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Chemical Science and Technology Laboratory
Technical Activities
1997

U.S. DEPARTMENT OF COMMERCE
Technology Administration
National Institute of Standards and Technology

Submitted to the Board on Assessment of NIST Programs,
National Research Council

Shown on the cover (clockwise starting at the bottom):

A data screen from the NIST Mass Spectral Database, showing likely matches between the mass spectrum of an unknown compound with several compounds from the database -- this database contains over 120,000 fully-evaluated entries. This is one of many important data activities in CSTL which provide critical data resources needed by industry and the scientific community.

Atomic and molecular-scale mapping of surfaces is a new area of measurement science based on scanned probe methods that provide a means to probe interactions of surface-attached molecular species. This class of measurement methods holds great promise for surface chemical characterization with atomic-scale spatial resolution.

The characterization of Standard Reference Materials (SRMs) is a core activity of CSTL. The SRM shown is SRM 956, Electrolytes in Human Serum. For measurements in chemistry, chemical engineering, and biotechnology, nation's traceability structure is based upon the availability of critically-evaluated measurement standards.

The development of critical biochemical measurements and methods advances the scientific basis and societal impact of biotechnology. The study and manipulation of the DNA molecule is one such focus in CSTL. Well-characterized materials have been produced that enhance quality assurance procedures of genetic testing (DNA Fingerprinting). Slab gel electrophoresis methods have been developed to detect single DNA-base mutations in the human p53 (anti-tumor) gene.

A micro-machined, thin-film gas sensor array (microhotplate) has three functional layers: a heater, a thermometer/heat distribution plate, and sensing film electrical contacts. These devices are being developed to provide inexpensive, real-time measurement technology with broad industrial applications, e.g., in process control, chemical identification, and auto emissions measurements. The view across the image is about 500 micrometers.

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Technology Laboratory

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Submitted to the Panel for the
Chemical Science and Technology Laboratory
Board on Assessment of NIST Programs
National Research Council

Hratch G. Semerjian, Director
Chemical Science and Technology Laboratory
National Institute of Standards and Technology

U.S. DEPARTMENT OF COMMERCE, William M. Daley, Secretary
Technology Administration, Gary R. Bachula, Acting Under Secretary for Technology
National Institute of Standards and Technology, Raymond G. Kammer, Director

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William F. Koch, Deputy Director
James R. Whetstone, Associate Director
W. Mickey Haynes, Assistant Director for Boulder

Program Overview

Since its creation by Congress in 1901, NIST then the National Bureau of Standards, has been the Nation's leading reference laboratory for measurements and standards with the express mission of supporting U.S. industry, commerce, scientific institutions, and all branches of the U.S. Government. The Chemical Science and Technology Laboratory (CSTL), one of the seven NIST Measurement and Standards Laboratories, is an integral part of the unique NIST mission to promote U.S. economic growth by working with industry to develop and apply technology, measurements, and standards.

Mission:

As the Nation's Reference Laboratory, the **mission of CSTL** is to provide the chemical measurement infrastructure to enhance U.S. industry's productivity and competitiveness, assure equity in trade, and improve public health, safety, and environmental quality. CSTL is a world class research laboratory recognized by the Nation as the primary resource for chemical, biomolecular, and chemical engineering measurements, data, models, and reference standards required to enhance U.S. industrial competitiveness in the world market. These capabilities are provided for the Nation - U.S. industry, government agencies, and the scientific community. CSTL seeks to accomplish its mission by setting and meeting the following goals:

- Measurement Standards: Establish CSTL as the pinnacle of the national traceability and international comparability structure for measurements in chemistry, chemical engineering and biotechnology, and provide the fundamental basis of the nation's measurement system.
- Chemical and Process Information: Assure that U.S. industry has access to accurate and reliable data and predictive models to determine the chemical and physical properties of materials and processes.
- Measurement Science: Address current, and anticipate next-generation, measurement needs of the nation, by performing cutting-edge research in measurement science.

Organizational Structure:

CSTL is a multifaceted, synergistic organization with a broad customer base. The Laboratory has technical capabilities in analytical chemistry, surface chemistry and microanalysis, chemical and physical properties, process measurements and modeling, and biotechnology. The primary customers we serve are: industry (chemical, electronics, automotive, petroleum refining, instrumentation, biotechnology, environmental technologies, and health care); federal, state, and local government agencies; standards and industrial trade organizations; and the academic and scientific community. CSTL is organized to reflect the technical expertise that is the foundation of our technical program and allows us to accomplish our mission. The Laboratory consists of five Divisions:

- Biotechnology Division,
- Process Measurements Division,
- Surface and Microanalysis Science Division,
- Physical and Chemical Properties Division, and
- Analytical Chemistry Division.

Each Division employs a group structure organized to achieve synergy and critical mass in the technical areas of its program. To accomplish our mission CSTL maintains expertise in a broad range of technical areas. Our technical staff consists of chemists, physicists, engineers, biologists, and computer specialists located at the NIST sites in Gaithersburg, Maryland and Boulder, Colorado.

Div.	Pubs.	Talks	Committees[1]	Seminars	Conferences	CRADAs	Patents	SRMs	SRDs	Cals.[2]
830	1	11	36	13	0	0	0	0	0	0
831	100	133	40	28	7	10	2	1	1	0
836	79	125	95	18	5	11	3	5	2	997
837	81	111	54	8	5	4	0	6	6	3
838	188	169	90	25	7	3	0	4	11	3
839	174	121	120	19	12	9	0	134	1	351
Totals	623	670	435	111	31	37	5	149	20	1354

[1] Committee totals include 62 editorships
[2] Calibrations were performed for over 400 customers

Division Key:

830	Laboratory Office
831	Biotechnology Division
836	Process Measurements Division
837	Surface and Microanalysis Science Division
838	Physical and Chemical Properties Division
839	Analytical Chemistry Division

To achieve its goals, CSTL maintains an experienced, well-educated professional staff. The permanent staff numbered 279 in FY97, in addition to 111 temporary and part-time employees. Also, there were almost an equal number (257) of guest researchers who work closely with CSTL staff. The technical staff consisted of 153 chemists, 48 physicists, 54 engineers, 21 biologists or computer specialists, and 35 technicians. Almost 75% of the technical staff hold PhD degrees

The needs of our customers are reflected significantly in our program priorities. Customers purchase our products and services (such as Standard Reference Materials, Standard Reference Data and calibration services), collaborate with us through consortia and CRADAs, contract for our services, and interact through round robins, conferences, workshops, and informally with our technical staff. Some of the CSTL outputs and interactions in FY97 are summarized in the table shown above. Our research program results in new measurement methods, critical information for design of new or improved chemical or biochemical processes, and analytical methods or procedures supporting new standard reference materials.

Research Program Assessment and Evolution: We balance our programs between provision of essential measurement technologies and standards and basic research to ensure a healthy science and infrastructural technology base for the future. Each Division in CSTL performs basic and applied research, and maintains close contacts with the appropriate industrial and scientific communities to assess and anticipate the future measurement needs of our customer base. As part of our strategic planning process, in the fourth quarter of each fiscal year we assess and prioritize future needs and re-orient our research program accordingly. At the beginning of FY98 we began or enhanced five program areas:

- standards for Raman spectroscopy
- chemical analysis at critical surfaces and interfaces
- determination of non-metals in advanced materials,
- computational chemistry, and
- molecular scale materials characterization.
-

The computational chemistry and molecular scale materials characterization areas have been continued as areas of additional emphasis within CSTL. Re-orienting parts of CSTL's research effort is accomplished with existing resources through identification of new areas where CSTL's work is anticipated to have significant impact on U.S. industry. Resources are redirected from activities where CSTL's efforts have reached maturity and produced their anticipated results.

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Major Facilities Additions: Major progress has been made with facility additions that affect CSTL operations in FY97. Construction of CARB 1B, a state-of-the-artaddition to the original facility, was completed this year, providing an additional

~2,600 m^2 (28,000 ft^2) of state-of-the-art laboratory space for biotechnology research. The three floors of the new building are staffed jointly by investigators from CSTL and the University of Maryland Biotechnology Institute. Substantial progress has been made in constructing the Advanced Chemical Sciences Laboratory (ACSL) on the Gaithersburg Campus of NIST. The ACSL is scheduled for completion in the Fall of 1998. It will provide CSTL with 7,605 m^2 (~82,000 ft^2) of state-of-the-art laboratories to be used by the Analytical Chemistry and Biotechnology Divisions. Occupancy is scheduled for early 1999.

Technical Achievements: There were many noteworthy technical achievements made by the CSTL scientific staff during FY97 that contribute to long term accomplishment of the CSTL goals. Examples of these are discussed briefly below. More detailed information about these activities can be found in the appropriate Division's technical reports.

Measurement Standards: The nature of international trade and industrial development is rapidly changing, becoming more global and more competitive. As regulatory barriers are reduced, technical barriers, associated with mutual acceptance of products, materials, and services, are becoming more important. Emphasis on conformity assessment issues continues to increase the demand for product quality certification, calibration and testing laboratory accreditation, and quality systems registration. Recognition of the intercomparability of measurement results between national trading partners is a fundamental issue. Intercomparability between national standards is fundamental because it supports the technical and metrological comparability needs for product testing standards and performance measures inherent to measurement laboratory accreditation and product certification processes.

CSTL has developed and maintained close working collaborations with the national standards laboratories of major U.S. trading partners for specific physical and chemical measurements. Intercomparability of national measurement standards is a U.S. treaty obligation under the Treaty of the Meter that supports improvement in the competitive position of U.S. industry in world markets. As the U.S. government agency responsible for such intercomparisons, NIST works with the International Committee on Weights and Measures (CIPM) to develop international inter-comparisons of measurement standards. CSTL, working with our counterparts in other nations, participates in the prioritization, organization, and execution of key measurement intercomparisons. These activities are designed to form **the basis of declarations of comparability** for specific measurement parameters and standards.

CSTL continues to aggressively expand efforts to document the comparability of NIST primary methods and standards with those of other nations and metrological regions through both multilateral agreements, e.g., through the Consultative Committee on the Amount of Substance (CCQM) of the CIPM, and several strategic bi- and trilateral collaborations. Our bilateral program with the Netherlands Measurement Institute (NMi), representing the European Union (EU), has demonstrated the equivalence of primary gas standards and has resulted in a formal "Declaration of Equivalence". This Declaration is mutually recognized by the U.S. EPA and European environmental regulatory bodies and documents the comparability of seven NIST and NMi primary gas mixture suites critical for acceptance of vehicle emission compliance in the U.S. and the EU.

Collaborations for assessing the comparability of chemical measurement standards have been established with several national measurement laboratories in specific chemical measurement areas:

- the **Danish Institute of Fundamental Measures** (DFM) and **the Hungarian Office of Mea**sures, (OHM) for standards for electrolyte conductivity,
- the **Physikalisch-Technische Bundesanstalt** (PTB) for pH measurement standards,
- with National Institute of Materials and Chemical Research (NIMC, Japan) and Bundesanstalt fur Materialforschung und -prufung (BAM, Germany) for elemental solution standards, and
- NIMC for volatile organic compound standards.

CSTL establishes and maintains the infrastructure for providing national traceability and assessing and realizing international comparability for chemical and certain physical measurements. Vertical traceability of physical measurements in the U.S. for temperature, pressure, vacuum, leak rate, humidity, fluid flow rate, liquid volume and density, and air speed are supported and strengthened by developing improved primary measurement standards and methods. The provision of instrument calibration and test services is a primary means to disseminate U.S. national standards to industrial users and federal and state government laboratories.

CSTL provided 73% of the Standard Reference Materials (SRMs) and 12% of the calibration services provided by NIST. CSTL also provided 69% of the databases provided by the Standard Reference Data (SRD) Program in FY97. In FY97 the Process Measurements Division achieved an important NIST goal in completing the realization of **International Temperature Scale of 1990** in terms of its fundamental definition. CSTL's achievements in this area places NIST in the lead among all national standards laboratories, not only in terms of completing the scale, but also in terms of the low levels of uncertainty of our realization. This accounts, in part, for our major role in four key comparisons of realizations of ITS-90 organized by the Consultative Committee on Thermometry of the CIPM where we have established leadership positions.

To support pressure and vacuum measurements, CSTL provides national standards and calibration services over 16 decades of pressure, from 10^{-7} to 10^{9} Pa. Two new low-pressure calibration systems were implemented this year. These provide calibrations in the pressure range of 0.1 Pa to 133 Pa, a factor of 10 improvement in accuracy, and the capability to calibrate low-differential pressure measurement devices at elevated line pressures (up to 200 kPa). The latter provides new capabilities to support high accuracy calibrations for differential pressure measurements associated with flow metering devices. As in the temperature standards area, international comparisons have grown in importance with NIST participating in six key comparisons dealing with pressure and vacuum standards. These are organized under the Consultative Committee for Mass and Related Quantities of the CIPM. Additionally, we have organized a multi-laboratory comparison for near atmospheric pressure measurements within NORAMET (North America) and SIM (Inter-American Metrology System).

CSTL establishes and maintains the chemical measurement infrastructure for national traceability and for assessing international comparability. The provision of Standard Reference Materials (SRMs) and NIST Traceable Reference Materials (NTRMs) are important tools in this effort. These capabilities are used to establish and maintain chemical measurements in the U.S. and to compare NIST primary methods and standards with other national metrology laboratories for chemical measurements. Stadard Reference Materials are certified reference materials issued under NIST trademark that are well-characterized using state-of-the-art measure-ment methods and/or technologies for chemical composition and/or physical properties. Currently, NIST provides nearly 1300 different types of SRMs and in FY97 sold nearly 40,000 SRM units to approximately 5,000 unique customers; approxi-mately 20,000 units of these represent about 850 different types that are certified for chemical composition. CSTL does not have all of the resources necessary to provide the quantities and specific varieties of SRMs needed to meet the increasing needs of U.S. industry. CSTL has created the NIST Traceable Reference Materials program to address this problem. An NTRM is a commercially produced reference material with a traceability linkage to existing NIST standards for chemical measurements. CSTL establishes the criteria and protocols necessary to maintain the traceability linkage which are tailored to meet the needs of the metrological community to be served. Initially developed for gas standards, the success of this approach has been such that it has been broadened to include other mature, high volume measurement areas this year.

In the area of human identity testing CSTL, working with the **Department of Justice**, has completed inter-laboratory testing program to evaluate methods for DNA-based human identification on an annual basis. SRMs have been developed to allow accurate characterization of DNA profiles for forensic and paternity testing. Completion of all inter-laboratory testing occurred in 1997 for prototype SRM 2392 human **mitochondrial DNA**.

Chemical and Process Information: Realistic design and modeling of chemical processing systems is critically dependent upon chemical and physical data to accurately describe materials and processes, and to model the mechanisms controlling these systems. CSTL activities provide or contribute to:

- standard/evaluated benchmark data for properties of important substances, classes of substances and systems
- data collections, data prediction methods, and models to meet high priority/immediate industrial and/or national needs,
- development of consensus standards for key properties, substances, and processes, and
- protocols or procedures for data access, facilitation of data exchange, and dissemination of appropriately formatted data.

CSTL has established the **NIST WebBook** to provide ready access to chemical reference data. The WebBook **(http://WebBook.nist.gov)** provides internet access to an extensive set of chemical data with a common interface featuring ease of use and ready expansion capability as additional data becomes available. During FY97 the Web-Book's content was expanded as follows:

- the number of compounds available increased from ~11,000 to 22,300,
- data on vapor pressure, infrared spectra, and mass spectra were added,
- correlations of vapor pressure with temperature for over 1500 compounds were added in the form of Antoine coefficients,
- phase-transition enthalpy data were added that included enthalpy-temperature dependence for selected compounds,
- high accuracy thermophysical property data for 13 industrially-important fluids (including computational capability to calculate selected properties along an isotherm, isobar, or the saturation line), and
- an extensive dataset of negative ion energetics.

CSTL continues to provide industry with **high accuracy, physical property data for alternative refrigerants**, CFC and HCFC refrigerant replacements, that do not deplete stratospheric ozone. These data are provided in the REFPROP database which was expanded in FY97 and will be released in early FY98. As interest in the 'natural refrigerants' and their mixtures has increased, measurements of heat capacity and the PVT and VLE behavior of the propane/isobutane system have been completed.

Continued efforts with the **forensic testing** community led to development of a Web Site (http://ibm4.carb.nist.gov:8800/dna/home.htm) for **Short Tandem Repeats** (STR) that includes a database of all currently used genetic testing systems. Use of STRs by crime laboratories throughout the world is rapidly becoming the preferred method of human identification.

CSTL continues its efforts to provide the industrial community that uses mass spectrometry as an important process and diagnostic tool with high quality mass spectral data. This year a detailed evaluation of the NIST mass spectral database was completed. The NIST Mass Spectral Database is included by the manufacturers of these instruments as an imbedded database in the analysis software. In FY97 3,864 copies of the mass spectral database were sold, the majority going to manufacturers of mass spectrometers as part of the spectrometer system.

Chemical and process models, and the data support them, describing **production of high technology materials** provide industry with the base necessary for development of advanced processes. In a joint project with the NIST Materials Science and Engineering Laboratory, CSTL is studying multiphase combustion synthesis of sodium/metal halide chemistry to synthesize metals and non-oxide ceramic particles and films, e.g., SiC, required for high-temperature, high-durability applications in the aerospace industry. This novel processing method offers a relatively low temperature (low energy consumption) route with promise for bulk-synthesis of these generally difficult-to-prepare materials. It also has the advantage of essentially zero emissions providing an inherently "green" processing approach for the production of high technology materials.

Measurement Science: CSTL maintains a strong research program to support the Nation's measurements and standards infrastructure, establish new measurements capabilities supporting new or advanced technology development and dissemination, and provide a fundamental basis for global scientific decision making. There have been many noteworthy research achievements by CSTL scientists and engineers during FY97 examples of these are presented below. More detailed information is contained in the technical reports of the respective Divisions found in the remainder of this report.

In the Process Measurements Division optical methods are being investigated as **species specific, partial-pressure measurement methods and**

standards for monitoring process gases in both vacuum and at process pressures. The initial focus is on the optical measurement technique cavity-ring-down-spectroscopy (CRDS) which holds promise for measurements of water vapor concentration in vacuum, perhaps down to the 10^{-8} Pa range, and for nanogram/gram-level measurements in process gases, e.g., humidity, at ambient and higher pressures. The quantitative capabilities of CRDS were demonstrated with preliminary measurement of absorption levels of approximately 10^{-10}/cm in a 10 cm cell (an improvement of a factor of 100 this past year). This work has excellent potential to benefit many industries, including semiconductor manufacturing.

Methods for detecting and quantifying **DNA damage and repair** are critical to the understanding of mechanisms of tumor initiation or tumor blockage. GC/MS techniques have been developed to characterize DNA damage on a molecular scale at levels approaching one base per million. These methods enable study of the kinetics and specificity of DNA repair by newly discovered enzymes and the interaction of DNA damage with cellular processes that initiate apoptosis, or programmed cell death, critical to the understanding of fundamental biochemical mechanisms. Knowledge of specific biochemical pathways and their measurement also supports development of valuable kinetic databases for the biotechnology industry.

As part of the effort to understand the **sensing applications of self-assembled mono-molecular layers (SAMs)**, two methods were demonstrated for absolute quantitative determinations of coverage and hybridization efficiency of single stranded DNA probes immobilized on gold surfaces. The immobilization relies on a two-component SAM monolayer discovered and patented by NIST. The DNA probes were shown to attach at approximately 60% of theoretical coverage, have negligible non-specific absorption, high specificity for complementary targets, and near unity hybridization efficiency.

Recent research efforts in **organic mass spectrometry** focused on electro-spray ionization as a tool for quantitative determination of proteins in biological matrices. Reference methods for important biomarkers such as troponin-I (a new marker of myocardial infarction), glycohemoglobin (an important new marker for diabetes), serum thyroxine (an important marker for thyroid function), and cortisol (a marker for endocrine function) are being established.

New **metabolic pathways to manufacture chemicals from renewable resources** (e.g., glucose from crop spoilage) have great potential as replacement for the current energy-intensive methods. The separate enzymatic steps in these pathways are not well-characterized. Information on biocatalytic rates, enzyme structure/function relationships, genetic and allosteric control of reactant specificity are needed to support bioprocess development. CSTL research is focused on the pathway leading from glucose to chorismate and its aromatic derivatives. This metabolic pathway is being developed as a model system for bioprocess measurement and modeling technology.

To test the **theory for the viscosity of a fluid closer to the liquid-vapor critical point** than is possible in earth's gravity, CSTL scientists measured the viscosity near the critical point of xenon onboard the Space Shuttle, where the typical acceleration is one millionth of the earth's gravity. Within 1 mK of the critical temperature, the critical fluctuations caused the xenon to become viscoelastic, resulting in frequency-dependent data that could not be obtained on earth. In FY98, the analysis of the data will be completed and the results will be compared with theory.

The **near-field optical microscope** (NSOM), which combines scanned probe technologies with optical contrast mechanisms, holds the promise of molecular contrast at high spatial resolution. However, improved theories and characterization artifacts are needed to correctly interpret NSOM images because the signal arises from a complex interplay of optical and topographic sources. Simultaneous shear-force AFM, transmission NSOM and reflection NSOM images were obtained for a series of samples, consisting of various coverages of size selected Au nanoparticles on a glass substrate, with diameters ranging from 15 nm "to 150 nm. Use of the well-known optical-field scattering properties of small metal spheres should provide a good test of near-field probe models.

The unique operating capabilities of the **environmental scanning electron microscope** (ESEM) provided the means to observe in real time the nucleation and growth of thin films of tin oxide.

The ESEM chamber functioned as a low-pressure CVD reactor while simultaneously collecting ESEM images of the film nucleation and growth. An unexpected result was the observation of mechanical stresses in the silicon micro-machined supporting structures. The images record the initial formation and widening of cracks in the top oxide layer as the device is operated at 450 °C. These results are important for improving the reliability of the device platform.

Conferences and Workshops:

CSTL sponsored or co-sponsored the following major international conferences.

- **Thirteenth Symposium on Thermophysical Properties**, June 22-27, 1997, Boulder, CO. This Symposium is the premier international conference for theoretical, experimental, and applied aspects of the thermophysical properties of gases, liquids, and solids. It brings together leading international experts from industry, academia, and government laboratories in these areas. Scientists from 36 countries other than the U.S. attended. NIST, in conjunction with the Thermophysical Properties Committee of the ASME Heat Transfer Division, has had primary responsibility for organization of this conference for more than 20 years.
- **Fourth International Conference on Chemical Kinetics**, July 14-18, 1997, Gaithersburg, MD. This conference brought together scientists from different disciplines to present recent research results and discuss topics of common interest in chemical kinetics. 64 Scientist from 21 countries outside the U.S. attended the conference.

The Workshop on **NIST Traceability in Chemical Spectrophotometry** was attended by 32 participants from pharmaceutical and chemical companies, instrument and optical component manufacturers, and government regulatory agencies. The attendees endorsed the NTRM concept and agreed that commercial production of NIST-traceable optical filter standards was viable based on public and regulatory agency acceptance of NTRMs.

The workshop on **Molecular Binding and Recognition Data** was held at NIST. A database containing information on noncovalent binding affinities will facilitate the discovery of molecules that bind to selective target molecules. The participants came from drug companies (DuPont Merck, Agouron, Bristol-Myers Squibb, and Glaxo Wellcome), from academic institutions (U. California San Francisco, Rutgers, Harvard, U. Pittsburgh, U. North Carolina) and from NIST. Consensus was reached on database content and on the next steps to be taken in implementation.

Awards and Recognition:

Many CSTL scientists received awards and recognition in FY97. Jan V. Sengers was elected a **Fellow of the American Society of Mechanical Engineers** for outstanding contributions to the field of thermophysical properties of fluids and fluid mixtures. John A. Small was recognized by **The Microbeam Analysis Society** with its **Presidential Award**. The National Organization for the Professional Advancement of Black Chemists and Chemical Engineers recognized Marlon L. Walker with the first **Lloyd N. Ferguson Young Scientist Award** this year at its annual meeting. Hratch G. Semerjian received the Brown Engineering Alumni Medal, during Brown University's Engineering Sesquicentennial celebration. Stephan J. Stranick was recognized by **Ithaca College** as its **Outstanding Young Alumni.** William R. Kelly was awarded the **Federal Laboratory Consortium Award for Excellence in Technology Transfer** for 1998. Richard F. Kayser was awarded the **Senior Executive Service Presidential Rank Award for Meritorious Service**. Rance Velapoldi received the **DoC Gold Medal** for leadership in the "...development of the Rapid Integrated Nuclear Analysis capability that enables measurements 5-10 times faster than previously possible". James Whetstone was awarded the **DoC Silver Medal** for his long-term leadership of CSTL efforts to meet semiconductor industry needs for improved measurement standards. Three 1997 **DoC Bronze Medals** were awarded to CSTL staff members. Donald Burgess was recognized for "...development and application of chemical reaction computational tools for managing and interpreting very large chemical kinetic simulations;" George Klouda for "...leadership in developing advanced technologies and standards for trace isotopic measurements of atmospheric gases and particles;" and Frank Guenther for "...development and implementation of programs for the realization of national traceability and international comparability of chemical measurements". Billy Mangum received NIST's **Allen V. Astin Award** for his career-long achievement and leadership of NIST's program in temperature standards and thermometry.

George Burns was awarded the **NIST Edward Bennett Rosa Award** for career-long contributions to national and international measurement standards for thermocouple thermometry. Christopher W. Meyer and Martin L. Reilly (retired, guest scientist) were recognized with the **1997 CSTL Technical Achievement Award** for their work in completing the realization of the ITS-90 in the 0.65 to 5 K range. Stuart Tison and Stephen Doty were awarded the **1997 Best Technical Paper** at the Annual Meeting and Workshop of the National Conference of Standards Laboratories for the paper "Low Gas-Flow Proficiency Tests". John Wright received the **NIST Measurement Services Award** in the calibration category for his outstanding efforts in developing and applying the Heated Gas Mixture Test Facility. Eric Steel and Alline Myers were awarded 2nd Prize for Best Poster at annual meeting of **The Microbeam Analysis Society**. The NIST Chapter of Sigma Xi recognized David Bright for his **Outstanding Service to the Society** and Teresa Petralli-Mallow for the **Outstanding Poster Presentation** at its Annual Postdoctoral Symposium.

Technical Highlights:

In the following pages, recent activities and technical directions of the CSTL Divisions are presented.

II. Biotechnology Division (831)

Gary L. Gilliland, Chief

A. Division Overview

Mission:
The Biotechnology Division is the focus of the NIST effort addressing critical measurement and data needs for the rapidly developing biotechnology industry. The mission of the Biotechnology Division is to provide the measurement infrastructure necessary to advance the commercialization of biotechnology. This is achieved by developing a scientific and engineering technical base along with reliable measurement techniques and data to enable U.S. industry to produce biochemical products quickly and economically with appropriate quality control. The Division has established a variety of long-range research programs to maintain critical expertise needed for the development of advanced measurement methods, standard reference materials and databases for use by industry and other research enterprises. The Division fosters collaboration among NIST scientists conducting biotechnology research, and raises the visibility of the NIST Biotechnology program, which leads to enhanced collaborations with industries, universities and other government agencies.

Programs:
To plan and guide Division research programs effectively, Division scientists are active in many forums that provide feedback on long-term and short-term needs for biotechnology commercialization. These activities supplement the high level of Division participation in scientific meetings and topical workshops. For example, during FY97 the Division continued active participation in the Biotechnology Industry Organization (BIO), in the IUPAC Commission on Biophysical Chemistry, and in the ASTM Committee E-48 on Biotechnology. Division members were also active participants in a number of important workshops held at NIST. The Division also worked closely with the NIST Advanced Technology Program (ATP) in a variety of ways. Division members served as NIST technical representatives in the annual review of a number of active ATP grants. They also participated in ATP sponsored workshops and public meetings presenting the results of Division research programs. Additionally, it should also be noted that Division members have been involved in generic research that is directly related to ATP focus areas, and also involved in research directly related to specific ATP projects. Throughout the year, the Biotechnology Division continued to play a major role in the planning and coordination of Federal biotechnology research through member-ships in the working groups associated with the Subcommittee on Biotechnology of the National Science and Technology Council (NSTC).

The staff of the Biotechnology Division consists of 48 NIST employees and a comparable number of contract researchers, guest scientists, and postdoctoral fellows. The Division is organized in four groups: 1) **DNA Technologies**; 2) **Bioprocess Engineering**; 3) **Structural Biology**; and 4) **Biomolecular Materials**. FY97 was a very productive year for scientists of the Biotechnology Division. A brief overview of each Group in the Division, and highlights of several research programs are given below:

Selected Program Highlights:
The **DNA Technologies Group** conducts a research program in DNA and molecular biology to enhance measurement technologies in **mutation detection** and **genetic toxicology** and to provide standard reference materials (SRM) for application in areas related to the detection and characterization of DNA. The Group has conducted interlaboratory tests designed to evaluate methods for DNA-based human identification on an annual basis. Standard Reference Materials have been developed to allow accurate characterization of DNA profiles for forensic and paternity testing. Completion of all interlaboratory testing occurred in 1997 for a prototype SRM 2392 human **mitochondrial DNA**.

The Group has focused efforts on methods and standards for **mutation detection**, a burgeoning area of testing in genetic and clinical laboratories. At this time, no national standards are available for genetic testing protocols. Work in FY97 delineated the characteristics of a set of materials for use in the standardization of DNA-based mutation detection systems (initially, the p53 tumor suppressor gene) for diagnostic testing and as research tools for determining parameters that affect the quality of measurements that are produced by various assay systems. Continued work with Single-Strand Conformation Polymorphism (SSCP) assays by capillary electrophoresis has been a fruitful area of research through a cooperative research and development agreement (CRADA) with a prominent biotechnology company. Use of a new class of enzymes to cleave polynucleotides has led to other collaborations with the biotechnology industry.

Continued work with the **forensic testing** community led to development of a Web Site for **Short Tandem Repeats** (STR) that includes a database of all currently used genetic testing systems. Use of STRs by crime laboratories throughout the world is rapidly becoming the preferred method of human identification. The Web Site includes a comprehensive reference listing, a compilation of population statistical studies, and a listing of researchers who have experience with STRs.

Long-range research in the Group includes the development of methods for detecting and quantifying **DNA damage and repair**, processes that are critical to the understanding of mechanisms of tumor initiation or tumor blockage. Methods have been developed to characterize DNA damage on a molecular scale at levels approaching one base per million using GC/MS techniques. These methods have been used to study the kinetics and specificity of DNA repair by newly discovered enzymes. Additionally, the interaction of DNA damage with cellular processes that initiate apoptosis, or programmed cell death, is critical to the understanding of fundamental biochemical mechanisms. Knowledge of specific biochemical pathways and their measurement can lead to NIST's development of valuable kinetic databases for the biotechnology industry.

Finally, working in several areas of **molecular biology**, the Group is actively manipulating DNA to produce cloned and/or engineered enzymes with specific functions useful to the biotechnology community. These enzymes include a specific DNA polymerase derived from a thermophilic mycobacterium for DNA sequencing. Additionally, studies are ongoing to uncover mechanisms of adenyl cyclase modulation by catalytic site mutants of protein IIA in *E.coli*.

The **Bioprocess Engineering Group** is focused on the development of measurement methods, databases, and generic technologies related to the use of biomolecules and biomaterials in manufacturing. Measurement methods and data have been developed in the protein **spectroelectrochemistry** area that will lead to improved understanding of intra- and inter-protein electron transfer processes. This understanding helps industrial biocatalyst development through more efficient utilization of carbon sources (e.g., renewable resources) and nutrients, and in developing new ways to drive organic syntheses such as the stereospecific hydroxylation of pharmaceutical precursors. In the **biothermo-dynamics** of enzyme-catalyzed reaction project, chromatography and micro-calorimetry measurements have been combined with chemical equilibrium analysis to develop thermodynamic data for several industrially important biotransformations. A comprehensive review of the thermodynamics data in the literature has been incorporated into a web-accessible database. The metabolic pathway by which microorganisms and plants convert glucose to aromatic amino acids is a current focus of our biothermodynamic measurements. This **chorismate metabolic pathway** is under current investigation by several large chemical companies as an environmentally friendly source of aromatic hydrocarbons. In the preparative **bioseparations** project, electrochromatographic/electrophoretic separation equipment and methodology are being applied to the separation of different physical forms of DNA (supercoiled plasmid, relaxed circular plasmid, linear genomic). Large scale purification of these materials is an emerging need in industries developing gene therapies and diagnostic materials. New biocatalytic systems projects in enzyme characterization by nitrogen-15 nmr spectroscopy, x-ray diffraction of protein crystals and computational chemistry have been initiated. These techniques will be used to address focused, industrially important biotransformation problems such as those found in hydroxylation and aromatic amino acid metabolic pathways.

The **Structural Biology Group** is located at the Center for Advanced Research in Biotechnology (CARB) on the University of Maryland Shady Grove Campus about four miles from NIST. CARB is a joint collaboration of the Biotechnology Division and the University of Maryland Biotechnology Institute (UMBI). Scientists at CARB develop and apply state-of-the-art measurement methods, databases, and modeling techniques to advance the understanding of **macromolecular structure/function relationships** in biological systems. The structures of prototypical macromolecular assemblies, including enzymes and proteins, nucleic acids, and their complexes, are being determined by high-resolution **x-ray crystallography** and **nuclear magnetic resonance** (NMR) **spectroscopy**. These three-dimensional structures not only provide a database for the development of theoretical models for macromolecular interactions, but also guide the Group's efforts in **protein engineering and design** using state-of-the-art methods in molecular biology. An essential, complementary component to the ongoing structural and theoretical studies is the development and application of advanced physical measurement methods to provide kinetic and thermodynamic information on the functional properties of proteins and nucleic acids. New applications using **calorimetry**, **spectroscopy**, **immunology**, **ultracentrifugation** and **rapid kinetic approaches** are being devised to address general problems currently facing the biotechnology industry. The multidisciplinary approach to research at CARB is vital for expanding industry's ability to exploit structure/function relationships such as thermodynamic stability and folding, macromolecular interactions with solvent, small molecule ligands, proteins, or nucleic acids, and enzymatic reaction pathways to design novel biomolecules for unprecedented use in medicine and biotechnology.

Construction of CARB IB, a state-of-the-art addition to the original facility, was completed this year, providing an additional ~2,600 m^2 (28,000 ft^2) of state-of-the-art laboratory space for biotechnology research. The three floors of the new building are staffed jointly by investigators from both NIST and UMBI who are focusing on both experimental and theoretical problems in structural biology. Speci-fically, the building will support an expansion in the **computational biology, chemistry and modeling research** programs, house the original **500** and a new **600 MHz NMR spectrometers**, and support investigators employing modern solution methods to characterize the physical and chemical properties and functions of biological macromolecules.

The technical activities in the Structural Biology Group are focused in three main areas, but there is also broad overlap in interest and interactions among the staff. Advanced methods for the determination of macromolecular structures are being developed using x-ray diffraction and NMR spectroscopy by scientists in the structural group. Newly determined structures for retinal **nucleoside diphosphate kinase**, an essential component of the visual signal transduction cascade, and **uracil DNA glycosidase**, a key enzyme involved in the repair of damaged DNA, have yielded important insights into their biochemical mechanisms. The aims of the computational group are to develop, validate and apply new theoretical and computational approaches in the study of macromolecular interactions in order to account for, and ultimately predict, the physical and chemical basis for their reactivity. The correlation of calculated pK_a values for ionizing residues with those estimated experimentally shed interesting light on the interpretation of NMR and x-ray structures of the immunoglobulin binding region of *Streptococcal* Protein G. Additionally, new quantum chemistry approaches that approximate the potential in the active sites of enzymes have been used to suggest new mechanisms for the hydrolysis of β-lactam antibiotics. Scientists in the molecular and cellular biochemistry group are using mosaic approaches to probe intricate structure/function relationships for a variety of experimental systems. The mechanism of the folding and assembly of membrane-embedded proteins, the control of the activation of transcription, and mechanisms for the fidelity of DNA modifying enzymes are under intensive investigation, and are yielding to the biochemical techniques employed by CARB researchers. Finally, the database activities of the Group have expanded. New entries for nucleic acid crystallization conditions have been incorporated into the NIST/NASA/CARB WWW-based Biological Macromolecule Crystallization Database, and, as mentioned above, a workshop was held at NIST this year to discuss the development of a database on noncovalent binding interactions.

The research program of the **Biomolecular Materials Group** is based on the underlying need of many biotechnology applications for control of biological molecules at interfaces. Chemically controlled surfaces which are engineered for specific biomolecular interactions are essential components of biosensors, bioelectronics, biocatalytic systems, and many diagnostic devices. *Biomolecular materials* thus influence such diverse applications as pharmaceutical development, health care, environmental pollution monitoring, and chemical manufacturing. A major focus of the group is a rugged artificial membrane system that mimics cell membranes. This **hybrid bilayer membrane** is composed of both artificial and natural lipid components, and is a unique membrane matrix that is both an excellent research tool as well as a commercially important development. Fundamental understanding of the structural characteristics of biological molecules such as cell membrane receptors, optically active proteins and redox enzymes in this and other biomimetic matrices, and the relationship between structure and functional activity, are key to successful commercial applications. Molecular details are provided by **vibrational spectroscopies** such as infrared and surface plasmon resonance enhanced Raman, and by **nonlinear optical spectroscopies**. The development of models based on electro-magnetic wave theory permits the development of simulated spectra which aid data interpretation. **Neutron reflectivity measurements** (made in collaboration with the NIST Neutron Research Facility) provide high-resolution data of these membranes and the location of protein complexes in them. Genetically engineered proteins, light-sensitive **bacteriorhodopsin** and pore-forming **α-hemolysin** are used in systematic studies of how membrane protein structural changes lead to functional changes. The development of stochastic models aid in interpretation of results and design of new experiments. **Sensor applications** development demonstrate the potential commercial usefulness of these proteins and matrices. Synthetic chemistry efforts are providing novel materials to allow assembly of matrices that are even more biomimetic. These tools need to be in place to permit assessment of the activity of biological molecules in high throughput formats, and to allow the successful engineering, characterization, and application of biomolecular materials for development of future products of biotechnology.

Meeting the future needs of the biotechnology industry will require the strengthening of existing Division programs and the development of technical expertise in new areas. The expansion of the DNA technologies effort to include measurement tools and quality assurance standards for **DNA diagnostic measurements** will continue to be a high priority in FY98 because of the rapid growth of industrial applications in this area. At CARB, the establishment of a state-of-the-art NMR facility in collaboration with the University of Maryland is a high priority. Included in Division plans are a broadening of the Biomolecular Materials Group's program to include an emphasis on generic needs common to many kinds of surfaces and materials that are components in sensors, processing, diagnostics and other applications. This is a reflection of the importance of biomolecular structures in the future development of biotechnology, particularly in pharmaceutical development and biomanufacturing. Additionally, expanded emphasis will be placed on the development of modeling that relates molecular structure to the properties of biomolecules, biomaterials, and bioprocesses. The use of biological macromolecules in non-biological applications such as **chemical manufacturing** and **environmental bioremediation** continues to be a promising area of biotechnology. The Division will continue to build expertise in bioprocess technology, with an emphasis on measurements and data to help industry solve generic problems that limit technology development. Also planned for the Division in FY98, will be an expanded effort in the area of **bioinformatics**, which includes the development of computational methods for using large biomolecular structure and sequence databases to identify, analyze or predict the structure and/or function of new biomolecular species. These expanded capabilities will enhance our Division's research programs and aid industry in the efficient use of chemical and biochemical data in the development of new products and processes.

B. Selected Technical Reports

1. *Detection of DNA Point Mutations by Single Strand Conformational Polymorphism (SSCP): Analysis by Capillary Electrophoresis*

D.H. Atha *and H-M. Wenz (Perkin Elmer, Applied Biosystems)*

Objective: Capillary electrophoresis SSCP is being developed as an alternative analytical tool for rapid and efficient screening of DNA point mutations.

Problem: There is an increasing need in DNA diagnostics for more efficient methods of detecting mutations associated with disease. Most of the established methods use amplification technologies and slab gel electrophoresis for detection. Continuing improvements in the sensitivity and automation of capillary electrophoresis, including improved capillary systems and separation conditions make it an increasingly attractive alternative for the detection of these mutations.

Approach: 139 base-pair (bp) fragments of DNA were amplified from reference samples (H596, Colo320, Namalwa and wild type) and site-directed mutagenesis samples (RDES 11, RDES 21, RDES 30, Nam 1and Colo 5) using exon 7 specific fluorescently-labeled PCR primers. In a blinded study, we analyzed these p53 mutations by single strand conformational polymorphism capillary electrophoresis (CE-SSCP) using the Perkin Elmer ABI PRISM™ 310 Genetic Analyzer with GENESCAN™ software.

Results and Future Plans: In the blinded study, the mobility profiles of the ten p53 samples were matched automatically using Genotyper™ software against the four reference samples. Of these ten samples, six were correctly identified as containing one of the reference mutations, two corresponded to the wild type, and two were correctly identified as non-reference mutations. This approach should prove helpful in the rapid screening of target sequences that are known to bear a limited number of mutations. Future experiments are aimed at determining the limits of detectability of a wide range of p53 mutations. From this, a statistical evaluation will be made of the ability to detect these mutations in large numbers of clinical samples that are known to contain only small percentages of mutated DNA.

Publication:

Atha, D.H., Wenz, H-M., Morehead, H., Tian, J., and O'Connell, C., ***"Detection of P53 Point Mutations by Single Strand Conformational Polymorphism (SSCP): Analysis by Capillary Electrophoresis,"*** Electrophoresis (in press).

2. *Oxidative DNA Base Damage and Its Repair in Nickel-treated Rats*

M. Dizdaroglu*, K. Kasprzak (National Cancer Institute, Frederick, MD), P. Jaruga (Medical Academy, Bydgoszcz, Poland), T. Zastawny (Medical Academy, Bydgoszcz, Poland), and R. Olinski (Medical Academy, Bydgoszcz, Poland)*

Objective: To determine oxidative DNA damage in kidneys and livers of rats treated with carcinogenic Ni(II)-compounds and follow the cellular repair of such damage.

Problem: Ni(II)-salts such as Ni(II)-acetate induce DNA damage in kidneys and livers of experimental animals, but initiate carcinogenesis in kidneys only. The reasons for this difference remain unclear. Some of them could be related to different types of the DNA damage and different capacity of cellular repair in these organs. This study was designed to investigate the type and repair of oxidative DNA damage in kidneys and livers of Ni(II)-treated rats up to 14 days post-injection.

Approach: Oxidative damage generates a multitude of modified bases in DNA. An accurate measurement of these lesions is achieved by the use of the GC/MS technique. Because of its ability to simultaneously measure a large number of DNA lesions, this technique also permits the study of the cellular repair of DNA lesions. We used this unique approach to determine a multitude of DNA base lesions and their repair in kidneys and livers of rats after treatment with Ni(II)-acetate.

Results and Future Plans: DNA base damage was assayed using GC/isotope-dilution MS in renal and hepatic chromatin of rats up to 14 days after a single intraperitoneal injection of 90 μmol Ni(II)-acetate/kg body weight. Ten different DNA base lesions were quantified. The damage became significant only from day 1, with magnitude and persistence depending on the organ and DNA base. In livers, the levels of five DNA lesions were significantly elevated over those in control rats. The elevation was highest at day 1 post-injection followed by a decrease in later days. In kidneys, the levels of four base lesions increased. Unlike those in the liver, the renal increases of levels of DNA base lesions persisted for 14 days. The results revealed a tissue specific response to Ni(II)-mediated oxidative DNA base damage with apparently faster repair in liver than in kidney. Longer persistence of promutagenic DNA base damage by Ni(II) in the rat kidney compared with that in the liver may be associated with susceptibility of the kidney, but not the liver, to Ni(II)-initiated carcinogenesis.

This work will be extended to other carcinogenic compounds such as Co-salts, and oxidative DNA damage induced by Co(II) will be determined in various organs of rats.

Publication:

Kasprzak, K.S., Jaruga, P., Zastawny, T.H., North, S.L., Riggs, C.W., Olinski, R., and Dizdaroglu, M., ***"Oxidative DNA Base Damage and Its Repair in Kidneys and Livers of Nickel(II)-treated Male F344 Rats,"*** Carcinogenesis 18, 271-277 (1997).

3. *Interlaboratory Evaluation of Short Tandem Repeat Triplex CTT*

M.C. Kline, D.L. Duewer (839), J. W. Redman, and D. J. Reeder

Objective: To evaluate the interlaboratory comparability of DNA typing results for Short Tandem Repeat (STRs) at the GenBank loci HUMCSF1PO, HUMTPOX, HUMTH01, and HUMVWFA31 using the CTT triplex and CTTv quadruplex.

Problem: The field of Human Identification using DNA techniques is growing rapidly, not only in the variety of genetic loci used, but also in the analytical methods and instrumentation used to acquire typing data. Since laboratories will exchange DNA typing data possibly obtained from different analytical methods, standardization of reporting is required. The newer analytical techniques make use of fluorescently-labeled products that are sized with internal sizing ladders, while older techniques visualize the products with either fluorescent or silver staining techniques and results are compared with allelic ladders that have known size repeats assigned to each band.

Approach: An interlaboratory comparison of typing results for Short Tandem Repeats (STRs) has been evaluated. These STRs all have a nominal four basepair (bp) repeat. However, there are known one- and two-base pair variants present, with several loci represented. For the comparison test, seven different samples were distributed to forty-one DNA laboratories (Federal, State, local, or commercial) in North and South America. Laboratories were given commercially available multiplex STR kits (donated by two different vendors) that fit their DNA methods. One manufacturer did not supply allelic ladders in their kit while the other vendor did.

Results and Future Plans: The 34 laboratories that returned results used a wide variety of commercial analytical systems. Comparable results were obtained for all samples at all loci when results were reported as an allelic name (or type). Raw sizing results obtained from internal-lane sizing standards differed by nearly five bp at some loci. Many different factors contribute to this observed sizing variability, including choice of sizing standards and matrix composition. While sizing results can be made more comparable by locus-specific offsets or calibration to a comprehensive set of alleles at each locus, samples typed to the allelic name can now be validly compared regardless of analytical method. Interlaboratory comparison of raw allelic size remains problematic. At the beginning of this study there was a movement in the DNA community to exchange STR typing data as basepair sizing. This movement was based on the precision of analytical data that that could be obtained from some of the fluorescent based technologies. While the data within a laboratory or within a gel was excellent, data obtained between laboratories that used the same analytical methods could not be reliably compared. The DNA results obtained by many different methods were comparable as long as each laboratory called the results by the allelic type and not the basepair size of the DNA product. Thus, the current reporting method for STR typing results is the allelic name. Additionally, all manufacturers of STR typing kits now supply allelic ladders to allow proper calibration.

Plans are underway to conduct several more interlaboratory tests with STRs to validate their usefulness in human identity and to assure the forensic and paternity testing community that the metrology is robust and accurate.

Publication:

Kline, M.C., Duewer, D.L., Newall, P., Redman, J.W., Reeder, D.J., and Richard, M., ***"Interlaboratory Evaluation of Short Tandem Repeat Triplex CTT,"*** J. Forensic Sci. 42(5), 897-906 (1997).

4. *Characterization of a Prototype Mitochondrial DNA Standard Reference Material*

B.C. Levin, *H. Cheng (Geo-Centers), and D.J. Reeder*

Objective: To develop a human mitochondrial DNA standard reference material (SRM) for quality control in sequencing, forensic identification, medical diagnostics and mutation detection.

Problem: Sequence data is being generated at an unprecedented rate both to sequence the entire human genome and to determine if various individuals are genetic carriers of polymorphisms or mutations which have been associated with a multiple of diseases. The problem is that there is little or no quality control to assure that the sequence data is correct. The effects of false positives or false negatives can be disastrous. False positives can lead to loss of insurance or worse - perhaps drastic surgery to prevent a future illness. False negatives could lead to a incorrect sense of security allowing a disease to occur that might have been prevented. A sequencing DNA SRM would provide the necessary quality control, which will prevent both false positives and false negatives.

Approach: A human mitochondrial DNA (mtDNA) standard reference material (SRM 2392) is in the final stages of development at the National Institute of Standards and Technology (NIST). It was prepared to provide quality control to investigators who sequence human mtDNA for forensic identifications, medical diagnosis, mutation detection or any other purpose. The mtDNA SRM will include extracted DNA and all the information necessary to perform the polymerase chain reaction (PCR) amplification process, cycle sequencing steps, gel separation and data analysis to determine the DNA sequence of the two templates (CHR and 9947A). All materials necessary to ascertain the accuracy of results are provided in this SRM. The SRM also will include cloned DNA from the HV1 region of the CHR cell line. Sequence information on a third human mtDNA template, GM03798, will be given for comparison, although the DNA will not be provided as part of this SRM. The sequences of fifty-eight sets of unique primers will be supplied to allow any area or all of the mtDNA (16,569 base pairs) to be amplified and cycle sequenced.

Results and Future Plans: Compared to the Anderson (Anderson et al., 1981) sequence, none of the differences found in these three templates correspond to the published mtDNA mutations associated with specific disease states (Wallace et al. 1997). An interlaboratory evaluation of the amplification, sequencing, and analysis of the data from the CHR template conducted by four laboratories indicated that three laboratories experienced no difficulties in obtaining the correct sequence. One laboratory, however, did experience difficulties. This laboratory could use this SRM to help identify analytical problems and ultimately improve their analytical techniques. Investigators will be able to purchase this SRM by June 1998 to use it as a control when they amplify and sequence their test samples. Corroboration of the SRM results provides quality assurance that any unknown mtDNA is being sequenced correctly and the resulting forensic identifications or medical diagnoses are accurate.

5. *Development of Standard Reference Materials for Diagnosis of p53 Mutations: Analysis by Slab-Gel SSCP*

C.D. O'Connell, J. Tian (Geo-Centers), and D. Johnsonbaugh

Objective: To provide well-characterized materials intended for use 1) in the standardization of DNA-based mutation detection systems for diagnostic testing and 2) as research tools for determining the parameters affecting the quality of measurements resulting from these assay systems, and from the numerous mutation detection systems under development.

Problem: The American Cancer Society estimated that 1,359,150 new cancer cases would occur in 1996. The p53 gene is mutated in over half of all human cancers. Mutation of this gene is associated with presenting a poorer survival frequency in breast cancer patients. If this correlation is supported for other cancers, detection of p53 mutations in tumors will be used to determine the aggressiveness of therapy and provide valuable prognostic information for patients and clinicians. The difficulty in diagnostic testing for p53 mutational status, as well as for the breast cancer-associated genes BRCA1 & 2, is that mutations occur throughout the gene coding regions and RNA splice junctions. As the p53 gene is 393 amino acids in size, the coding region is 1179 nucleotides in length, any of which may be mutated in cancer. If we are to begin screening cancers with molecular diagnostic tests capable of detecting all mutations, the costs of these tests need to be reduced substantially, and the sensitivity of the detection systems improved.

Approach: In this study, we focused on two important aspects for designing standards that are appropriate for use in the numerous test formats under development for mutation detection. These include: 1) the drawbacks to using established cell lines for this purpose, and 2) the sensitivity of assay formats and the variables that affect sensitivity and specificity of the test results. We use automated fluorescent gel separation and detection of mutations in the p53 gene under nine different gel systems for this study.

Results and Future Plans: We amplified by PCR a 2.0 kilobase region of the p53 gene containing exons 5-9 from seven cell lines reported in the literature to contain common mutations for this gene. We analyzed the seven-p53 single point mutations by single strand conformational polymorphism (SSCP) analysis using fluorescence slab gel electrophoresis (SG-SSCP). Fluorescently-labeled PCR primers were used for amplification of specific exons for mutation detection. SG-SSCP was conducted using a Perkin Elmer ABI 373 Sequencer with GENESCAN^{TM} Software. Nine different gel systems were tested for their ability to resolve the p53 mutations. Two gel systems were capable of resolving all of the mutations that were screened. Optimal results were obtained with 12% acrylamide 50:1 + 10% glycerol. We are using this system to examine a much larger panel of p53 mutation clones that has been constructed by a technique known as site-directed mutagenesis. The p53 sequences contained in the clones are being verified, and the panel has been made available to collaborators to determine whether different mutation detection systems are capable of detecting the mutations present within the clones. We intend to use the information gained from these studies to determine which clones to include in the SRM. The final configuration of the panel will include clones containing mutations most commonly found in human cancer, as well as others that are difficult to detect by the mutation detection assays under investigation. The results of two collaborative studies were presented recently at the 4th International Workshop on Mutation Detection, Czech Republic.

Publication:

O'Connell, C.D., Tian, J., Juhasz, A., Wenz, H.M., and Atha, D.H., ***"Development of Standard Reference Materials for Diagnosis of p53 Mutations: Analysis by Slab-Gel SSCP,"*** Electrophoresis (in press).

6. Biothermodynamics

***R.N. Goldberg**, Y.B. Tewari, and N. Kishore (Indian Institute of Technology, Bombay, India)*

Objective: The overall aim of the research is the characterization of the thermodynamics of enzyme catalyzed reactions that can benefit biotechnology.

Problem: Knowledge of the position of equilibrium is essential for predicting the feasibility of chemical reactions and for the optimization of industrial processes. Reaction conditions such as temperature, pH, ionic strength, and co-factor concentrations can substantially affect the position of equilibrium of many biochemical reactions.

Approach: Chromatography, microcalorimetry, thermodynamic modeling, and literature data are used to measure thermodynamic quantities and assemble databases for enzyme-catalyzed reactions. The microcalorimetric capability has been particularly important in allowing for the extrapolation of data to higher temperatures. This effort has also resulted in the development of estimation schemes based upon limited and carefully chosen sets of data.

Results and Future Plans: An example of a recently completed study involves the conversion of chorismate to prephenate, catalyzed by the enzyme chorismate mutase. This reaction is a rare example of a biochemical Claisen rearrangement and is central to many of the metabolic pathways that are being investigated in biotechnology for the manufacture of aromatic compounds. In collaboration with scientists at The Scripps Institute, and the Universities of Notre Dame and UCLA, we have completed an investigation into the energetics of this reaction using micro-calorimetry and a monofunctional chorismate mutase enzyme. The enzyme, derived by the Scripps scientists from an engineered host strain, was devoid of enzymatic activities that could have led to interfering side reactions. At NIST, we measured the standard molar enthalpy change for the conversion of chorismate to prephenate and were able to set a lower bound for the value of the equilibrium constant for the reaction. The university collaborators used this data to validate a novel and extensive quantum chemical calculation of the enthalpy change that for the first time accounts for the effect of water solvation and solvent polarization. These calculations also provided the absolute and relative energies for chorismate and prephenate both in the gas phase and in aqueous solution. The calculated and measured values of the standard molar enthalpy change differed by only 9 kJ mol^{-1}. This good agreement between measurement and theory suggests significant advance in our understanding of the energetics of this reaction, and helps to establish a basis for extension of quantum mechanical calculations to other biochemical reactions. From a practical standpoint, these results also may prove useful in understanding why one branch in the pathway leading to the synthesis of aromatic amino acids is favored over an alternative one, and to what extent rigorous kinetic control at the chorismate branch point is required to direct metabolic flow. Finally, our comprehensive reviews for all classes of enzyme catalyzed reactions has recently been made available as a database on the web (http://aer.nist.gov//bioprocess).

Publication:

Kast, P., Tewari, Y.B., Wiest, O., Hilvert, D., Houk, K.N., and Goldberg, R.N., ***"Thermodynamics of the Conversion of Chorismate to Prephenate: Experimental Results and Theoretical Predictions,"*** J. Phys. Chem. B 101, 10976-10982 (1997).

7. *Preparative Bioseparations*

***K.D. Cole** and C.M. Tellez (University of Illinois)*

Objective: To develop new high-resolution techniques for large-scale purification of different physical forms of DNA.

Problem: Large-scale purification of nucleic acids is necessary to meet the needs of research and development laboratories and for uses as new classes of therapeutic agents. Nucleic acid molecules selected from combinatorial libraries that are capable of high affinity binding to target molecules are examples of ligands that could be used therapeutically or for diagnostic purposes. Production of large amounts of DNA for these experiments is a new challenge in bioprocessing.

Approach: Electrophoresis has proven to be a highly successful method for the separation of nucleic acids on an analytical scale. Electrophoresis in gels and capillaries is a high resolution analytical method, but scale-up is difficult. Electrochromatography (EC) is proving to be a promising method to scale up the electrophoresis of nucleic acids. EC is the application of an axial electrical field to a chromatography column. This research has been done in collaboration with the company Life Technologies, Inc. LTI has provided a crude cellular extract that contained supercoiled circular DNA, nicked circular plasmid DNA (relaxed), linear genomic DNA (from host bacteria), RNA, and other cellular constituents. Another approach is gel electrophoresis with reversible media. Gel electrophoresis is another high resolution technique that is not widely used as a preparative tool because of the difficulty of getting DNA or proteins out of the gel when the separation is achieved. We are investigating the use of gel-forming polymers that change to solutions when the chemical environment is changed. We are also developing a new technique, helical-flow free solution electrophoresis, that uses hydrodynamic as well as electrokinetic phenomena to induce separation.

Results and Future Plans: Electrochromatography was effective at separating the supercoiled plasmid, relaxed circular plasmid, and linear genomic DNA. The separation of different physical forms of DNA was determined by the electric field strength, the flow rate, and the porosity of the chromatography packing material. Plasmid DNA of differ molecular weight was size-fractionated by varying the electrical field strength. At a given electrical field strength and flow rate, lower molecular weight DNA plasmid fragments were not as strongly retained as higher molecular weight plasmid fragments. By selecting a specific set of conditions (packing material, flow rate, and electrical field strength) the molecular weight of DNA fragments retained by the column was adjusted. In the future, we will examine the behavior of very large DNA (such as bacterial artificial chromosomes) and small DNA (oligonucleotides).

Publications:

Cole, K.D., ***"Preparative Concentration and Size Fractionation of DNA in porous Media Using a Combination of Flow and Electrical Field Strength,"*** Biotechnology Progress, 13, 289-295 (1997).

Cole, K.D. and Cabezas, Jr. H., ***"Improved Preparative Electro-chromatography Column Design,"*** Journal of Chromatography A, 760, 259-263 (1997).

8. *Biocatalytic Systems*

***B. Coxon,** D.T. Gallagher, M.J. Holden, M.P. Mayhew, A.E. Roitberg, (GeoCenters, Inc.), N. Sari (CARB/University of Maryland)*

Objective: To develop measurement and modeling techniques for characterizing enzymatic transformations that are important to industrial applications of biocatalysis and metabolic engineering.

Problem: Many new metabolic pathways are being discovered and promoted for use in making chemicals from renewable resources (e.g., glucose from crop spoilage). The separate enzymatic steps in these pathways are not well-characterized, and information such as biocatalytic rates, enzyme structure/function relationships, genetic and allosteric control of reactant specificity are needed for successful bioprocess development.

Approach: This research uses molecular biology to engineer and produce proteins whose coordinated activity is then characterized and modeled by various measurement and computational chemistry techniques. Site-directed mutagenesis, NMR spectroscopy, and X-ray crystallography/diffraction are used to determine and analyze molecular structure, while various molecular modeling techniques are used to interpret function.

Results and Future Plans: Two projects are producing structural information on component proteins to model dynamic interactions during biocatalysis. One project deals with protein electron transfer. This biocatalytic system involves cytochrome P450 (CYP101) and its electron transfer partners putidaredoxin (Pdx) and Pdx reductase. *In vivo*, this *Pseudomonad*-based system derives reducing power from NADH. The P450 stereospecifically hydroxylates a variety of carbon rich compounds and thus is of interest to both chemical synthesis and bioremediation industries. We are investigating the intermolecular interactions with regard to the flow of reducing power and exploring ways of engineering the system to reduce the need for cofactor regeneration.

The biosynthetic pathway leading from glucose to chorismate, and its aromatic derivatives, has major industrial potential and is a second focus of study. Through collaborations with industry and government laboratories, we have begun enzymology and structural investigations of several key components that may be amenable to engineering for improved pathway throughput. A database that combines existing structural and other information with new measurements from the biothermodynamics laboratory has been created. This metabolic pathway is being developed as a model system for bioprocess measurement and modeling technology.

Publications:

Holden, M., Mayhew, M.P., Bunk, D., Roitberg, A.E., and Vilker, V.L., ***"Probing the Interactions of Putidaredoxin with Redox Partners in Camphor P450 5-monooxygenase by Mutagenesis of Surface Residues,"*** J. Biol. Chem., 272, 21720-21725 (1997).

Roitberg, A.E., ***"A Molecular Dynamics Study of Fe2S2 Putidaredoxin: Multiple Conformations of the C-Terminal Region,"*** Biophysical J., 73, 2138-2148 (1997).

Coxon, B., Sari, N., Holden, M.J., and Vilker, V.L., ***"Investigation of the Paramagnetic Domain of Putidaredoxin by Nitrogen-15 NMR Spectroscopy,"*** Mange. Reson. Chem. (in press).

9. Spectroelectrochemistry

A.K. Gaigalas*, V. Reipa (UCLA), W. Yap, T. Ruzgas (Vilnius State University, Vilnius, Lithuania), V.L. Vilker*

Objective: Measure the structural changes occurring in proteins during redox processes on modified electrodes, measure electron transfer rates associated with these redox processes, and develop models for electron transfer in proteins that explain and correlate the experimental results.

Problem: Commercial application of redox enzyme biotransformations is hampered by the lack of data and models for intra- and inter-protein electron transfer, and by lack of inexpensive and reliable sources of reducing power. Knowledge of the structure-function change of biomolecules at electrode interfaces is important in the design and development of biocatalysts and biosensors.

Approach: Spectroscopic and electrochemical measurements such as linear sweep voltammetry (LSV), surface enhanced Raman spectroscopy (SERS), electroreflectance spectroscopy (ER), and spectroellipsometry (SE) are being used to characterize electrode surfaces and to measure electron transfer (ET) in several redox proteins.

Results and Future Plans: SERS has been used to identify metal site vibrations in cytochrome c, putidaredoxin (Pdx) and azurin. SERS and surface-enhanced resonant Raman spectroscopy (SERRS) are used to measure the vibrational modes of adsorbed enzymes and small molecules that effect enzyme behavior at interfaces. This allows identification of various groups that affect the binding interaction, and provides methods for inferring orientation and redox state of the active site. Electroreflectance spectroscopy (ER), which detects changes in electronic absorption induced by potential modulation, is being developed to measure electron transfer kinetics and large scale structural changes in redox proteins. Recently, this technique has been extended to the measurement of shifts in the static dipole moment of ground state and excited state solvated tryptamine adsorbed on a gold electrode. This measurement was made possible through a collaboration with investigators at NIST's SURF II facility where application of ultraviolet synchrotron radiation to electroreflectance of adsorbed proteins is being developed. Spectro-ellipsometry (SE) is the multiple wavelength equivalent of standard ellipsometry used to measure the thickness of thin films. We are developing this technique to measure the complex index of refraction and the thickness of adsorbed protein layers, or of small molecule modifiers that are bonded to electrodes to improve protein electron transfer. SE is also combined with traditional electrochemical techniques such as linear sweep voltammetry, electrochemical impedance, and pulsed chronoammperometry in order to monitor electrode modification processes, to interpret ET mechanisms and kinetics. Such spectroelectrochemical investigations on the iron-sulfur protein, putidaredoxin, have proven useful in the development of an electrode-driven, biocatalytic process for stereospecific hydrocarbon hydroxylation using the CYP101(P450cam) enzyme system. Further research using semiconductor and modified electrodes is in progress.

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10. Control and Structure of Oligomeric Enzymes Regulating Amino Acid Biosynthesis

__E. Eisenstein__, D. Chinchilla (CARB, University of Maryland), K.E. Fisher (CARB, University of Maryland), G.L. Gilliland and D.T. Gallagher

Objective: The goal of this research is to forge a quantitative mechanism for the regulation of the specificity of substrate binding and catalysis by a family of pyridoxal phosphate-dependent threonine deaminases.

Problem: A pressing problem facing biotechnology is to develop alternative approaches for the production of raw materials for chemical synthesis and bioprocesses. One approach to meet this challenge is to use protein engineering to manipulate the specificity of regulatory enzymes that control cellular biosynthetic pathways. The nature and consequences of regulatory ligand binding on the properties of allosteric threonine deaminase is providing essential information for the design of altered enzyme variants by recombinant DNA technology. These new biocatalysts are being used to direct three or four carbon α-keto acids into metabolic pathways to produce novel chemicals, including biodegradable plastics.

Approach: Our approach consists of analyzing complementary information from structural, genetic, thermodynamic and kinetic studies to yield more accurate insights into the fundamental interactions between subunits that give rise to cooperative ligand binding, and the feedback regulation of substrate binding and catalysis in threonine deaminse by isoleucine and valine. These insights are providing a rationale for the construction of novel enzymes with specific regulatory properties that are being used to increase the yield and efficiency of certain end-products in branched-chain amino acid metabolism.

Results and Future Plans: The three dimensional structure of unliganded tetrameric threonine deaminase has been determined to 2.8 nm resolution by X-ray crystallography, and is being used to guide site-directed mutagenesis efforts to reveal the molecular mechanism of allosteric regulation. The four identical chains of the enzyme possess three, two-fold molecular symmetry axes, yielding a 'dimer of dimmers' quaternary structure. The interface between subunits at one of the two-fold axes is conspicuously small. Certain amino acid substitutions at this interface yield dimeric variants that display sigmoidal steady-state kinetics, and cooperative isoleucine and valine binding. Interestingly, sedimentation studies performed in the absence and presence of active-site ligands indicate that liganded dimers show a tendency to form tetramers. This result was confirmed by analyzing the binding isotherms for active-site ligands as a function of protein concentration, which reveal that ligand affinity increases with protein concentration. These complementary approaches show unequivocally that active site ligands stabilize the tetramer, and indicate that the cooperative free energy for active-site ligand binding to threonine deaminase is negative.

Future work will be directed at introducing additional substitutions at this dimeric interface to establish the complete energetics linkage between ligand binding and subunit assembly for threonine deaminase. The elucidation of enzyme structures in the presence of regulatory ligands will also be undertaken to reveal the stereochemical changes that occur when the enzyme adopts either the active or inactive conformations. The regulatory variants constructed in these studies will also be introduced into cells to examine their effects on three and four carbon α-keto acid production in order to determine their fate in metabolism.

11. Bovine Retinal Nucleoside Diphosphate Kinase: Purification, Characterization, Cloning, Heterologous Expression, and Three-Dimensional Structure

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Objective: To biochemically and structurally characterize retinal nucleoside diphosphate kinase (NDP-kinase), an essential component of the visual signal transduction cascade.

Problem: The key role of guanine nucleotides in signal transduction in photoreceptor cells is well documented. What remains unclear is how the visual phototransduction cascade blends with the biochemical pathways of nucleotide metabolism. To address this and other questions, a study was undertaken to biochemically and structurally characterize NDP-kinase, a key enzyme supporting high levels of guanosine triphosphate (GTP) for guanine nucleotide-binding protein activation and cyclic guanosine monophosphate (cGMP) synthesis in photoreceptor cells.

Approach: Protein chemistry, recombinant DNA technologies, immunochemical techniques, biophysical methods, and crystallization were used to gain information about the chemical aspects of NDP-kinase, its subcellular localization, the cDNA sequence(s), the general build up of the molecule, and the three-dimensional structure(s) with bound cGMP.

Results and Future Plans: NDP-kinase from the retina is shown to consist of two different subunits with apparent molecular masses of ~17.5 and 18.5 SI. Gel filtration shows that NDP-kinase behaves as a tetramer in solution while analytical ultracentrifugation suggests a hexameric structure. Like other NDP-kinases, the retinal enzyme shows broad specificity for the nucleotide substrate. Carbohydrate analysis of the individual NDP-kinase subunits shows that both contain minor amounts of O-linked oligosaccharides. Immunocytochemical localization of NDP-kinase in retinal sections with anti-NDP-kinase antibodies shows arrays of the enzyme on the plasma and disc membrane surfaces. Two isoforms of the enzyme (NBR-A and NBR-B) have been cloned from a retinal cDNA library and overexpressed in bacterial cells. The recombinant enzymes differ slightly from the native NDP-kinase in their subunit molecular mass and the level of enzymatic activity. Both NDP-kinase isoforms were subjected to crystallographic analysis and their 2.4 nm resolution three-dimensional structures were determined by molecular replacement. In agreement with NDP-kinase structures from other biological sources, each monomer has four anti-parallel β strands surrounded by six α-helices and the subunits are arranged as a trimer of dimers. Future efforts will investigate the physical association of NDP-kinase with already known members of the visual transduction pathway or still unknown factors that contribute to the regulation of GTP levels. The three-dimensional structures of these NDP-kinase/target protein complexes are expected to provide important insights into the mechanism of communication between the visual transduction and guanine nucleotide metabolism pathways.

12. Theoretical Analysis of the Electronic Structure of the Active Site of a Zinc Lactamase

M. Krauss and H.S.R. Gilson

Objective: Use *ab initio* quantum calculations to interpret the spectra of metalloprotein enzymes. The zinc-containing β-lactamase from *Bacteroides fragilis* is considered here.

Problem: Determine the detailed electronic structure of an enzyme's active site through analysis of its spectra. Use this information to gain insight in the catalytic mechanism.

Approach: Model the active site of an enzyme by treating the chemically and/or spectroscopically active site as an all-electron super-molecule. The protein and solvent surrounding this site is represented by effective fragment potentials (EFP). These potentials allow the electrostatic, polarization, charge-transfer and repulsion from the surrounding protein to be incorporated into the calculation. The EFPs are implemented in the code GAMESS maintained by Dr. Mark Gordon's laboratory at Iowa State University.

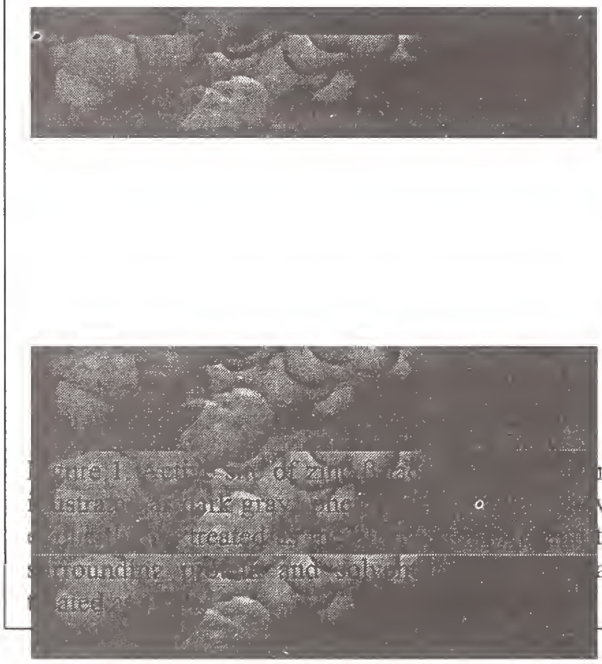

Figure 1. [illegible] of zinc β-la[illegible] atoms illustra[illegible] dark gray [illegible] shown [illegible] treated [illegible] the surrounding protein and solvent [illegible] are treated [illegible]

Results and Future Plans: The spectrum of zinc-containing β-lactamase has been obtained experimentally by substituting the optically inactive zinc ions with cobalt ions. As can be seen in Figure 1, there are two zinc ions which organize the active site of this enzyme. Model calculations show that both metal sites contribute to the observed spectrum. Different hydrogen-bonding arrangements representing different ionicities are shown to modify the position as well as the intensities of the peaks. Rules are being developed to correlate the observed spectrum to the coordination number of the metal and the ionicity of the site.

Preliminary calculations replacing the all-electron histidines by EFPs show that the EFP representations do not have a large effect on the calculated spectra when compared to the all-electron calculation. Using the EFPs for the histidines will make it possible to do a full active site calculation.

The effect of the second shell of residues and of substrate binding on the spectra will be examined using the EFPs. The active site models developed based on these calculations will be used as a basis for interpreting and predicting the effects of mutations in the protein on both the spectral properties and the reactivity of enzyme.

13. Molecular Mechanism of Site Recognition and Catalysis by DNA Repair Glycosylases: The Role of DNA Base Flipping

***J.T. Stivers**, G. Gilliland, R. He (CARB/University of Maryland), and S. Garber (CARB/University of Maryland)*

Objective: The aim of this research is to elucidate the molecular mechanism by which DNA repair glycosylases recognize and catalyze the removal of damaged premutagenic bases in DNA.

Problem: DNA repair glycosylases recognize and catalyze the removal of damaged premutagenic bases in DNA that are present at a relative concentration of less than 1 per 107 base pairs in human DNA. Thus, these impressive enzymes must solve the formidable problems of finding the specific site in a sea of nonspecific sites, and then forming specific interactions such that the transition-state for the reaction is stabilized. A general mechanism that is used to solve these problems is to couple the processes of recognition, binding and catalysis by conformational changes in the enzyme or DNA. A molecular-level understanding of these enzymes is of increasing interest for enhancing the effectiveness of cancer chemotherapy treatments, the design of new antiviral drugs, and for mutation detection in DNA diagnostic applications.

Approach: We have taken a comprehensive approach in obtaining the highest level structural and mechanistic information on the prototypic DNA repair enzyme uracil DNA glycosylase (UDG) using X-ray crystallography, NMR spectroscopy and novel rapid kinetic studies.

Results and Future Plans: UDG catalyzes the hydrolysis of premutagenic uracil (U) residues from single-stranded or duplex DNA producing free U and abasic DNA (AB-DNA). Structural evidence indicates that U is "flipped-out" of the DNA helix during catalysis, suggesting that this induced conformational change in the DNA is a key component of specificity and catalysis. Two general mechanisms for base flipping have been proposed and tested for the first time in our lab. In the first mechanism the enzyme actively accelerates the spontaneous rate of base flipping, and in the second mechanism, the enzyme increases the spontaneous equilibrium for base flipping. To elucidate the mechanism, we have developed a rapid kinetic assay based on the incorporation of the fluorescent nucleotide probe, 2-aminopurine (AP), opposite to U in duplex DNA oligonucleotides. These rapid kinetic studies using substrates with different propensities for base pair opening indicate that the rate of base flipping (k_{flip} = 310 s^{-1} to 500 s^{-1}) is independent of the base pair stability, and is faster than the subsequent step of glycosidic bond cleavage (k_{max} = 100 s^{-1} to 150 s^{-1}). Since these enzymatic base flipping rates are similar to the spontaneous rates of base pair opening in free DNA (k_{spon} = 200 s^{-1} to 1000 s^{-1}), then the enzymatic mechanism does not involve significant acceleration of the rate of base flipping. Instead, UDG increases the spontaneous equilibrium for base pair opening by stabilizing the flipped-out base, and by straining the bound substrate before the base flipping step.

In collaboration with the crystallography group at CARB, the 0.14 nm crystal structure of free UDG has been solved, as well as the structure of a UDG-DNA complex. These structures reveal the molecular interactions and conformational changes that are involved in base flipping by UDG, thus providing a structural framework for interpretation of the kinetic results. Future work will focus on protein engineering and NMR studies of the active site of UDG to quantify the roles of key residues in specificity and catalysis.

Publication:

Stivers, J.T., He, R., and Garber, S., ***"Rapid Kinetic Studies of Escherichia coli Uracil DNA Glycosylase: Evidence for Fast Base Flipping and Rate-Limiting Uracil Hydrolysis,"*** Biochemistry (in press).

14. A Database for Molecular Binding and Recognition

M.K. Gilson

Objective: Facilitate the discovery of molecules that bind to selected target molecules by providing a public database with information on noncovalent binding affinities.

Problem: Information on the noncovalent association of molecules is necessary for a range of activities in the biotechnology, pharmaceutical, and chemical industries. A tremendous amount of such information is being generated daily. However, it is difficult to find the data relevant for a given application because the information is disseminated only in journals.

Approach: Develop a web-accessible database that will facilitate access to a large body of information on the noncovalent binding of molecules in solution.

Results and Future Plans: A workshop was held at NIST on August 21-22, 1997, to discuss the planned database. The participants came from drug companies (DuPont Merck, Agouron, Bristol-Myers Squibb, and Glaxo Wellcome), from academic institutions (U. California San Francisco, Rutgers, Harvard, U. Pittsburgh, U. North Carolina) and from NIST. A number of conclusions were reached by consensus; notably: 1) The database would be a valuable resource for the scientific community. 2) The database would provide a welcome mechanism for publication of large datasets not currently publishable in journals. 3) It would also permit publication of experimental details that are useful in assessing the quality of data, but that are not normally accommodated by journals. 4) The database should include information on many types of molecules, including proteins, nucleic acids, and small organic molecules. 5) Provision should be made for various different methods for measuring affinities; e.g., calorimetry, enzyme-inhibition, and NMR spectroscopy. 6) Provision should be made for experimentalists to enter their data directly via the WWW. 7) A range of queries should be provided, including SQL, free-text, and chemical substructure. 8) Detailed specifications should be generated in advance of implementation. 9) Users should be involved in developing the user-interface. A detailed report of this workshop is available.

A series of smaller workshops will define the data fields necessary for describing specific types of binding measurements. The first of this series, held at Rutgers on October 17, 1997, assembled calorimetry experts from three drug companies and from academia to discuss calorimetric measurements of binding affinity. The report of this workshop is in preparation.

Further work on this project will be in collaboration with Dr. Phillip Bourne, a database expert at the San Diego Supercomputing Center. It is envisioned that the data definitions will be written as extensions to the macromolecular crystal information file format (mmCIF). This will facilitate linking the binding database with other databases holding structure information on proteins and small molecules. The core of the database will be implemented with commercial software. However, specialized search engines and interfaces will also be needed.

15. *Cross-referencing the Biological Macromolecule Crystallization Database (BMCD) with the Nucleic Acid Database (NDB)*

__J.E. Ladner__, M. Tung, G.L. Gilliland, J. Westbrook (Rutgers University), G. Patel (Rutgers University), M. Huang (Rutgers University), and H. Berman (Rutgers University)

Objective: To cross-reference the NIST/NASA/CARB/BMCD and Rutgers University NDB databases for nucleic acid macro-molecules and to test a user-friendly data input tool for submission of data to the BMCD.

Problem: There are NDB x-ray structures for crystals of macromolecules which are not in the current version of the BMCD and no convenient tool exits for submission of data about the crystallization of macromolecules by the experimenters.

Approach: Engage students at Rutgers University to search the literature for the NDB structures that are not included in the BMCD and to enter the data in a form that is easily included in the BMCD.

Results and Future Plans: The NDB is a database administered by Helen Berman at Rutgers University with the atomic coordinates for nucleic acid macromolecules that have been solved by X-ray crystallographic or NMR techniques. The BMCD is a database that has the crystallization conditions used to produce crystals of macro-molecules, including proteins and nucleic acids. The two databases have been developed independently. Data is submitted to the NDB by the authors at the time of publication. Data is taken from the published literature for entry into the BMCD.

An input tool and a program for checking the cross-referencing of the two databases was developed by John Westbrook at Rutgers University. After identifying the macromolecules that were in the NDB but not in the BMCD, Gnanesh Patel and Michael Huang used the input tool to make files of the data needed by the BMCD by accessing the journal articles that are archived with the NDB entries. These files are now being incorporated into the BMCD. This work is continuing and plans for the future include a thorough cross-referencing of the BMCD with particular emphasis on all of the proteins whose three-dimensional structures are deposited in the Protein Data Bank (PDB). With a useful software tool to deposit crystallization conditions for biological macromolecules, it is anticipated that future entries into the BMCD will be submitted by authors at the same time as structure coordinates.

16. *Thermodynamics of PNA/DNA Hybridization Reactions*

__F.P. Schwarz__ and J.M. Butler

Objective: The two primary objectives of these studies are to develop a data base consisting of the free energy change, enthalpy change, and entropy change for the binding of peptide nucleic acid sequences (PNA) to their complementary DNA sequences and to use this data as the basis of a model for predicting these thermodynamic binding quantities from a nucleotide sequence of the PNA.

Problem: PNAs are a new class of nucleic acid sequences connected by a peptide backbone linkage which bind to their complementary DNA sequences with an affinity comparable or greater than the binding of an identical DNA sequence. The high PNA binding affinities make them suitable as probes for identifying specific DNA sequences using microchip arrays and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. A sequence-based model for predicting thermodynamic information on the hybridization of DNA by PNA is necessary for the design of suitable PNA probes for DNA diagnostics and DNA technology.

Approach: High-precision isothermal titration calorimetry (ITC) was employed to determine the free energy change, the enthalpy change, the entropy change, and the stoichiometry for the hybridization reaction between a variety of PNA sequences and their complementary DNA sequences. Results from accurate ITC measurements are being compared to thermodynamic parameters derived from the widely employed, but indirect method of analyzing the UV melting curves of PNA/DNA duplexes. These thermodynamic quantities will be used to develop a model for predicting the thermodynamics of PNA/DNA hybridization reactions by assigning thermodynamic parameters to the Watson-Crick nearest neighbor pairs in the PNA/DNA duplex. A similar predictive approach has been successfully applied to DNA/DNA self-complementary reactions.

Results and Future Plans: Thermodynamic data have been collected from ITC measurements at 297 K on 16 binding reactions between PNA sequences and their self-complementary DNA sequences, in addition to the 16 corresponding DNA/DNA binding reactions. The reactions are exothermic, occurring with the free energy changes ranging from -43 kJ/mol to -35 kJ/mol, and with enthalpy changes from -140 kJ/mol to -77 kJ/mol. A comparison of the energetics for DNA/PNA association with the same quantities seen for corresponding DNA/DNA binding reactions indicates that for 75% of the sequences investigated, a given sequence binds more tightly to a complementary PNA sequence than to a complementary DNA sequence. This striking result stems from the differences in the entropic contributions to the binding thermodynamics. The entropic cost for the PNA/DNA hybridization reaction is less than that for its corresponding DNA/DNA binding reaction, which may be attributable to the well-ordered, stacked conformation of the PNA reactants in solution at 297 K. The different conformational states of the PNA at 297 K and at the higher temperatures where UV melting transitions are seen may also explain the difference between the ITC results and those obtained from analysis of the UV melting curves of duplex molecules.

From the stoichiometry of the hybridization reactions, a more accurate method of calculating the UV absorptivities of PNA sequences is being developed. The thermodynamic data is now being used to derive the thermodynamic contributions of the nearest neighbor Watson-Crick pairs for the predictive model. To evaluate the validity of the predictive approach, model-derived thermodynamic quantities for a variety of hybridization reactions involving sequences of different lengths and compositions will be compared to their corresponding experimental quantities.

17. Hybrid Bilayer Membranes

A.L. Plant, C.W. Meuse, V. Silin, and D. Vanderah

Objective: The desire to assemble organized arrays of biological molecules for structure/function determinations, and for applications in sensors, bioelectronics and novel materials has led to an intense interest in biomimetic materials. A novel supported lipid bilayer, with a structure analogous to the membranes of living cells, is being investigated for its application as a rugged, biomimetic matrix for studying the structure and function of active membrane proteins.

Problem: The characteristics of lipid membranes such as their insulating properties, self-assembling components, dynamic responses, and the fact that they provide a matrix for membrane proteins, are important for potential applications in biocatalysis, sensors, and electro-optical materials. An especially important class of proteins is cell membrane receptors, which are sites for control of many metabolic aspects of living cells and are potentially important targets for pharmaceutical delivery. Commercial uses of cell membrane-like lipid systems for research and applications have been limited by difficulties associated with lipid bilayer stability, and by difficulties associated with handling membrane proteins in a way that conserves membrane protein structure and function.

Approach: We have developed a hybrid bilayer membrane (HBM) system consisting of both natural (phospholipid) and synthetic (alkanethiol) components, which is easily formed by self assembly, is supported on a conductive metal surface, and is stable for very long periods of time. This cell membrane-like material is rugged enough and easy enough to fabricate that it has practical applicability to industrial-scale use. One focus of this project is to use this membrane mimetic system as a research tool for studying the structure and activity of membrane proteins. Using impedance analysis and cyclic voltammetry, we have demonstrated that this membrane has many characteristics that are consistent with those of other model membrane systems, including its insulating properties and its response to the protein toxin, melittin. In collaboration with the NIST Neutron Research Facility, neutron scattering from these bilayers is providing sub-nanometer level resolution in the Z-axis. Together with molecular vibrational information from Fourier transform infrared spectroscopy, we are achieving in-depth analyses of the molecular structure of these bilayers and membrane proteins inserted in them.

Results and Future Plans: These stable and rugged membranes can be formed and studied in aqueous conditions and in dry air. Aided by dynamic simulation modeling results (in collaboration with the NIST Neutron Research Facility), comparison of surface enhanced Raman and Fourier transform infrared spectroscopy results has provided details on the subtle changes that occur in the alkanethiol layer when a bilayer is formed Neutron reflectivity from these membranes has provided new and fundamental information on the degree of hydration of the polar region of lipid membranes Neutron reflectivity data on bilayers containing the pore-forming toxin melittin are providing important and unambiguous information about where this protein complex resides in the membrane. New chemistries currently under study will provide a tethered layer that is more accommodating to transmembrane proteins. Surface plasmon resonance measurements are being employed to understand the mechanism of spontaneous self assembly of HBMs from phospholipid vesicles, and are part of a collaborative effort with Los Alamos National Laboratory on sensor applications using HBMs. In another collaboration, CRADA partner, SmithKline Beecham, has used HBMs to study the agents involved in blood clotting initiation at cell surfaces. The demonstration of the use of this approach to form highly complex supported bilayers from red blood cell membranes suggests that this may be a tool by which cell membrane proteins can be studied that circumvents the difficult and sometimes impossible step of membrane protein purification.

Publications:

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18. Vibrational Spectroscopy of Biological Interfaces

*C. **Meuse** and V. Silin (Institute of Biochemistry, Lithuanian Academy of Sciences, Lithuania)*

Objective: To develop new vibrational spectroscopic tools to study the formation and structure of biological interfaces and biomimetic models of cell membranes.

Problem: The utilization of biomimetic surfaces to study biological problems such as the structure and function of transmembrane proteins, biocatalysis, sensors and DNA diagnostics requires the development of sensitive characterization and quantitation techniques. Commercial interest in these techniques is evident in the rise in the use of surface plasmon resonance to measure the kinetics of biomolecular interactions at surfaces and the recent introduction of a commercial infrared spectroscopic ellipsometer. As the complexity of the questions about the structure of biological interfaces increases, the need for techniques to study these systems will grow.

Approach: Both Raman and infrared spectroscopy are being used to obtain complimentary vibrational spectroscopic information about surface structures. An opto-mechanical unit is being developed to utilize surface plasmon resonance to enhance the signal observed by Fourier Transform Raman spectroscopy. Since surface plasmons are excited at smooth metal surfaces, this technique allows sensitive analysis of the molecular structure of a biological interface without the need to roughen the surface as is required for conventional surface-enhanced Raman scattering. A second approach involves the development of an electromagnetic wave theory model that allows a better interpretation of the structural details of biomolecular surfaces by comparing Fourier transform infrared spectroscopy data with simulated spectra. Sampling techniques include internal and external reflection to study both hydrated and dehydrated sample.

Results and Future Plans: One biomolecular material under study is a cell membrane mimic composed of alkanethiols and phospholipids. Infrared spectroscopy and surface enhanced Raman spectroscopy have been used to determine that the changes in alkanethiol monolayers upon the formation of a phospholipid-containing hybrid bilayer are consistent with increases in both trans/gauche and torsional ordering of the thiol acyl chains. Infrared spectroscopy and electromagnetic wave theory have been used to characterize the number of trans bonds and to determine the orientation of the acyl chains of the lipid layer in dry hybrid bilayers. Surface plasmon resonance FT-Raman capability now exists and is being tested. It will allow future studies of supported cell membrane mimics under aqueous conditions, and will improve our ability to interpret SPR kinetic data. The capability to acquire infrared ellipsometric data and analyze it using electromagnetic wave theory models is being developed to increase our capabilities to characterize the spatial orientation of biomolecular materials at interfaces.

Publications:

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19. Self-Assembling Nanoscale Pore-Forming Proteins

*J.J. **Kasianowicz,** D.W. Deamer (UC Santa Cruz), D. Branton (Harvard University), H. Bayley (Texas A&M), and S. Bezrukov (NIH)*

Objective: Studying an important class of naturally occurring pore-forming proteins will increase our understanding of membrane channel proteins, as well as aid in rational design of biomolecular materials for the separation and sensing of a wide variety of water-soluble analytes.

Problem: Nanometer-scale self-assembling pore-forming proteins function by opening passages for certain ions and macromolecules in otherwise impermeant cell membranes. In addition to their biological functions as toxins and in nerve cell response, these protein channels, or biomimetic structures like them, could play a significant role in separation and sensing applications. To develop an understanding of the role that specific molecular sites play in the functioning of these proteins in membranes, we study the passage of different kinds of solvated molecules through these pores. We have discovered that we can design pores that distinguish, characterize and separate different polymers (e.g., DNA), and different heavy metal divalent cations. Improving the ease and efficiency of selecting, separating, and identifying the sequence of DNA segments is of interest for both forensic and diagnostic applications. Better ways of detecting and removing heavy metal ions will benefit manufacturing and military applications.

Approach: A combination of electrophysiological techniques and genetic engineering is being used to redesign and adapt proteins that self-assemble to form well-defined nanoscale pores in lipid bilayers. The ability of polymers or cations to interact with these pores are determined by the changes in the pore's ionic current caused by these analytes.

Results and Future Plans: Our recent work on the interaction of DNA and RNA, nonelectrolyte polymers and cations with the ion channel formed by *Staphylococcus aureus* α-hemolysin (α-HL) suggest that nanoscale pores could be used in separation and sensing applications. First it was demonstrated that single stranded (but not double stranded) RNA and DNA polynucleotides could be driven through an ion channel by an applied electric field. The passage of individual polynucleotides through the pore caused brief blockades in the ionic current that otherwise flowed freely. The duration of the current blockades was proportional to the length of the polynucleotides. Secondly, it was shown that an ion channel can discriminate between differently-sized poly(ethlyene glycol) nonelectrolyte polymers, and the period over which the polymer and pore interaction occurred. Third, genetic engineering and electrophysiological techniques were used to redesign and adapt α-HL pores that exhibit different sensitivities to different heavy metal divalent cations.

The crystal structure of the α-HL pore was recently determined by others to 0.19 nm resolution. This will greatly aid the design of pores with the desired properties for separation and sensing applications. In addition, we are interested in producing pores with different diameters for characterizing and separating different sized polymers.

Publications:

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20. Sensor Applications Using Enzymes and Membrane Channel Proteins

S.A. Glazier *and J. J. Kasianowicz*

Objective: To develop strategies for potential applications of protein-based electrochemical biosensors using electrodes modified with active proteins in rugged matrices.

Problem: Because of their specificity in molecular recognition, proteins such as enzymes and toxins have great potential as electrochemical sensor components. To be effective in such applications they must be associated with matrices in which they are active, stable, and in electrical contact with an electrode that is protected from degradation. Matrices in which proteins may function optimally in sensor applications are under examination.

Approach: Through a CRADA with Nitrate Elimination Co., the redox state of a water-soluble nitrate reductase was used to detect the presence of nitrate in drinking water. A polymer film was used to trap the enzyme at the electrode surface. Using a different approach to electrode modification, a rugged supported lipid bilayer was formed at a gold electrode surface using alkanethiols and phospholipids. The pore-forming toxin, α-hemolysin, spontaneously assembles into this biomimetic bilayer membrane with its ion channel activity intact. The channels are specific for, and can be used as, sensors for certain heavy metal ions by assessing the electrochemical response of the modified electrode.

Results and Future Plans: For nitrate detection, the highly stable, water soluble nitrate reductase from corn seedlings was an effective sensor component. Electrodes responded to nitrate ion at levels near or below the 10 mg/L set by the EPA for nitrate in drinking water. The performance of these electrodes was comparable to those of other nitrate assay techniques. The supported bilayer membrane has a high electrical resistance in the absence of the channel forming protein. Adding a genetically engineered mutant of α-hemolysin to the solution bathing the membrane causes a decrease in the resistance. Transition divalent cations (e.g. Zn^{+2}) which are known to block this channel mutant in suspended lipid bilayers, also appear to block it in these supported rugged membranes. Next-generation chemistries for forming rugged membranes with more biomimetic character are currently being characterized in order to optimize the function of these channels and other membrane-bound proteins.

21. Nonlinear Optical Studies of Biological Surfaces

***T.P. Petralli-Mallow**, J.C. Stephenson, L.J. Richter, and A.L. Plant*

Objective: To develop surface-specific, structure-sensitive nonlinear optical methods for *in-situ* studies of biological surfaces to facilitate the engineering of more effective biomimetic materials.

Problem: A critical need for surface structural information exists in many biotechnology applications including the development of bioimplants, biosensors, and biocatalysts. The architectures and mechanisms of surface-associated biological molecules can be very different from those in solution due to the interfacial forces, energies, and gradients which may direct orientation, structure, aggregation, and reactivity. Both surface-induced denaturation and organization can significantly alter the activity of these molecules. Studying surface-bound biological molecules is difficult due to inherently small surface concentrations and the fact that native structures involve buried aqueous interfaces.

Approach: Nonlinear optical laser techniques, second harmonic generation (SHG) and sum-frequency generation (SFG), are being adapted to study biological molecules at or within biomimetic membranes. SHG and SFG offer powerful advantages due to their flexibility as optical probes, high surface selectivity, submonolayer sensitivity, and excellent spatial, spectral and temporal resolution. Though not yet widely applied to biological macromolecules, SHG and SFG are capable of *in-situ* measurements at biological interfaces and can potentially provide direct information about structure, orientation, aggregation, and organization of surface-associated biomolecules. SHG and SFG signals are only generated by molecules at the interface and thereby have zero background from molecules in solution.

Results and Future Plans: Currently, SHG studies of ubiquinone (coenzyme Q) are underway. Ubiquinone is found in all native cell membranes and can activate electron transport in proteins in biomimetic membranes. The SHG studies aim to determine the orientation of the quinone head group in biomimetic membranes containing ubiquinone and determine whether and how the quinone orientation changes as a function of redox state. This work strives to address current controversy concerning the mechanism of ubiquinone in electron and proton transport and further the Biomolecular Materials group's fabrication of redox-active biomimetic membranes. Future SHG studies will concentrate on protein incorporation in and interactions with biomimetic membranes. SFG studies will query the conformation of its isoprenoid tail as a function of redox state.

III. Process Measurements Division (836)

Gregory J. Rosasco, Chief

A. Division Overview

Mission:
The Process Measurements Division develops and provides measurement standards and services, measurement techniques, recommended practices, sensing devices, instrumentation, and mathematical models required for analysis, control, and optimization of industrial processes. The Division's research seeks fundamental understanding of, and generates critical data pertinent to, chemical process technology. These efforts include the development and validation of data-predictive computational tools and correlations, computer simulations of processing operations, and provision of requisite chemical, physical, and engineering data.

Programs:
Process and quality control and equity in commerce ultimately depend on the accuracy of measurements. This generally requires calibration of instruments against, or use of procedures assuring traceability to, national standards. Therefore, **measurement standards and calibration services** are a very major part of the Division's activities. We provide support critical for **temperature, humidity, fluid flow rate, pressure, vacuum, leak rate, liquid density and volume, and air speed measurements** with more than 1000 standard tests and calibrations performed this year. The Division's commitment to provision of these services involves many facets: the establishment, maintenance, and improvement of the primary standards; continuing intercomparisons of these standards to those of other nations; development of suitable mechanisms for transferring the requisite measurement accuracy to customers in the field and in secondary calibration laboratories; and continual attention to service efficiency and measurement quality.

While these measurement and calibration services are provided to a wide range of customers, we also have measurement support programs focused on specific strategic technologies, such as maintaining U.S. leadership in semiconductor device manufacturing. As part of NIST's National Semiconductor Metrology Program (NSMP), the Division is selecting, developing, evaluating, and validating **process measurement technologies important in semiconductor manufacturing**. These efforts include provision of improved thermocouples for control of thermal processing equipment including RTP systems, low-range gas flow standards, evaluations and models of the performance of residual gas analyzers used to monitor gaseous contamination in fabrication tools, methods to determine plasma electrical properties, and very low-level moisture measurements for contamination control in process gases. In some of these efforts we make use of a reference processing-reactor prototypical of industrial manufacturing environments. This allows critical tests of the measurement approach and its utility for the intended application. Because processing systems are typically complex, with strongly coupled chemistry and mass transport, and electrical characteristics, reference reactors are subject to extensive modeling and validation efforts as an integral part of the measurement support activity. These models and supporting data play a critical role in all elements identified by the Semiconductor Industry Association's (SIA) National Technology Roadmap for Semiconductors. In fact, modeling is specifically identified not only as a "crosscutting technology", but as "pervading all crosscuts". Our program in this area, partially supported by NIST's NSMP, seeks to develop and validate **benchmark chemical mechanisms and supporting thermochemical and kinetic data, for equipment and process design**.

The technical approach described above, which emphasizes measurement technology development, provision of process models and supporting data, and validation on prototypical systems, characterizes not only our semiconductor-related efforts, but also is representative of our process technology related research in the areas of materials chemistry, spray combustion, and hydrothermal oxidation. The first of these, highly synergistic with the semiconductor models and data program, develops **chemical and process models and data to support the production of high technology materials**. In a project joint with the Materials Science and Engineering Laboratory, we are studying multiphase combustion synthesis of nano-scale magnetic oxides, important for information storage technology, and seeking to use sodium/metal halide chemistry to synthesize metals and non-oxide ceramic particles and films, e.g., SiC, required for high-temperature, high-durability applications in the aerospace industry. This novel processing method offers a relatively low temperature (low energy consumption) route with promise for bulk-synthesis of these generally difficult-to-prepare materials. It also has the advantage of essentially zero emissions providing an inherently "green" processing approach for the production of high technology materials.

Addressing industrial problems associated with the operation and design of thermal reactors is the main focus of the other two Division programs in process technology. Based upon a unique combination of spray measurement capabilities and a laboratory-scale prototype spray combustion facility, the spray combustion program emphasizes measurement of the role of droplet dynamics (generation, transport, and mixing) in determining the performance (efficiency and emissions) of spray-based energy production and waste destruction systems. The primary objective of this effort is to **provide benchmark data for the validation of computational models for combustor performance and to establish a means to correlate performance with operating conditions**. Major concerns in the development of hydrothermal oxidation (HTO) as a zero-emission treatment technology for aqueous wastes are unknown processing conditions and poorly understood "unit operations", specifically with respect to salt formation and deposition, metallic corrosion, and heat transfer in near-critical fluids. Addressing the measurement and data issues associated with these technology barriers forms the core of the Division's **research in HTO technology**.

The Division has a significant effort in the area of chemical sensor technology with two research programs: **micromachined gas sensor arrays** and **sensing applications of self-assembled monolayers (SAMs)**. The first effort is collaborative with the Semiconductor Electronics Division of the Electronics and Electrical Engineering Laboratory. The technology is based on CMOS-fabricated SiO_2 bridge structures formed with silicon micromachining to make 'micro-hotplate' arrays. Chemical sensing capability is achieved by depositing metal oxides, e.g., SnO_2, and surface-dispersed catalytic metal-additives to form robust, electrical-conductance based sensing elements on the micro-hotplates. Because of their small mass the micro-hotplates can be heated to near 1000 °C and cooled back to ambient temperature with time constants in the millisecond range. This enables temperature programmed sensing (TPS) which can lead to enhanced sensitivity, selectivity, and repeatability of the sensing response. Combined with selection of metal oxides and catalysts, TPS arrays offer excellent potential for real-time sensing of multi-component gas mixtures. NIST holds three patents on the fabrication and application of these devices. To date, more than 26 companies have contacted us to discuss licensing this technology. The objectives of our effort are to develop the knowledge-base required to optimize multi-species detection and quantitative analysis and to resolve generic device-processing issues which could limit commercial application.

Alkanethiol monolayers, of the general formula $X(CH_2)_nSH$, self-assembled on the surfaces of noble metal substrates are a second focus of the Division's sensor program. These molecules attach via the thiolate headgroup to form strongly chemisorbed and densely packed assemblies with surfaces having terminal-group (i.e. the moiety 'X') controlled functionality. The SAMs can be 2-dimensionally patterned, for example via a NIST patented photo-process, to produce arrays of two or more alkanethiol molecules with different terminal functionalities selected to enhance or prevent physior chemisorption of specific biological or organic molecules. Our research is currently focused on the attachment of active DNA probes with the goal to develop the means to reliably produce the desired SAM arrays, including studies of the roles of chemical and structural "forces" in the self-assembly process, and to develop approaches to sensing and identifying molecular recognition events, such as DNA hybridization. SAM based sensors hold great promise for applications in medicine, pharmacology, and biotechnology.

Selected Program Highlights:

The Division provides and disseminates the International Temperature Scale of 1990 (ITS-90) over the range 0.65 – 1235 K. This year we have achieved an important Division goal in completing the NIST realization of the scale in terms of its fundamental definition. NIST's achievements in this area place us in the lead among all national standards laboratories, not only in terms of completing the scale, but also in terms of the low levels of uncertainty of our realization. This accounts, in part, for our major role in four key comparisons of realizations of ITS-90 organized by the Consultative Committee on Thermometry of the International Committee on Weights and Measures (CIPM). We have leadership positions, as coordinator or sub-coordinator, in two of these comparisons and full participation in the other two. Additionally, we are participating in comparisons of transportable cryogenic triple-point cells and are leading a number of international efforts examining non-uniqueness issues in many sub-ranges of the ITS-90. We also continue efforts, joint with the Physical and Chemical Properties Division and the Optical Technology Division (Physics Laboratory), to improve the accuracy of thermodynamic temperature measurements in the range above 500 K. The plan calls for extension of high accuracy acoustic thermometry to 933 K (the Al-point). The Optical Technology Division will link to our measurements at the Zn- (693 K) and Al-points and extend them to the Au-point (1337 K) with an accuracy goal of 10 mK.

In practical process control applications, thermocouples (TCs) are the most widely employed of all thermometers. This year we completed in collaboration with IMGC (the national measurement institute of Italy) development of a reference function for Pt/Pd TCs. This TC has demonstrated remarkable high temperature performance with stability of ±20 mK for temperatures up to 1200 K and ±100 mK for temperatures up to 1775 K. These devices will be increasingly important in semiconductor manufacturing which requires very accurate temperature control in wafer processing furnaces. We also are developing the Pt/Pd couple and other noble metal systems as thin film thermocouple thermometers to provide accurate surface-temperature measurement for control of rapid thermal process (RTP) systems used in semiconductor manufacturing.

The Division provides the national standards and calibration services for pressure and vacuum measurements over 16 decades of pressure, from 10^{-7} to 10^{9} Pa. Recent advances in the measurement of pressure and vacuum include the development of new standards and calibration services as well as significant improvements in instrumentation. Two new low-pressure calibration systems were implemented this year. The first, based on an oil ultrasonic interferometer manometer, provides calibrations in the pressure range of 0.1 Pa to 133 Pa with expanded uncertainties of 0.01% at a pressure at 133 Pa, a factor of 10 improvement in accuracy in this range. The second new standard, based on a mercury ultrasonic interferometer manometer, was designed for low-differential pressure measurements at elevated line pressures (up to 200 kPa) and provides new capabilities to support high accuracy calibrations of differential pressure flow devices. As in the temperature standards area, international comparisons have grown in importance with NIST participating in six key comparisons dealing with pressure and vacuum standards. These are organized under the Consultative Committee for Mass and Related Quantities of the CIPM. We are leading, i.e., serving as pilot laboratory, three of these comparisons. Additionally, we have organized a multi-laboratory comparison for near atmospheric pressure measurements within NORAMET (North America) and SIM (metrology collaboration for the Americas).

In the general area of fluid transfer measurements, the Division provides gas flow and leak rate standards and calibrations over the range from 10^{-14} to 10^{2} mol/s and similar services for liquid flows in the range from 10^{-3} to 10^{3} L/s. To support measurement needs in industries such as semiconductor manufacturing, new high accuracy primary standards for low range gas flows are under development. A series of ultra-stable, laminar flow meters have been developed to generate flows over a range of 10^{-7} to 10^{-3} mol/s. These instruments have demonstrated long term stability (over the course of two years) of ±0.1% and have been used by NIST personnel to conduct on-site tests of industrial primary flow standards at 15 facilities over the past two years. We are also developing these laminar flow elements for use as *in-situ* calibration devices for industrial flowmeters, such as mass flow controllers. To this point the majority of international comparisons of flow standards have been bi-lateral, for example, results of a preliminary comparison between Japan and NIST was completed this year. However, interest in coordinated international comparisons of flow standards is growing. New transfer standards, such as the laminar flow meter discussed above, should play an important role in these developing efforts.

Another long-term Division goal was reached this year with the commissioning of a new reference low frost point generator capable of delivering humidity levels down to approximately 5 nmol/mol (−100 °C frost point) at atmospheric pressure. The system has shown long-term stability of better than 0.5 mK, and an uncertainty (k=2) of less than 10 mK in saturator temperature. Interest in international comparability in humidity measurements also continues. Under the auspices of the Consultative Committee on Thermometry, NIST is serving as chair of a 13-nation comparison of national humidity standards. This year, a third round of comparison, utilizing a high-precision dew point hygrometer, were made with INTA (the national measurement institute of Spain). This transfer standard has circulated in Europe over the past few years and allows assessment of NIST's humidity generators relative to those in Europe. A similar comparison, based on the dew point hygrometer transfer standard which is circulating in the Asia Pacific Region, also was completed at NIST this year. Although publication of the results must await final analysis and approval, preliminary indications support agreement within stated uncertainties.

Increasingly industry is turning to NIST for flow calibrations for reactive and/or corrosive gases (e.g., for semiconductor manufacturing applications), for gas mixtures and for gases at elevated temperatures (the latter two conditions are important in combustion and for automotive applications). Our current efforts to address these needs include the development of new metering technology, e.g., an acoustic doppler-shift flowmeter, and the provision of new calibration facilities, i.e., the Heated Gas Mixture Flow Facility (HGMFF). Initial tests of the doppler-shift flowmeter have demonstrated a flow resolution of 10^{-7} mol/s for an instrument with a maximum flow range of 10^{-3} mol/s. The new flowmeter can be applied to any gas, requiring only conventional gas handling hardware for its construction and knowledge of the gas density near room temperature and 1 atmosphere pressure, i.e., nominally ideal gas conditions. It has the additional advantage of relatively high speed, i.e., measurements in 10-100 ms, which can be important in many processing applications. The HGMFF provides variable composition (high concentration mixtures of air, N_2, CO_2, H_2O, and additions of 1 or more low concentration species), variable temperature (to 700 K) flows in the range 1 to 36 standard (1 atm at 273.15 K) liters per second ($\cong 0.04$ mol/s). This new facility has been very important in testing a number of prototype meters being developed for the U.S. automotive industry as part of it push to ultra low emission vehicles. We have interacted directly with commercial meter manufacturers who are attempting to meet meter performance specifications set by the American Industry/Government Emissions Research consortium. A five-fold improvement in meter performance has been realized from this collaborative work, and a NIST developed Reynolds-number scaling relationship holds promise for simplifying calibration of these important automotive exhaust measurement systems.

Proficiency testing at 13 air-speed calibration facilities was completed this past year to quantify their performance relative to NIST's standards. These tests were conducted under the auspices of a CRADA to protect the confidentiality of participants' data. These tests used 2 types of transfer standards: a thermal anemometer and a pitot tube. Testing covered the range from 0.3 to 15 m/s. Results showed facility variations up to 30% relative to NIST values. These assessments have enabled participants to identify errors in their procedures and establish traceability to the NIST reference. A second round of testing is being planned with the goal of establishing agreement at the level of approximately 2%. Also in the fluid flow area, research continued under two CRADAs, involving the Electric Power Research Institute and meter manufacturers, to investigate the use of non-intrusive acoustic flow meter technology for improved accuracy in measurements of cooling-water flows in power plants. Preliminary results from testing these clamp-on acoustic devices suggests rather good precision, of the order of 1%, but the need to addresses biases in the methods used to calculate average flow rates from the acoustic time-of-transit information. The promise of ultrasonic multi-path flowmeters to provide accurate (primary) measurement of pipe flow has been studied both theoretically and experimentally for the past few years. Measurements with an uncertainty (k=1) of the order of 0.2% appear to be achievable with today's technology. Computational simulation of the flows and the flow measurement device plays an increasingly important part of the assessment of all our flow measurement standards. Refinement and validation of computational tools for both incompressible and compressible high Reynolds number (turbulent) flows, which are characteristic of many of our applications, is an important part of the overall program plan. This work has the vision of developing portable, scaleable primary flow measurement standards. These could play a vital role in establishing flow traceability within the US and also in establishing flow measurement comparability internationally.

A major thrust in the Division is to develop species specific, partial-pressure measurement methods and standards to calibrate instrumentation used to monitor process gases. This effort will expand vacuum metrology beyond the traditional inert gases to include identification and quantitation of low-level contaminants, even in higher-pressure background gases. Such contaminants play a critical role in determining the quality of vacuum-processed components and represent a major challenge from the point of view of real-time process monitoring and control. Our initial focus is on the optical measurement technique cavity-ring-down-spectroscopy which holds promise for measurements of moisture in vacuum, perhaps down to the 10^{-8} Pa range, and for parts per billion measurements of water in gases, e.g., humidity. Building on our previous theoretical and experimental studies, we have identified three critical elements for success in this effort: 1) the need for a versatile narrow-bandwidth frequency-stable light source, 2) the use of length-stable ring-down cavities, and 3) the excitation of single TEM cavity modes to obviate mode-beating effects. Significant progress was made in realizing these requirements this past year. At present, we can measure individual cavity-ring-down times with an imprecision of 0.05% (within a factor of 4 of the theoretical, shot-noise, limit) and absorption at the level of approximately 10^{-10}/cm in a 10 cm cell (an improvement of a factor of 100 this past year).

The work on optical measurements of partial pressures will benefit many industries, including the semiconductor manufacturing sector. In many areas of our measurement support for this sector, we are now transferring technology to the industry. Hardware and software that we have developed in recent years to make accurate measurements of RF electrical parameters in the Gaseous Electronics Conference (GEC) cell are now finding application in industry. This year, a new technique was developed for measuring the ion current at wafers exposed to high-density plasmas. A provisional patent was filed on this technique, which is well suited for use as an ion current sensor in industrial reactors. Unlike traditional methods of measuring ion currents, it does not require any hardware to be inserted into the reactor (thus avoiding the possibility of contaminating wafers), it does not require the application of voltages or currents that would perturb the plasma, and it does not fail if insulating layers are present on reactor surfaces. Also this year, planar laser induced fluorescence (PLIF), optical emission, and electrical probes were used to study the optimization of O_2/CF_4 and O_2/C_2F_6 chamber-cleaning plasmas. This work significantly advances our previous collaborative studies with Air Products and Chemicals, Inc. by providing a detailed, 2-D characterization of plasma spatial-uniformity.

In recent years, we have developed a unique model for micro-contamination in a spinning-disk thermal CVD reactor. The newly developed model focuses on realistic chemical kinetics in addition to (the more typical) energy and mass transport. It also contains a model, drawn from our work on nano-phase materials chemistry, which accounts for the formation and coagulation of particles in the reactor. A production-quality, spinning-disk reactor is currently being installed in our laboratory. This system, in analogy to the GEC cell, will serve as the reference reactor for development of measurement standards and validation of models for a range of thermal CVD processes employed by the semiconductor industry.

Using sodium vapor/metal halide chemistry, we demonstrated this year a new, low-temperature, energy-efficient CVD process for the production of metal and ceramic thin films. We have successfully grown metallic titanium and ceramic titanium nitride films on copper and silicon substrates at a temperature of only 600 °C (compared to 1000 °C for conventional titanium CVD). These lower temperatures greatly reduce unwanted changes, e.g., chemical or morphological changes, in the substrate and generally lead to good film quality and adhesion. A "green" aspect of this process is that the by-products are solid-phase salts which are both easy to capture and environmentally benign.

In the HTO program, we completed two studies associated with corrosion and plugging of reactors. The first study demonstrated the use of Raman spectroscopy to measure, *in-situ* at elevated temperatures and pressures, corrosion on the surfaces of iron, nickel, chromium, and a number of common corrosion-resistant alloys. For the conditions of operation, i.e. up to 800 K and 25 Mpa, a variety of films were observed, mainly metal oxides of various stoichiometries and oxidation states. Some species were present only at elevated temperatures indicating chemical inter-mediates not evident from normal, *post-facto* analyses. In the second study, done in collaboration with the Massachusetts Institute of Technology, data were collected on salt nucleation phenomena and deposition kinetics for near-supercritical sodium sulfate solutions. A model of the deposition rate was developed that included fluid mechanics, heat and mass transfer, and was applied successfully to the sodium sulfate data.

Efforts continued this past year to refine the design and processing of the micro-hot plate sensor arrays to allow routine, extended high temperature operation. The use of high temperature, tungsten-titanium alloys to replace the Al metal layers used in the first generation micro-machined arrays is vital in this regard. The high-temperature capability of these devices was exploited this year to alter the microstructure of a Pt-doped SnO_2 sensing film via high temperature (750 °C) processing. This has yielded increases in sensitivity for detection of CO down to the 100 ppB level. We have also examined some new device designs this past year. A differential micro-calorimeter and an approach for growing epitaxial, single crystal sensing films on the hot plates were demonstrated.

As part of the effort to understand the sensing applications of self-assembled monolayers, we demonstrated this year two methods for absolute quantitative determinations of coverage and hybridization efficiency of single stranded DNA probes immobilized on gold surfaces. The immobilization relies on a two-component self-assembled monolayer discovered and patented by NIST. The DNA probes were shown to attach at approximately 60% of theoretical coverage, have negligible non-specific absorption, high specificity for complementary targets, and near unity hybridization efficiency. Surface-plasmon resonance spectroscopy and electrochemical methods were used to provide these new quantitative measures.

Awards in FY97:
The Division is especially proud of the achievements of many of its staff this year. Dr. James R. Whetstone was awarded the Department of Commerce Silver Medal for his long-term leadership of CSTL efforts to meet semiconductor industry needs for improved measurement standards. Dr. Donald R. Burgess was awarded the Departments' Bronze Medal for development and application of chemical reaction computation tools for managing and interpreting very large chemical kinetic simulations. Dr. Billy W. Mangum received the Allen V. Astin Measurement Science Award for his career-long achievement and leadership of NIST's program in temperature standards and thermometry. Mr. George W. Burns was given the Edward Bennett Rosa Award for career-long contributions to national and international measurement standards for thermocouple thermometry. Dr. Christopher W. Meyer and Mr. Martin Reilly (retired, guest scientist) earned the 1997 CSTL Technical Achievement Award for their work in completing the realization of the International Temperature Scale of 1990 in the range from 0.65 to 5 K. The paper "Low Gas-Flow Proficiency Tests" by Mr. Stuart A. Tison and Mr. Stephen W. Doty was cited as Best Technical Paper at this year's Annual Meeting and Workshop of the National Conference of Standards Laboratories. Mr. John D. Wright received the NIST Measurement Services Award in the calibration category for his outstanding efforts in developing and applying the Heated Gas Mixture Test Facility.

Organizational Structure:
In FY97, the Division was organized into six Groups: Fluid Flow, High Temperature Processes, Reacting Flows, Process Sensing, Thermometry, and Pressure and Vacuum. The following pages present more detailed discussions of some of the accomplishments and plans for the coming year for many of the Division's programs.g

B. Selected Technical Reports

1. *Calibration and Test Services Provided by the Process Measurements Division*

G.J. ***Rosasco****, V.E. Bean, B.W. Mangum, G.E. Mattingly, S.A. Tison, and J.R. Whetstone*

Objective: To realize and maintain national standards according to the definitions of the relevant units, and to disseminate the NIST-realized units to industrial users and government laboratories (DoD, NASA and state governments) that require calibrations against and direct traceability to national standards.

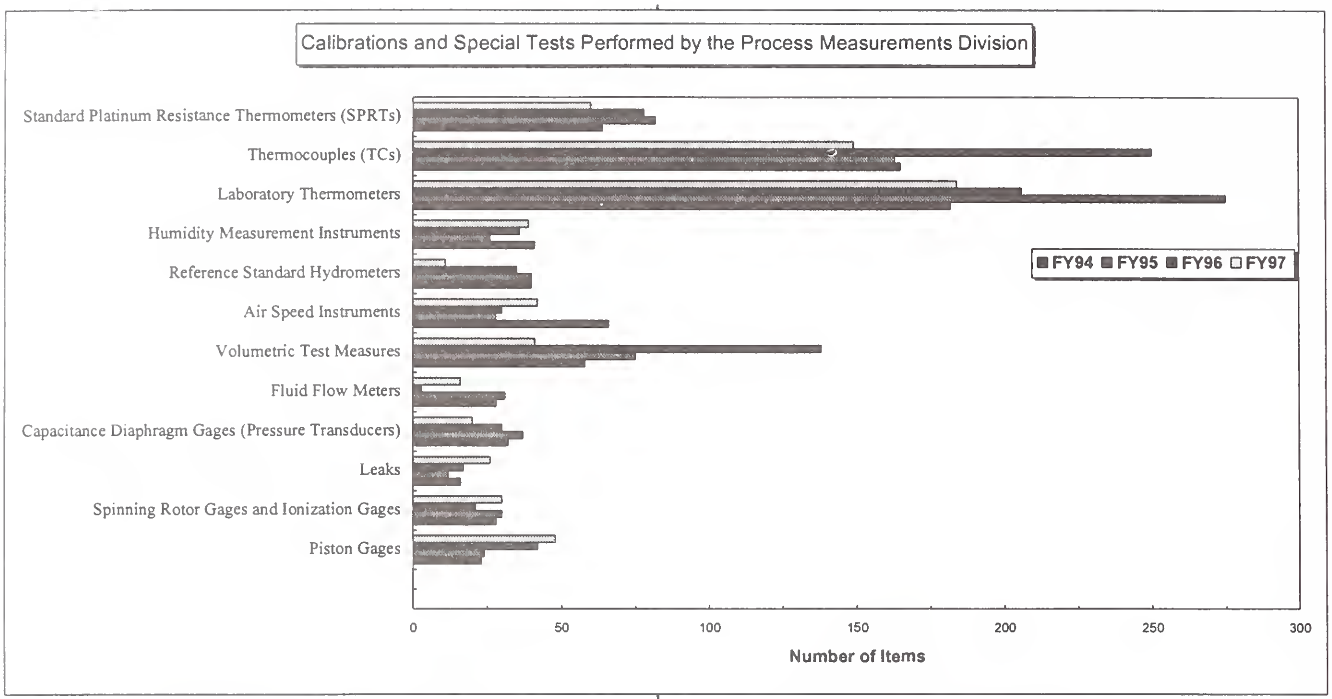
Problem: The Process Measurements Division is responsible for realizing, maintaining, and disseminating the national standards for measurement of temperature (in the range 0.65-1235 K), pressure, vacuum, leak rate, humidity, fluid flow rate, liquid volume and density, and air speed. Issues of primary importance in this area involve assessing and meeting, to the extent practicable, customer requirements for accuracy in their measurements, improving the efficiency of calibration services, developing methods to enable appropriate realization of standards in the customer's laboratories, and serving as the primary resource supporting the national measurement system.

Approach: Provision of customer-appropriate access to national standards of measurement involves a range of activities: maintenance and improvement of primary standards, participation and leadership in U.S. and international standards activities, performance of instrument calibrations and tests, operation of Measurement Assurance Programs, proficiency and round-robin tests, development of mechanisms for realization of secondary standards in customer laboratories, and a wide-range of consultation and customer assistance services. The calibration and test services provided by the division are described in NIST SP250, NIST Calibration Services Users Guide, and its supplements.

Results and Future Plans: The chart below summarizes the level of activity in each service area over the past 4 years. Large fluctuations in numbers of items are often encountered; however, the total calibration workload for each service, measured by staff years (or costs), typically varies by less than 10%. Our capabilities, experimental techniques, and the facilities used to provide these services are continually upgraded, with concomitant improvements in efficiency and in measurement uncertainties.

Improvements in realization of standards and highlights of activities for temperature, humidity, air speed, variable composition and temperature gas flows, low-range gas flows, and liquid density are discussed in separate reports below. Also presented elsewhere are descriptions of activities involving international comparisons, a critical element in maintaining NIST services at the pinnacle of the Nation's measurement system.

Two new low-pressure calibration systems were implemented this year. The first, based on an oil ultrasonic interferometer manometer (UIM), provides calibrations in the pressure range of 0.1 to 133 Pa with expanded uncertainties of 0.01% at a pressure at 133 Pa. The second calibration system, a mercury ultrasonic interferometer manometer, was designed for making low-differential pressure measurements at elevated line pressures (0 to 200 kPa). Both of these systems have been used this year to calibrate industrial instrumentation. Implementation of the oil UIM has reduced uncertainties by as much as an order of magnitude and implementation of the low-differential pressure standard has initiated new measurement capabilities in a critical measurement area. Plans for FY98 include the incorporation of a new gas piston gage pressure standard and continued development of high-stability pressure transducers in the near-atmospheric range.



In the area of air speed measurements, a program involving round robin testing with meter manufacturers and secondary calibration laboratories was completed this year as part of an Air Speed Proficiency Testing CRADA. Testing covered the range from 0.3 to 15 m/s. Results showed facility variations up to 30% (for the lowest air speeds) relative to NIST values. These assessments have enabled participants to identify errors in their procedures and establish traceability to NIST. A second round of testing is being planned with the goal of establishing agreement at the level of approximately 2%. This program grew out of requests from industry to resolve measurement discrepancies existing among different calibration facilities.

Efforts (described in previous reports) to establish a new primary standard gravimetric hygrometer and to upgrade our hydrocarbon fluid flow loop, to achieve a factor of 4 reduction in uncertainty, continued in FY97. In each case, major modifications of these systems were required this past year in order to meet operational and performance goals. Good progress has been made and completion of these new standards is expected in the coming year.

The Division made significant progress this year in producing the required documentation that supports our compliance with ANSI/NCSL Z540-I-1994. This is the U.S. standard, specific to calibration laboratories, defining the requirements for the ISO 9000 series of standards and ISO/IEC Guide 25 as they apply to calibration laboratories. The documentation is contained in the Division Quality Manual. Part I, which applies generically to all services provided by the Division, was completed this year, and Part II, which deals with the specifics of each service, will be completed in FY98.

Publications:

Tilford, C.R. and Miiller, A.P., ***"Development of a Low Differential-Pressure Standard,"*** Proceedings of the 1997 Meeting of the National Conference of Standards Laboratories Conference, Vol. 1, pp. 221 (1997).

Miiller, A.P., ***"Measurement Performance of Capacitance Diaphragm Gages and Alternative Low-Pressure Transducers,"*** Proceedings of the 1997 National Conference of Standards Laboratories Conference, Vol. 1, pp. 287 (1997).

Schmidt, J.W., Tison, S.A., and Ward, D.B., ***"Research at High Pressure,"*** Proceedings of the 1997 National Conference of Standards Laboratories Conference 1, pp. 183, (1997).

Abbott P.J. and Tison, S.A., ***"Commercial Helium Leak Standards: Their Properties and Reliability",*** J. Vac. Sci. Technol. A 14(3), 1242 (1996).

2. Implementation and Dissemination of the International Temperature Scale of 1990

***B.W. Mangum**, C.W. Meyer, W.L. Tew, G.F. Strouse, D.C. Ripple, G.W. Burns, K.M. Garrity, C.D. Vaughn, G.T. Furukawa (Guest Researcher), W.C. Ausherman, E.Y. Xu (Contractor) and N.P. Moiseeva (VNIIM, D. I. Mendeleyev Research Institute of Metrology, St. Petersburg, Russia)*

Objective: To realize and maintain the International Temperature Scale of 1990 (ITS-90) as it is defined over the range from 0.65 K to 1235 K, to investigate the non-uniqueness of the ITS-90 over this temperature range, and to disseminate the scale to the user community.

Problem: The ITS-90 extends upward from 0.65 K. The realization of this scale, as it is defined, has been completed at NIST over the ranges from 0.65 K to 24.5561 K and from 83.8058 K to 1234.93 K, as reported in "Guidelines for Realizing the International Temperature Scale of 1990 (ITS-90)," *NIST Technical Note 1265*, U.S. Govt. Printing Office, Washington, DC 20402, August 1990, and in several papers published in: *Temperature: Its Measurement and Control in Science and Industry*, Vol. 6 (Edited by J.F. Schooley), New York, American Institute of Physics, 1992; *Metrologia*; and *Proceedings of TEMPMEKO '96, 6th International Symposium on Temperature and Thermal Measurements in Industry and Science*, 1997. The realization over the range from 24.5561 K to 83.8058 K, however, has not been completed. Consequently, NIST still uses a "wire scale", based on previous NBS work and on thermometers calibrated by NPL, as the NIST reference for calibrations in the region 13.8033 K to 83.8058 K. Realization of the ITS-90, as it is defined, between 13.8033 K and 83.8058 K will free us from the wire scale and will reduce our uncertainty of calibrations in that range. Also, construction and evaluation of sealed triple-point cells of Ar, O_2, Ne and equilibrium H_2 are needed for maintaining the realization of the scale in the cryogenic region and for participation in international comparisons. Although our partial realization of the scale has reduced the uncertainties in some ranges of calibrations, there still are potential uncertainties of calibration resulting from the non-uniqueness of the scale over the range from 13.8033 K to 1243.93 K that have not yet been evaluated. The magnitudes of these non-uniquenesses must be determined in order to arrive at the total uncertainties of realization and in calibrations. Also, new and/or better methods for dissemination of the ITS-90 (apart from calibration of thermometers) are needed to get the scale to users requiring high accuracy.

Approach: The completion of the implementation of the ITS-90 will be accomplished through the realizations of the triple-point temperatures of Ar (83.8058 K), O_2 (54.3584 K), Ne (24.5561 K) and e-H_2 (13.8033 K) in large non-transportable cells, and in transportable cells that are required for maintaining the scale over this range of temperatures and that also are suitable for use in international comparisons. The non-uniqueness of the ITS-90 will be determined by investigating its sources in the various temperature ranges from 13.8033 K to 1234.93 K and determining its magnitude in the different ranges. Since many thermometers are required for this investigation, collaborations with national laboratories of other countries are desirable for a meaningful investigation. The ITS-90 is disseminated through calibrations of thermometers, SRM fixed-point cells of pure materials, SRMs of pure metals of the defining fixed-point materials, and SRM thermometers.

Results and Future Plans: Our goal of the realization of the ITS-90 from 13.8033 K to 83.8058 K was reached this year. This realization was at high precision and the scale in that temperature range was retained on SPRTs or RIRTs, depending on the range. Some of the thermometers involved in the realizations will be used in international comparisons of the realizations of the ITS-90. This scale work completes our realization of the ITS-90 from 0.65 K to 1234.93 K, but the non-uniqueness in the range from 13.8033 K to 24.5561 K, arising from the use of SPRTs and an ICVGT, and that at higher temperatures resulting from use of SPRTs will be completed in FY98.

For purposes of maintaining realizations of the cryogenic triple points of the ITS-90 and for key international comparisons of realizations of the scale, sealed transportable cells of e-H_2, Ne, O_2, and Ar will be constructed and evaluated in FY98. Also, comparisons of the fixed-point cells will begin in FY98.

Efforts to determine the non-uniqueness of the ITS-90 in the ranges 273.16 K to 933.473 K and 933.473 K to 1234.93 K were continued this year. Since our supply of HTSPRTs is inadequate for the range 933 K to 1235 K, we organized a collaborative effort with the national laboratories of Italy (IMGC) and the Netherlands (VSL). Seven of the HTSPRTs of NIST that had been selected for investigation on the basis of their stability upon high-temperature exposure and that had been calibrated from 273.16 K to 1234.93 K, underwent comparison measurements between 875 K and 1235 K in our high-temperature comparator. Measurements in this range were delayed because heater elements of the comparator corroded destructively and had to be replaced. Also, one of the HTSPRTs appeared to become "wet" inside the sheath and was replaced. Measurements on the 7 HTSPRTs indicate a non-uniqueness (less than 2 mK) that is significantly smaller than that observed at IMGC for their set of HTSPRTs. The investigation of all of the NIST HTSPRTs will be completed and the work on the IMGC HTSPRTs will begin by the end of FY98.

In recent years, we have made a significant effort in developing fixed-point cells, and in certifying thermometers and high-purity metals (for use in preparing fixed-point cells), with the goal of disseminating the ITS-90, or providing materials for use in its realization, to secondary calibration laboratories and others requiring high accuracy. In this effort, work began in FY97 on the certification of 99.9999+ % pure Sn for SRM 741a (Sn freezing-point standard). SRM 741a will replace SRM 741. This new SRM will be available in FY98. Work on a new SRM (SRM 1750) of calibrated capsule SPRTs, covering the range from 13.8033 K to 429.7485 K, began in FY97 and will be completed in FY98. Also, the dissemination of the ITS-90 to those requiring high accuracy (± 0.01 K) at temperatures up to 1273 K is provided by highly-stable and accurate thermocouples (TCs) that require no recalibration. In this regard, the certification of 18 Au/Pt TCs as SRM 1749 was completed in FY97.

3. High-Temperature Thermocouple Research and Sensor Development

*G.W. **Burns**, D.C. Ripple, K.G. Kreider, B.W. Mangum, D.P. DeWitt (Purdue University), D.W. Allen (Contractor), and M. Battuello (IMGC)*

Objective: To develop new sensors (e.g., wire and/or thin-film thermocouples) as reference thermometers for secondary calibration laboratories and/or as fairly-inexpensive, high-accuracy, high-stability, high-temperature thermometers for industrial use, including use in surface-temperature measurements.

Problem: The problems being addressed are two-fold. 1) The lack of stable thermocouples (TCs) to serve as reference standards in secondary calibration laboratories and/or as high-quality thermometers for industrial applications. TCs currently used as reference standards (types S, R and B, all of which contain Rh), and as the best-available thermometers for most industrial applications, have uncertainties of about 0.1 K at the Au freezing point (1337 K) at the time of calibration. These uncertainties increase rapidly with increase in temperature above 1337 K to about 1.6 K at 1725 K. Also, due to unstable inhomogeneities, arising primarily from selective oxidation of Rh, the emfs of these TCs drift with use, becoming much more uncertain, perhaps increasing the error by as much as a factor of 10 at 1337 K. 2) Unreliable measurements of surface temperatures resulting from the use of traditional contact thermometers or non-contact radiation thermometers, e.g., in the semiconductor industry. Accurate, high-speed measurements of temperatures of surfaces are especially critical in semi-conductor wafer preparation by rapid thermal processing (RTP) because accurate control of temperature, during short, high-temperature exposures, is critical to product quality and device performance.

Approach: To address the need for stable TCs, as indicated above, TCs of pure noble metals, such as Au, Pt and Pd, are being investigated. These metals can be produced at very high purity (5-6 nines, depending on the metal) and are generally resistant to oxidation in high temperature environments. Since the TCs are constructed of these pure metals, inhomogeneities are small, defects can be removed by annealing, the TCs are stable, and, in the case of

Au/Pt, interchangeability is excellent. To address the need for accurate measurements of temperatures of surfaces, the feasibility of thin-film TCs is being investigated. These devices become part and parcel of the surface and thereby obviate the uncertainties associated with conventional contact thermometers (uncertainty of the quantitative relationship of the measured temperature and the surface temperature) and with radiation thermometers (uncertainty with respect to the time-dependent, effective emissivity of the surface, stray radiation, and changes in the optical path).

Results and Future Plans: In our efforts to develop stable, high-accuracy TCs, Au/Pt TCs have been found to be an excellent choice for temperatures up to 1275 K (stability of a few mK). Previously, we developed a reference function for them and this year we completed the construction and certification of Au/Pt TCs as SRM 1749. A paper on Au/Pt TCs will be written in FY98. In an effort to develop a TC for use to about 1775 K, the investigation of Pt/Pd TCs continued. Previously, some of these TCs have been heat treated at 1375 K for more than 1000 h and stabilities of 5 mK to 10 mK per 100 h at 1375 K were obtained and inhomogeneities equivalent to only 4 mK to 16 mK were observed. In a collaborative project with IMGC to determine the reference function for these TCs, experiments were completed on obtaining emf vs. t_{90} and stability data up to about 1775 K. Those TCs had been constructed and evaluated at NIST for that purpose. NIST performed the measurements from 273 K to 1337 K (by fixed points using the ice point and the freezing points of In, Sn, Zn, Al, Ag and Au; by comparison against an SPRT from the ice point to 723 K; and by comparison against three calibrated Au/Pt TCs from 693 K to 1273 K and type S TC's from 973 to 1775 K), and IMGC performed measurements from 1073 K to 1775 K (by comparison against a radiation thermometer). The reference function, necessary to facilitate the use of these TCs in industrial applications and as high-temperature transfer standards has been completed. A paper on these TCs will be written in FY98. Industrial trials of Pt/Pd TCs in diffusion furnaces used by the semiconductor industry also will be performed.

In order to develop improved surface temperature measurements in the semiconductor manufacturing industry (especially for RTP), some of the most promising metals for thin-film TCs on Si wafers were evaluated with regard to their stability at elevated temperatures. Pt and Pd were chosen as the first candidates for temperatures up to about 1100 K. Also, Pt and Pd wires of 0.1 mm and 0.25 mm diameter were used for constructing TCs to measure the temperature of the wafers at their periphery and also to serve as leads to the thin-film TCs. The emfs of TCs made from these diameter wires agreed with our reference function values to the equivalent of 0.3 K at 1235 K, both before and after heat treatment at 1400 K for approximately 500 hours. Thin-film Pt/Pd TCs were deposited on test wafers designed for evaluation in an RTP tool. SensArray, Inc., instrumented the wafers with small-wire TCs for evaluating these calibration wafers in the RTP tool, using different types of TCs and a radiation thermometer. The initial measurements indicated that the RTP tool must be redesigned in order to reduce the uncertainties of the radiation measurements. The alteration of the tool is in progress and measurements of the surface temperature of the wafers will be continued in FY98. Investigation of materials for higher-temperature operation will begin in FY98, as will modeling of the heat flow in the test coupons containing thin-film TCs.

4. *Thermodynamic Temperature Measurements*

***D.C. Ripple**, B.W. Mangum, D.W. Allen (Contractor), D. DeFibaugh (838), M. Geide (838), K. Gillis (838), and M. Moldover (838)*

Objective: To improve the accuracy of thermodynamic temperature measurements above 500 K by a factor of 3-8.

Problem: There remain unresolved inconsistencies in previous measurements of thermodynamic temperatures at 500 K and above by two groups of researchers at NIST (each group used a different gas-thermometry apparatus). Those inconsistencies led to unnecessarily-large uncertainties in the thermodynamic values assigned to the defining fixed points of the ITS-90 and, hence, to all temperatures measured on the ITS-90 by radiation techniques, for which reference is made to either the freezing-point temperature of Ag, Au, or Cu.

Approach: Thermodynamic temperatures between 500 K and 933 K will be measured by acoustic techniques using spherical resonators. Acoustic thermometry relies on the relationship of the speed of sound in an ideal gas to the thermodynamic temperature. Speed of sound measurement via spherical resonator techniques, previously applied to the high accuracy determination of the Boltzmann constant, will be extended to high-temperature operation. Gas purity will be controlled to a very high degree, a major challenge in this high-temperature environment. We expect reductions in the uncertainty of the thermodynamic temperature of various high-temperature fixed points by factors of 3 to 8. The goal for the Au point is a reduction by a factor of 5 to an uncertainty of 10 mK. The results will have application to radiometric measurements of temperature to much higher temperatures (upward to maximum measured temperatures of about 4000 K), since the new, more accurate values of the thermodynamic temperatures will be the basis for the radiometric measurements.

Results and Future Plans: The work to improve the accuracy of thermodynamic temperature measurements above 500 K, using acoustic resonators between 500 K and 933 K, was started in FY95. During FY97, the stainless-steel resonator used for determination of the gas constant was altered so that it could be used in the present investigation. The highest temperature at which it will be used will be about 775 K. Capacitance diaphragm-type acoustic transducers (source and detector), using very thin discs of pure Si, were constructed. Also, the pressure vessel that will enclose the resonator was constructed. The high-stability furnace that will be used with the resonator and that will have very uniform temperatures over the volume of the resonator was designed, and its construction has begun. The temperature of the resonator will be controlled to 1 mK. The temperature fluctuations due to purging of the resonator will be at the tenths of millikelvin level. A gas chromatograph to be used in monitoring the purity of the argon gas in the resonator was received, evaluated, and installed in the high-purity gas-handling system. Since microwaves will be used for measuring the volume of the resonator, the microwave transducers were designed and the effect of the transducer positions on the measured resonator volume was investigated.

In FY98, the assembly of the acoustic resonator suitable for operation at temperatures as high as 775 K, complete with its pressure vessel, high-stability furnace, and the remainder of the thermodynamic temperature measurement system will be completed, and measurements of temperature will be begin.

5. *International Comparisons of Temperature Standards and Scale Realizations*

B.W. Mangum, *G.F. Strouse, W.L. Tew, and C.W. Meyer*

Objective: To serve as coordinator for, and/or participate in, comparisons of national realizations of the International Temperature Scale of 1990 (ITS-90) and to participate in direct comparisons of some transportable cells of the defining fixed points of the scale, all comparisons being performed at the highest levels of accuracy.

Problem: Although there have been some bilateral as well as multi-national comparisons of fixed-point cells of some defining fixed points, there have been no general comparisons of realizations of the ITS-90 or of the defining fixed points over the entire range of the scale at the highest levels of accuracy. Results of such comparisons are needed in order to develop a basis for bilateral agreements between the U.S. and other countries on the realizations of the kelvin (through the ITS-90) and of the other SI units. Such agreements are necessary for trade purposes.

Approach: We will participate in four key comparisons of realizations of the ITS-90 organized by the Consultative Committee on Thermometry (CCT) of the International Committee on Weights and Measurements (CIPM), and in a comparison of transportable cryogenic triple-point cells organized by PTB. Of the key comparisons, NIST is coordinating those covering the range from 83.8058 K (Ar triple point) to 933.473 K (Al freezing point), with 14 national laboratories plus BIPM participating. NML (Australia) and PTB (Germany) are serving as sub-coordinators for NIST for some of the laboratories. Also, NIST is serving as sub-coordinator for the comparisons covering the range from 933.473 K to 1234.93 K (Ag freezing point), with four laboratories in North America, Germany and Italy participating.

Both sets of comparisons involve circulating some fixed-point cells and an HTSPRT. After measurements on the devices at each of the participating laboratories, the devices are returned to NIST or the appropriate sub-coordinator, for another set of measurements before they are sent to the next participant. In addition to these comparisons, we are participating in key comparisons of realizations of the ITS-90 over the ranges 0.65 K to 24.5561 K, involving rhodium iron resistance thermometers (RIRTs), and 13.8033 K to 273.16 K, involving capsule SPRTs.

Results and Future Plans: The key comparisons covering the range from 83.8058 K to 933.473 K were initiated this year. The protocol and schedule for the measurements were developed with the various participants. Three sets of Ga and Cd fixed-point cells to be used in the comparisons were prepared and evaluated. Six SPRTs for use in the comparisons were evaluated for stability and they were measured at all of the defining fixed points, and at the Cd freezing point, in the range. After measurements here, one set of cells and an SPRT were sent to each of the two sub-coordinators, NML and PTB. After repairing some serious damages incurred in shipping the devices, measurements were made at NML and PTB and then the devices were sent to D.I. Mendeleyev Institute for Metrology (VNIIM, Russia) and Measurement Standards of the Industrial Research Limited (New Zealand) (MSL/IRL) for measurements. Measurements at MSL/IRL and VNIIM were completed and the devices have been returned to NML and PTB, respectively, for further measurements before shipping the devices to the next participants. The results have not yet been received from any of the laboratories. Further comparison measurements will be made throughout FY98.

6. *Measurement and Standards for the Metering of Low-Gas Flows*

***S.A. Tison** and A.M. Calabrese*

Objective: To develop primary flow standards in the range of 10^{-7} to 10^{-3} mol/s and transfer this flow measurement capability to U.S. industry, government, and academic institutions.

Problem: Many industrial processes require the accurate metering of mass flow over the range of 10^{-7} to 10^{-3} mol/s. In particular, the SEMI/SEMATECH Mass Flow Controller working group identified the need to measure flows in this range with uncertainties of 1% or less and identified the need for national flow standards in the range with uncertainties of 0.2% or less. To meet these needs new primary flow standards and improved techniques for measuring flow for industrial applications must be developed.

Approach: We have implemented a program to develop primary flow standards that would operate over a range of 10^{-7} to 10^{-3} mol/s with uncertainties of 0.1% or less. To transfer this measurement capability to industrial users, the properties of commercially available flow meters will be investigated, and the development of highly repeatable flow meters will be explored.

Results and Future Plans: A constant volume primary flow meter was constructed which operates over a range of 10^{-9} to 10^{-3} mol/s with uncertainties of 0.1% or less. The system is of all metal construction with high vacuum type fittings and is compatible with all non-corrosive gases. This system was compared with existing flow standards in the Pressure and Vacuum Group over their overlapping ranges of 10^{-8} to 5×10^{-6} mol/s. The two standards agreed to within their total uncertainties of ±0.1%. The system was also compared with flow standards in the Fluid Flow Group over the range of 10^{-4} to 10^{-3} mol/s, and the systems agreed to within their estimated uncertainties.

A series of ultra-stable laminar flow meters have been developed that use pressure differentials as large as 1.2 MPa to generate flows over a range of 10^{-7} to 10^{-3} mol/s. These instruments have demonstrated long term stabilities (over the course of two years) of ±0.1%. The NIST-designed laminar flowmeter is being commercialized by two companies. The first application of this meter is for use as an *in-situ* calibration device for industrial flowmeters, such as mass flow controllers. The second implementation is as a stable transfer standard to validate the performance of primary flow standards. In the latter area, we have used the laminar flowmeters to conduct on-site proficiency tests with industrial primary flow standards at 15 facilities over the past two years. The results of the proficiency tests with nitrogen reveal that the tested industrial standards were within their specified uncertainties for flows larger than 10^{-4} mol/s but many were significantly outside of their estimated uncertainties for lower flows. Proficiency testing with other gases, such as sulfur hexafluoride, argon, and helium, indicated greater measurement deficiencies.

Because current meter designs often have unknown (*a priori*) dependence on gas properties, such as viscosity, thermal conductivity, and heat capacity, an ideal mass flowmeter would be totally self-compensating for gas type or composition. A possible candidate for a self-compensating flowmeter is one which operates by acoustically measuring the velocity of the gas stream. During the past year an acoustic doppler-shift flowmeter that measures the velocity and the speed of sound of the gas has been investigated. The volumetric flow is computed from the known tube area, and converted to mass flow from knowledge of the equation of state (nearly ideal for our measurement conditions) by making an appropriate pressure and temperature measurement. The initial performance with argon indicates a flow resolution of 10^{-7} mol/s for an instrument with a maximum flow measuring range of 1×10^{-3} mol/s (0.01% of full scale). This technique has great promise for providing accurate flowmetering of toxic and/or corrosive gases, and will be pursued in FY98 with particular emphasis on use with semiconductor processing gases and improvements in the design for robustness required for industrial use. Also, in FY98 a constant pressure flowmeter which operates over a range of 10^{-7} to 10^{-3} mols/s will be tested and used for characterization of laminar flowmeters, acoustic flowmeters, and other flow measuring instrumentation.

Publications:

Tison, S.A., ***"Accurate Flow Measurement in Vacuum Processing"***, Solid State Tech. 39, 73 (1996).

Tison, S.A. and Doty, S.W., ***"Low-Gas-Flow Proficiency Testing,"*** in Proc. of the 1997 National Conference of Standards Laboratories (NCSL) Annual Meeting, NCSL, Boulder, CO, 55 (1997)

Tison, S.A. and Berndt, L., ***"High-Differential-Pressure Laminar Flow-Meter,"*** in Proc. of the 1997 ASME Fluids Engineering Summer Meeting, FEDSM97-3207 (1997).

7. Comparison of International Pressure Standards

***A.P. Miiller**, J.W. Schmidt, CR. Tilford, and S.A. Tison*

Objective: Establish the agreement between national pressure and vacuum standards for pressures between 3×10^{-7} Pa and 500 MPa.

Problem: International trade is, in part, based upon the equivalence of measurement. One of the largest segments of industrial measurements are in the areas of pressure and vacuum. To alleviate technical trade barriers, the relative agreement of national measurements standards needs to be determined and maintained.

Approach: A number of 'key' international comparisons in Pressure and Vacuum have been identified by the Consultative Committee for Mass and Related Quantities (CCM). These comparisons include the following ranges:

1) 3×10^{-7} to 1×10^{-3} Pa (absolute)
2) 1 Pa to 1000 Pa (absolute)
3) 1 Pa to 1000 Pa (differential)
4) 5 kPa to 120 kPa (absolute)
5) 50 kPa to 7000 kPa (gauge)
6) 50 MPa to 1000 MPa (gauge)

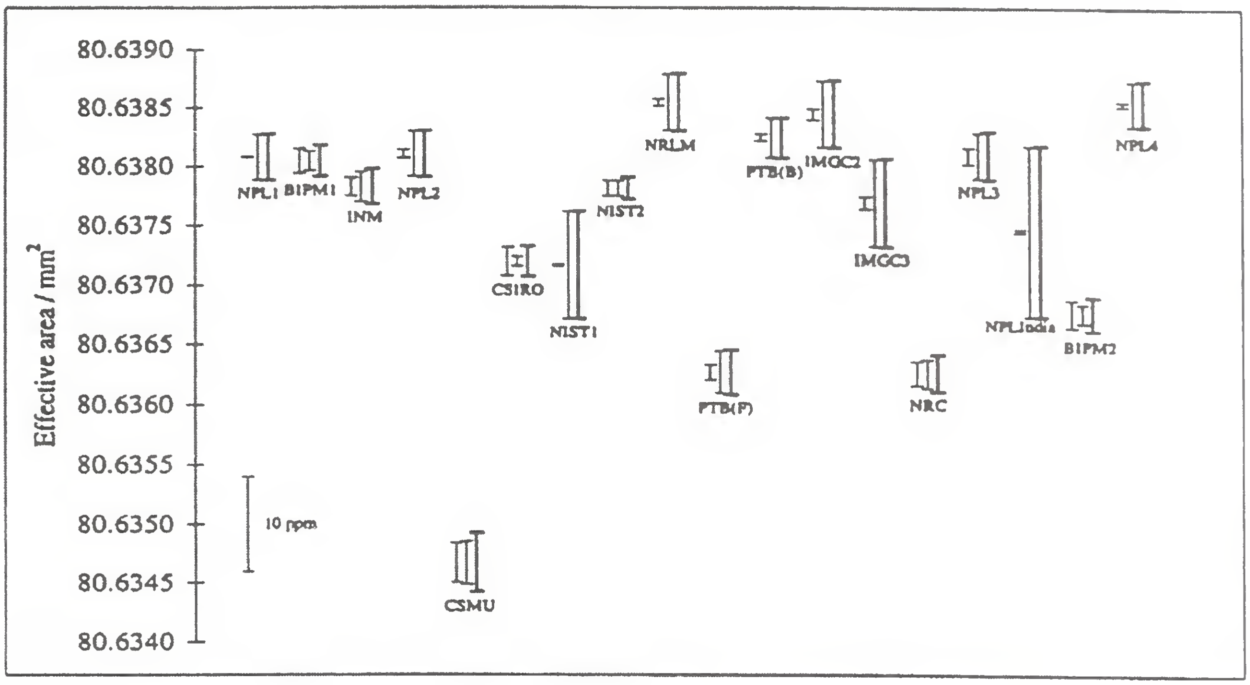


Figure 1. Measured effective area of a transfer standard piston gage. The NPL1-4 indicate multiple measurements made by the pilot laboratory. NIST1 and NIST2 are two NIST primary standards. The participating laboratories included; the National Physical Laboratory-NPL (United Kingdom), Bureau International des Poids et Meaures-BIPM, Insitut National de Metrologie-INM (France), Slovak Institute of Metrology-CSMU (Slovokia), Commonwealth Scientific and Industrial Research Organization-CISRO (Austriale), National Research Laboratory of Metrology-NRLM (Japan), Physikalisch-Technische Bundesanstalt-PTB (Germany), Instituto di Metrologia "G. Colonnetti"-IMGC (Italy), National Research Council-NRC (Canada), and the National Physical Laboratory-NPL (India).

Results and Future Plans: A comparison of intermediate gas pressures, item 5, has been organized by the High-Pressure Working Group of the CCM. The Laboratoire National D'Essais -Paris (LNE) agreed to serve as pilot laboratory for a first phase. This phase, between 50 kPa and 1 Mpa, has been carried out between five laboratories: NIST, the National Physical Laboratory - Teddington (NPL), the Istituto di Metrologia "G Colonnetti" - Torino (IMGC), the Physikalisch-Technische Bundesanstalt - Braunschweig (PTB), and LNE. The data for phase one is complete and is now being analyzed as phase two is implemented. Phase two is a comparison over the range of 500 kPa to 7 Mpa and includes the laboratories in phase one with the addition of the National Research Laboratory of Metrology - Japan (NRLM).

The 1 Pa to 1000 Pa (absolute), item 2, comparison is scheduled to begin in early 1998 with the start of the other comparisons not yet established.

The results of an earlier comparison corresponding to item 4, including data for two NIST standards, have been documented and were recently submitted for publication in Metrologia. The laboratories included in this comparison are identified by acronyms in the figure below. The figure shows the effective area of a transfer piston gage as measured by the laboratories at a pressure of 100 kPa in absolute mode. As can be seen in the figure, significant differences exist between some standards (the larger error bars indicate the one total uncertainties). Efforts are underway to complete a second phase of the comparison using a new transfer standard.

8. *Study of MEMS-type Pressure Sensors*

A.P. Miiller, W.J. Bowers, Jr., C.R. Tilford, and S.A. Tison

Objective: Characterize measurement performance parameters of MEMS-type pressure sensors to determine their suitability for pressure measurements in applications that require high-accuracy and long-term stability.

Problem: In recent years, a new technology known as MEMS (microelectromechanical systems) has emerged in which well-established fabrication techniques developed for the manufacture of IC's are being applied to the construction of miniature sensors and actuators. This technology has considerable promise for advancing the state-of-the-art in pressure measurements in several ways: by reducing the cost of manufacture, by increasing reliability, by decreasing size and power requirements, and by improving performance. MEMS-type pressure sensors are now commercially available with advertised performance characteristics that are at par with the most expensive traditional pressure transducers. If true, these sensors would be attractive for use as transfer standards in calibration laboratories and for regional/international comparisons of pressure standards, as well as in the demanding applications found in the aerospace, defense and electrical power industries. In addition to long-term stability, their performance under conditions of high-line pressures and varying temperatures has not been well established.

Approach: Using the unique pressure measurement capabilities of the Pressure and Vacuum Group, which include Ultrasonic Interferometer Manometer primary standards and gas-operated piston gage pressure standards, we intend to quantify the long-term stability, zero stability, temperature dependence and line-pressure dependence of selected MEMS-type pressure sensors.

Results and Future Plans: A comprehensive study of measurement performance of traditional transducers that will provide a baseline for comparing the MEMS-type sensors has been completed recently. In the present study, data has been obtained for two basic types of microprocessor-based MEMS sensors, namely, piezoresistive silicon sensors and resonant silicon sensors with full scale (FS) ranges between 1 and 130 kPa. The results, though still preliminary, indicate that these sensors have promising long-term stability's of ~ 0.01% FS, which is comparable to the highest quality traditional pressure instrumentation. Their performance at lowest pressures (zero stability and resolution) appears to be not as good as that observed for capacitance diaphragm gages. Plans for FY98 include:

1) Continued evaluation of high-repeatability MEMS sensors in the pressure range of 1 kPa to 130 kPa absolute.
2) Study of industrial type MEMs pressure sensors and development of novel calibration techniques in the range of 10 kPa to 1MPa absolute.
3) Evaluation of MEMs sensors for low-differential pressure (high common mode pressure) applications typically used for industrial flow measurements.

Publication:

Miiller, A.P., ***"Measurement Performance of Capacitance Diaphragm Gages and Alternative Low-Pressure Transducers"***, in Proc. of the 1997 National Conference of Standards Laboratories Workshop and Symposium 1, 287-299 (1997).

9. *Characterization and Optimization of Residual Gas Analyzers for Semiconductor Processing*

***C.R. Tilford** and S.A. Tison*

Objective: Characterize and improve the metrological properties of residual or partial pressure analyzers (RGAs or PPAs), and develop *in-situ* calibration techniques for processing applications.

Problem: Residual gas analyzers have been widely used for qualitative vacuum system diagnostics. The increasing complexity of semiconductor processing has generated a further need for real-time process monitoring, typically to monitor gaseous contaminants or for process control. Both of these require quantitative measurements if they are to be successful in a large-scale manufacturing environment. However, to the extent that they are known, the quantitative capabilities of most RGAs are not adequate for these tasks. There is a need to better understand these instruments, improve their performance, and ensure consistent results by providing the users with access to national standards.

Approach: Obtain quantitative test data for commercial RGAs and develop generic RGA operation models that will allow a determination of critical performance parameters, optimum operational conditions, and instrument design improvements. Transfer NIST vacuum standards capabilities to users through *in-situ* calibration techniques.

Results and Future Plans: Experimental data and analytic modeling completed this past year strongly indicate that the most important undesirable performance characteristics of RGAs are caused by the effects of electron and ion space charge throughout the instrument. While the evidence is quantitative - it is difficult to model these instruments, and the designs are so varied that experiment performance for different instruments is not always consistent - the preponderance of the evidence is that the severe nonlinearities with pressure, and the dependence of the sensitivity for one species on the pressure of other species, are caused by a combination of three distinct space charge effects.

The first of these effects is a competition between electron and ion space charges in the ion source. The electron space charge, which dominates at low pressure, decreases the ion energy and the transmission efficiency of the quadruple mass filter, in some cases by as much as two orders of magnitude. As the total pressure increases there is a corresponding increase of ion space charge that counteracts the electron space charge, with a corresponding increase in the ion energy, transmission efficiency, and instrument sensitivity. While this model had been previously proposed, the present data are the only direct evidence that this model applies to most instruments.

With further increases in pressure the sensitivity change is reversed to a rapid decrease with increasing pressure. Although previously thought due to ion-neutral collisions, NIST-sponsored modeling completed this past year predicts that the sensitivity decrease is due to expansion of the ion beam in the region between the ion source and mass filter, caused by self-repulsion of the ions. At even higher pressures a further decrease in sensitivity is caused by ion space charge in the mass filter. An extensive series of measurements with different gases validates this explanation.

Fortunately, with this new understanding, space-charge effects can be detected and minimized for most instruments. Decreasing the electron emission current directly reduces the perturbation of ion energy within the ion source and in addition causes a corresponding decrease in the ion current throughout the instrument. Increasing the ion energy further reduces the ion space charge density. Performance data for a new, small-geometry RGA are consistent with the model prediction that reducing the distance between the ion source and the mass filter will reduce beam expansion in that region and extend the linear range of the RGA to higher pressures - by at least an order of magnitude for the instrument tested.

In FY98, the techniques for calibration of RGAs will be implemented in a chemical vapor deposition tool for validation of the proposed calibration methodology in an industrial application. RGAs installed and calibrated *in-situ* on this system will be used for contamination monitoring and for process control (film thickness monitoring). Our characterization of traditional open ion source

RGAs will be extended to closed ion source RGAs, typically used for these higher pressure processes.

Publication:

Tilford, C.R., "***Optimizing Residual Gas Analyzers for Process Monitoring,***" in Proc. of the Symposium on Process Control, Diagnostics, and Modeling in Semiconductor Manufacturing, Ed. by M. Meyyappan, D.J. Economou, and S.W. Butler, The Electrochemical Society, PV 97-7, 184 (1997).

10. Quantitative Optical Measurements of Gas Partial Pressures

J.P. Looney, R.D. van Zee, and J.T. Hodges

Objective: To develop measurement standards for partial-pressure measurements of low-level gaseous contaminants, with particular emphasis on H_2O, CO_2, CO, O_2, and CH_4.

Problem: Low-level gaseous contaminants cause deleterious effects in many chemical processing systems and drive the demand for improved measurement instrumentation and capabilities, as well as the primary standards which underpin measurement accuracy and reliability. As an example, the Semiconductor Industry Association National Technology Roadmap identifies water vapor measurements as one of the key metrological parameters for contamination-free manufacturing in the next generation of devices, with a stated measurement capability of 100 ppt_v (parts per *trillion*) by the year 2001. Traditional techniques for generating low partial pressures of active gases, including water, are severely limited due to surface interactions and long time constants. Furthermore, the technical approaches used in the development of existing standards for vacuum and humidity are not capable of meeting many of the identified industrial measurement requirements. The development of a fundamentally new approach to this measurement problem is required.

Approach: Develop quantitative high sensitivity optical absorption measurements, to establish a new primary standard for low-levels of gaseous contaminants. Cavity Ring-Down Spectroscopy (CRDS) has been identified as the most suitable approach to achieve quantitative low-level gas density measurements. The centerpiece of CRDS is a state-of-the-art high-Q Fabry-Perot etalon. By measuring the Q of the cavity, for example, by determining the time constant for photon decay of an injected light pulse, one obtains directly the optical losses of the cavity. The introduction of an absorbing species into the cavity degrades the cavity-Q and is a direct measure of the gas absorption. The realization of this approach has been enabled by recent advances in high quality mirrors used to form the optical cavity. Using these ultra low-loss mirrors, cavities with Q's as high as 10^{10} have been constructed, for which ultimate water partial pressure sensitivities below 10^{-6} Pa (100 ppt_v) are projected.

Results and Future Plans: During this past fiscal year, we worked to develop an optimal experimental configuration which is designed to realize CRDS at the highest levels of sensitivity. Our modeling and previous laboratory experience highlighted three critical elements for this effort. Specifically, the need for a versatile narrow-bandwidth frequency-stable light source, the use of length-stable ring-down cavities, and the excitation of single TEM cavity modes to obviate mode-beating effects.

As there is a dearth of broadly tunable and commercially available light sources in the near infrared, during this past year we constructed an injection seeded, pulsed optical parametric oscillator (OPO). The optimum spectral properties and frequency stability of this light source enable CRDS measurements at unprecedented levels of sensitivity. The tunability of this light source allows a number of critical molecules to be detected using CRDS, most notably water vapor near 1.37 microns.

Due to the spectral filtering properties of high-Q ring-down cavities, precise control of the length of high-quality optical cavities is crucial. To investigate the improvements to be gained, we first constructed a length-stable cavity which uses a passive stabilization scheme. This cavity was constructed from low thermal expansion material and housed in a temperature regulated, vibration isolated enclosure. A piezo-electric element is used to vary the cavity length in a controllable fashion. The length of this cavity was found to be stable to about 5 nanometers over the course of a measurement. Measurements made with this cavity show significant improvement over those made with non-length-stable cavities; imprecisions were lowered by one order of magnitude. Encouraged by these results, we have designed and built a larger, UHV-compatible system that is designed with an active length stabilization scheme, based upon locking of the cavity to a frequency stable helium-neon laser. This system will be used to make quantitative water measurements during the coming fiscal year.

Combining our previously developed theoretical models, the unique light source, and ring-down cavities constructed this past year, we have been the first group to demonstrate high sensitivity levels achievable using single-cavity mode ring-down spectroscopy with pulsed lasers. At present, individual optical ring-down signals can be measured with an imprecision of about 0.05%, only about a factor of 4 larger than the ultimate (shot-noise limited) levels theoretically achievable. From these measurements, we currently have achieved an absorption sensitivity of ~ 10^{-10} cm^{-1} in a 10 cm long cell. This represents a 100-fold improvement during the past year.

Publication:

Hodges, J.T., Looney, J.P., and van Zee, R.D., ***"Response of a Ring-Down Cavity to an Arbitrary Excitation"***, J. Chemical Physics 105, 10278-10288 (1996).

11. Low Concentration Humidity Standards

J.T. Hodges, *P.H. Huang, G.E. Scace, J.R. Whetstone and D.C. Hovde (Southwest Sciences)*

Objective: To provide absolute standards for humidity generation and measurement in the concentration range 1 to 1000 nmol/mol.

Problem: Strict monitoring and control of trace (nmol/mol and lower) water vapor levels is required in numerous industrial processes related to the fabrication of microelectronics and semiconductors. Regrettably, metrology-grade standards are not well established in the nmol/mol range, and existing hygrometers are inadequate as they often suffer from hysteresis, irreproducibility, and relatively slow response. Further, measurements of low humidity levels are complicated by poorly understood interactions between water vapor, carrier gases, and transfer lines, as well as uncertainty in thermodynamic properties of ice/water vapor mixtures.

Approach: Two types of precision humidity generators are being considered; Type I or thermodynamic- and Type II or permeation-dilution-based systems, in which the delivered humidity level depends upon mixture pressure and saturator temperature (Type I), and empirically determined water vapor diffusion rates and measured gas dilution ratios (Type II). Prediction of the output of Type I generators at nmol/mol levels requires extrapolation of the vapor pressure measured at higher temperatures. Type II generators suffer from the fact that permeation rates must be empirically determined and are subject to long-term drift. These generators are intercompared using various custom as well as commercially available and customer-supplied hygrometers. International intercomparisons with other national standards laboratories are also underway. Sensors investigated include chilled-mirror devices, optical absorption spectrometers, electrolytic and capacitative units, and vibrating crystal microbalance-type transducers, with studies intended to quantify the stability and accuracy of precision generation systems and hygrometers.

Results and Future Plans: A new Type I generator has recently been realized which is capable of delivering humidity levels down to approximately 5 nmol/mol at atmospheric pressure, with long-term stabilities better than 0.5 mK and absolute accuracies better than 10 mK in saturator temperature. Intercomparison of the new generator with another NIST Type I generator having a 25 year history indicates that for the region of overlap between the two systems, the two agree to within the stated uncertainty of the reference generator.

The precision generators developed here will also be compared to our gravimetric primary standard of humidity. Further, in conjunction with theoretical considerations, the foregoing efforts will allow us to assess the expanded uncertainty of the precision generators. It is intended that the new Type I generator be commissioned to provide calibration services for clients desiring direct traceability to national standards of humidity measurement. At present, the accuracy of the generated water vapor concentration is limited largely by uncertainties in the vapor pressure of ice which are estimated to be of the order of 2%.

As an independent check on the output of precision generators, we are developing quantitative measurement techniques based on absorption of laser light by water vapor. It is expected that such optical methods will have sufficient sensitivity, dynamic range, and accuracy to provide a critical link between the primary gravimetric measurements of water vapor concentration made at relatively high concentrations and trace levels that cannot be determined gravimetrically. Preliminary experiments indicate that absorption measurement of precision humidity via optical absorption is a very promising method for measuring absolute humidity in the nmol/mol range of concentration.

Publications:

Scace, G.E., Huang, P.H., Hodges, J.T., Olson, D.A., and Whetstone, J.R., ***"The New NIST Low Frost-Point Humidity Generator,"*** in Proc. of the 1997 National Conference of Standards Laboratories Workshop and Symposium 1, 657-673 (1997).

Huang, P.H., ***"Determining Uncertainties in Standard Dew/Frost-Point Generators for Humidity Measurements,"*** in Proc. of TEMPMEKO'96, 577-582 (1997).

12. Heated Gas Mixture Flow Facility: Usage and Results

J.D. Wright and P.I. Espina

Objective: Provide a variable gas composition and temperature gas flow facility to support customer calibrations and advanced flow meter development.

Problem: Accurate flow measurements of gas mixtures such as humid air and the gases produced by the combustion of carbon based fuels (i.e., gasoline, coal, natural gas) are needed by U.S. industry for process control and to comply with regulations. Unfortunately, little is known about the sensitivity of the available flow measurement techniques to changes in the mixture composition or temperature. The need for accurate flow meters for car exhaust is particularly important for the testing of ULE vehicles. Also, the methodologies for extending calibrations made under easily attained conditions, i.e., room temperature and dry air composition, to the extreme conditions of real meter applications have not been thoroughly validated for the various meter types in use.

Approach: In 1996, a research and calibration facility was constructed which would serve as a test bed for flow meters used in variable temperature and composition flows. To provide gas mixtures of known flow, composition, and temperature, the Heated Gas Mixture Flow Facility (HGMFF) first mixes flows of pure air, nitrogen, carbon dioxide, and argon that have been metered with calibrated critical flow nozzles. Water vapor is added using a saturator vessel and the mass flow of water is calculated from the dew point temperature. Before entering the meter under test, the gas mixture can be heated with an electric circulation heater to temperatures from 293 to 700 K. The HGMFF can generate simulated combustion product flows over the 60 to 2000 standard liters per minute (slm) flow. In an alternate mode of operation, the HGMFF can also provide humidified air flows from 85 to 6200 slm.

Results and Future Plans: Since the completion of the HGMFF in August 1996, the facility has been qualified via internal calibration checks for usage by outside customers. This work included a published description of the facility operating principles and uncertainty analyses for a wide range of operating conditions. The velocity profile entering the test section was measured with a hot wire anemometer and found suitably uniform for calibration purposes. A standard test program for efficiently stepping through various temperature, composition, and flow conditions also was developed.

Laminar flow elements and ultrasonic flow meters for the measurement of vehicle exhaust flows were tested in FY97. The tests conducted cover wide ranging conditions of gas composition, temperature, and flow that are designed to expose unwanted sensitivities which would cause measurement errors during vehicle testing. Each performance test takes about one week to carry out, running the automated facility around the clock.

Five ultrasonic meters of three design iterations have been tested in this manner. Each design iteration has been a significant improvement over its predecessor thanks to test data from the HGMFF and the interaction of industry and NIST engineers. In the most recent ultrasonic design, the data scatter at low flows has been reduced by a factor of five when compared to the original design. Also, the ultrasonic performance tests have shown that the flow meter calibration coefficient is a function of the flow Reynolds number over the entire range of temperatures and compositions tested. With this knowledge, the meter behavior can be predicted for conditions even more extreme than those tested. Further, now that it is known how the ultrasonic meter behaves as a function of composition and temperature, it can be calibrated with room temperature air flows instead of the elaborate, week long test schedule. It is hoped that similar efforts applied to laminar flow elements and vortex shedding flow meters (scheduled for testing in FY98) will result in several viable alternatives for exhaust flow measurement.

Publication:

Wright, J.D. and Espina, P.I., ***"Flowmeter Calibration Facility for Heated Gas Mixtures,"*** in Proc. of the 1997 National Conference of Standards Laboratories Workshop and Symposium 1, 401-421 (1997).

13. Fluid Mechanics and Flow Metering Research

*G.E. **Mattingly**, T.T. Yeh, P.I. Espina, and J.M. Allingham*

Objective: To expand our capabilities for applying Computational Fluid Dynamics (CFD) to flow measurements, to improve the accuracy of existing flowmeter technology and to develop new primary measurement methods.

Problems: Flow meter accuracy can be highly dependent on installation conditions. Since very long straight lengths of constant diameter pipe are required to achieve "fully developed," "ideal" pipe flow conditions, it is rare that these are achieved in metering practice. Therefore, unless meters are calibrated in their specific pipe work and under actual flow conditions, accuracies can deviate markedly from desired performance. This situation is prevalent in many industries but it is especially so in electric power plants where it is not feasible to calibrate specific pipe arrangements in flow labs and impossible to duplicate required flow conditions because of the extreme Reynolds numbers. However, current advances in ultrasonic technology and in CFD provide potential solutions. Additionally, this technology offers prospects for constituting primary flow standards. Ultrasonic metering methods have the potential to serve as transfer standards which, for example, could be clamped on the outside of pipes to calibrate installed meters, and they can feasibly serve as primary flow standards to greatly improve our abilities to establish and to disseminate references for flow measurement.

Approach: We have significantly improved our CFD capabilities by completing our program to apply compressible turbulence modeling to industrial flow problems, and we have used our incompressible CFD capabilities to simulate the performance of a range of ultrasonic techniques that have the potential to benefit wide ranges of flow measurements in the U.S. industry. Additionally, with the Electric Power Research Institute (EPRI), we have initiated a collaborative program (CRADA) to improve critical flow measurements in power plants. This program complements our CFD modeling and ultrasonic simulation efforts with a meter testing program in which commercially available clamp-on type units are tested in both "ideal" and non-ideal" installation conditions. We have also bought and initiated testing of a multi-path, in-line, ultrasonic flow meter which has contributed significantly to our program with EPRI and it is enhancing our efforts to assess ultrasonics as potential primary flow standards.

Results and Future Plans: This year our compressible fluid dynamics work benefited from the evaluation of various k-epsilon turbulence models in an axisymmetric supersonic base flow. The results obtained showed that conventional turbulence models have trouble predicting the turbulent kinetic energy dissipation rate, thus leading to errors in complex metering/industrial flows. However, improved turbulent distributions were obtained by damping the production of dissipation by 10%. The improved modeling is now enabling us to assess the potential of critical nozzles as potential portable primary flow standards over wide ranges of flows, temperatures, pressures, and gas species.

Our CFD results in incompressible pipe flow enabled computer simulations of ultrasonic measurement techniques in both "ideal" and "non-ideal" pipe flows. These results have not only enhanced our ultrasonic flow meter testing program with EPRI, but also they clearly show levels of ultrasonic metering performance that can feasibly achieve primary standard reference levels using single and multipath techniques for wide ranges of flow conditions. These simulations are especially useful to ultrasonic flow meter manufacturers who are upgrading their software capabilities. These simulations also complement our testing of our in-line multipath flow meter installed in "ideal" pipe flows. This unit has been assessed as having accuracies of ±0.2% or better in 250 mm pipe flows for Reynolds Numbers up to 3 x 10^6.

In the future, we plan to continue both our CFD efforts and the associated simulations of ultrasonic flow meters. We will continue our testing program with EPRI by assessing clamp-on type ultrasonic flow meters downstream of a conventional elbow and after this downstream of a concentric reducer. These results are expected to provide industry, especially the electric power generating industry with a very valuable assessment of the potential of these clamp-on meters for improving their flow measurements.

Publications:

Espina, P.I. and Piomelli, U., ***"Validation of the NPARC Code in Supersonic Base Flows,"*** AIAA 97-0032, Amer. Inst. Aero. Astro., Washington, DC (1997).

Yeh, T.T. and Mattingly, G.E., ***"Computer Simulation of Ultrasonic Flow Meter Performance in Ideal and Non-Ideal Pipeflow,"*** in Proc. of the 1997 American Society of Mechanical Engineers Fluids Engineering Division Summer Meeting FEDSM'97-3012 (1997).

14. Air Speed Measurement Standards

V.E. Bean, J.M. Hall, P. Espina, and J. Mu

Objective: To provide calibration services for air speed instrumentation over the range of 0.15 to 67 m/s with improved uncertainty levels as needed by U.S. Industry.

Problem: Two technologies upon which air speed calibration services are based are the Pitot-static tube and the laser Doppler anemometer (LDA). The former is useful for speeds above about 2.5 m/s while the latter can be applied over the entire range with varying uncertainties. The calibration of the LDA depends upon the angle between the intersecting laser beams. Until recently, this angle was controlled by external mirrors and was unstable due to environmental factors influencing the mirrors. Thus, the Pitot-static tube was considered to be the primary standard and was used to calibrate the LDA. This situation added a large type-B uncertainty to all air speed calibrations.

Approach: Recently, we have installed an LDA system utilizing securely anchored fiber optics to deliver the laser beams. Measurements under operating conditions have shown the angle to be constant. The new LDA has been calibrated by two methods:

1) by directly measuring the angle between the beams and calculating the calibration coefficient, and
2) by providing a "particle" of known speed and calculating the calibration coefficient from the response of the LDA and the known speed. The

"particle" is a tungsten wire, 5 μm in diameter, mounted in front of a light trap on the cylindrical section of a rotating disk. The speed is calculated from measurements of the rotation rate and the disk diameter.

Results and Future Plans: The two calibrations agree to within 0.06%. The LDA, characterized using the rotating disk, is now regarded as the primary standard. The total uncertainties in the LDA measurements are speed dependent varying from 2.3% at 0.15 m/s to 0.6% at 1 m/s to 0.2 % above 5 m/s (with a coverage factor of 2). The uncertainties are dominated by the standard deviations from the means of 260 calibration measurements, each based on a few hundred observations of the "particle" speed.

Intercomparisons between the LDA and the Pitot-static tube indicate the Pitot-static tube results have been systematically low by 1.65%, which appears to be due to differences in the idealizations heretofore assumed in applying hydrodynamic theory to the Pitot-static tube. Rigorous hydrodynamic calculations initiated in FY97 are attempting to clarify these realities using CFD.

Now that the primary standard is on a firm basis, intercomparisons with other national metrology laboratories are being planned. The feasibility of a portable LDA is also being investigated as a transfer standard.

15. Liquid Density Standards

***V.E. Bean** and J.F. Houser*

Objective: To provide measurements of liquid densities appropriate to characterizing NIST standard reference materials (SRMs) that are needed by U.S. industry.

Problem: Commercially available liquid densimeters may have resolutions approaching a few parts per million, however, these instruments are not primary and require calibration. The current stock of liquid density SRMs is totally depleted.

Approach: We are working with the NIST Office of Measurement Services to measure the density of SRM toluene and SRM isooctane and to certify the required 5 ml samples. Our method is based on hydrostatic weighing of a 200 g single crystal of silicon of known density in both air and in the liquid for which the density is to be measured.

Results and Future Plans: As a proof test of our apparatus and methods, we measured the density of distilled water in tests comprised of six determinations per day on each of three days with a new water sample employed each day. The average of the 18 measurements is within 0.4 parts per million of the average based on the distilled water density equation due to Kell. The expanded uncertainty of our approach is 7 parts per million.

Unfortunately, shortly after these measurements were finished, a critical temperature control system failed and was sent to the factory for repair. The SRM toluene and isooctane will be produced early in FY98 with a target expanded uncertainty of 15 parts per million.

16. Measurements and Models for Plasma Processing of Semiconductors

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Objective: Develop advanced chemical and electrical measurement methods and models needed to characterize plasma etching and deposition processes important to the semiconductor industry, enabling continued progress in process optimization, process control, and model-based reactor design.

Problem: Plasma processing reactors have historically been designed and operated using empirical methods alone, but continued evolution of these tools requires a much greater reliance on process and reactor modeling. Indeed, model-based process design and control is a need identified in the *National Technology Roadmap for Semicon-*

ductors. To obtain more reliable predictions of the spatial uniformity, chemistry, and electrical properties of processing plasmas, further progress in model development and validation is required. Also, to enable improvements in process control, a need exists to develop sensors that are compatible with the manufacturing environment.

Approach: Our experimental program has made use of reference reactors as a testbed for validating models and testing new measurement techniques. The reactors, known as Gaseous Electronics Conference Radio-Frequency Reference Cells (GEC Reference Cells), provide a well-defined basis for comparison of measurements between laboratories. The cells are equipped with a wide variety of plasma diagnostic tools that measure the chemical, physical, and electrical properties of the plasma. Information provided by the set of diagnostics allows testing of models. Also, sensors designed for manufacturing environments can be installed on the cells and compared with diagnostic results.

Results and Future Plans: This year a new technique was developed for measuring the ion current at wafers exposed to high-density plasmas. A provisional patent was filed on this technique, which is well-suited for use as an ion current sensor in industrial reactors. The sensor relies on radio-frequency current and voltage measurements, drawing on the expertise we have developed in this area in previous years. Unlike traditional methods of measuring ion currents, it does not require any hardware to be inserted into the reactor (thus avoiding the possibility of contaminating any wafers), it does not require the application of voltages or currents that would perturb the plasma, and it does not fail if insulating layers are present on reactor surfaces. Tests to determine if rf electrical measurements can also be used to determine information about ion energies were begun this year and will continue in FY98.

We continue to investigate 2-D species densities in the GEC Reference Cell using 2-D planar laser-induced fluorescence (PLIF) imaging. In these studies, the concentration of CF_2 in fluorocarbon etching and chamber-cleaning plasmas is monitored as a marker of uniformity and chemistry for validation of 2-D plasma models. This year, PLIF, optical emission, and electrical probes were used to study the optimization of O_2/CF_4 and O_2/C_2F_6 chamber-cleaning plasmas. This work significantly advances our previous collaborative studies with Air Products and Chemicals, Inc., by providing a detailed, 2-D characterization of the plasma spatial uniformity. We also continued to investigate the effect of precursor and elemental composition on the chemistry of etching plasmas. CF_2 PLIF and light scattering from particulates are monitored as a function of elemental composition (C:H:F ratio) and of precursor structure (combinations of CH_xF_y precursors). In FY98 we plan to extend our PLIF work to study etching plasmas in a high-density, inductively-coupled GEC cell. Experiments are also planned in a new research reactor to be constructed, which is designed to mimic state-of-the-art industrial reactors for 300 mm wafers.

Perfluorocompounds emitted by plasma reactors are global warming gases. Draft reports were prepared for the Semiconductor Industry Association (SIA) and SEMATECH by the NIST-chaired task force on Sampling and Measurement Methodologies for Perfluorocompound (PFC) Emissions Reduction. Techniques addressed in the report include quadruple mass spectrometry Fourier transform infrared spectrometry and gas chromatography with mass spectrometry. In cooperation with Air Products and Chemicals, 3M, and Dupont, the methodologies were prepared and have been incorporated in an INTEL Corporation Tech-Transfer Document. Also, the electrical, chemical, and environmental properties of SF_6 gas and SF_6 mixtures with N_2, He, and CF_4 were evaluated in a NIST Technical Report on alternatives to pure SF_6 for electrical insulation and interruption. This report will impact the electrical industry and the semiconductor industry.

Publications:

McMillin, B.K. and Zachariah, M.R. ***"Two-Dimensional Imaging of CF_2 Density by Laser-Induced Fluorescence in CF_4 Etching Plasmas in the Gaseous Electronics Conference Reference Cell,"*** J. Vac. Sci. Tech. A 15, 230 (1997).

Sobolewski, M.A., ***"Experimental Test of Models of Radio-Frequency Plasma Sheaths,"*** Appl. Phys. Lett. 70, 1049 (1997).

Sobolewski, M.A., ***"Dynamic Model of the Radio-Frequency Plasma Sheath in a Highly Asymmetric Discharge Cell,"*** Phys. Rev. E 56, 1001 (1997).

17. Models and Data for Semiconductor Processing

M.R. Zachariah, *D.R. Burgess, Jr., M.J. Carrier, R.W. Davis, E.F. Moore, J. Maslar, W. Tsang (838), C.F. Melius (Sandia National Laboratories), and R. Berry (Wright-Patterson Laboratories)*

Objective: To provide the necessary information and scientific infrastructure to enable the application of semiconductor process models and controllers that are well grounded in fundamental chemical and physical laws.

Problem: Reactor and process design are often limited to empirical trial and error approaches that tend to converge slowly, if at all, to semi-optimized states. This implies that, for an industry where rapid changes are the norm, important processes are not adequately investigated prior to final implementation. This situation manifests itself in more expensive, lower quality products produced by processes that may be less environmentally acceptable.

Approach: Process simulation has the potential to significantly enhance the design phase of process development so as to improve both efficiency and quality. This is because computational power has evolved to the point where highly sophisticated models can be constructed for a variety of complex semiconductor processes. However, the increasing complexity of these models implies a greater need for accurate fundamental thermochemical and kinetic data, which are not presently available. Our approach is both to develop and use methods for reliably generating (from first principles) the data necessary for process modeling. Techniques for handling, collating, and disseminating this information in an efficient and timely manner are an important component of this task. The reliability, quality, and utility of the generated data must also be demonstrated to the user community. Consequently, the development of process models of wide applicability is essential, as is model validation carried out in reference reactors prototypical of industrial processing equipment. This typically requires the development of reacting flow computer simulations that employ the aforementioned data for input.

Results and Future Plans: Our effort in the area of microcontamination in reactors continued with the development of aerosol models for the plug flow and perfectly-stirred configurations. These two cases have long been employed to study the two extremes in reacting mixtures: no mixing and perfect mixing. We have embedded an aerosol model in the Sandia codes (SENKIN and PSR), which are widely used to simulate these two extreme cases. This model accounts for the formation and coagulation of particles in the two reacting systems by employing a lognormal distribution function in conjunction with a moment formulation. Results obtained here can be utilized to estimate the behavior of actual reactor systems that exhibit characteristics in the range between the two extremes being simulated. During FY98, our rotating disk CVD reactor experiment is expected to generate the first data for comparison with our microcontamination model of this reactor. Temperature, species, and particle field data will be acquired from this experimental apparatus and utilized to validate the numerical model.

We continued our work in the area of physical/chemical properties data for species of importance in semiconductor processing. During FY97, the properties of Si_1 and Si_2 silicon hydrides were added to our Web site (CKMech). Although the chemistry for silicon hydrides is relatively refined, their oxidation chemistry is not well understood. We have been working on a mechanism which reflects experimental observables such as ignition delay and product distribution. However, ready access to reliable data is an essential precondition for improving this situation. Related activities here have included further development of a Unix graphics post-processor for analysis of chemical kinetic calculations (Xsenkplot) and a PC Windows compatible pre-processor (CKMech PC) for ready generation of chemical kinetic mechanisms, physical and chemical property data, and supporting bibliographic citations. For FY98, it is planned to assemble a working reaction-set or mechanism for silicon hydride oxidation that will be made available to other researchers through Web access or archival publications. Data will also be made available for silicon oxy-hydrides.

Publications:

Burns, T.J., Davis, R.W., and Moore, E.F., ***"Dynamical Systems Approach to Particle Transport Modeling in Dilute Gas-Particle Flows with Application to a Chemical Vapor Deposition Reactor,"*** Aerosol Sci. & Tech. 27 (1), 1-21 (1997).

Dufaux, D.P. and Zachariah, M.R., ***"Aerosol Mineralization of Chlorofluorocarbons by Sodium Vapor Reduction,"*** Environmental Science and Technology 31 (8), 223-228 (1997).

McMillin, B.K. and Zachariah, M.R., ***"Two-Dimensional Imaging of CF_2 Density by Laser-Induced Fluorescence in CF_4 Etching Plasmas in the Gaseous Electronics Conference Reference Cell,"*** J. Vac. Sci. Tech. A 15 (2), 230-237 (1997).

Zachariah, M.R. and Melius, C.F., ***"Theoretical Calculation of Thermochemistry for Molecules in the Si-P-H System,"*** J. Phys. Chem. A 101, 913-918 (1997).

18. *Synthesis and Characterization of Nanostructured Materials*

__M.R. Zachariah__, M. Aquino-Class, M.J. Carrier, N. Gorchkov, J.H. Hendricks, C. Scurlock, E. Steel (837), R.D. Shull (MSEL), R. Axelbaum (Washington University), and R. Ziolo (Xerox Corporation)

Objective: To develop a knowledge base for vapor-phase processing of nanostructured materials including both particulates and thin films.

Problem: Various theoretical and experimental results have shown that materials can demonstrate new and enhanced properties (mechanical, optical, electrical, etc.) when constructed from components whose composition, and size have been tailored on nanometer-scale dimensions. However, methods to grow such materials reliably with specified size, composition, and morphology need development. In addition, the knowledge base necessary to design and control the chemical/physical processes inherent in vapor phase gas-solid transformations requires further development.

Approach: Our approach has been to systematically study methods for the synthesis of nanostructured materials in both particulate and thin-film form, with an emphasis on methods that have the potential to be extended to the production of materials on a large scale. The vapor-phase route has been pursued as potentially the most robust generic method for producing quality materials in a cost-effective manner. There are two synergistic approaches being pursued: 1) development and investigation of new methods and chemistries for materials production; 2) application of advanced *in-situ* diagnostics for characterization of these processes in conjunction with the development and application of molecular-level models for predicting nucleation and growth of nanoscale materials.

Results and Future Plans: This year we continued our study of a gas phase sodium reduction process for the production of titanium nanoparticles in a $TiCl_4$/Na counterflow reactor. Our efforts focused on utilizing Laser-Induced Breakdown Spectroscopy (LIBS) to investigate the particle growth region in this reactor. The results provided a spatially-resolved profile of the entire reacting flow, thus yielding qualitative information regarding the elemental species, and their physical states, present in the reactor. Our success here has demonstrated that the reaction zone in this type of system can be interrogated *in-situ* using LIBS. Furthermore, while previous studies of particles using LIBS were performed only at atmospheric pressure, our operations at low pressure (<13 kPa) have clearly shown how the breakdown mechanism associated with this technique is pressure dependent. The plasmas that form in our system from the laser-induced breakdown are derived solely from the particles interacting with the laser, not from the surrounding carrier gases as occurs at higher pressures. This nonlinear pressure effect changes both the plasma temperature and volume, each of which dramatically alters the observed LIBS emission spectrum. Thus, we have conclusively demonstrated that, in order to obtain reliable results, users of LIBS must account for any pressure changes inherent in their systems. A companion study involving sodium vapor reacting with metal chlorides was carried out in a coflow flame configuration and succeeded in producing nanoparticles exhibiting technologically important magnetic properties including superparamagnetism.

Our molecular dynamics simulations continued with a study of the growth of silicon nanoparticles via particle-particle interactions. The computations showed that particle coalescence is very dependent on size and temperature when the particles are solid-like and considerably less sensitive when they are liquid-like. These atomistic computations have been used to validate for the first time previously postulated phenomenological models for both solid and liquid particle coalescence. Future work will focus on metal oxide clusters.

A new aspect of this activity has been an experimental effort that has demonstrated that sodium vapor/metal halide reaction chemistry can be used as a new low temperature energy-efficient CVD process for the production of nanostructured metal and ceramic thin films. We have successfully grown metallic titanium and ceramic titanium nitride films on copper and silicon substrates at a temperature of only 873 K (compared to 1250 K for conventional titanium CVD). An additional advantage of this process is that the by-products are solid-phase salts that are both easy to capture and environmentally benign. Investigations during FY98 will focus on the production of silicon carbide and titanium carbide films as well as further study of the process parameters (pressure, reactant concentrations, substrate temperature, etc.) required for optimal film quality.

Publications:

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Shapiro, A.J., Shull, R.D., Gorchkov, N., and Zachariah, M.R., ***"Mossbauer Study of Na-Coated Fe Nanoparticles,"*** Hyperfine Interactions C (in press).

Zachariah, M.R., Carrier, M.J., and Tsang, W., ***"Particle Nucleation and Growth: A Molecular View,"*** in Proc. of the 13th International Conference on Chemical Vapor Deposition, The Electrochemical Society, Pennington, NJ, 1-8 (1996).

19. Self-Assembled Monolayers for Diagnostics and Sensing

M.J. Tarlov, T.M. Herne, G.E. Poirier, R. Levicky, A.B. Steel, C. O'Connell (831), G. Gillen (837), and R. Georgiadis (Boston University)

Objective: Use self-assembled monolayers (SAMs) as model systems to develop fundamental, quantitative knowledge of sensing reactions of ultrathin films. Develop and apply ultrathin film measurement methods to correlate molecular-scale structure of films with their diagnostic and sensing performance.

Problem: Future biosensors will be required to perform multi-analyte measurements rapidly, accurately, and at lower cost. One promising approach is to use surface-confined arrays of highly selective sensing elements. For example, arrays of immobilized single-stranded DNA (ssDNA) probes, so-called DNA chips, may revolutionize genetic analysis for disease detection, toxicology, forensics, industrial processing, and environmental monitoring. In spite of the promise of this technology, little is known about the optimal film structure and composition for promoting hybridization of surface-bound probes. A sound scientific understanding of surface hybridization reactions, the linchpin of DNA chip technologies, must be attained for greater acceptance of these devices. In achieving this goal it will be necessary to develop and refine measurement methods for correlating the structure of these biomolecular layers with their molecular recognition properties.

Approach: Alkanethiol SAMs impart chemical sensitivity to Au surfaces by forming robust, ordered structures with highly tunable surface characteristics. The thiol functionality bonds strongly to the gold surface, forming a densely packed monolayer with the opposite ends of the thiol molecule forming the SAM surface. Fully functional biomolecular films are prepared by derivatizing a biological molecule (protein or nucleic acid) of interest with a thiol group, and then self-assembling the modified biomolecule on gold. Our studies are currently focused on the surface characterization of thiol-derivatized, ssDNA monolayers. The surface density, hybridization activity, and molecular orientation of the surface-bound DNA probes are characterized with a variety of surface-sensitive methods, including electrochemical techniques, neutron reflectivity, grazing angle FT-IR, surface plasmon resonance, 32P radiolabeling, x-ray photoelectron spectroscopy, ellipsometry, surface enhanced Raman spectroscopy, scanning tunneling microscopy (STM), and secondary ion mass spectrometry.

Results and Future Plans: DNA monolayer films can be prepared with high hybridization activities and precisely controlled probe coverages using a two-component film of thiol-derivatized ssDNA and a passivating thiol, mercaptohexanol. High specificity for complementary targets with near unity hybridization efficiencies is observed, while nonspecific adsorption of non-complementary targets is negligible. Steric and electrostatic repulsion effects are important factors in surface hybridization reactions as indicated by the dependence of hybridization efficiency on probe coverage. An electrochemical method using redox molecules electrostatically bound to DNA phosphate groups was also developed to quantitate both probe coverage and the amount of DNA target molecules undergoing hybridization. Future work will focus on *in-situ* measurements of surface hybridization reactions with the aim of correlating kinetic behavior with surface molecular architecture. Factors to be examined include base pair mismatches and target sequence length. STM has also been used to elucidate the molecular packing of alkanethiol monolayers in an effort to correlate the nanometer scale structure of SAMs with the macroscopic chemical and physical properties important in sensing and diagnostic applications. The mechanism by which thiols organize into monolayers was determined from molecular-resolution STM topographs obtained in real time during gas phase dosing experiments.

Publications:

Herne, T.M. and Tarlov, M.J., ***"Characterization of DNA Probes Immobilized on Gold Surfaces,"*** J. Amer. Chem. Soc. 119, 8916-8920 (1997).

Poirier, G.E., ***"Characterization of Organosulfur Molecular Monolayers on Au(111) Using Scanning Tunneling Microscopy,"*** Chemical Reviews 97 (4), 1117-1127 (1997).

20. Gas Sensing with Microhotplate Sensor Arrays

J.R. Whetstone*, R.E. Cavicchi, S. Semancik, C.E. Kendrick, M.J. Nystrom, R. Walton, S. Wight (837), J.D. Allen, B.L. Shomaker, J.S. Suehle (EEEL), T. McAvoy (University of Maryland), T. Kunt (University of Maryland), J. Kelliher (Microelectronics Res. Lab. of the Department of Defense)*

Objective: Demonstrate feasibility and manufacturability of silicon micromachined, thin-film sensor array technology for multi-analyte, real-time detection, and concentration measurement of gases.

Problem: Increasing global competition has placed new demands on the chemical process industry for more efficient use of materials, better process reproducibility, and environmental safety. Similar concerns are encountered in the automotive field where engine performance and reduced emissions are issues. Meeting these demands would be greatly aided by a low-cost technology for the measurement of gas species, which can provide immediate, on-site analysis for the detection of reaction products, exhaust gases, leaks, etc.

Approach: Advances in microfabrication technology now make possible miniaturization of conventional low-cost metal oxide sensors into a planar array form. At NIST, a sensor array platform has been developed which uses a "microhotplate" as the generic device structure. The microhotplate has three functional layers: a heater, a thermometer/ heat distribution plate, and sensing film electrical contacts. Devices are fabricated using CMOS processing combined with post-CMOS process silicon micromachining and sensor film deposition. NIST holds three patents on this technology. Advances are required in three areas: materials, measurement techniques, and transducing mechanisms.

The most important challenge is developing methods for fabricating (on arrays) sensing films with the desired characteristics of sensitivity, selectivity, and stability. Catalyst-doped metal oxide materials, which have shown good characteristics in conventional sensors, must now be produced in thin film form. Reactive sputter deposition and chemical vapor deposition (CVD) methods are adapted to take advantage of the self-heating of the micro-hotplates for thermally processing the sensing film. With CVD, varying the precursor composition and selecting which micro-hotplates in an array are activated yield array elements with different materials.

Because of their 50 to 250 µm size the elements can be heated and cooled rapidly with time constants of 1-2 milliseconds over a large operating temperature range (>800 °C). This capability supports a novel sensing approach, temperature programmed sensing (TPS), in which effects that produce a response signal are based on thermally-activated processes, such as adsorption, reaction, and desorption. By varying the temperature in a defined, repeated pattern using millisecond scale temperature changes, the sensor generates "response-signatures" that are characteristic of adsorbed species/sensing material combinations. Neural network based approaches are being used to optimize the generation of signatures and for signal analysis in TPS.

The third area of research is to discover the mechanisms behind the signal transduction process. Depending on whether the thin film structure is polycrystalline, oriented polycrystalline, or epitaxial, the dominant mechanisms may be related to grain-boundaries or the properties of the oriented-surface. The rapid temperature variations used to generate signals require a better understanding of reaction kinetics on these materials. Surface analytical techniques combined with electrical measurements are used to address these issues.

Results and Future Plans: Accelerating the pace of research this year is a new set of devices produced by advanced CMOS processing at MRL. These devices have a tungsten-titanium alloy (instead of aluminum) in the metal layers which makes the device more compatible with subsequent etching and film deposition steps. Some problems which are associated with high residual stress in the tungsten films and the non-planar surface on which the sensor film is grown still must be resolved. A new set of devices fabricated by Lincoln Laboratories (MIT) is planned for FY98 to address these issues.

Using self-lithographic CVD methods, sensing films of SnO_2, Al-doped ZnO, TiO_2, and Pt have been grown. By heating a device in a scanning electron microscope we found that post-annealing of Pt catalytic layers produces "islanding" which enhances the sensitivity of devices. Using an environmental SEM, the movies of a CVD film growth were obtained. Simultaneous acquisition of film conductance data with SEM imaging relates the microstructural data with the electrical behavior. In addition to the CVD work, studies continue on the epitaxial growth of SnO_2, which has the potential for a more stable and selective sensor form. Research on sensing materials will continue with three components: the systematic optimization of a SnO_2/Pt system by comparing the effects of grain size, composition, Pt doping method, and anneal treatments; the addition of new sensing materials, possibly including polymers, to a four-element array; and the continued development of the single crystal platform for epitaxial film growth.

TPS data for single chemical species in air have been obtained for a number of species including CO, and organic materials, e.g., ethanol, methanol, propanol, acetone, perchloroethylene. Sensitivities at the 1 mg/kg level have been observed for CO in air on Pt-dosed SnO_2 films. Neural net optimization methods were used to maximize chemical separation between ethanol and methanol while minimizing the detection time. The data-based optimization methods are now turning to the probem of concentration measurements and mixtures of two gases.

Work has been started to study the mechanisms behind the TPS response data. Sequential dosing of simple single gases such as O_2, CO, and H_2 in a vacuum system has been used to investigate the desorption and reaction kinetics on tin oxide surfaces. These experiments show the temperatures at which significant conductance changes occur with each gas. The signal changes are correlated with controlled changes in the sensing ambient to deduce the mechanisms responsible in a sensing cycle.

Publications:

Semancik, S., Cavicchi, R.E., Kreider, K.G., Suehle, J.S., and Chaparala, P., ***"Selected Area Deposition of Multiple Active Films for Conductometric Microsensor Arrays,"*** Sensors and Actuators B 34, 209-212 (1996).

Ratton, L., Kunt, T., McAvoy, T., Fuja, T., Cavicchi, R.E., and Semancik, S., ***"A Comparitive Study of Signal Processing Techniques for Clustering Microsensor Data,"*** Sensors and Actuators B 41, 105-120 (1997).

DiMeo, Jr., F., Semancik, S., Cavicchi, R.E., Suehle, J.S., Tea,, N.H., Vaudin, M.D., and Kelliher, J.T., ***"Silicon Microhotplate Arrays as a Platform for Efficient Gas Sensing Thin Film Research,"*** in Proc. of the Materials Research Society 441, 69-74 (1997.)

21. Measurement Technology for Benchmark Spray Combustion Data

C. ***Presser***, *S.R. Charagundla, I.P. Chung Hsu, J.D. Widmann, C.A. Cook, A.K. Gupta (Univ. Maryland), A. Nazarian (SAIC), G. Gmurczyk (SAIC), J. Dressler (Fluid Jets Assoc.), R. Cope (Dow Chemical), J. Smith (Cabot), D. Brown (StreamWise), B. Shomaker, J. Allen, M. Megerle (Univ. Maryland), T. Damm (Univ. Maryland), I.W. Wang (ACS SEED)*

Objective: Develop measurement technology to provide benchmark experimental data for input/validation of multiphase combustion models, optimization of process control architecture, calibration of instruments/sensors, and development of advanced diagnostics. Establish correlations between operating conditions and the resultant spray flame characteristics, thermal gradients, and level of chemical byproducts in combustion systems.

Problem: Control of process efficiency and the formation of species byproducts from industrial combustion systems (e.g., power generation and treatment of process liquid chemical wastes) is relying increasingly on computational fluid dynamics (CFD) simulations to provide relevant process information in a cost-effective manner. However, there is a dearth of reliable data for specifying model initial/boundary conditions and a need for experimental/numerical comparative analysis of conditions within the reactor. The need to provide benchmark data on the characteristics of the droplet field, flame structure, heat transfer, and particulate/gaseous byproducts, and its interrelationship with the system operating conditions (e.g., desired stoichiometry) is crucial for the development and calibration of advanced computational models, diagnostics, and instrumentation.

Approach: The NIST spray combustion test bed has evolved into a well-characterized and controlled system that can handle different process liquid fuels and wastes, atomizer designs, and combustor configurations. A variety of diagnostics are employed or being developed to characterize the input fuel stream (fuel composition), spray flame (droplet size, velocity, and temperature), and flame emissions (particulates and chemical species). A coupled experimental/computational approach is used to involve modelers from our industrial partners in the program directly.

Results and Future Plans: In FY97, efforts focused on examination of state-of-the-art fuel injection concepts. Fuel atomization is essential to enhance process performance and control the formation of chemical byproducts. Currently, two atomizer concepts are under investigation, namely: acoustic atomization, and gas-assist atomization. In collaboration with Fluid Jets Associates, a commercially available pressure-jet nozzle, modified with a piezoelectric driver, was used to study fundamental liquid sheet disintegration processes. Driving frequency and the input perturbation power were investigated to determine their effect on the conical sheet breakup length. The results indicated quantitatively that atomization quality is dependent primarily on the liquid sheet breakup length which is controlled by both the driving frequency and input perturbation power directly.

Air-assist atomization is another commonly used technique to enhance atomization. Conceptually, one does not have to use air for assisting atomization, i.e., any gas can be introduced into the atomizer. We have undertaken an effort to characterize the advantages of steam-assisted atomization, as compared to that with normal and preheated air. The results showed a marked enhancement in droplet atomization, vaporization, and observed flame luminosity over normal air.

In collaboration with Science Applications International Corporation (SAIC), we have developed a new capability at NIST to determine the thermal properties and chemical reaction characteristics of solid and liquid multiphase (such as hazardous waste) substances through rapid and controlled heating with laser radiation. Wastes containing both sodium nitrate and sodium nitrite were studied because of their substantial concentration (up to 30 %) in high-level radioactive wastes and concerns about safe storage of these wastes. Conventional techniques can only study these wastes under equilibrium conditions and at slow heating rates. Such analyses often conceal thermal characteristics that occur at higher temperatures because of material decomposition. Thus, high heating rates must be used to reach these higher temperatures before material decomposition and chemical reactions are completed. This year, we have uncovered such characteristics with our reactor and simulant wastes, i.e., detection of exothermic processes that are associated with reactions occurring at higher temperatures. A better understanding of the thermal behavior of chemical wastes can lead to improved and safer destruction strategies.

In FY98, we expect to direct our efforts toward obtaining benchmark experimental data for input and validation of CFD codes that are used by our industrial partners.

Publications:

Gupta, A.K., Damm, T., Cook, C., Charagundla, S.R., and Presser, C., ***"Effect of Oxygen-Enriched Atomization Air on the Characteristics of Spray Flames,"*** AIAA 97-0268, Amer. Inst. Aero. Astro., Washington, DC (1997).

Chung, I.P., Presser, C., and Dressler, J.L., ***"The Effect of Acoustic Modulation on Liquid Sheet Disintegration,"*** in Proc. of the American Society of Mechanical Engineers 1997 National Heat Transfer Conference 4, HTD-342, New York, NY, 67-74 (1997).

22. *Engineering Measurements for Hydrothermal Processes*

***A. Lee**, W.J. Bowers, Jr., J.J. Horvath, W.S. Hurst, J. Maslar, D. Olson, J.M.H.L. Sengers (838), W. Allmon (Babcock & Wilcox), S. Freeman (ACS SEED), J. Gallagher (Contractor), M. Hodes (Massachusetts Institute of Technology), and S.H. Lee (University of Texas at Austin)*

Objective: Near-term objectives are the development of *in-situ* measurement techniques that identify reaction and corrosion intermediates, and map velocity and thermal profiles, while withstanding the aggressive hydrothermal environment. In the longer term, data gathered will be used for developing engineering design models.

Problem: Hydrothermal processes range from treatment of industrial wastes to power generation in boilers. Major challenges to the large scale implementation of these processes include inadequate destruction of particular compounds, vessel corrosion, salt deposition and scaling, poor understanding of the near-critical heat and mass transfer, and lack of on-line process sensors and engineering models. To overcome these challenges, it is necessary to understand and develop engineering models and data for the chemical reactions, transport phenomena, and thermodynamics in this medium. However, experimental data for these models have been limited by a lack of robust, *in-situ* measurement techniques that can withstand the harsh, high temperature, high pressure, and high gradient environment.

Approach: Each area of the program addresses a major challenge (i.e., corrosion, reactor operation, salt deposition, transport phenomena). For understanding corrosion processes and validation of other reaction mechanisms, Raman spectroscopy has been developed as an *in-situ* technique to identify key species. For developing reactor operation models, we investigate different reactor geometries and their ramifications on operating conditions, with results being quantified via an *ex-situ* (effluent) analysis for aqueous pH, specific ions, and total carbon. For studying salt deposition and heat transfer processes, experiments in various near-critical fluids, flow regimes, and chemical compositions will employ various visualization and measurement technique (e.g., video, Schlieren interferometry, laser Doppler velocimetry, thermocouples). Salt deposition experiments will also provide phase boundary data that support thermodynamic modeling efforts.

Results and Future Plans: During FY97, *in-situ* Raman spectra were collected from iron, nickel, chromium, 304L stainless steel, alloy 600, and zirconium-base alloy in air-saturated water at temperatures up to 800 K and pressures up to 25 MPa. On some surfaces, chromium (VI) oxides were observed at elevated temperatures, but not upon cooling, demonstrating the value of an *in-situ* probe.

The effect of reactor shape and flow orientation on waste destruction was studied by the oxidation of acetic acid in various reactor sections under identical temperatures and residence times. Destruction was greater in the higher surface-area-to-volume ratio tubular reactor of constant diameter, whereas destruction was reduced in the lower surface-area-to-volume ratio reactor with small inlet and exit diameters and large internal diameter. Based on surface area effects previously reported for ammonia, the differences in conversion we observe most likely are associated with the enhanced mixing in the smaller diameter reactor.

In collaboration with the Massachusetts Institute of Technology, data were collected on salt nucleation phenomena and deposition kinetics for near-supercritical sodium sulfate and potassium sulfate solutions. A method was demonstrated that drastically reduced the time for collecting data to identify the solubility line. A model of the deposition rate based on fluid mechanics and heat and mass transfer was developed and applied successfully to sodium sulfate data. These results demonstrate that deposition first occurs on the hottest surface that the solution contacts, and as the solid layer grows deposition can occur internally within the porous structure.

Construction of a supercritical CO_2 heat transfer research facility was completed this year. An effort was begun with the University of Texas at Austin to calculate flow patterns in supercritical fluids using commercial CFD software and accurate fluid equations of state. The experiment and CFD models will explore the strong coupling between non-linear fluid property variations and large buoyancy forces that occur in supercritical fluids.

For FY98, we will acquire heat transfer data in turbulent supercritical CO_2 and attempt to validate the CFD models.

Publications:

Hodes, M.S., Smith, K.A., Hurst, W.S., Bowers, Jr., W.J., and Griffith, P., ***"Measurements and Modeling of Deposition Rates from a Near Supercritical Aqueous Sodium Sulfate Solution to a Heated Cylinder,"*** Proc. of the American Society of Mechanical Engineers 32nd National Heat Transfer Conference 12, HTD-350, New York, NY, 107-119 (1997).

Lee, A., ***"Effect of Shape and Orientation on the Performance of Supercritical Water Oxidation Reactors,"*** Proc. of the American Society of Mechanical Engineers 32nd National Heat Transfer Conference 12, HTD-350, New York, NY, 99-107 (1997).

IV. Surface and Microanalysis Science Division (837)

Rance A. Velapoldi, Chief

A. Division Overview

Mission:

The Surface and Microanalysis Science Division serves as the Nation's Reference Laboratory for chemical metrology research, standards, and data to:

- Characterize the spatial and temporal distribution of chemical species; and
- Improve the accuracy, precision, sensitivity, and applicability of surface, microanalysis, and advanced isotope measurement techniques.

The Division provides the tools for the Nation's measurement communities to enhance U.S. industry's productivity and competitiveness, assure equity in trade, and improve public health, safety, environmental quality, and national security. We perform research to: a) determine the chemistry and physics of surfaces, interfaces, particles, and bulk materials, and their interactions with a broad spectrum of species including electrons, photons, ions, atoms, and molecules; b) determine the chemical and isotopic composition, morphology, crystallography, and electronic structure at scales ranging from millimeters to nanometers; c) determine the energetics, kinetics, mechanisms, and effects of processes occurring on solid surfaces as well as within materials and devices; d) study the total chemical measurement process as well as source apportionment in atmospheric chemistry using advanced isotope metrology and chemometrics; and e) develop and certify key Standard Reference Materials and Standard Reference Data. Emphasis is placed on performing fundamental and applied measurement research to push the measurement envelope by anticipating measurement, standard, and data needs through interactions with a broad base of customers. This infrastructural information can provide the basis for advances in various technologies, such as chemical catalysis, advanced electronics and materials science and provides the tools that industry can use to solve their measurement problems.

Division staff were productive in technical research and program planning. In program planning, we expanded our programs from six to seven major programs, providing increased visibility for **Molecular Scale Chemical Measurements**. Additionally, we proposed and were successful in obtaining funding to expand our existing project in Auger electron spectroscopy under the **Nanoscale Chemical Characterization** program. With these advances, we have addressed two of the three needed components for our proposed National Facility for Chemical and Materials Microanalysis. Objectives of the programs, as well as selected accomplishments for each, are given below to provide a flavor of the research performed as well as the directions in which each program is going.

Programs:

Nanoscale Chemical Characterization: Our objectives are to push the measurement envelope and provide infrastructural tools for the measurement communities to determine the chemical composition of various samples, ultimately at very high spatial resolutions and very low concentrations. In a broader context, the measurements include the chemical characterization (elements, isotopes, and molecules) of materials at millimeter to nanometer and smaller spatial scales with major, minor, and trace chemical concentrations. In addition to determining qualitative and quantitative chemical composition, the measurements also include determining crystallography (species and molecules) and morphology (structure). Instrumental methods include electron, ion, photon, and x-ray probes. These measurement tools can then be applied across a broad range of problems in the private and public sectors such that the 'microspatial' relationships of chemical species can be correlated with specific macroscopic properties of high technology materials such as electronic devices as well as to determine the effects of individual manufacturing steps on a system or product.

Selected Accomplishments:

- Established the capability for Telepresence Microscopy and Microanalysis and demonstrated its utility by solving processing and measurement problems for industry, academia, and government
- Improved measurement parameters (resolution, count rate, and window transmission) for the new NIST micro-calorimeter Energy Dispersive Spectral detector and demonstrated that it has an energy resolution comparable to conventional wavelength dispersive spectral detectors
- Performed definitive measurements to identify chemical state of species using low energy x-ray emission spectroscopy
- Determined utility of algorithms to detect low intensity peaks in energy x-ray spectra
- Characterized defects in a manganese oxide microporous material and compared experimental results with computer simulations

Particle Characterization and Standards: Our objectives are to focus on the special case of individual particles or samples that contain 'particles' and to provide measurement capabilities to 1) characterize individual particles, and 2) characterize a sample by the chemical composition of each particle summed into "particle populations", a micro to macro concept. In this concept, automated measurement methods are developed by optimizing sample and instrument measurement parameters, and developing or extending software for data collection, visualization, and interpretation. These methods are then used for the identification of samples, contaminants, or to analyze particle starting materials or products in advanced materials production an in the development of particle SRMs. We also apply these measurement capabilities to: characterize actinide and other materials of interest; develop standards, data, and measurement protocols appropriate for use in quality assurance by various laboratories; and transfer these measurement capabilities to the appropriate measurement communities, e.g., DoD, DoE, and IAEA. These latter efforts aid the Nation in monitoring the Nuclear Test Ban Treaty and determining the spread of nuclear weapons, and help the IAEA carry out worldwide nuclear monitoring.

Selected Accomplishments:

- Developed and provided measurement capabilities and standards to the International Atomic Energy Agency for the automated determination of uranium isotopes, providing a more efficient method for monitoring nuclear production on a worldwide basis
- Integrated phosphor-imaging plates with X-ray micro-diffraction equipment to provide increased capabilities for data collection and detection of preferred orientation
- Developed radioactivity speciation method using auto-radiography and microscopy
- Finished certification of SRM 2806 Medium Test Dust in Hydraulic Fluid in collaboration with the National Fluid Power Association

Electronic and Advanced Materials Characterization: Objectives are to apply measurement techniques for the chemical and morphological characterization of electronic devices and components (e.g., semiconductors, superconductors, opto-electronics) and advanced materials (e.g., coatings, ceramics); and to develop needed standards and data. The projects, chosen to demonstrate the application of our developed measurement techniques, range from needs defined by the Semiconductor Industry Association (SIA) roadmap to determining contaminants in finished products from various industries.

Selected Accomplishments:

- Planned and developed the 2nd depth profile standard, SRM 2134: Arsenic Implant in Silicon for calibration of secondary ion mass spectrometers
- Collaborated with MIT Lincoln Laboratories; used multidisciplinary diagnostic tools to solve problems in deep μm CMOS technology
- Developed protocol to repeatably measure Si dopant concentrations in GaN thin films
- Applied automated SEM and compositional mapping to characterize starting particles of yttria-stabilized zirconia and the thermal barrier coatings on turbine blades in jet engines
- Obtained improved vibrational spectra of synthetic zeolite reference materials using near-infrared Fourier transform Raman spectroscopy

Chemical Measurement Process: Objectives are to investigate the Chemical Measurement Process and establish generic methods, standards, data, and definitions, as bases for overall quality assurance. Several aspects of these objectives are important aids to industry in achieving ISO 9000 certification and providing the basis for traceability among national and international standards bodies, industries, and governments. Examples include:

calibrations, data analysis and interpretation, process design, model validation, estimates of uncertainties and bias, Standard Reference Data and Standard Test Data, Standard Reference Materials, and Documentary Standards (i.e., terminology and reference procedures).

Selected Accomplishments:

- Published IUPAC document on evaluation of analytical methods and definition of calibration
- Established a Surface Analysis Data Center
- Released version 2.0 of the X-Ray Photoelectron Spectroscopy Database (SRD 20) and Version 1.0 of the Elastic-Electron-Scattering Cross-Section Database (SRD 64)
- Developed Electron Inelastic-Mean-Free-Path Database (SRD 71)
- Provided new data services on the World Wide Web: Interactive Standard Test Data for XPS and a Database of Isotopes in Atmospheric Methane
- Determined homogeneity of a prototype urban dust particle filter Reference Material
- Performed international comparison of carbon dioxide isotopic Reference Materials
- Built new ozone Standard Reference Photometers for the National Physical Laboratory, Great Britain and the Environmental Protection Authority, Australia (21 in international network: 12 in the U. S. and 9 worldwide – inquiries SRPs from Spain, the Netherlands, and Korea)
- Applied the measurement technique of x-ray standing waves to study quasicrystals

Surface and Interface Chemistry: The program develops measurement tools for the characterization of, provides fundamental data on, and produces models for, the basic chemical events that occur in surface and interface reactions. Laser and electron spectroscopies and mass spectrometry are applied to the study of advanced surface processes including photoreactions at surfaces, energetic radical reactions with surfaces, and the details of thin-film growth and surface structure formation. Optical probes are also used to study both solid/solid and liquid/solid interfaces.

Selected Accomplishments:

- Investigated strain effects in heteroepitaxial thin film growth and reactions on GaAs
- Developed inclusive theory using breathing mode excitation in near harmonic systems to describe systems from laser-cooled atoms in optical lattices to molecules adsorbed on solid surfaces
- Determined mechanism for hyper-thermal H-atom abstraction of D adsorbed on Si
- Designed and constructed "second generation" system to measure the interaction of atoms and radicals with surfaces, critical to providing the needed mechanistic and reaction rate data for modeling of semiconductor processing
- Used the environmental SEM to perform real-time monitoring of the nucleation and growth of tin oxide CVD films on silicon microdevices

Advanced Isotope Metrology: Objectives are to develop basic procedures and provide tools to measure isotope ratios of chemical species in processes such as combustion, atmospheric gas-particle interactions and transformations, and contaminant transport, all critical for atmospheric source apportionment. Included here are the general objectives for chemical species source apportionment:

- Apply isotopic and molecular chemical characterization techniques to measure atmospheric contaminants on local, regional, and global bases;
- Determine sources of the contaminants;
- Model results considering meteorology to develop optimum sampling locations and strategies; and
- Provide results to interested sectors so they can devise control strategies for pollutant or contaminant reduction.
- Various emissions can be differentiated including woodburning, gas and diesel vehicles, power production, fast food frying, biomass burning, biogenic sources as well as chemical species used in or contaminants produced by manufacturing processes. Other measurement capabilities include dual isotope dating, authentication, actinide analyses, and individual pulse characterization in low-level counting.
-

Selected Accomplishments:

- Discriminated completely two sources of a single reactant (monomer) and the correct quantitative apportionment of source components through dual isotopic characterization of the commercial product (high-tech copolymer)
- Identified isotopic and molecular fire tracers in the polar atmosphere and cryosphere
- Finished collaborative source apportionment study (fossil/biomass) for Denver, the State of Colorado, and the CRC to provide information for pollution abatement strategies

- Identified mass spectrometer measurement bias in stable isotope measurements and decreased measurement bias for the most exacting measurements by a factor of ten through instrument redesign

Molecular Scale Chemical Characterization of Organic and Biomolecules: The critical dimensions of emerging technologies have shrunk to the point that current, infrastructural, spatially-resolved surface-microprobes of molecules and species cannot meet the projected chemical measurement needs of industry. The Division has addressed this challenge *via* the development of two categories of advanced, non-destructive surface probes. The first is to leverage the NSOM competence project into this robust program by developing chemically resolved scanned probe microscopies (e.g., chemical force AFM, heterodyne scanning tunneling microscopy (STM), and the SIMS/TOF-SIMS measurement methods. The second is to focus on the development of a project under the **Nanoscale Chemical Characterization** program to develop capabilities in spatially resolved AES and XPS. The molecular information from the scanned probes and SIMS techniques, and elemental and oxidation state information from the probes of electronic states, will provide complementary, information on surfaces of technological interest.

Selected Accomplishments:

- Designed and built near-field scanning optical microscope for the visible region
- Obtained images simultaneously using shear-force AFM, transmission NSOM, and reflection NSOM and developed models to explain images using point polarizable dipoles for the sample scatter and tip
- Demonstrated Raman NSOM on diamond films
- Investigated effects of tip parameters on NSOM signal response
- Developed and applied measurement procedures for imaging organic molecules and elemental species in and on human hair using SIMS
- Developed and applied FEG-TEM quantitative, nanometer-scale analysis of carbon bonding environment on field emission devices for flat panel displays

Other areas for future consideration as either new programs or emphasized major projects include **Chemical and Process Information for Surface Engineering** and **Source Apportionment of Important Chemical Species**.

Staff Recognition: Honors our staff received this year include: George A. Klouda, the Department of Commerce Bronze Medal for "...leadership in developing advanced technologies and standards for trace isotopic measurements of atmospheric gases and particles."; Rance A. Velapoldi, the Department of Commerce Gold Medal for leadership in the "...development of the Rapid Integrated Nuclear Analysis capability that enables measurements 5-10 times faster than previously possible.", Marlon L. Walker, the Lloyd N. Fergusen 'Outstanding Young Scientist' Award for "...his outstanding contributions and achievements as a young chemist in research"; Stephan J. Stranick, the "Ithaca College Outstanding Young Alumni Award"; John A. Small, the 1997 Microbeam Analysis Society "Presidential Award"; for "...dedicated support and service to the Society. "; and Alline F. Myers and Eric B. Steel (with collaborators from NC State Univ. M.L. Ding and J.J. Cuomo) for the 2nd best Poster - Physical Sciences (out of several hundred posters) at the joint Microscopy Society of America and the Microbeam Analysis Society Conference. These internal and external awards were based on long-term efforts develop accurate measurements, standards, and data.

Interactions: Strong interactions by the staff with our constituents and effective technology transfer are shown by substantial technical outputs, participation on 10 editorial review boards, close interactions with national (e.g., ASTM, ANSI, MAS, EMSA, NFPA) and international (e.g., ISO, IUPAC, IAEA, VAMAS) organizations, and participation on established committees. In addition, staff participated on evaluation and consulting panels for DoE, DoD, NSF, EPA, NRC, USGS, WHOI, and industrial groups. Finally, we have organized, co-organized, or participated in several international and national conferences.

B. Selected Technical Reports

1. *High Resolution X-ray Spectrometric Analysis with the NIST Micro-calorimeter Energy Dispersive Spectrometer*

***D.E. Newbury** (CSTL), J.M. Martinis, D.A. Wollman, K.D. Irwin, and G.C. Hilton (EEEL)*

Objective: Bring the revolutionary Micro-calorimeter Energy Dispersive X-ray Spectrometer (EDS) developed by NIST into use for analytical applications.

Problem: The NIST Micro-calorimeter EDS has the potential to fundamentally alter the manner in which analytical x-ray spectrometry is performed. To speed the entry of this device into the market-place, critical device performance improvements are needed and test/demonstration measurements must be performed on problems of analytical importance.

Approach: Optimize detector design to improve resolution, limiting count rate, and window transmission. Compare micro-calorimeter EDS performance with conventional semiconductor EDS and wavelength dispersive (i.e., diffraction) spectrometry (WDS).

Results and Future Plans:

Resolution: A resolution of 8.7 eV for Al Kα radiation (FWHM, full width at half peak maximum) has been demonstrated, the best performance ever reported for a micro-calorimeter. Recent design modifications have improved the resolution to 4 eV. This resolution performance is critical to the measurement of chemical state through peak shape and position shifts.

Count rate: The initial limiting count rate of 200/s has been increased to 800/s. The combination of high resolution and count rate is critical to realizing the full potential of energy dispersive operation for simultaneous trace-minor-major detection.

Window transmission: Photon energies as low as 250 eV have been successfully detected through a window array that attenuates the infrared radiation by nine orders of magnitude. This permits the detection of C K-radiation at 282 eV and gains access to the spectral energy range where chemical shifts occur.

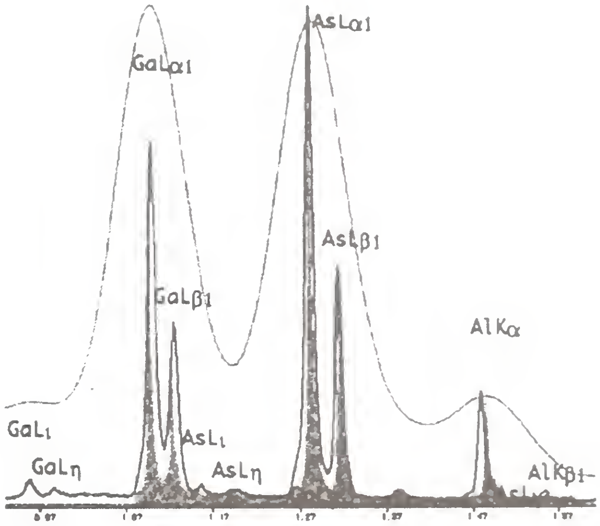


Figure 1

To examine analytical performance limits, x–ray spectra have been compared among the micro-calorimeter EDS, the semiconductor EDS, and the wavelength dispersive (diffraction) spectrometer (WDS). As shown in Figure 1 for AlGaAs, the micro-calorimeter EDS (dark line) performance is very similar to the scanned WDS (filled, gray), and far superior to the semiconductor EDS (gray dashed line), upon which the analytical spectrometry field now mostly depends. The spectrum for carbon, demonstrating low photon energy performance, is shown in Figure 2.

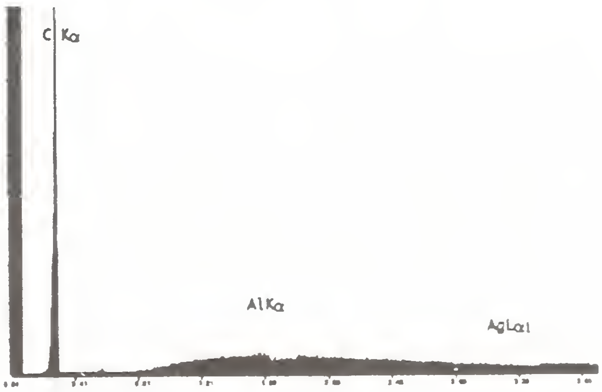


Figure 2

Further improvements to the micro-calorimeter EDS are anticipated, especially to the solid angle of collection and the window transmission. The process to select an industrial partner to develop the micro-calorimeter EDS was officially started with a meeting at NIST Boulder on August 7, 1997.

2. *Surface Analysis Data Center*

C.J. Powell, J.R. Rumble (231), A. Jablonski (Poland), and S. Tougaard (Denmark)

Objective: To provide needed reference data for applications in surface analysis.

Problem: Surface properties are crucial for the fabrication and performance of a wide range of materials (e.g., ceramics, composites, alloys, polymers, superconductors, diamond thin films, and biomaterials), semiconductor devices, optoelectronic materials, high-density magnetic-storage media, sensors, catalysts, thin films, and coatings. Surface analysis is used not only to correlate the composition of an exposed surface with specific material properties but also for the investigation of interface properties if intervening material is removed. While there are many successful applications of surface analysis (e.g., for failure analysis in manufacturing and for monitoring steps in product fabrication or process development), the reliability and efficiency of many analyses are often limited by the lack of reference data.

Approach: NIST has established a Surface Analysis Data Center to give greater visibility to its existing and planned databases developed for applications in surface analysis. These databases are currently intended for use in Auger-electron spectroscopy (AES) and x-ray photoelectron spectroscopy (XPS), the most commonly used surface-analysis techniques.

Results and Future Plans: Two databases are now available for AES and XPS applications, a third will be released soon, and planning for another has commenced. These databases will be described in turn.

Version 1 of the X-Ray Photoelectron Spectroscopy database (SRD 20) was released in 1989, and version 2.0 was released in September, 1997. Version 1 has been widely used to obtain binding energy and related data for the surface analysis of a wide range of materials by XPS. Version 2.0 contains completely redesigned software and about 16,000 line positions, chemical shifts, and line splittings. Pull-down menus are available to initiate searches for:

- identification of unknown lines in an experimental spectrum,
- retrieval of core-level binding energies,
- retrieval of chemical shift data,
- searching for compounds containing selected elements or for specified material classes,
- searches based on compound names and other fields, and
- to display Wagner plots,
- effort is ongoing to provide additional evaluated data for this database.

Version 1 of the Elastic-Electron-Scattering Cross-Section Database (SRD 64) was released in August 1996. This database provides differential and total elastic-electron-scattering cross sections for simulations of signal-electron transport in XPS and AES and for other applications involving electron transport. Such simulations are important in developing improved methods that separate chemical information from effects due to the complex morphologies of many practical materials such as semiconductor structures. The database provides elastic-electron-scattering cross sections for elements with atomic numbers from 1 to 96 and for electron energies between 50 and 9,999 eV.

The Electron Inelastic-Mean-Free-Path Database (SRD 71), to be released in spring, 1998, will provide needed data for quantitative surface analyses by AES and XPS. This database contains calculated and measured electron inelastic mean free paths (IMFPs) for elements, inorganic compounds, and organic compounds. If no calculated or measured IMFPs are available for a material of interest, values can be estimated from a predictive formula. A wide range of options is available so that a user can display IMFPs as a function of electron energy, can determine IMFPs for selected energies, and can compare IMFPs for different materials or from different sources.

Planning has commenced for a new database to be used for AES and XPS analyses of materials with complex morphologies. These data will access the data from SRD 64 and SRD 71 and, with additional data, will enable comparisons to be made of measured and simulated spectra for particular analytical conditions.

3. Identifying Isotopic and Molecular Fire Tracers in the Polar Atmosphere and Cryosphere

***L.A. Currie**, J.M. Conny, G.A. Klouda, D.B. Klinedinst, S.R. Biegalski (PDA), J. VanValkenburgh (GR), B.A. Benner (839), and J.E. Dibb (Univ. NH).*

Objective: To provide direct information on the origins, transport, and history of climate-changing combustion aerosol ("soot") in the Arctic, through the application of uniquely sensitive and specific isotopic and organic tracers for fossil and biomass burning.

Problem: Natural and anthropogenic sources of combustion aerosols are having an increasingly important impact on global pollution and climate. Along with the Greenhouse gases, black carbon ("soot") is of major importance because of its radiation interactions that can contribute to global warming. It is thus essential to develop and validate measurement and modeling approaches that relate to the origins of this material, and that can discriminate between the two source classes.

Approach: We report here on a multi-institutional project, supported in part by NASA and NSF, to track fossil and biomass burning aerosol from industrial and remote source regions to Summit, Greenland. These results begin to develop the historical record of global combustion as recorded in natural snow and ice core archives. The initial measurements were triggered by an unusually severe firestorm in central Canada (lower Hudson Bay) on August 5, 1994, that sent a large biomass burning plume to Summit Greenland, the site of the Greenland Ice Sheet drilling Program-2. Measurements of aerosol carbon and ^{14}C arriving at Summit showed a six-fold increase in biomass carbon on that date, with little change in the fossil carbon contribution. Supporting evidence came from ion chromatography data, satellite imagery, and back-trajectory analysis.

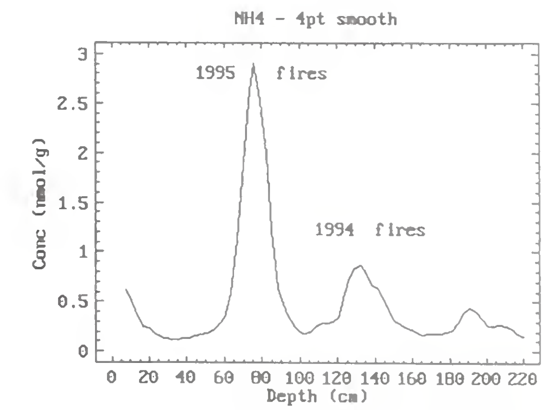


Figure. 1 1996 Snowpit: NH_4 concentration vs depth.

Results and Future Plans: During the past year, we have developed a suite of isotopic and molecular fire tracers, applied them to the location, and quantified combustion aerosol trapped in the Summit snow. To illustrate, Figure 1 shows an ammonium ion trace in a snowpit from the summer of 1996. This biomass-burning tracer shows distinctive peaks marking the forest fire seasons of 1995, 1994, and 1993, with increasing depth. (The snow accumulation rate near the surface is about 70 cm/y.) NIST's unique capabilities to measure ^{12}C, ^{14}C, and trace polycyclic aromatic hydrocarbons (PAH) in combustion aerosol have now been applied to sections of the 1996 snow core to quantify long range transport and deposition from fossil and biomass burning events in the Northern Hemisphere. Our first data, from a "baseline" region at a depth of about 40 cm, indicate comparable impacts of fossil and biomass burning aerosol based on independent evidence from both the carbon isotopic tracers and the pattern of PAH tracers, retene, benzo(*e*)pyrene, and benzo(*ghi*)-perylene. This represents the very first time that aerosol ^{14}C has been measured in the polar snow or ice, and the first combined polar application of the particulate carbon isotopic and PAH fire tracers. Concentrations are so low (ng/g for carbon, pg/g for PAH) that our metrological capabilities are pushed to the extreme. Following the identification of regional sources of climatically active "soot," our measurements will be extended to interdisciplinary studies to validate transport, deposition, and satellite imaging models for the global circulation of atmospheric particles.

Publication:

Currie, L.A., Dibb, J.E., Klouda, G.A., Benner, Jr., B.A., Conny, J.M., Biegalski, S.R., Klinedinst, D.B., Cahoon, D.R., and Hsu, N.C., *"The Pursuit of Isotopic and Molecular Fire Tracers in the Polar Atmosphere and Cryosphere,"* Proc. 16th Int. Radiocarbon Conference Groningen, 1997 (manuscript accepted).

4. *New Data Services on the World Wide Web: Interactive Standard Test Data for X-Ray Photoelectron Spectroscopy (XPS) and a Database of Isotopes in Atmospheric Methane*

J.M. Conny, C.J. Powell, L.A. Currie, J.N. Lee (SU), G.W. Mallard (838), and T. Levitsky (GR, 838)

Objective: In keeping with NIST's efforts to provide high quality chemical data, we are implementing new data services on the World Wide Web for the surface science and the atmospheric science communities. The first service provides Standard Test Data (STD) to the surface spectroscopist for assessing quality in computer-based data analysis procedures and then provides on-line evaluation of the results of the customer's data analyses. The second service is a database of isotopic measurements for use in studying the role of the atmospheric methane in global climate change.

Problem: Like NIST Standard Reference Materials (SRMs), STD are used to assure the quality of the chemical measurement process. While SRMs are used to assess the complete chemical measurement process from sample preparation/measurement through data evaluation, STD are used solely to assess the quality of the data evaluation domain; in particular, computer-based data-analysis procedures that convert instrument responses to relevant chemical information. For atmospheric scientists and geochemists, the sources and sinks of atmospheric methane, which are important in global climate change, are encoded in its isotopic composition. Thus, isotopic data are essential to modelers who quantify the global or regional atmospheric methane budgets by comparing the isotopic compositions of methane in ambient air with the isotopic compositions of the aggregate of flux-weighted sources.

Approach: For the surface science community, simulated x-ray photoelectron spectra have been developed (XPS-STD). Following a factorial design, the XPS-STD consist primarily of polymer carbon 1s doublet spectra that present varying degrees of overlap between peaks, varying levels of relative intensity between peaks, and varying levels of Poisson noise (Figure 1). At the XPS-STD web site, customers 1) download the XPS-STD and analyze the spectra for peak binding energies, 2) upload their results back to the web site, and 3) have their results evaluated on-line. For the atmospheric science community, we have created a WWW database of over a thousand reported measurements of ^{2}H, ^{13}C and ^{14}C abundances in methane for ambient air and methane sources.

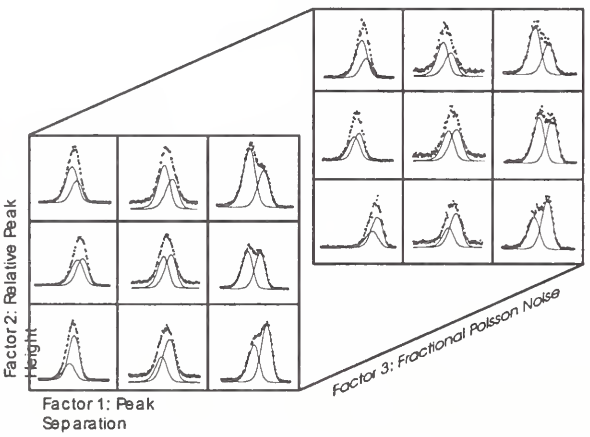


Figure 1. Factorial design for simulated XPS C^{1s} doublet spectra binding energies for each spectrum measured to the left along the horizontal axis. Solid traces show the pure spectra of the doublet components.

Results and Future Plans: Curvefits of the XPS-STD by 20 analysts using a variety of software procedures, revealed peak binding energies that deviated substantially from the true binding energies. These deviations from true values, calculated as biases and random errors, serve as the evaluated results of the test group. Customers using the XPS-STD web site may compare the on-line evaluation of their data analysis with that of the test group. By minimizing biases and random errors in the evaluated results for particular spectral conditions modeled by the XPS-STD, customers may determine which analysis procedures produce high accuracy and precision. In the future, the XPS-STD web site will also evaluate peak intensity (area) determinations. Within the web pages of the database of methane isotopic compositions, there are numerous links to numeric and text information on: 1) methane source types, 2) sampling times, locations, collection procedures and measurement procedures, 3) sampling and measurement uncertainties, 4) isotopic measurements and associated statistics, and 5) data interpretation. The URL for both the XPS-STD web site and the isotopic database web site is http://silicon.nist.gov.

5. *The Homogeneity of a Prototype Urban Dust Particle Filter Reference Material*

G.A. ***Klouda****, D.B. Klinedinst, J.J. Filliben (898), B.A. Benner (839), H.J. Parish (SRI International), and R.B. Kellogg (ManTech Environmental, Inc.)*

Objective: To evaluate a method for production of particle filter Standard Reference Materials (SRMs) as industrial and regulatory standards.

Problem: It is well known that atmospheric aerosols influence climate, public health, and visibility throughout the world. To determine their origins, the standard approach is to collect particulate material on filter substrates and measure their chemical and isotopic compositions. These data provide a link to understanding relationships between source emissions and air quality. In the case of regional air quality, state implementation plans are formulated to address specific control strategies based on these data using regional air quality models. The revised U.S. EPA National Ambient Air Quality Standard (NAAQS) for air particulate matter (PM) addresses the size range from <10 µm to <2.5 µm diameter particles (U.S. EPA, *Air Monitoring Technical Informational Center News, V.6, No. 1, 1997*). This new standard presents the scientific and monitoring communities with a greater challenge in calibrating and intercomparing analytical techniques. Successful production and certification of an air particulate filter SRM on quartz-fiber filters and on polytetrafluoroethylene (PTFE) filter materials will provide the best means to assure that attempts to meet the NAAQS are based on high quality measurements.

Approach: A prototype filter Reference Material has been produced by re-suspending the NIST SRM 1649 (Urban Dust) in air and collecting the material on tared 37 mm diameter quartz-fiber and PTFE membrane filters using SRI's dust generation and collection system. The goal is to evaluate this method for producing up to 2000 filters — six batches of 320 filters (four arrays, 8 x 10 filters per array) — each filter loaded with 3-4 mg of SRM 1649. The SRI system, originally designed for the National Institute for Occupational Safety and Health Proficiency Analytical Testing Program that normally requires deposits of less than 50 µg, is expected to provide a means to distribute about one milligram of any fine particle (dust) material uniformly on filter medium. Particles re-suspended in air are less likely to change in their original composition compared to methods that rely on liquid re-suspension. The homogeneity of the re-deposited material within and across filters, *i.e.*, across arrays and batches, has been determined gravimetrically and chemically. The chemical homogeneity within and across filters was determined at the percent level *via* total-C, organic-C, and elemental-C measurements and at the trace (µg/g) level *via* polycyclic aromatic hydrocarbon and inorganic elemental measurements.

Results and Future Plans: The particle mass variability across filters ranges from 13-15% relative standard deviation (RSD) within arrays and as much as 20% RSD across arrays within a given batch. This variability is partially a result of:

1) an inadequate seal between the filter and the cassette sections that resulted in particle losses,
2) the sample collection chamber dynamics: filters positioned in the center have a greater mass loading than filters positioned along the edge, and
3) the particle size distribution of the SRM 1649 (50% volume with a median diameter of 24 µm) which favors agglomerated particles (Poster *et al.*, submitted to *Env. Sc. & Tech.*, 1997).

The within-filter variability, based on total carbon measurements, is 4-13% RSD at the edge and 4-8% RSD in the middle for an ≈0.1 mg SRM. In comparison, the SRM 1649 has a total carbon variability of 2-5% RSD (at 0.3-9 mg SRM level). The across-filter variability of elemental carbon relative to total carbon is 16% RSD (*cf.* the thermal-optical method). The inorganic elemental composition variability on PTFE filters is less than 8% RSD based on elemental ratios relative to iron. We expect that the following changes to the protocol would improve the homogeneity for future particle-filter materials:

1) a <2.5 µm diameter contemporary urban dust,
2) a cyclone size-segregator between the re-suspension and collection chambers to remove agglomerates, and
3) optimized filter packs to avoid particle losses.

The production and certification of a particle filter SRM on quartz-fiber filters using SRI's system and on Nucleapore® filters using liquid filtration has been proposed for FYs 1998-1999. The particle filter SRM would meet the EPA's revisions to the Reference Method for collecting $PM_{2.5}$.

6. International Comparison of Carbon Dioxide Isotopic Reference Materials

R.M. Verkouteren

Objective: To provide critically evaluated and internationally recognized carbon dioxide isotopic Reference Materials (RMs) for the environmental, medical, industrial, and forensic science communities that cover the natural range of carbon and oxygen isotopic abundances.

Problem: The isotopic composition of a material can be a superb tracer. Despite natural, or industrial, chemical processing, a conserved element will retain its isotopic signature through any chemical identity, being altered only slightly, and predictably, through subtle isotopic fractionation. Multi-national consortia that study the global carbon cycle, relevant to climate change through environmental effects of carbonaceous aerosols and "greenhouse" gases, require measurement reproducibility of 0.002% (RSD) for ^{13}C abundance. This value is typical of intra-laboratory precision. However, inter-laboratory reproducibility is 3 – 10 times poorer due to limitations in available standards and quality assurance practices. While the global monitoring community has the most stringent measurement needs, other communities also suffer from limitations in the isotopic measurement and standards infrastructure. For example, the isotopic resolution of natural and synthetic additives in many consumer goods (e.g., foods, pharmaceuticals, perfumes, and advanced materials) is not advanced enough to protect comprehensibly U.S. industries and consumers from patent infringements and illegal adulteration of products. Also, the isotopic analyses of controlled substance residues (e.g., narcotics, toxins, and explosives), which help to identify their origins, are limited by existing interlaboratory reproducibility and traceability that are insufficient for legal prosecution, especially across international jurisdictions.

Approach: Measurements of ^{13}C abundance are typically performed through isotope ratio measurements of carbon dioxide (derived from the carbonaceous sample), and standardized with measurements of reference CO_2. Due to technical challenges in the production of carbon dioxide isotopic RMs, none existed with the requisite sample-to-sample isotopic reproducibility until NIST developed RMs in 1996. This year, an international intercomparison exercise was organized among twelve laboratories with expertise in carbon dioxide isotopic measurements. Countries included were Australia, Austria, England, Germany, India, The Netherlands, New Zealand, Japan, and the United States. Each laboratory was given several units of three different RMs to analyze these replicates using standard procedures for the determination of ^{13}C and ^{18}O abundances standardized by the CO_2 derived from the primary limestone standard ($NBS19\text{-}CO_2$).

Results and Future Plans: Results are summarized in Figure 1. Horizontal lines above the bottom axis mark true sample-to-sample ^{13}C and ^{18}O heterogeneities (standard uncertainties, u_s) of the RMs ($n = 50$). For ^{13}C and ^{18}O abundances, true u_s values were less than 0.0007% and 0.0025%, respectively. Shaded bars (left members of the six displayed pairs) are medians of the sample-to-sample intra-laboratory reproducibilities (apparent u_s) for RM replicates ($n = 2$ or 3), slightly larger than their true values. Unshaded bars (right members of the six displayed pairs) are inter-laboratory reproducibilities (u_i), which are three to ten times poorer than the apparent u_s values. Dispersion in the reported isotopic compositions surprisingly increases with increasing compositional distance from the primary standard (NBS19-CO_2), suggesting the presence of proportional instrumental errors, in addition to variations induced by the difficult carbonate standardization procedures. The use of these "chemistry-free" isotopic CO_2 RMs as calibration materials, therefore, should improve inter-laboratory reproducibility significantly. The RMs have been stored for one to two years and representative samples will be reanalyzed to determine RM stability characteristics before general distribution.

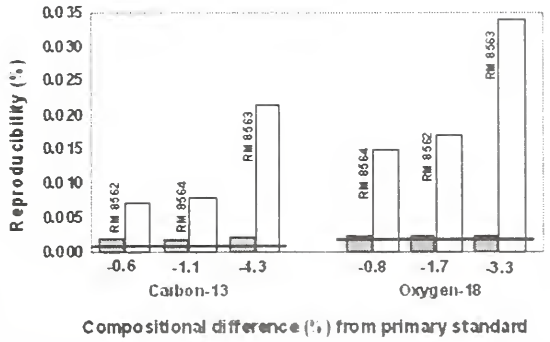


Figure 1. Carbon-13 and oxygen-18 intercomparison results: true sample-to-sample heterogeneities (lines), intra-laboratory reproducibilities (shaded bars), inter-laboratory reproducibilities (unshaded bars), and dependency on isotopic difference from the primary standard (see text).

7. *Telepresence Microscopy and Microanalysis: A New Paradigm for Solving Problems and Transferring Information*

***E.B. Steel**, B.B. Thorne, A.J. Fahey, J.A. Small, A.F. Myers, and D.E. Newbury*

Objective: To develop methods to transfer microscopy images, microanalytical qualitative and quantitative spectroscopic information, and compositional mapping images to remote sites in real-time.

Approach: Participating in the National Advanced Manufacturing Test-bed for Telepresence Microscopy, we designed and implemented a method that allows remote collaborators to utilize and participate in the Division's microanalysis and microscopy measurement capabilities. Several possible approaches were possible. We chose a low-cost method that is applicable in virtually any microscopy laboratory to maximize the method's utility. Commonly available Macintosh and WinTel computer platforms with World Wide Web (WWW) connectivity and browser capability were used. This method, coupled with low cost software and hardware add-ons, provides a system that costs between $2K - $5K. This capability provides real-time images and analyses originating in our laboratories. The design allows our instruments, including electron, ion, and light microscopes, and an x-ray optical bench, "to be connected to customers" who have direct WWW access to the advanced microscopy and microanalysis instrumentation and technical expertise at NIST.

Results and Future Plans: We have implemented the telepresence system and applied it to a variety of industrial and technological problems. We have tested the system by "telepresenting" analytical results in live time to several industrial, government, and university collaborators and found that the NIST microanalysts and collaborators unanimously agreed that the use of the telepresence approach aided the analysis. The analysts found that they no longer were required to become an expert in the collaborator's field, but rather they (microanalyst and collaborator) could use their combined knowledge about the analysis and specimen to develop simultaneously an understanding of the analytical needs, problems, and solutions. We have termed this mode "over-the-shoulder" telepresence microscopy. We estimate the telepresence approach has decreased the analysis and reporting process by an order of magnitude through more efficient and effective communication. Since live video over the WWW is only a few years old and the technology of Internet communication is evolving at a rapid rate, we expect to expand and improve this approach as the WWW technology improves and as we implement the next step, remote control. Remote control can be applied in several useful ways:

1) to remove our sensitive instruments from the effects of laboratory environmental degradation (including the presence of the analyst) that significantly reduces our analytical capabilities and reproducibility,
2) to allow knowledgeable users remote access to microscopy and microanalysis facilities, and

3) to allow equipment manufacturers to remotely inspect, calibrate, and possibly repair instruments in the field.

We have already implemented some simple remote control features that allow basic two-way communication among the local and remote participants, but true remote control will require instrument modification and improved Internet communication speed and methods, possibly through fiber optic connections.

Several areas need to be addressed to make full use of telepresence microscopy. All researchers using the system were concerned about security issues, i.e., how secure the WWW communication is from other competing or inquisitive parties. Live-time performance dramatically increases the pressure on the microanalysts, and we must develop new analytical approaches to answer these new demands for immediate results and interpretation. Similarly, the need for live-time quality assurance, uncertainty determinations, and statistical evaluation, and possibly even review of NIST results, is a new requirement that will take further research to determine good solutions. Telepresence microscopy may be considered the analytical analogy of "just-in-time" manufacturing and moves microanalysis into a new age of high efficiency, speed, and rapid communication, truly a new paradigm for problem solving and information transfer.

8. Complexities in Chemical State Identification by Low Energy X-ray Emission Spectroscopy

J.T. Armstrong

Objective: To determine the extent to which low energy x-ray emission spectroscopy using wavelength dispersive spectrometers on electron micro-beam instruments can be used to determine the chemical state (elemental valences and bonding environments) of analyzed micro-volumes.

Problem: The ability to obtain *in-situ* chemical information from individual micro-particles and micro-inclusions has a variety of important commercial applications in materials science ranging from defect and failure analysis of composite materials and semiconductor devices to characterization of fine-grained intergrowths in high-temperature superconductors. Although one can perform accurate *elemental* analysis of such specimens using conventional electron and ion microprobes, *chemical* data obtainable with these techniques are usually limited to deductions that can be made based on the relative proportions of different elemental species present. A number of investigators have proposed use of low energy x-ray emission spectroscopy, obtained with conventional electron micro-beam instruments, as a means of determining oxidation state and other chemical bonding information. In particular, numerous papers have been published proposing that line energies, peak shapes and relative intensities of the L_α and L_β lines of the first row transition elements vary systematically with oxidation state. However, the results reported in these papers are not consistent, and in most cases had not considered the effects of self-absorption due to the LIII edge energy occurring between the L_α and L_β lines. These problems have prevented low energy x-ray spectroscopy from being utilized for chemical state determination routinely.

Approach: High-precision measurements were made of the x-ray line energies, x-ray peak shapes and relative x-ray intensities for the L_α and L_β series spectra of Mn, Fe, Ni, Cu, Zn, and Ge in the pure elements and in a variety of metal alloys, oxides, sulfides and silicates. The data were collected using conventional wavelength dispersive detectors on two commercial electron microprobes. Extensive replicate measurements on standards were conducted to insure that the measured peak energies, shapes, and intensities were not affected by instrumental artifacts. The data were processed using the NIST DTSA spectral analyzer program to determine relative intensities of overlapping lines. Intensity data were corrected for differences in the excitation energy, absorption, and fluorescence of the L_α and L_β lines using Monte Carlo calculations and NIST/Caltech 'CITZAF' correction algorithms. Data were collected at more than one beam energy to test for the self-consistency of these corrections.

Results and Future Plans: The measurements showed that most published conclusions regarding the interpretability of soft x-ray spectra in unambiguously determining the specimen's chemical state are overly optimistic or simply in error. Significant variations in the peak energies and shapes of the L-series lines were observed in many cases from compound to compound, but systematic variations with oxidation state were not observed. Contrary to what was proposed in many publications in the literature, measured variations in the L_α/L_β for transition elements in different compounds cannot unambiguously be ascribed to differences in the oxidation state. Some compounds, e.g., FeS, Fe_3O_4, Fe_2SiO_4, NiO, ZnO, show significant increases in L_α/L_β ratio over the pure metal that are not explained by differential self-absorption, others do not, e.g., FeS_2, Ni_2S, CuS, $YBa_2Cu_3O_{6.85}$, GeO_2. No simple rules governed the presence or absence or magnitudes of these effects. In cases where spectral variations occur, comparison of standard spectra to an unknown could be made to determine whether an element is present in a particular chemical environment. As is done in Auger electron spectroscopy and x-ray photoelectron spectroscopy, libraries of standard spectra could be collected and used for comparison. With the high lateral resolution and variable depth ranges obtainable by electron microscopy, such library comparisons could be used for many valuable applications. We plan to continue our systematic measurements of L_α - L_β spectra of the first row transition elements at multiple accelerating potentials as a bases for such a reference data set. In addition, similar measurements for low energy K and M lines will be made.

9. A New Approach to Determine the Structure of Quasicrystals.

__T. Jach__, Y. Zhang and R. Colella (Purdue Univ.), M. de Boissieu and M. Boudard (Univ. of Grenoble, France), S. Thurgate (Murdoch Univ., Perth, Australia), A. I. Goldman, T. Lograsso, and D. Delaney (DoE Ames Lab and Iowa State Univ.), and S. Kycia (Cornell Univ.)

Objective: To determine the crystal structure symmetry of quasicrystals.

Problem: Quasicrystals are novel, highly ordered materials, which are nonetheless aperiodic. Discovered at NIST in 1984, they are typically binary or ternary metal alloys that show x-ray diffraction patterns with symmetries that were thought to be impossible. After many years of study, atomic maps have been proposed that reproduce many of the diffraction spot intensities that are observed. However, because there are an infinite number of diffraction peaks (and no unit cell!) for these materials, diffraction intensities by themselves may not be able to verify the positions or underlying correlations of specific elements.

Approach: We have undertaken a new approach of studying quasicrystals using x-ray standing waves. High quality specimens of certain quasicrystals, such as AlPdMn, have been grown which exhibit the diffraction behavior normally seen only in defect-free periodic crystals. The behavior includes very narrow diffraction peaks and a distinct interference inside the material between the incident and diffracted x-ray wave fields. By looking at characteristic x-ray fluorescence radiation coming out of the quasicrystal during diffraction, it is possible to determine how the specific elements correlate with the periodic waves set up by the conditions of the diffraction.

The measurements require intense, highly monochromatic radiation at relatively low x-ray energies (2-5 keV). Fortunately, one of the few good sources of this radiation is the X-24A beamline, supported by NIST groups in MSEL, Physics, and CSTL, and operated by CSTL at the National Synchrotron Light Source, Brookhaven National Laboratory. All of the data has been obtained there. The work is collaborative with Iowa State University, which grows the quasicrystals, Purdue University, where they are characterized, and the University of Grenoble, which is active in the theory of quasicrystals.

Results and Future Plans: Our approach has allowed us to determine some surprising results. The atoms of specific elements in the quasicrystal can be highly correlated over thousands of atoms even though the material is aperiodic. While many theoretical models have been based on structure that is statistically centrosymmetric, our data indicate that different elements show correlations that are not consistent with centrosymmetry. We are able to make direct comparisons between theoretical models and the standing wave measurements that provide adjustments to the models.

Further measurements along different reflections that represent different symmetry axes will lead to a better three-dimensional understanding of the surface chemistry of quasicrystals. A collaborative effort using a combination of surface analysis methods (LEED, Auger) with diffraction and x-ray standing waves at the European Synchrotron Radiation Facility (ESRF) is being planned.

10. The Detection of Low Intensity Peaks in Energy Dispersive X-Ray Spectra from Particles

J.A. Small

Objective: To evaluate computer-based peak-finding algorithms used to detect and identify x-ray peaks.

Problem: A critical step in the processing of energy dispersive (EDS) x-ray spectra from the automated scanning electron microscopy (ASEM) analysis of particles is the detection and identification of elemental peaks. Since there are often several hundred to several thousand spectra for each ASEM analysis, it is important that this step operate rapidly and with a minimum of interaction between the analyst and the program. This requires that the algorithm for finding and identifying peaks be robust, *i.e.* minimize the number of false positives and negatives. For peaks with large peak-to-background (P/B) ratios (greater than 0.5), most peak-finding or peak-fitting methods perform adequately, even when the spectra have low signal-to-noise (S/N) ratios (less than 5.0). The detection of peaks with small P/B ratios (less than 0.34) is much more problematical. Peak identification and fitting procedures may not work well on low intensity peaks particularly in spectra with low S/N ratios.

Approach: In this study, three procedures for identifying x-ray peaks, with small P/B ratios and varying S/N ratios, were evaluated. The first method was to have human analysts look at the individual x-ray spectra and identify which ones contained the low-level peaks. The results from the human analysts were then used to establish a benchmark for the performance of the computer-based procedures. The second method included computer procedures based on the qualitative identification/analysis methods common on most commercial x-ray analyzer systems. These methods use digital filtration of the spectra to remove the spectral background and noise. In this study, the qualitative procedures from three manufacturer's systems were compared. The third method was a quantitative analysis procedure that employs a multiple-linear-least-squares (MLSQ) peak-fitting routine to separate the x-ray peaks from the background and noise. For this study, we measured the intensity of Fe Kα x-rays from glass particles 1-10 μm in size. The particles were made from two glasses with similar compositions except one contained 0.007 wt.% Fe (used to evaluate false negatives) and the other contained no Fe (used to evaluate false positives). The P/B ratio for the 0.007 wt.% Fe is 0.34. X-ray spectra were collected from particles for live times of 15, 60, and 200 s which correspond to average S/N ratios for Fe of 4.5, 9.2, and 17.1 respectively. These counting times were selected to span a range of spectrum quality. Many of the Fe peaks were marginally detectable in the 15 s spectra and easily detected in the 200 s spectra.

Results and Future Plans: At the lowest S/N ratio only 1 of the 6 human analysts met the benchmark for false positives (13 out of 35 analyses) and false negatives (0 out of 35 analyses) while none of the computer-based procedures were successful. Three of the remaining analysts, one of the three qualitative methods, and the quantitative procedure, met the benchmark for false negatives but not for false positives. For the 60 s data with a S/N ratio of 9.2 and a benchmark of 0 false positives and negatives, 5 of the 6 analysts, and the quantitative procedure met the benchmark. A wide variation in the performance of the different qualitative methods was observed and is related to the width of the digital filter used to suppress the spectral background and noise. The qualitative method with the fewest false negatives, was the one with the widest filter width. As a result, this method was the most sensitive in finding the small broad peaks that were common in the spectra with the lowest S/N ratio. This method also had the highest number of false positives that actually increased for the spectra with the higher S/N ratios. The results show that for finding low-intensity peaks, the quantitative analysis procedure performed as well as the best human analysts and better than the qualitative procedures. This, coupled with the ability to evaluate whether an element is missed in the residual plots from the MLSQ fit, makes the quantitative method the most robust for the analysis of ASEM data sets. The results also indicate that increasing the S/N ratio above 9.0, significantly improves the reliability of the different peak-finding procedures. During this next year, we plan to incorporate a MLSQ fitting procedure into our ASEM analysis software and to test it against various ASEM data sets.

11. High-Resolution TEM of a Microporous Material with Potential Industrial Applications

***S. Turner** and P.R. Buseck (Arizona State University)*

Objective: To characterize defects in a manganese oxide microporous material using high-resolution transmission electron microscopy (TEM) and computer simulation.

Problem: The manganese oxide material todorokite consists of interconnected manganese-oxygen octahedra that form tunnels or channels resembling those found in the zeolites. Both todorokite and the zeolites are categorized as microporous structures - structures containing open channels less than two nanometers wide. Zeolites have found extensive industrial applications, in particular as catalysts and molecular sieves. There has been considerable interest in the potential industrial applications of todorokite. In the past five years, the physical and chemical properties of the material have been intensively studied - including thermal stability, surface area, redox properties, electrical resistivity and efficiency at photocatalysis. The studies performed thus far have not considered the effect of microstructure on the bulk properties of the material. The goal of this work has been to characterize defects in todorokite.

Approach: Naturally-occurring samples from several localities were studied. The most intensively studied sample was from Charco Redondo, Cuba. Most samples were prepared by grinding and deposition on a TEM grid. Fibrous samples were prepared by cross sectioning and ion milling perpendicular to the tunnel direction. Images were simulated from atomic models of the structures and defects using commercial software.

Results and Future Plans: Initial study of the material shows that defects are prevalent in naturally-occurring todorokite viewed down and across the tunnel direction. Samples viewed across the tunnel direction showed cooperative terminations of octahedral chains forming the sides of tunnel structures. In most cases the termination was gradual indicating that the termination occurs at an angle to the electron beam direction. In one todorokite grain, the termination was abrupt,

Figure 1, indicating a termination parallel to the beam direction. An atomic model for this termination was developed and an image simulated from this model. A comparison of the experimental and simulated images shows good agreement. Similarly, defects in the todorokite viewed down the tunnel direction were imaged. An image simulated from an atomic model of one defect was a good match to the experimental image.

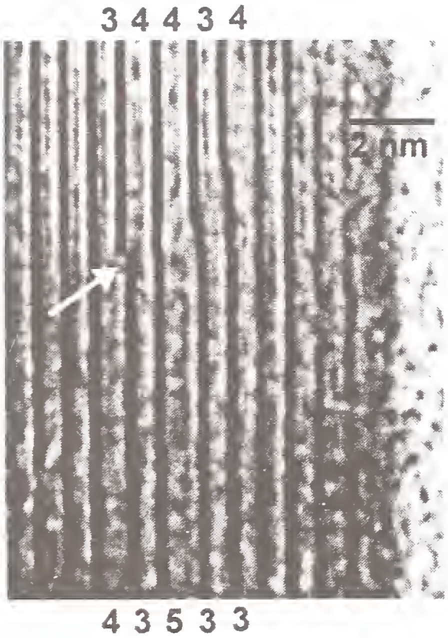


Figure 1. High-resolution TEM image of todorokite viewed perpendicular to the tunnel direction. Numbers refer to number of octahedral chains. The arrow indicates a termination of an octahedral chain

Such defects likely affect the physical and chemical properties of todorokite. Further effort is needed to more fully characterize the defects. Use of more sophisticated simulation software is planned along with further acquisition of high-resolution TEM images. The understanding of the types of defects that occur in todorokite will aid in the understanding of defects in other manganese-oxide microporous materials such as hollandite, romanechite and manganite.

12. Real-time Monitoring of the Nucleation and Growth of Tin Oxide CVD Films on Silicon Micro-devices

S.A. Wight, M.J. Nystrom (836), and R.E. Cavicchi (836)

Objective: To observe in real time the nucleation and growth of thin films of tin oxide by chemical vapor deposition onto micromachined silicon devices.

Problem: Metal oxide thin film conductance sensors[1] are an emerging technology for the measurement of gas concentrations in mixed atmospheres. The gas sensing properties of these materials are dictated by the microstructure of the polycrystalline films. Typically, films grown by chemical vapor deposition (CVD) are characterized after growth by removing them from the CVD reactor and investigating the morphology and chemical composition of the film in an electron microscope. This process is disruptive and time consuming for monitoring the morphological or chemical progress of film growth. An *in-situ* method of monitoring the film growth was needed.

Approach: The environmental scanning electron microscope (ESEM) is unique in that its chamber does not operate at high vacuum. The low vacuum specimen chamber can be operated with a user defined gas at a designated pressure. The pressure range 133-2660 Pa (1-20 Torr) is compatible with the pressures used in a CVD reactor. We used the ESEM chamber as a low-pressure CVD reactor while simultaneously collecting ESEM images of the film nucleation and growth. We modified the ESEM to allow for the introduction of tetramethyl tin and oxygen, required for tin oxide deposition, and implemented electrical feed-throughs and vacuum compatible chip sockets for operation of the micro-hotplate. The resulting system has the capability for *in-situ* monitoring of thin film nucleation, coalescence, and growth by both secondary electron and backscatter electron imaging techniques.

Results and Future Plans: The system has been used for a variety of process conditions. Evaluation of the film growth process consists of simultaneous measurement of the film electrical conductance and sequential image collection. Images clearly show contrast between two micro-hotplates (Figure 1) in the CVD environment in which one element is heated and growth occurs on the heated surface, while a neighboring element remains at room temperature. Micro-hotplates that have been seeded with platinum, prior to growth, have large grain growth with clearly observed facets.

Figure 1. Device before (left) and after (right) *in situ* tin oxide growth by CVD in the ESEM

We have investigated the possibility of electron beam effects on the growth. High resolution images using the field emission gun scanning electron microscope, show no difference between the morphology of the portion of the films that were grown under the rastered region of the ESEM and the portion outside the rastered region. The beam does, however, produce transient changes in conductivity in the growing film as revealed by periodic structure in the conductivity growth curves that are synchronized with the image collection period. Modifications to the ESEM to allow for a dry pumping method (sorption pumps) have been implemented. This should reduce the incorporation of carbon that influences the grain size of the resulting tin oxide film. An unexpected benefit of the research is that we discovered mechanical stresses in the micro-hotplate structures. The images record the initial formation and widening of cracks in the top oxide layer as the device is operated at 450 °C. These results are important for improving the reliability of the device platform.

Publication:

Cavicchi, R.E., et al., Appl. Phys. Lett. 66(1995) 812.

13. *Mesoscale Optics of Gold Nanoparticles Probed with Near-Field Scanning Optical Microscopy*

L.J. Richter, ***S.J. Stranick,*** *and R.R. Cavanagh*

Objective: To explore the feasibility of using size selected Au nanoparticles as characterization artifacts for near-field optical microscopes.

Problem: The near-field optical microscope (NSOM), which combines scanned probe technologies with optical contrast mechanisms, holds the promise of molecular contrast at high spatial resolution. Unfortunately, the interpretation of NSOM images is fraught with difficulty, as the signal arises from a complex interplay of optical and topographic sources. Improved theories and characterization artifacts are needed.

Approach: Simultaneous shear-force AFM, transmission NSOM and reflection NSOM images were obtained for a series of samples, consisting of various coverages of size selected Au nanoparticles on a glass substrate, with diameters ranging from 15 nm to 150 nm. The well-known scattering properties of small metal spheres should provide a good test of near-field probe models.

Results and Future Plans: Shown in Figure 1 are simultaneously recorded topographic (a) and transmission (b) NSOM images from a sample consisting of 100 nm Au nanoparticles. In the field-of-view are both isolated particles, and clusters. A striking feature in the optical image is the 'wave' structure, centered on the Au nanoparticles. The wave has a spatial period of ½ the probe wavelength (488 nm), suggesting that it is a

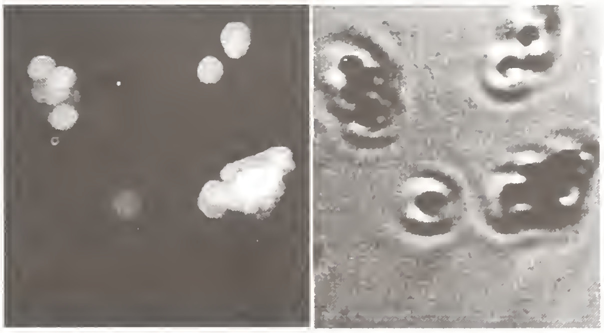


Figure 1(a) Figure 1(b)

standing wave, arising from the coherent interaction of light scattered by the Au nanoparticle with light 'backscattered' from the NSOM tip.

The hypothesized origin of the wave is supported by numerical calculations shown in Figure 2. In the calculation, both the Au scatter and the Al cladding of the near-field tip are modeled by point polarizable dipoles, with polarizabilities derived from the Clausius-Mosotti relationship. The initial aperture fields are treated as a dipole source at tip center. Given the simplicity of the model, the agreement with Figure 1 is remarkable.

The waves are a manifestation of 'middle-field' effects in NSOM. They conclusively demonstrate that one must account for the entire tip structure when modeling near-field optics, and not treat them as simple diffraction apertures. The large polarizability of the tip structure, apparent in these measurements, suggests that optimal tip designs may lead to local-field enhanced spectroscopies, such as Raman. We are actively pursuing such tip designs.

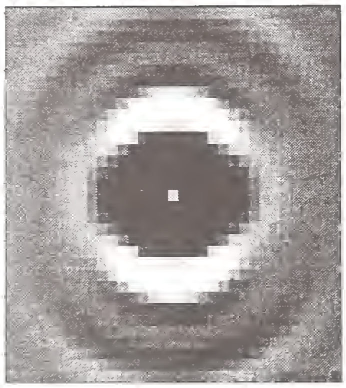


Figure 2

14. *Strain Effects in Heteroepitaxial Thin Film Growth and Reactions*

S.W. Robey

Objective: To identify the influence of strain on epitaxy and surface morphology in the growth and reaction of oxide and metal films on GaAs.

Problem: Heteroepitaxial thin-film growth - growth of a thin film on a dissimilar substrate - is prevalent in a wide range of technologies including semiconductor electronics, chemical catalysis, optoelectronics, etc. Finding solutions to the problems inherent in heteroepitaxy, i.e., chemical reactions, lattice mismatch induced strain, is an important issue in any technology that attempts to combine the functionality of disparate materials. Success of a given device architecture often hinges on issues of growth morphology that is governed by surface energy, interfacial reaction, and crystalline compatibility. Strain in a thin film, due to crystalline lattice mismatch, can drastically influence growth energetics and kinetics, producing undesirable surface morphologies and misfit-accommodating dislocations. These act as device-killing recombination sites in semiconductor LED's and lasers. However, strain can also lead to a variety of interesting and potentially useful effects including the formation of coherent one-dimensional and two-dimensional nano-scale 'dots' and 'wires', and self-organization of these structures into ordered arrays.

Approach: Various aspects of heteroepitaxial growth of oxide and metallic layers on GaAs were investigated using *in-situ* electron diffraction (Reflection High Energy Electron Diffraction) and spectroscopic (Auger spectroscopy) techniques to provide structural and chemical information on interfacial reaction products and growth morphology. These techniques were supplemented with Atomic Force Microscopy (AFM) to provide real-space imaging of surface morphology at the nanometer scale. Of particular interest were effects due to strain.

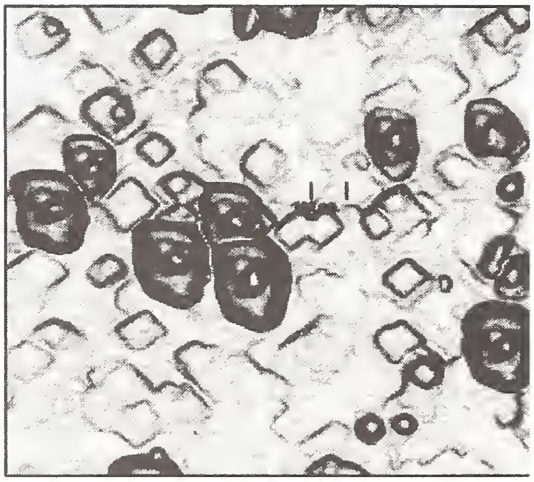


Figure 1. MgO Film Growth on GaAs Substrate

Results and Future Plans: MgO growth on GaAs holds promise as a potential buffer layer to allow integration of GaAs device capabilities with oxide materials, e.g., $BaTiO_3$ and $LiNbO_3$, resulting in interesting ferroelectric or electro-optical properties. Due to strong reaction, these materials cannot be grown directly on GaAs. *In-situ* growth studies indicated that reactivity issues can be overcome in the case of MgO growth on GaAs. However, AFM studies show that the large lattice mismatch between the two materials leads to a rough surface morphology as the growing film relaxes strain by developing a 3-dimensional growth mode and nucleating large, strain-relieving, misoriented grains as shown in Figure 1. This morphology is highly undesirable, particularly for optical applications.

Mg reaction with GaAs was investigated both to understand the role of this reaction in the growth of MgO and as a potential ohmic contact to GaAs. The reaction produces an epitaxial overlayer with a cubic structure but a lattice constant about 9% larger than the underlying GaAs. The formation of two-dimensional, wire-like structures was observed by AFM when thin films of Mg were annealed to drive the reaction. Detailed studies of the growth characteristics of these structures again implicated strain in producing this novel growth mode. Strain induces the formation of 3D structures that can relieve some strain elastically. These structures grow to a critical size, ~ 40 nm wide and 4 nm high. At this size the accumulated strain triggers anisotropic relaxation processes that initiate rapid growth along the GaAs [110] direction. Future work on these systems is planned to investigate interesting magnetic or optical properties that may result from this nanoscale structure.

15. Breathing Mode Excitation in Near Harmonic Systems: From Laser-cooled Atoms in Optical Lattices to Molecules Adsorbed on Solid Surfaces

J.W. Gadzuk

Objective: To provide useful theoretical models with predictive power that describe the quantum dynamics of driven atomic systems within the natural vibrational timescale of laser-cooled and trapped atoms and/or chemically bound adsorbed molecules.

Problem: Real time observation and control of transient quantum motion in chemical systems is the holy grail whose pursuit drives a large component of the chemical physics world in all sectors (academic and government) of the research community. Theoretical modeling of the fundamental atomic and molecular processes occurring in a controlled chemical reaction, particularly at solid surfaces, is the area of concern here.

Approach: This work has been inspired by a number of ideas involving some gedanken experiments. These were sequentially conceived in a progression moving from femtochemistry to breathing-mode-excitation in resonant neutron-capture-processes to a special realization of electron stimulated desorption, all in confluence with some beautiful real-world experiments from the Phillips' group (PL) at NIST involving ultra-cold atoms trapped in optical lattices. These examples have as a common theme the excitation of quantum mechanically localized atoms by some form of transient wave packet squeezing and spreading. The observable consequences of such compression include bound vibrational oscillations or free translational motion associated with bond breaking, as manifest by delocalization/desorption. Analytic wave packet theory for these (up-to-now-unrelated) processes has been devised which constructively exploits the temporal scaleability of the near-harmonic systems under investigation, thus rendering irrelevant the fact that on an absolute time scale the vibrational period of the quantum oscillator in the optical lattice and in the adsorbed state differ by ten or more orders of magnitude. The motivation for focusing on this parallelism is to use recently obtained ultra-cold atom experimental results as a confirmation of the basic theory which, now verified, can be temporally scaled down to the domain of surface femtochemistry and used there with confidence.

Results and Future Plans: Striking experimental observations of oscillatory wave packet spreading and compression (i.e., breathing mode excitation) were made using time-resolved Bragg scattering from Cs atoms in the partially occupied optical lattice, upon suddenly switching the oscillator force constant, hence frequency. (A similar change in frequency would occur in the gedanken neutron capture process due to the sudden switch of oscillator mass!) Our theoretical wave packet results such as the mean-square wave packet width as a function of time, shown in Figure 1, reproduce well, without adjustable parameters, most aspects of the experimental results such as the observed oscillatory amplitude, the observed anharmonic dephasing decay, and the correct revival period. Gaining this independent confirmation of the model, the theory can now be applied to the original chemical physics problems which initiated this inquiry and will be pursued in future investigations.

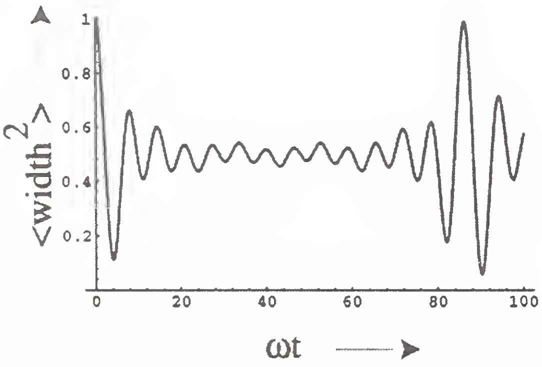


Figure 1. Normalized width of breathing mode wave packet (=> excited Cs atom trapped at optical lattice site) as a function of time after excitation (multiplied by the lattice atom oscillator frequency)

16. Solving Problems in Semiconductor Device Processing

*L.M. **Struck**, J.A. Small, E.B. Steel, D.S. Simons, P.H. Chi, A.F. Myers, E.S. Windsor, and J.R. Whetstone (836)*

Objectives: To solve problems in deep submicrometer CMOS process technology by utilizing multidisciplinary diagnostic tools.

Problem: A collaborative effort has been established between scientists in CSTL and the Microelectronics Laboratory at M.I.T. Lincoln Laboratory to solve problems in deep submicrometer CMOS process technology affecting the maximum operating frequency of individual logic elements. Signal propagation times anticipated at the 0.15 to 0.2 μm size level were not being realized. This effort utilizes multidisciplinary diagnostic tools and scientific expertise available in the Surface and Microanalysis Science Division (837) and the Process Measurements Division (836) to investigate processing issues. The M.I.T. Lincoln Laboratory group fabricates deep submicrometer silicon-on-insulator (SOI) CMOS devices with the goal of developing advanced processing technology. The combination of the expertise of the two groups allows more direct identification of problems encountered in deep submicrometer CMOS manufacturing process development efforts.

Approach: The approach was to characterize actual devices and blanket films of the material of interest that were processed by the same procedure as in the device. The analytical techniques that we have used to investigate various properties of the devices or thin films have included scanning electron microscopy (SEM), Secondary Ion Mass Spectrometry (SIMS) depth-profiling measurements, and Transmission Electron Microscopy (TEM).

Results and Future Plans: The image in Figure 1 shows the cross section of an individual transistor that was obtained using a Field Emission SEM. The contrast for this image was improved by etching the device in dilute HF. The etch rate is different for different materials and even within the same material, areas having more defects will etch preferentially. The image shows the layers used in forming the transistor in its gate-drain region. These are:

(a) silicon wafer substrate,
(b) buried silicon oxide,
(c) cobalt silicide layer to the right,
(d) top layer of silicon oxide,
(e) silicon channel to the left,
(f) polysilicon gate, and
(g) spacer oxide.

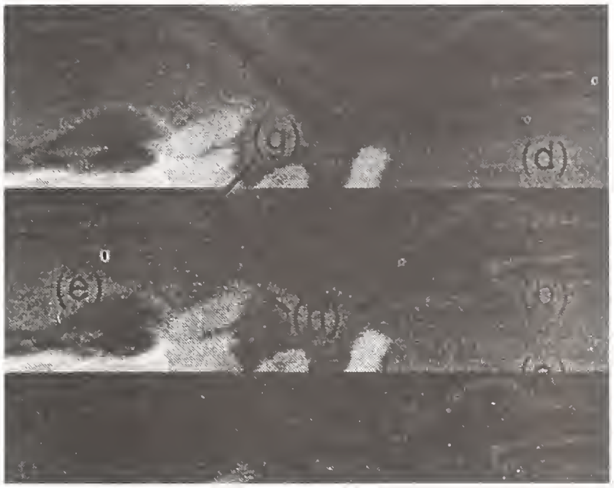


Figure 1. Field Emission SEM micrograph of a cleaved and etched cross section of the Gate region of a ~0.2 µm design rule CMOS transistor

Additionally, a void (h) was consistently seen between the cobalt silicide and the silicon channel in these devices. The poor performance of these devices may well be due to these voids or their precursors. Insights into other important aspects of the processing parameters have also been gained by characterizing the quality of areas of the transistor, e.g., the top layer of silicon oxide, the polysilicon gate, and the spacer oxide. In another series of experiments, degradation in device characteristics after thermal treatment was initially thought to be due to dopant redistribution. Three sets of n-doped and p-doped silicon wafers with $CoSi_2$ films were analyzed by SIMS to determine dopant depth profiles. The SIMS analyses concluded that there is no evidence of significant dopant redistribution as a function of heat treatment. We are currently investigating the effects of several processing parameters and steps (such as the use of a TiN capping layer) on the quality of titanium silicide film with high resolution transmission electron microscopy, selected area electron diffraction, scanning TEM, energy dispersive x-ray spectroscopy, and electron energy loss spectroscopy.

17. *Phosphor Imaging Plates for X-ray Microdiffraction*

***J.R. Verkouteren** and C.J. Zeissler*

Objective: To integrate an imaging plate (IP) in the x-ray microdiffractometer for use as an area detector. The advantages of a 2-D detector over a line detector are increased data collection and detection of preferred orientation.

Problem: X-ray microdiffraction is a tool to determine the crystalline phase(s) of micrometer-sized samples using powder x-ray diffraction. A problem inherent in microdiffraction is the potential for poor powder averaging due to insufficient numbers of crystallites. A problem common to all powder diffraction techniques is the potential for preferred orientation. Our microdiffractometer compensates for both problems by 3-axis rotation of the sample to improve the homogeneity of the Debye-Scherrer rings that are sampled in a linear fashion by a position-sensitive detector (PSD). The approach used in another commercially-available system is to hold the sample fixed, collect the data on an area detector, and integrate along the diffraction rings to achieve representative intensities. We think there are advantages to both approaches, and tested the feasibility of incorporating an area detection system into our current diffractometer.

Approach: An IP based on the photo-stimulable phosphor $BaFBr:Eu^{2+}$ was used as an x-ray area detector. The IP is a 20 x 25 cm flexible plate that is scanned after exposure to produce a digital image. The characteristics of the IP that make it superior to x-ray film have been documented previously, and include higher sensitivity, larger dynamic range, and digital data format. The IP is erased by exposure to light, and is reusable. There are options in scanning the IP that determine the resolution of the data, including pixel size (a minimum of 25 µm/pixel), dynamic range (a maximum of 10^5), and image depth (8 or 16 bits). These parameters can be varied and the IP rescanned without significant degradation of the signal to determine the most efficient settings. Samples were prepared for microdiffraction analysis and the IP was placed over the PSD and exposed for 30 minutes. The sample goniometer was restricted to single axis movement due to geometric constraints.

Results and Future Plans: The integration of the IP in the microdiffractometer was a success in terms of providing significant information that was not available using the PSD. An image collected on the IP from a 30 µm ZrO_2 particle is shown in Figure 1 and the approximate location and sampling area of the PSD is indicated. Using the single-axis rotation and a much longer collection time (3 hours), no diffraction pattern was recorded by the PSD. An image collected on the IP of the same particle in a fixed position showed fewer than 10 discrete spots. A combination of approaches (sample rotation and area detection) seems to be ideal. Additional information from the IP image includes sources of background radiation (uneven background gray level indicates fluorescence of the beam stop) and differences in particle sizes for the monoclinic *versus* the tetragonal+cubic phases. Future work involves quantitative analysis of the imaging plate data.

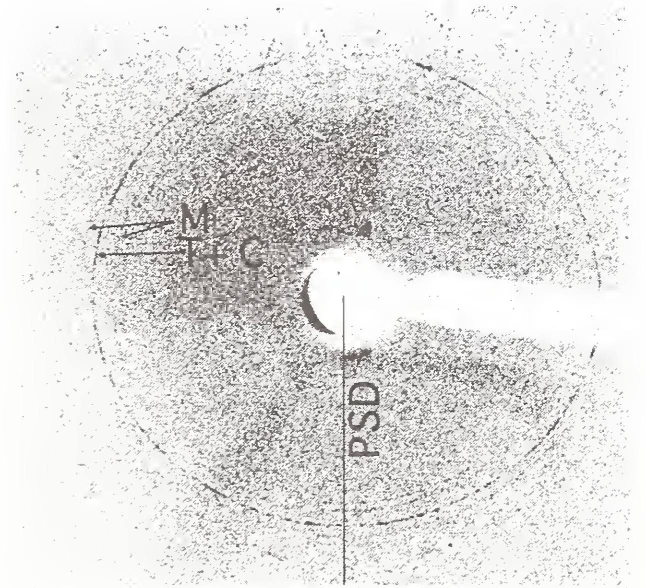


Figure 1. IP image of monoclinic (M) and tetragonal + cubic (T + C) reflections for 30 µm ZrO_2 particle

18. Development of Radioactivity Speciation Method Using Autoradiography and Microscopy

C.J. Zeissler, S.A. Wight, and R.M. Lindstrom (839)

Objective: To expand conventional radionuclide speciation to nondestructive chemical analyses of individual microscopic particles that contain low levels of alpha, beta, and gamma-emitting radionuclides. The method accommodates single- to multi-particle analyses, from microgram to supergram quantities of heterogeneous samples such as dust and soil, with an emphasis on those with low radioactivity signal-to-noise ratios.

Problem: The determination of the chemical form of radioactivity present in samples (speciation) is commonly approached by destructive wet chemical methods leading to an averaged bulk sample measurement. However, it is sometimes desirable to retain the isotopic, chemical, size, and morphologic information from individual particles. Discrete particle information can be used to understand the environmental behavior of radionuclides, to aid in the development of appropriate remediation methods, elucidate radioactivity contamination events, and assist the development of other analytical methods that can be used to distinguish multiple isotopic populations from identical chemistries. Until recently, other non-destructive radionuclide speciation methods existed, but were often limited to very small sample volumes (e.g., microscopy constraints), or involved tedious and relatively insensitive methods (e.g., film autoradiography limitations).

Approach: Only since early 1996 has one key component of this analytical approach become available, a commercial instrument designed for a different purpose, that of digital large-format medical autoradiography. The laser-scanned phosphor technology used by this instrument is more sensitive and has larger dynamic range than photographic film, and has a two-fold improvement in spatial resolution over earlier, but otherwise similar, technologies. The quantum signal efficiency and point-source performance characteristics are being studied and integrated with measurements produced by other recent advances in microanalysis, such as environmental scanning electron microscopy. This enables discrete particle characterization from even super-gram quantities of soil or dust. Crucial to realizing this capability are developments in signal discrimination and particle isolation methods that allow sample exchange between energy-dispersive x-ray spectrometry (EDS) and autoradiography.

Results and Future Plans: Radioactive particles have been detected, isolated, and chemically analyzed from three test samples using this new technique. Examples include the detection and chemical characterization of a 0.01 ng ^{239}Pu particle from 3 g of Rocky Flats, Colorado soil, and sub-Bq level ^{152}Eu and ^{60}Co particles (Figure 1) from two activated dust samples. Cation oxidation states can sometimes be inferred from EDS data, but we plan to augment the results with other microanalytical methods to determine the crystallographic phases present, and therefore, the valence forms of the elements of interest.

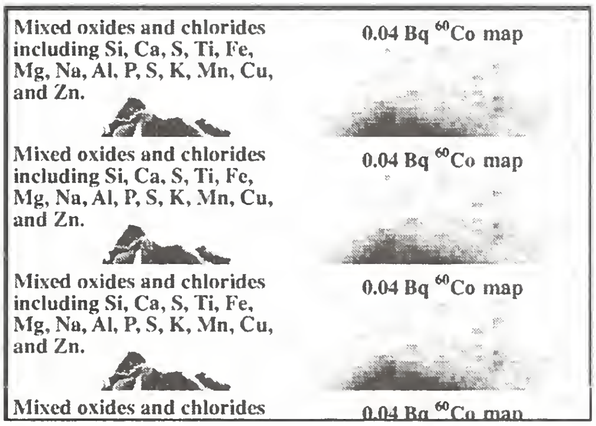


Figure 1. A mixed oxide/chloride particle containing ^{60}Co activity

Publications:

Simons, D.S., Gillen, G., Zeissler, C.J., Fleming, R.H., and McNitt, P.J., ***"Automated SIMS for Determining Isotopic Distributions in Particle Populations,"*** SIMS XI, Orlando, 1997.

Zeissler, C.J., ***"Comparison of Semiconductor Pixel Array, Phosphor Plate, and Track-Etch Detectors for Alpha Autoradiography,"*** Nucl. Instrum. Meth. Phys. Res. A392 (1997) 249-253.

Zeissler, C.J., Wight, S.A., and Lindstrom, R.M., ***"Detection and Characterization of Radioactive Particles,"*** accepted for publication by Applied Radiation and Isotopes, 1998.

19. *Second Depth Profile Standard Produced - SRM 2134: Arsenic Implant in Silicon for Calibration of Secondary Ion Mass Spectrometry*

***D.S.** Simons, R.M. Lindstrom (839) and W.F. Guthrie (898)*

Objective: To develop a Standard Reference Material for calibration of arsenic concentration in silicon by secondary ion mass spectrometry (SIMS) based on ion implantation of arsenic in silicon.

Problem: The U.S. semiconductor industry increasingly relies on SIMS for measurement of dopant concentrations of boron, arsenic, and phosphorus in silicon. The *repeatability* of these measurements has improved to the point that daily variation of no more than a few percent are possible when the measurement process is carefully controlled. The uncertainty of measured doses or concentrations is usually dominated by the uncertainty in the known doses of the reference samples required for SIMS calibration. In the past, individual laboratories used their own in-house reference materials (RMs) because certified reference materials (CRMs) were unavailable. The demand for ion-implanted CRMs to support the semiconductor industry has increased recently for several reasons, among them the pressure for analytical laboratories to obtain ISO 9000 certification. NIST issued a boron-10 implant in silicon in 1993 as the first ion-implanted Standard Reference Material, SRM 2137, with the boron dose certified by neutron depth profiling. An arsenic implant in silicon was the next obvious candidate for certification based on the prioritization of the SEMATECH Analytical Laboratory Managers Working Group. However, a technically feasible certification method needed to be identified, and a source of high quality implanted material needed to be obtained.

Approach: In 1995, Charles Magee of Evans East organized a round robin exercise to measure the implanted dose of arsenic in silicon by SIMS. A major ion implanter manufacturer supplied three 200-mm diameter wafers that had been implanted in the same batch with arsenic at an energy of 100 keV. An additional wafer from the batch had been annealed and subjected to sheet resistance mapping to check the uniformity of the implant, which had an impressive relative standard deviation (RSD) of 0.17%. One of the wafers was diced and distributed to 12 participating laboratories. The doses, measured by SIMS based on in-house RMs, showed a maximum variation of nearly a factor of 10, although the typical RSD for repeat measurements was less than 5%. The round-robin results provided additional justification for producing a SRM. The organizer donated the remaining two high quality implanted silicon wafers as source material. Each wafer could provide 221 SRM units of 1 cm x 1 cm, enough for an estimated 10-year supply. Instrumental neutron activation analysis (INAA) was identified as a viable certification method for the arsenic dose. It was estimated that less than 1% relative measurement uncertainty could be attained from the ~90 ng of arsenic in one SRM unit. One of the remaining wafers was diced into 1 cm x 1 cm pieces with a wafer saw. For the INAA measurements, 10 test pieces were selected for even coverage of the wafer surface. Two silicon blanks and two independent arsenic solution standards deposited on filter papers were included in the irradiation stack. The INAA measurements showed a RSD of 0.4% among the 10 analytical specimens. The resulting certified arsenic dose value is 7.27×10^{14} atoms/cm^2, with an expanded uncertainty of 7.69×10^{12} atoms/cm^2. The arsenic depth distribution was determined by SIMS with cerium ion bombardment and negative ion detection.

Results and Future Plans: This reference material, designated SRM 2134, is expected to be available early in 1998. Its relatively rapid certification compared with boron implant SRM 2137 can be attributed to the use of a state-of-the-art implanter, the availability of an established certification method, and the larger size of the silicon wafers that permitted the entire certified lot to be taken from a single wafer. Future plans call for the investigation of possible certification methods for a phosphorus implant in silicon.

20. Repeatability of Si Concentration Measurements in GaN Films by SIMS

***P.H. Chi**, D.S. Simons, A.E. Wickenden (NRL), and D.D. Koleske (NRL)*

Objective: To develop the measurement protocol for Si dopant concentration in GaN thin films repeatably through careful control of measurement parameters such as sample chamber pressure, type of sample holders, and the energy distribution of the measured species.

Problem: Concentration measurements of Si in GaN measured by secondary ion mass spectrometry (SIMS) must be made at high mass resolution to discriminate against interference from CO and N_2. In high mass resolution measurements, the secondary ion intensity ratio of the $^{28}Si^-$ signal to the matrix $^{69}Ga^-$ signal had poor repeatability. In some cases the $^{69}Ga^-$ signals from adjacent windows of a sample holder showed large intensity variations (a factor of two) even though the $^{28}Si^-$ signal intensities were similar. The relative sensitivity factor (RSF) method of quantification is based on the ratio of dopant to matrix signals. Variation of the $^{69}Ga^-$ matrix signal from run to run produces an unacceptable uncertainty in measuring the Si concentration in a GaN film when the RSF method is used.

Approach: The changes in $^{69}Ga^-$ intensity from repeated measurements were suspected to be affected by the sample chamber vacuum condition, ion energy distribution, and type of sample holder used in the measurement. In routine depth profiling, profiles are normally taken after the sample chamber pressure has reached 1.3×10^{-4} Pa, which usually requires about 10 minutes of pumping time after sample introduction. By observing the correlation of the chamber pressure with the $^{69}Ga^-$ signal, we found that the Ga signal, but not the Si signal, was affected by the chamber pressure if it was above 1×10^{-5} Pa. The presence of oxygen on the sample surface is suspected of enhancing the Ga^- signal more strongly than the Si^- signal. The repeatability of Si concentration measurements was also expected to be influenced by the different energy distributions of Ga^- and Si^-. The Ga^- distribution is narrower than that of Si^- This can affect ion trajectories and collection efficiencies from different locations on a sample holder. A factor of two variation in Si/Ga ion ratio was observed for profiles of the same sample taken at center and edge positions of a holder.

Results and Future Plans: After the critical parameters that needed to be controlled were determined, the RSF from a ^{28}Si ion implant in GaN was measured 11 times by SIMS over a 5 month period. All measurements were made when the sample chamber pressure was below 1×10^{-5} Pa, and a single sample holder with a large rectangular hole in the Ta cover mask was used throughout the experiments to minimize possible ion trajectory variations. Si profiles were taken from the center of the hole at high mass resolution. The RSFs showed a relative standard deviation (RSD) of 13% over this period. For a uniformly Si-doped GaN film, the RSD of the RSFs was 8%. This level of repeatability now allows Si concentrations in GaN to be determined with much greater confidence than before.

Publications:

Chi, P.H., Simons, D.S., Wickenden, A.E., and Koleske, D.D., ***"Repeatability of Si Concentration Measurements in Si-doped GaN Films"***, J. Vac. Sci. Technol. **A15**, 2565 (1997).

21. Improved Vibrational Spectra of Phyllosilicate Minerals through Near-Infrared Excited FT-Raman Microspectroscopy.

E.S. Etz, D.A. McKeown (Howard Univ.), and M.I. Bell (Naval Research Laboratory)

Objective: To obtain improved vibrational spectra of natural silicate minerals, virtually free from interfering luminescence, through excitation of their Raman spectra in the near-infrared (NIR) with a Fourier-transform (FT) Raman spectrometer.

Problem: The vibrational behavior of natural silicates is central to our understanding of many geological processes, such as those governing the adsorption capacities of natural clays for the removal of environmental contaminants in soils. Raman spectroscopy plays a major role in the study of such minerals. The goal here is to obtain spectra devoid of interfering non-Raman signatures, allowing the vibrational analysis of a chosen mineral assemblage. Raman measurements of natural minerals are often degraded by substantial sample luminescence upon laser excitation. This has been a pervasive experimental problem in the common use of visible (VIS) Raman lasers for mineral studies. The advent of FT-Raman techniques employing excitation in the NIR opens up new horizons for recording Raman spectra of minerals virtually free from luminescence interferences.

As part of a larger study of phyllosilicates, we have focused on two representative members of this mineral class, phlogopite, $KMg_3(Si_3Al)O_{10}(OH,F)_2$, and muscovite, $KAl_2(Si_3Al)O_{10}(OH,F)_2$, to report their near-IR excited Raman spectra correlated with lattice dynamics calculations. The motivation is to provide vibrational assignments to the Raman spectra of these complex sheet silicates, which requires detailed spectroscopic information. Knowledge of the normal mode frequencies of these minerals is essential to predicting their perturbed mode frequencies that arise from adsorption and complex formation with interacting species.

Approach: Earlier Raman measurements on well-characterized specimens of both phlogopite and muscovite were carried out employing VIS (488.0 and 514.5 nm) excitation using a dispersive (non-FT) Raman system. These approaches produced only marginally useful spectra due to intrinsic laser-excited sample luminescence originating from trace level impurities. Examining the same mineral specimens in the FT-Raman instrument with 1064 nm excitation, both in macro- (bulk) and micro-measurements (~ 8 μm probe spot) provided high quality polarization-dependent spectra yielding normal mode frequencies that were readily correlated with crystallographic structure and lattice dynamics calculations.

Results and Future Plans: By using FT-Raman spectroscopy with NIR excitation to analyze these minerals, luminescence has been avoided, Figure 1, and some sample heterogeneity has been detected by the micro-sampling measurements. The FT-based technique, referenced to a He-Ne laser, has provided high-accuracy characteristic Raman frequencies. These results have led to a detailed vibrational analysis of these structures and new fundamental mode assignments. The spectra can serve as a basis for studying these minerals as perturbed structural entities due to complexation by either heavy metal ions or uptake of organic molecules from environmental pollutants.

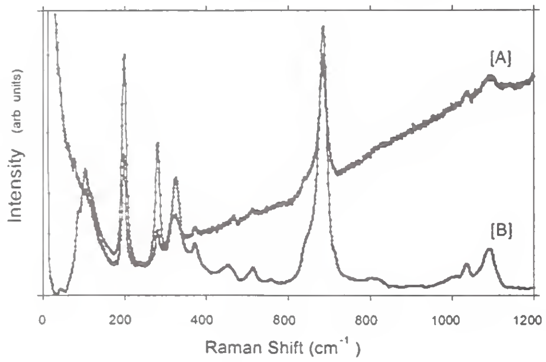


Figure 1. The micro-Raman spectra of mineral phlogopite: (A) Dispersive Raman, 514.5 nm excitation (with sample luminescence); (B) FT-Raman, 1064 nm excitation (no sample luminescence)

22. *Elemental and Molecular Imaging of Species in Human Hair Using SIMS*

J.G. Gillen and S.J. Roberson

Objective: To develop procedures for spatially resolving organic and elemental species in cross-section and on the surface of human hair using secondary ion mass spectrometry (SIMS).

Problem: The elemental composition of human hair can be used as a unique source of information about the biomedical and environmental history of an individual. Elemental hair analysis has been used for examining environmental exposure, studying the nutritional status of the body, helping to diagnose certain diseases and evaluating the incorporation of heavy metals. Organic characterization of hair is of current interest because human hair can serve as a long term (months, years) monitor for drug use as opposed to the hours-to-days type of information obtained from blood or urine analyses. Many of the analytical techniques that have been applied to the analysis of hair are bulk techniques that give limited spatially resolved information. However, there is a growing need, particularly in the personal care product industry, to develop analytical methods that provide spatially resolved elemental and molecular surface analysis of biological materials such as hair and skin. Analyses of these non-planar, non-conductive samples present several analytical challenges for SIMS. Because hair is not conductive, experimental conditions must be used that minimize or compensate for charge build-up during the analysis. Preparation procedures for surface and cross-sectional analysis must preserve elemental and molecular surface information while minimizing contamination and redistribution of analytes.

Approach: For analysis of hair surfaces, individual hairs are placed onto conductive silver tape substrates. For cross-sectional analysis, a variety of procedures are used depending on the information required. To minimize charge build up during analysis, the SIMS instrument is operated in two different modes. For detection of species that produce positive secondary ions, the sample is analyzed with a ~0.5 µm diameter, 15.0 keV O^- microbeam with no auxiliary electron bombardment. For detection of species that form negative secondary ions, an ~0.2 µm diameter, 10.0 keV Cs^+ microbeam is used with normal incidence, low energy electron bombardment.

Results and Future Plans: Figure 1 shows a SIMS image of the surface of a human hair. In this example (in collaboration with a personal care product company), we have mapped the dimethicone distribution, an ingredient in shampoo formulations. Figure 2 shows a typical cross-sectional image of a human hair that was treated with a solution of fluorinated cocaine. In this example, the SIMS signal for fluorine was used to map the penetration of the cocaine into the hair sample. This information may be useful for characterizing procedures for preparing standards for drugs of abuse in hair. Our future work involves continuing to apply the SIMS imaging technique to address analytical issues of interest to various pharmaceutical and personal care product companies. At the same time we are continuing to work on improving the technique. One area that appears to be quite promising is the use of negatively charged *molecular* primary ion beams for analysis. Our preliminary work has indicated that this approach may improve our analytical sensitivity by several orders of magnitude while minimizing charge build-up.

Figure 1. Distribution of dimethicone on the surface of a human hair

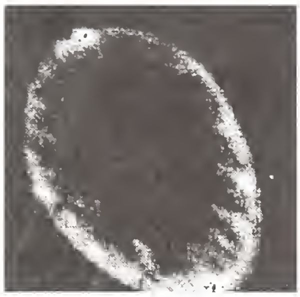


Figure 2. Human hair cross-section showing distribution of fluorinated cocaine

V. Physical and Chemical Properties Division (838)

Richard F. Kayser, Chief

A. Division Overview

Mission:

The Physical and Chemical Properties Division is the Nation's reference laboratory for measurements, standards, data, and models for:

- the thermophysical and thermochemical properties of gases, liquids, and solids – both pure materials and mixtures
- the rates and mechanisms of chemical reactions in the gas and liquid phases
- fluid-based physical processes and systems, including separations, low-temperature refrigeration, and low-temperature heat transfer and flow.

The Division provides technical research and services, Standard Reference Data, Standard Reference Materials, and calibrations to promote U.S. economic growth and to assist U.S. industry, other government agencies, and academia in solving problems of national importance.

Functions:

In the areas of thermophysics, thermochemistry, and kinetics, the Division

- develops, maintains, and uses state-of-the-art apparatus to perform experimental measurements on industrially and scientifically important systems
- compiles, evaluates, and correlates experimental data
- develops and evaluates state-of-the-art theories, models, estimation methods, and computational approaches
- disseminates results by a wide variety of mechanisms

In the area of cryogenic technologies, the Division provides engineering data, models, and research to support the development of advanced cryocoolers, and measurement methods, standards, and services for flow under cryogenic conditions.

Current Focus Areas:

Current focus areas include *Basic Reference Data and Computational Techniques, Data for Process and Product Design, Properties of Energy-Related Fluids, Environmental Fates of Industrial Chemicals, Tools for Chemical Analysis, Fundamental Studies of Fluids, and Cryogenic Technologies.* Brief descriptions of these areas follow, with references to selected Technical Highlights (see next section).

Basic Reference Data and Computational Techniques: Physical, chemical, and kinetic data and models are important in research and development, process modeling, process design, energy efficiency, safety, health, transportation and storage, custody transfer, and the environment. Scientists and engineers require sufficient data for many substances to determine parameters in commonly used models, to develop new and improved estimation methods and models, and to evaluate and intercompare estimation methods, models, and computational techniques. The principal components of this program are:

- to compile, evaluate, and disseminate data and predictive methods for chemical species and systems of broad interest to a large number of diverse users
- to develop, apply, and assess computational approaches for acquiring such data

During 1997, the Division initiated a new program in quantum chemistry focused on developing resources to aid industrial scientists and engineers in the computation of molecular properties. These resources will include:

- critical comparisons of computational results with the best available experimental data,
- interactive guidance for the non-expert on methods, reliability, and resource requirements,
- a searchable repository where scientists may submit or extract the results of standard calculations

For additional information on *Basic Reference Data and Computational Techniques,* see Technical Highlights 1-6 and 31.

Data for Process and Product Design: Process and product design in a wide variety of industries depends on the availability of high-quality physical and chemical properties data and models. The availability of such information has played a key role in the emergence of process simulators as a key enabling technology in the chemical and related industries. Large-scale process modeling and simulation is also growing in importance in areas such as semiconductor processing and the treatment of hazardous wastes. The Division's goal is to provide the underlying data and models needed to support such developments. Areas of current interest include:

- semiconductor processing
- chemical and materials processing
- separations
- advanced oxidation technologies
- combustion

For additional information, see Technical Highlights 7-12.

Properties of Energy-Related Fluids: Industry requires accurate and comprehensive equilibrium and transport properties data and models for energy-related fluids in several key areas, including the design and optimization of working cycles in refrigeration systems and power plants; the design, control, and optimization of gas processes; and custody transfer. Efforts in this area include the development of experimental apparatus, the acquisition of needed data, and the development and dissemination of high-accuracy correlations. Fluids under study include:

- alternatives to ozone-depleting chlorofluorocarbons and hydrochlorofluorocarbons for use in air-conditioning and refrigeration systems
- alternatives to steam for use in power cycles, e.g., ammonia-water mixtures
- noble gas mixtures for use in thermoacoustic refrigerators
- natural gas systems

During 1997, the Division developed plans to expand its experimental and modeling research on the properties of natural gas systems. Major goals of the program are to develop the means to accurately model and predict the thermodynamic, phase equilibrium, and transport properties of natural gas, liquefied natural gas (LNG), natural gas liquids (NGLs), substitute/synthetic natural gas (SNG), compressed natural gas (CNG), and wet, dry, and sour gases. For additional information on *Properties of Energy-Related Fluids*, see Technical Highlights 13-16.

Environmental Fates of Industrial Chemicals: A wide variety of physical, chemical, interfacial, and kinetic data and data prediction methods are essential to understand and assess the long-term fates of new and existing chemicals in the atmosphere and in ground water. Properties of interest include amospheric lifetimes, aqueous solubilities, ion-exchange equilibria, and partition coefficients. Current efforts are focusing on:

- the atmospheric chemistry and lifetimes of alternative refrigerants, alternative fire suppressants, and oxygenated fuel additives
- the thermodynamics and kinetics of selected species in aqueous solution

During 1997, the Division initiated a multi-year program on thermodynamic properties for environmental fate and risk analysis, with the principal emphasis on heavy-metal-containing species and the common ions with which these species come into contact in aqueous environments. This program will comprise:

- an assessment and analysis of the state of the literature regarding selected species and properties
- the development of needed experimental capabilities
- the acquisition of experimental data to fill gaps and resolve discrepancies in the data
- the development of comprehensive models for the thermodynamic properties of "key substances"
- the construction of a data-handling system to manage the resulting network of thermodynamic information in a thermodynamically consistent manner

For additional information, see Technical Highlights 17-18.

Tools for Chemical Analysis: The analysis of simple and complex mixtures and the identification of individual chemicals are tasks central to many aspects of the chemical and related industries, including research and development, production, and quality assurance and control. These tasks are also crucial in environmental monitoring, medical research, and health care. In this area, the Division strives to produce critically evaluated data, predictive models, and software to assist in the analysis and identification of as wide a range of species as possible. Areas of current emphasis include:

- mass spectral (MS) data and databases
- gas chromatographic (GC) data and databases
- infrared data and databases
- tools for automatically deconvoluting and analyzing GC/MS data files

In the latter area, the Division is working with the U.S. Defense Special Weapons Agency, the Organization for the Prevention of Chemical Weapons, and others to develop software for use in on-site inspections under the Chemical Weapons Convention. For additional information, see Technical Highlights 19-20.

Fundamental Studies of Fluids: The goals of this program are to develop and use unique experimental, theoretical, and simulational capabilities to study fluid systems under equilibrium and non-equilibrium conditions, with and without chemical reactions. Topics under investigation include:

- the effects of shear on the microscopic structure of colloids, gels, micelles, and emulsions and on the dynamics of processes such as coagulation, gelation, and association
- the behavior of the viscosity of a pure fluid very close to its critical point in microgravity
- hydrogen bonding in water and related systems
- fluid-solid phase transitions
- new primary standards for temperature and pressure

For additional information, see Technical Highlights 21-26.

Cryogenic Technologies: Cryogenic technologies such as pulse-tube refrigerators underpin a wide variety of technically important areas. These areas include the cooling of electronics for high-speed computing and communications, the production of ultra-clean environments for semiconductor processing, the liquefaction of natural gas from remote gas wells and for use as a clean fuel, the cooling of medical instruments, and the cooling of satellite-based infrared sensors for military and environmental applications. Research in this program addresses all of these topics, with the primary focus on:

- the development of improved measurement and modeling techniques for characterizing basic cryocooler components and processes in the temperature range from 120 K to below 10 K
- collaborations with industry and others to support the development of cryocoolers for specific applications
- the measurement of cryogenic flows

During 1997, the Division initiated a new program in microscale heat transfer. The goal is to develop and validate models and correlations for predicting heat transfer between fluids and solids when the length or time scale over which the heat transfer takes place becomes very small. For additional information, see Technical Highlights 27-28.

Selected Technical Accomplishments:

- release of two major upgrades of the NIST Chemistry WebBook (see Technical Highlight 1) publication of evaluated proton affinity database and primary scale based on data for 1700+ species (2)
- new facility for measuring the thermophysical properties of gases used in semiconductor processing (7)
- revision of refrigerant properties in the 1997 ASHRAE Handbook of Fundamentals (13)
- measurement of retention parameters of selected hydrocarbons on selected stationary phases and incorporation of results into the database used by the natural gas industry to analyze the C_6+ fraction of natural gas (15)
- completion of adiabatic twin-cell calorimeter for performing high-accuracy measurements of isochoric heat capacity of compressed gases and liquids (16)
- first-ever demonstration of the use of cavity-ring-down technology for studying transient phenomena in condensed phases (18)
- measurement of the viscosity of xenon near its critical point with state-of-the-art accuracy in a microgravity environment (23)
- use of molecular dynamics to delineate different regimes of hydrogen bonding in water over wide ranges of conditions (24)
- acquisition of comprehensive data on the thermal conductances of stacked screens for optimizing the design of regenerative heat exchangers (27)

Selected Conferences and Workshops:

Major international conferences:

- Thirteenth Symposium on Thermophysical Properties, June 22-27, 1997, Boulder, CO (Technical Highlight 29)
- Fourth International Conference on Chemical Kinetics, July 14-18, 1997, Gaithersburg, MD (Technical Highlight 30)

Topical meetings:

- DIPPR Liaison Forum, November 11, 1996, Chicago, IL
- Special Topics in Statistical Mechanics – A Symposium in Honor of Raymond D. Mountain, April 10-11, 1997, Gaithersburg, MD
- Meeting of International Energy Agency Annex 18 on the Thermophysical Properties of the Alternative Refrigerants, June 20, 1997, Boulder, CO
- Meeting of IUPAC Subcommittee on Transport Properties, June 21-22, 1997, Boulder, CO

Organizational Structure:

The Physical and Chemical Properties Division has research groups in Gaithersburg, Maryland and Boulder, CO, with the equivalent of 35-40 full-time staff in each location. Dr. William M. Haynes directs the Boulder part of the Division. The structure and technical activities of the Division are as follows:

Division-Office Programs (Gaithersburg and Boulder)

- study the behavior of fluid systems under both equilibrium and non-equilibrium conditions using unique experimental, theoretical, and simulational capabilities

Process Separations Group (Boulder)

- performs basic and applied research on a variety of separation processes, including distillation, supercritical fluid extraction, adsorption, and membrane separations
- provides critically-evaluated data and models needed to design and/or select more efficient and robust separation processes

Fluid Science Group (Gaithersburg)

- develops and applies state-of-the-art techniques based on acoustics and other novel approaches for measuring the thermodynamic and transport properties of fluids and fluid mixtures, including refrigerants and semiconductor processing gases
- performs research on next-generation primary standards in the areas of temperature, pressure, and low flow rate

Experimental Kinetics and Thermodynamics Group (Gaithersburg)

- develops and uses state-of-the-art measurement techniques to determine the rates and mechanisms of chemical reactions in the gas and liquid phases and the thermodynamic properties of industrially and environmentally important chemical species and materials
- develops new measurement methods for detecting and characterizing reactive intermediates
- certifies Standard Reference Materials for thermodynamic properties important to industry and science

Chemical Reference Data and Modeling Group (Gaithersburg)

- develops and evaluates new theories, models, estimation methods, and computational techniques for thermodynamic properties and rate constants
- compiles, evaluates, correlates, and disseminates Standard Reference Data
- develops and disseminates electronic databases and software on thermodynamics, chemical kinetics, and analytical mass and infrared spectra

Experimental Properties of Fluids Group (Boulder)

- performs experimental research and develops and maintains high-accuracy apparatus for measuring the full complement of thermodynamic and transport properties of fluids and fluid mixtures over wide ranges of temperature, pressure, and composition
- provides comprehensive thermophysical property measurements for technically important pure fluids and mixtures, including common organics and inorganics, hydrocarbons, refrigerants, and aqueous systems

Theory and Modeling of Fluids Group (Boulder)

- performs theoretical and simulational research on the thermophysical properties of fluids and fluid mixtures, including regions of fluid-fluid and fluid-solid phase separation
- develops models and correlations of high accuracy to describe and predict the thermophysical properties of fluids and fluid mixtures

- provides comprehensive and evaluated Standard Reference Data and electronic databases for the properties of technically important fluids and fluid mixtures

Cryogenic Technologies Group (Boulder)

- develops improved measurement and modeling techniques for characterizing basic cryocooler components and processes
- develops state-of-the-art cryocoolers for specific applications
- provides measurement methods, standards, and services for flow under cryogenic conditions

Staff Recognition for Fiscal Year 1997

- Richard F. Kayser, Senior Executive Service Presidential Rank Award for Meritorious Service
- Jan V. Sengers, Election to Fellow of the American Society of Mechanical Engineers for outstanding contributions to the field of thermophysical properties of fluids and fluid mixtures

B. Selected Technical Reports

1. *The NIST WebBook - NIST Chemical Reference Data for Industry*

W.G. Mallard, *P.J. Linstrom, J.F. Liebman (UMBC), H. Affefy (UMBC), and P.J. Christian*

Objective: To provide Internet access to a complete set of chemical data with a common interface that provides both ease of use and a simple method to expand as more data become available.

Problem: There is an enormous amount of organic thermochemical data (heats of formation, entropies, heat capacities, heats of reaction) that are largely unknown to the technical community. One part of this project is to find and evaluate those data. In addition, there is a need to make available ancillary thermochemical data such as phase-change enthalpies. Data on infrared (IR) spectra, mass spectra, and other analytical techniques are also important resources that are often difficult to find. For all of the data it is essential that tools be provided to make the data easy to access.

Approach: The rapid growth of the World Wide Web has been widely remarked upon. The most enthusiastic appraisal of the future of the Web is unrealistic, but it is clear that the Web has dramatically changed the way that science is done. The use of the Web as a publishing medium and as a resource for communication has been growing rapidly. What has not followed is the development of data resources for the Web. The WebBook is an effort to correct this. The WebBook will provide a quick and direct source of data available at all times. The initial efforts are tied to an approach based on compounds rather than properties. All the data on benzene, for example, are gathered together, rather than all the data on heat of combustion. While the major thrust of the WebBook is to supply data from NIST evaluations, the role of the WebBook in providing a resource for chemical data from all sources will expand. In parallel with the efforts to gather and evaluate data, another major part of this project is aimed at providing the mechanisms needed to make these and other NIST chemical reference data available on the Internet. These efforts are part of NIST's program on Systems Integration for Manufacturing Applications (SIMA).

Results and Future Plans: During FY97, the second and third editions of the NIST Chemistry WebBook* were released. The original data set, which included a number of estimated values, was edited to include only experimental data. The total number of compounds for which data was provided more than doubled in the second release (from 11,000 to 22,300 compounds) and was further increased in the third release (to 27,300 compounds). In addition, a number of new types of data were added. In the second release, data were added on vapor pressure, infrared spectra, and mass spectra. Data for vapor pressure as a function of temperature were added for over 1500 compounds in the form of Antoine coefficients. In addition, far more extensive data were provided for phase-transition enthalpy, including data for the temperature dependence of the enthalpy for a selected set of compounds. The third release included high accuracy thermophysical properties data for thirteen important industrial fluids. For these fluids, the WebBook allows the user to calculate selected properties along an isotherm, an isobar, or the saturation line (as either a function of temperature or pressure). In addition, an extensive set of data was added on negative ion energetics. The WebBook has been extremely well received, as demonstrated by the number and variety of users from industry, government, and academia. Both the number of users (5000 per week) and the number of repeat users (1800 per week) have continued to grow steadily. The WebBook is also a tool to aid future evaluation projects, both at NIST and in collaborations with others. A long-term goal is to provide a single point of entry for access to all chemical data at NIST.

*http://WebBook.nist.gov

2. *Evaluated Proton Affinity Database*

E.P. Hunter and S.G. Lias

Objective: To develop an evaluated proton affinity database for use in determining the thermochemistry of ions and ionic clusters.

Problem: The energy associated with ionizing a molecule can sometimes be determined to very high accuracy. However, for the majority of molecules, especially radicals, this is difficult at best.

Approach: Rather than measuring the enthalpy of formation of ionic species, it is generally easier to measure the difference between the energy of one species and another. The resulting energy differences can be formed into a thermochemical "ladder". Absolute thermochemical values can then be obtained by referring all of these differences, either directly or indirectly, to a relatively small number of molecules that together constitute a primary thermochemical scale. Great care is taken to ensure that the thermochemical values assigned to these primary molecules are consistent with absolute values that have been determined for the individual molecules and with differences that have been determined for pairs of molecules.

Results and Future Plans: The data from 1700+ compounds contained in 500+ references have been analyzed and evaluated. Discrepancies have been identified and, where possible, resolved. For the first time it has been possible to rely on some computational results to resolve experimental uncertainties. While in principal the experimental data are simple, in practice the level of detail needed to understand which of the multiple experiments are correct has meant that this work was a far more extensive undertaking than originally envisioned.

The results of the work have been submitted for publication in the Journal of Physical and Chemical Reference Data. In addition, they have been made available in the NIST WebBook (see Technical Highlight 1). It is anticipated that the use of this electronic medium will allow rapid feedback on any remaining points of controversy. Evaluations such as this are important in providing useful points of reference for future work. By providing all of the data in a single source and pointing out the remaining areas of disagreement, they allow for a refocusing of experimental and theoretical efforts.

The role of computation in the future of ion energetics has also been clearly established by this work. The computational results were essential in the effort to develop a consistent set of values that could be used as a primary scale. Future work will require that larger scale computations be attempted to establish reference values for larger molecules.

Publication:

Hunter, E.P.L. and Lias, S.G., ***"Evaluated Gas Phase Basicities and Proton Affinities of Molecules: An Update,"*** J. Phys. Chem. Ref. Data (in press).

3. *Reference Thermodynamic Formulations for Pure Fluids and Mixtures*

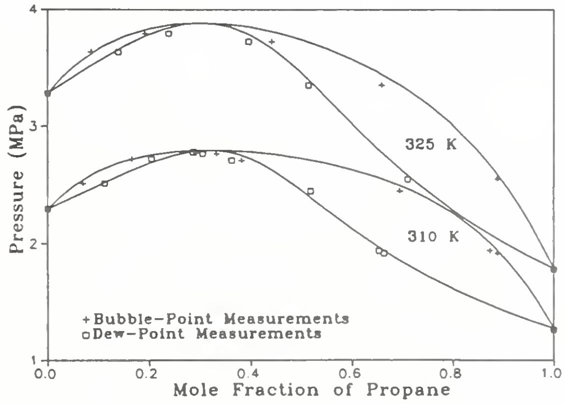
***E.W. Lemmon**, M.L. Huber, M.O. McLinden, J.C. Rainwater, A.H. Harvey, D.G. Friend, and S.L. Outcalt*

Objective: To develop reference thermodynamic surfaces for selected pure fluids and mixtures for calculating properties within the experimental uncertainties of measured data over large ranges of temperature, pressure, and composition.

Problem: The thermodynamic properties of fluid systems are required in numerous industrial applications. In particular, accurate property information is needed for the working fluids used by such industries as power generation and refrigeration for design and operation of their technologies. Custody transfer considerations demand such data for commodity chemicals and energy-related fluids including natural gases. Finally, such reference quality information is needed in the development of more broadly applicable engineering formulations and in a variety of calibration applications. In these and other areas, NIST provides the infrastructure for the Nation's thermodynamic property needs.

Approach: The systems chosen for study are determined by our customer's stated and anticipated needs, and generally fall into such classes as refrigeration fluids, cryogens, and natural gas systems, and are re-prioritized every few years based on industrial feedback. The general data infrastructure at NIST also demands that certain systems be described to fill important gaps and to serve as a basis for the predictive models used for less well-characterized systems. The models are usually in the form of Helmholtz energy equations, which allow calculation of all thermodynamic properties in the fluid phases in a consistent manner, and which are based on fundamental statistical mechanics, on empirical use of available data, and on advances in statistical correlation techniques. This work is coordinated with the experimental efforts of the Division.

Results and Future Plans: In conjunction with collaborators from Germany, a new thermodynamic formulation for nitrogen has been developed based on a structural optimization algorithm, that provides a dramatic reduction in the uncertainties associated with the NIST cryogenic flow calibration facility. A reference equation was completed for the refrigerant R143a (CF_3CH_3). Several other important refrigerants, as well as systems such as toluene and alcohols, are under study. (Our general program on refrigerants and work on the ammonia-water binary system are described in Technical Highlights 13 and 14, respectively.)



A mixture model, based on a corresponding states algorithm for the excess Helmholtz energy and reference quality formulations for the constituents, has been developed. This model has undergone testing as part of our commitment to the International Energy Agency in its study of mixtures containing R32 (CH_2F_2), R125 (CF_3CHF_2), and R134a (CF_3CH_2F), and forms the core of the thermodynamic modeling capability in NIST Refprop. The figure shows the model's extension to the calculation of phase behavior for propane + R32 mixtures.

Publications:

Lemmon, E.W. and Jacobsen, R.T., ***"A Generalized Model for the Thermodynamic Properties of Mixtures,"*** Int. J. Thermophys. (in press).

Outcalt, S.L. and McLinden, M.O., ***"An Equation of State for the Thermodynamic Properties of R143a (1,1,1-trifluoroethane),"*** Int. J. Thermophys. (in press).

4. *Transport Property Models for Fluids*

***D.G. Friend**, R.A. Perkins, M.L. Huber, M.O. McLinden, E.W. Lemmon, A. Laesecke, J.C. Rainwater, and S. Kiselev (Inst. Oil and Gas Res., Russia)*

Objective: To establish models to evaluate the viscosity and thermal conductivity of a variety of important pure fluids and mixtures to within uncertainties required by the relevant user community.

Problem: The viscosity and thermal conductivity of fluids and fluid mixtures are required in many engineering applications including those related to the refrigeration, petroleum, and natural gas industries. In addition to direct applications, reference quality formulations are used in the calibration of commercial instruments used to measure these properties. In certain contexts, transport properties can be used to ascertain stream composition, extent of reactions, product quality, etc., and, in other cases, they may be primary process design parameters. The data and modeling infrastructure provided by NIST promotes design innovation and optimization for industrial and commercial applications.

Approach: The transport property models developed at NIST are most easily transferred to our customers through standard reference databases such as NIST Refprop (see Technical Highlight 13) and NIST SUPERTRAPP, but they are also disseminated through traditional publications and our activities in various standards organizations. The models begin with an understanding of basic kinetic theory applied at the molecular level, incorporate empiricism based on conventional statistical approaches when necessary, and may involve significant approximations to account for poorly characterized constituents, multiparticle correlations, mixing effects, internal degrees of freedom, etc. This activity is very closely tied to the experimental measurements of viscosity and thermal conductivity conducted in the Division.

Results and Future Plans: An extension of our transport property extended corresponding states (ECS) model has enabled us to undertake the significant challenge of calculating the transport properties of petroleum fractions, which may contain literally hundreds of components and which are only characterized by a few key parameters which can be easily determined. This new model is described in a forthcoming publication, and will be incorporated in a version of a database to be available from NIST. In the course of this work, a new reference fluid formulation for the viscosity of propane was required and a preliminary version has been developed. Reference quality equations were also developed for the transport properties of R134a (CF_3CH_2F) (as the basis for refrigerant calculations), as well as the thermal conductivity of propane and toluene (a calibration fluid) and viscosity of n-pentane (a calibration fluid). Studies of additional key pure fluids are underway, including a major improvement to our calculations of the viscosity and thermal conductivity of pure water.

Work has been completed on an extension to the ECS model for viscosity that yields a significant improvement in our ability to calculate this property for the refrigerants. Similar work is underway for the thermal conductivity. This approach will also be applied to natural gas systems. Finally, we have developed a new approach to provide accurate values for the transport properties of air at extreme temperatures and pressures as part of a project associated with advanced wind tunnel designs.

Publications:

Baltatu, M.E., Chong, R.A., Huber, M.L., and Laesecke, A., ***"Transport Properties of Petroleum Fractions,"*** Int. J. Thermophysics (in press).

Klein, S.A., McLinden, M.O., and Laesecke, A., ***"An Improved Extended Corresponding States Method for Estimation of Viscosity of Pure Refrigerants and Mixtures,"*** Int. J. Refrig. 20, 108 (1997).

5. Critical Evaluation of Chemical Kinetics Data - New Tools and Old Problems

W. Tsang, *R.F. Hampson, V.I. Babushok (Guest Researcher), W.G. Mallard, D.H. Frizzell, J.J. Reed, F. Westley (Contractor), Y.A. Mirokhin (Guest Researcher), J.T. Herron (Contractor), and C-Y Lin (Contractor)*

Objectives: To collect and evaluate data on the rates of gas phase chemical reactions needed for modeling natural and industrial processes; to develop new calculational tools for evaluating data on pressure-dependent rate constants.

Problem: Understanding complex chemical processes – such as those that occur in the atmosphere, a furnace or a chemical vapor deposition reactor – often requires a detailed model of the chemical changes that are occurring. To create such a model, one requires a rate for each reaction in the system, usually as a function of temperature. While much of this information exists, it is often fragmentary and difficult to find. In addition, older analyses of experiments have often proven to be incomplete and the resulting rate constants reported incorrect. In addition to the collection and evaluation of temperature-dependent rate constants, efforts are also needed to understand the dependence on pressure.

Approach: There are several components of this work. First, the technical literature is routinely searched and all publications presenting data on the rates of chemical reactions are retrieved, and data relevant to on-going evaluation projects are abstracted for use by evaluators. Second, the data are compared to other similar systems, and when possible, models of complex systems are developed and compared to experimental results. The resulting kinetic parameters are examined to determine trends in reactivity and associated bond energies implied by the kinetic parameters. Comparisons of these results with theoretical calculations are made. The results of these studies are published in the literature and distributed as electronic data sets. One of the most important methods of making the data available is via the Chemical Kinetics Database for use on personal computers. Version 6.0 of this database, released in 1995, contains data relating to 8800+ reactant pairs.

Results and Future Plans: Production of a Windows version of the basic chemical kinetics software and entry system is progressing, and a Windows version of the Chemical Kinetics Database will be available in early FY98. In addition, a new set of tools for the analysis of complex unimolecular and recombination reactions has been developed. The analysis of data on these reactions has always been dependent on model calculations, the most common being the so-called RRKM model. The development of a detailed master-equation-based analysis of the thermal activation process of these complex systems has led to a better understanding of many recombination reactions for which there are multiple pathways. These reactions are especially difficult to model in cases in which radical recombination produces species that have sufficient energy to go into various other reactive channels as well as to return to the original products. The detailed solutions to these problems based on master equations have begun to yield predictive tools for these complex reactions. A long-range goal is to provide simple tools to allow the non-expert to perform pressure dependent calculations easily, perhaps as part of a single, integrated package.

Publications:

Tsang, W., Bedanov, V., and Zachariah, M.R., ***"Unimolecular Decomposition of Large Organic Radicals with Low Reaction Thresholds: Decomposition and Reversible Isomerization of n-Pentyl Radicals,"*** in Berichte der Busengesellschaft fur Physickalische Chemie (in press).

Atkinson, R., Baulch, D.L. Cox, R.A., Hampson, R.F., Kerr, J.A., Rossi, M.J., and Troe, J., ***"Evaluated Kinetic and Photochemical Data for Atmospheric Chemistry: Supplement VI – IUPAC Subcommittee on Gas Kinetic Data Evaluation for Atmospheric Chemistry,"*** J. Phys. Chem. Ref. Data (in press).

6. Ab Initio Prediction of Ionization Energies

R.D. Johnson III

Objective: To predict the ionization energies for important chemical species using modern methods of computational chemistry and to evaluate the methods for accuracy.

Problem: Many chemical properties can be related to the ionization energy of a molecule or radical, e.g., the electronegativity that correlates with chemical reactivity. The ionization energy can be problematic to measure, but is straightforward to calculate by *ab initio* methods. This is especially true for radicals. However, routine use of *ab initio* methods requires testing and validation to establish the accuracy and precision of predicted ionization potentials computed with a given method or level of theory.

Approach: *Ab initio* methods of quantum chemistry are powerful enough to generate ionization energies to better than 0.1 eV. The ionization energy is obtained by taking the difference between the calculated absolute energies of neutral and cationic species. The vibrational frequencies must be known or computed in order to obtain the correct zero point vibrational energy. The accuracy can be assessed by calculating the ionization energy of species with experimentally well determined ionization energies. Ongoing research is 1) exploring the accuracy of different levels of theory, and 2) exploring reaction schemes involving species with known ionization energies to improve accuracy by using calculated ionization energy differences in order to minimize systematic errors. This *ab initio* work is in collaboration with experimental work to determine ionization energies and thermochemical properties.

Results and Future Plans: Studies are underway on a series of stable fluorocarbon species, fluorocarbon radicals and species of atmospheric interest. The stability of simple perfluorocarbon cations had been questioned in the past, but ab initio calculations found them to be stable species. For example, the perfluoroethane cation has a C-C bond strength on the order of 90 kJ/mol, and perfluoropropane cation has a C-C bond strength on the order of 70 kJ/mol. Combined with calculated electron affinities the electronegativities have been calculated for a series of fluorocarbon radicals. This allows for the prediction of reactivities in organic reactions, where the fluorocarbon radicals are used as protecting groups. The ionization energy of HNO was calculated to compare with photoelectron experiments and establish a heat of formation for this molecule of atmospheric importance.

Publications:

Kuo, S., Zhang, Z., Ross, S.K., Klemm, R.B., Johnson, R.D., Monks, P.S., Thorn, R.P., and Stief, L.J., ***"Discharge Flow-Photoionization Mass Spectrometric Study of HNO: Photo-ionization Efficiency Spectrum and Ionization Energy and Proton Affinity of NO,"*** J. Phys. Chem. A101, 4035, 1997.

7. *Thermophysical Properties of Gases Used in Semiconductor Processing*

***J.J. Hurly**, K.A. Gillis, and M.R. Moldover*

Objective: To provide industry with high-accuracy data for modeling CVD (chemical vapor deposition) processes and for calibration of MFCs (mass flow controllers) used in semiconductor processing.

Problem: Many process gases are toxic, and/or corrosive, and/or pyrophoric. For such gases, measurements of their thermophysical properties are sparse and rarely accurate. Accurate thermophysical property data are required to model the hydrodynamics of the gas streams, i.e., the velocity and temperature profiles in the vicinity of the hot susceptor, together with the concentration and temperature gradients that evolve within the streams used in CVD processes. MFCs are used to deliver process gases (*e.g.*, Cl_2, HBr, BCl_3, WF_6) for CVD and for other processes (*e.g.,* plasma etching) throughout the semiconductor industry. Calibrated MFCs are needed to scale processes up from prototype to pilot plant and to production. The operation of MFCs depends upon heat transfer through the process gas; however, MFCs are sold based on calibrations for benign "surrogate" gases (such as N_2, CF_4, SF_6, and C_2F_6). Rationalization of this practice requires data for the density, heat capacity, thermal conductivity, and viscosity of the process gases as functions of temperature and pressure.

Approach: The Fluid Science Group will use acoustic techniques to measure the thermophysical properties of three classes of gases: 1) binary mixtures of CVD carrier gases with process gases, 2) pure process gases, and 3) surrogate gases. The Group will develop a comprehensive, reliable database for these gases that provides the heat capacity, thermal conductivity, viscosity, and the pressure-density-temperature relation for the gases and also diffusion coefficients for mixtures of the gases. The diffusion coefficient will be obtained from models for the intermolecular potentials between the carrier and the process gases.

Results and Future Plans: We have assembled and tested a facility in which acoustic techniques can be used safely for measuring the properties of these hard-to-handle gases. During the upcoming year, we shall measure speed of sound in the seven gases that were identified by the SEMATECH MFC Working Group as having the highest priority. They are the process gases Cl_2, HBr, BCl_3, WF_6, and the surrogate gases CF_4, SF_6, and C_2F_6. From the data, we shall obtain the ideal-gas heat capacity and the equations of state with uncertainties of approximately ±0.1%. Initially, the data will range from 0 C to 200 C and from 25 kPa to 400 kPa or 80% of the vapor pressure. The data will be extended to higher temperatures (until chemical instability becomes a problem) and transport property data will follow.

8. *Thermodynamic Data for the Industrial Application of Chemical Compounds*

***P.A.G. O'Hare** and D.R. Kirklin*

Objective: To obtain the basic thermodynamic data required for the industrial application of organic and inorganic materials.

Problem: Advances in the applications of many materials is limited by inaccurate or incomplete thermodynamic data. This can be particularly important in applications in which the phase of the material after processing determines key characteristics.

Approach: Fluorine and oxygen bomb calorimetric techniques are utilized to obtain the enthalpies of formation of the materials. This information is combined with data on the enthalpy increments to obtain a complete description of the thermodynamic properties of the material.

Results and Future Plans: During the past year, studies were completed on the fluorine-combustion calorimetry of several silicon compounds, including β-Si_3N_4. Future studies will be concentrated on the (boron + nitrogen) system, in which four distinct solid modifications have been identified. Those are amorphous, wurtzitic (formed at high pressures), hexagonal, and cubic. The cubic form has a hardness surpassed only by diamond but is superior to diamond in its high-temperature stability. Accordingly, cubic boron nitride has high potential for use in cutting tools. Some of the techniques utilized in depositing boron nitride may yield other forms, in addition to the cubic. Thus, it is important to understand the conditions under which only cubic BN will be produced. Unfortunately, the (boron + nitrogen) phase diagram is not well defined. Preliminary studies have shown that hexagonal and cubic boron nitride react with fluorine in our bomb calorimeter in a simple and straightforward way:

$$BN(cr) + (3/2)F_2(g) = BF_3(g) + (\tfrac{1}{2})N_2(g).$$

Because the standard enthalpy of formation of BF_3 is already well established, measurements of the energies of reaction will give the standard molar enthalpies of formation and, thus, a relative ranking of the stability of the different forms of BN. This information will provide a sound basis on which to construct a reliable phase diagram for the (boron + nitrogen) system to support technological applications.

Also during the past year, oxygen-combustion and differential-scanning calorimetric measurements were carried out on three structurally similar benzaldehydes: 1,4-benzenedicarboxaldehyde (terephthalaldehyde), 1,3-benzenedicarboxaldehyde (isophthalaldehyde), and 1,4- carboxybenzaldehyde. With the new data for the phthalaldehydes and the carboxybenzaldehydes, and data already available for the phthalic acids, estimations of the energetics of diacids, dialdehydes, and acid aldehydes are now possible.

Publications:

Kirklin, D.R. and Affefy, H.Y., ***"Enthalpy of Formation of 1,4-Benzenedicarboxaldehyde,"*** J. Chem. Eng. Data (in press).

Tomaszkiewicz, I., Hope, G.A., Beck. C.M., III. and O'Hare, P.A.G., ***"Thermodynamic Properties of Silicides. VI. Pentamolybdenum Trisilicide (Mo_5Si_3). Fluorine Combustion Calorimetric Determination of the Standard Molar Enthalpy of Formation at the Temperature 298.15 K,"*** J. Chem. Thermodynamics 29, 87 (1997).

O'Hare, P.A.G., Tomaszkiewicz, I., and Seifert, H.J., ***"The Standard Molar Enthalpy of Formation of β-Si_3N_4 by Combustion Calorimetry in Fluorine, and the Enthalpy of the α-to-β Transition at the Temperature 298.15 K,"*** J. Materials Res. (in press).

9. Measuring and Modeling Solute-Solvent Interactions in Supercritical and Subcritical Fluids

T.J. Bruno and A.F. Lagalante

Objective: To develop and test predictive models for solubilities of compounds in alternative solvents at supercritical, near-critical, and subcritical conditions using a combination of both physical and chemical variables as input into an empirical multivariate statistical model.

Problem: As a result of the Montreal Protoc many industrially important chlorinated solvents used in cleaning and extraction processes will become unavailable. The most important piece of thermophysical data to assess the feasibility of an extraction process is the solute-solvent phase equilibrium. Serious limitations exist in equation-of-state modeling approaches that use only physical properties of the solute and solvent to model supercritical and near-critical solute solubility.

Approach: Replacements for the chlorinated solvents are likely to come from fully or partially fluorinated alkanes, ethers, or ketones that possess negligible ozone depletion potential, as well as functionalized glycol ethers and siloxanes. Many of the fluorinated alternative solvents are gases under ambient conditions, and their thermophysical properties offer the promise of both conventional liquid extraction and the tunable solvent strength offered by near-critical and supercritical fluid extraction. In our approach, a given solution process is empirically modeled as the dependent variable in a multivariate statistical analysis. The independent variables to the multivariate statistical model include quantitative measurements of solute-solvent interactions and additional state-dependent terms. Solute-solvent interactions are quantified using the Kamlet-Taft solvatochromic chemical parameters. These parameters are empirically deter-mined values of three solvent-solute interactions: acidity, basicity, and dipolarity-polarizability. Work is in progress to significantly extend the Kamlet-Taft parameters to the fluorinated solvents in the subcritical and supercritical phases as well as the glycol ethers and siloxanes at ambient conditions. The resulting models will aid in the replacement of chlorinated solvents by making it possible to predict the solubility of industrially relevant compounds in alternative solvents.

Results and Future Plans: In recent years, we have designed and constructed numerous instruments for the quantitation of solubilities of solutes in subcritical and supercritical fluids. Solutes studied have ranged from classes of organometallic compounds (such as the metal ß-diketonates) to physiologically active natural products (ß-carotene, capsaicin). Recently, we have measured water-solvent partition coefficients for sets of organic solutes in fluorinated ethane solvents. The Kamlet-Taft parameters for the fluorinated ethane solvents have been measured using high-pressure equilibrium cells. Results show a constant basicity and density-dependent acidity and dipolaritypolarizability values over the gas-to-liquid density range. Kamlet-Taft parameters for the glycol ethers and siloxanes have been measured for both the pure compounds and aqueous solutions of the compounds. Based on the measured water-solvent partition coefficients and the measured Kamlet-Taft values for the fluorinated ethanes, a model was developed to predict the solute partition coefficients in 1,1,1-trifluoroethane and 1,1,1,2-tetrafluoroethane, as well as in carbon dioxide. In the future, we will model other types of equilibria, such as solubility and gas chromatographic retention times, in the alternative solvents. A predictive solubility model will suggest suitable alternative solvents and extraction conditions to substitute for an obsolete chlorinated solvent. Although initially the model will be tested using the pure fluorinated alternative solvents, we envision that the model can be applied to other classes of solvents as well as azeotropic mixtures of solvents.

Publication:

Lagalante, A.F. and Bruno, T.J., ***"Modeling of Water-Carbon Dioxide Partition Coefficients of Organic Solutes Using a Linear Solvation Energy Relationship,"*** J. Phys. Chem. A (in press).

10. Measurements and Database for Adsorptive Separations

T.J. Bruno, *J.E. Mayrath, H.J.M. Hanley, F. Tsvetkov (Daren Laboratories, Inc., Israel), and A. Lewandowska (Univ. Colorado)*

Objective: To provide basic data to facilitate the design of efficient and effective adsorptive separations for process and environmental applications.

Problem: Adsorptive separation techniques represent a versatile and selective family of methods that is especially applicable to dilute solutions. This is a concentration regime that is particularly problematical and costly for many industries, including chemical processing, energy, pharmaceuticals, and almost all phases of environmental remediation. As currently practiced, the design of adsorptive separations relies greatly on intuition. Adsorbents are customarily characterized in terms of surface area and pore size distributions, which are concepts that do not adequately account for the actual structures and attractive potentials that increase the concentrations of adsorbates on the surfaces of adsorbents. Moreover, thermodynamic properties (such as isotherms and enthalpies) measured on "standard adsorbents" cannot fully account for porosity and adsorptive capacities for other adsorbates, nor can such measurements account for properties at conditions differing from those of the standard measurements. This situation makes the rational design of adsorptive separations extremely complex.

Approach: This project consists of a data-oriented effort and an experimental measurement and modeling effort. The data work encompasses a literature review and critical evaluation of the literature focused on theory and measurements concerning adsorption from the gas phase on carbon, zeolites, and novel materials (polymers, urea, clathrates, etc.). Other physical property measurements of the adsorbents are correlated (where possible) with the customary or classical adsorption isotherms and areas and porosities. The current experimental effort concerns the enthalpy of adsorption of pollutants on unmodified clays (and clays modified with surfactants), and also the measurement of the skeletal density of adsorbents. We are using a chromatographic approach to measure the enthalpies, in which the clays (laponite, bentonite, montmorillonite, etc.) are deposited on glass spheres, which are then packed into columns. The temperature dependence of the specific retention volume provides the enthalphic information. The skeletal density apparatus consists of a microbalance enclosed in a vacuum chamber. Necessary gas manifolds allow the introduction of helium and other gases at known temperatures and pressures, and therefore, densities. One then measures the mass at several gas densities at several sample temperatures, ultimately yielding the adsorbent skeletal density.

Results and Future Plans: The results of the comprehensive literature search have been compiled into a 2000 entry database that is searchable by a variety of keyword approaches. Data are being added on an ongoing basis, after a critical evaluation is done. The results of the literature review have revealed that there are no recognized or *de facto* standard adsorbents suitable for characterization. Surface area and pore size distributions were found to be virtually meaningless for materials that were thought to provide material separation on the basis of size and/or shape. The skeletal density apparatus is fully operational and is now undergoing performance testing with a variety of carbonaceous materials and well-characterized synthetic adsorbents. Enthalpy of adsorption measurements have been completed for a large number of hydrocarbons and pollutant species on laponite clay, and on a laponite clay that had been modified by an organic surfactant. These data provide an insight into the relative strength of the adhesion of such pollutants on these common adsorbents. Correlations have emerged that relate structural features such as carbon number to the measured enthalpy. The measurements on the organic-modified laponite provide insight into the mechanism of pollutant adsorption and partitioning in real soil systems. In the next year, enthalpy of adsorption work on more highly branched hydrocarbons will be performed on both the modified and unmodified clay surfaces.

11. Measurements and Data for Membrane Separations

J. Pellegrino, M.R. Yetzbacher, J. Portnoy, T. Nguyen, B.R. Mattes (Los Alamos National Laboratory), and M. Guiver (National Research Council of Canada)

Objective: To develop improved quantitative structure/property prediction methods for polymeric membrane materials based on high quality measurements of sorption and transport of gases and vapors in several well-characterized systems and to compile property data on industrially-significant materials used for membrane-based separations.

Problem: Although polymeric materials are used in membrane and adsorptive separation processes, a significant barrier to the development of new materials and optimum use of existing materials is the lack of *a priori* predictive capabilities for the transport properties of mixtures in any selected polymer.

Approach: This program has a measurement and modeling component and a data component. Measurements of gas (and vapor) sorption and diffusion in polymers are critical for development of techniques to predict transport properties. These measurements provide a means to compile the effects of both chemical and structural subgroups in the polymer, and ultimately, to delineate rational design criteria for separations. Through our collaborations with Los Alamos National Laboratory and the National Research Council of Canada, we have access to materials whose chemistries can be varied in well-defined ways. In addition, the polymers under study (polysulfone, polyperfluorosulfonic acid, polytrimethylsilyl-propyne, and polyaniline) represent both commercial and cutting-edge materials. Improved processes for obtaining high purity oxygen and nitrogen from air, processing natural gas, recovering hydrogen from refinery streams, recovering and purifying olefin streams, and purifying water are examples of important industrial uses of membranes. The data component of this research program consists of the development of an Internet accessible database of polymeric material properties that are important for membrane separation design.

Results and Future Plans: Four (two fully automated) sorption apparatus (based on pressure decay methods) are currently in operation. During the past year, data have been obtained for determining the film density and sorption and diffusion coefficient for various permanent gases in the temperature range 293-308 K in polyaniline film doped with HF, and in the unmodified and silane-derivatized polysulfone base polymer. Also, refurbishment and recalibration of the multicomponent gas flow apparatus for measuring transport of gas and vapor mixtures through membranes were completed in preparation for designating it as a user test facility. An initial version of the membrane technology database, containing gas transport properties in hundreds of polymers, has been completed and is accessible internally via World-Wide-Web browser programs. A variety of software tools is still being developed to provide more complete querying capabilities and report generation. This work addresses a need within the chemical engineering community for comprehensive, critically evaluated information on separation membranes, and how these membranes interact with important chemical feedstock components. The current version of the database includes permeability, solubility, and diffusion coefficients; ideal and mixed gas separation factors; temperatures; primary reference; monomer repeat unit structure; and common names and abbreviations. Future work will expand the number of polymers and include additional solute interaction parameters of feed materials with the membrane materials. Membrane properties to be added include transition temperatures of membrane polymers, densities, and elastic moduli.

12. *Experimentally Validated Database for Neutral/Ion Kinetics for Plasma Processes*

***L.W. Sieck**, J.T. Herron (Contractor), D.S. Green (U. Md), T.J. Buckley, and E. P. Hunter*

Objective: To develop a laboratory-validated database for modeling the processes associated with non-thermal plasma treatment of gas streams.

Problem: Substantial advances in effective manufacturing and environmental cleanup can be achieved by exploiting non-thermal plasma treatment. In such discharges, chemical change is driven by a variety of processes including ionization, molecular excitation, ion-electron recombination, fragmentation of ions and excited molecules, and reactions of radicals, atoms, and ions. The quantitative modeling of these processes requires a reliable database describing the key elementary kinetics involved.

Approach: The program has centered around the creation and validation of an ion chemistry database for use in modeling plasma processes. In addition, a neutral-chemistry component will also be pursued to describe more completely the total chemistry. Creation of the database involves data collection and evaluation, experimental measurements of specific rate parameters, and verification of the model with the new NIST hybrid high-pressure mass spectrometer system, scheduled for full operation by January 1998.

Results and Future Plans: Current efforts are focused on the primary kinetics operative in plasma removal of volatile organic compounds (VOCs) and nitrogen oxides (NO_x) from humid air streams typical of jet-engine test beds and from diesel sources. The first effort was a survey and assessment of the available literature pertinent to positive ion chemistry in both wet and dry air at one atmosphere, and a recommended database was created for the temperature range 300-700 K. The database includes pressure effects and the conversion from third- to second-order kinetics (which is of particular importance in modeling atmospheric reactions), as well as switching reactions and the formation of cluster ions, and the effect of applied electric fields on the various rate parameters. The goal of this activity is to develop a reliable predictive scheme for air-only atmospheric-pressure reactors. This predictive scheme is based on modeling of the low-pressure scheme, which was validated and modified by comparison with direct results from the NIST high-pressure mass spectrometer.

During the past year, additional lab diagnostics were also carried out with toluene (as a representative VOC), and these studies will be extended in detail next year to CCl_4, which is one of the four target molecules chosen for intensive study by the IUPAC Hazardous Waste Task Force. These measurements demonstrated the dramatic effect that these additives have on the air system, including an apparently complete quenching of the NO_x ion chemistry. In the coming year, we will create a compact chemical kinetics database for ion chemistry at one atmosphere incorporating key reactions representative of VOCs that influence the destruction of NO_x during non-thermal plasma treatment. A generic recommended database for negative ion kinetics in humid air at atmospheric pressure including trace components such as O_3, NO, NO_2, and CO_2 will also be assembled. Laboratory validation of the competitive ion kinetics and important parent-daughter relationships will be conducted as required. The neutral database will also be extended to include excited state reactions of N_2, O_2, N, and O with both NO_x and C_1-C_2 hydrocarbons.

Publications:

Herron, J.T. and Green, D.S., *"Evaluated Chemical Kinetics Data for Neutral Reactions in Humid Air Plasmas."*

Sieck, L.W., Herron, J.T., and Green, D.S., *"Evaluated Chemical Kinetics Data for Positive Ion Reactions in Humid Air Plasmas."*

13. Thermophysical Properties of Alternative Refrigerants

__M.O. McLinden__, D.R. Defibaugh, K.A. Gillis, C.D. Holcomb, M.L. Huber, J.J. Hurly, A.R. Laesecke, E.W. Lemmon, J.W. Magee, M.R. Moldover, S.L. Outcalt, R.A. Perkins, and L.A. Weber (Contractor)

Objective: To provide industry with high-accuracy property data and models for alternative refrigerants and refrigerant mixtures.

Problem: The chlorofluorocarbon (CFC) and hydroclorofluorocarbon (HCFC) refrigerants must be replaced with fluids, which do not deplete stratospheric ozone. To evaluate the energy efficiency, capacity, etc. of any fluid in a thermodynamic cycle, or to design equipment using a new fluid, knowledge of the thermophysical properties is required.

Approach: Our work on alternative refrigerants represents a comprehensive approach to a major problem and has been supported by multiple government agencies and industry groups. Our work in this area includes experimental measurements and the compilation and evaluation of literature data. These data provide the input information for developing the models that form the basis of the REFPROP database. Also included are technology transfer activities and participation in international collaborations.

Results and Future Plans: The work on alternative refrigerants is shifting increasingly to mixtures and to transport properties. We have completed viscosity measurements on mixtures of R32 (CH_2F_2), R125 (CF_3CHF_2), R134a (CF_3CH_2F), and propane. Complementary work on the thermal conductivity is in progress. We have measured the viscosity of several fluorinated ethanes and propanes. Interest is increasing in the "natural refrigerants," and we have completed comprehensive measurements of the heat capacity and of the PVT and VLE behavior of the propane/isobutane system. Similar comprehensive measurements have been completed on several mixtures of the HFCs. We have also performed more limited thermodynamic measurements on several "developmental" fluids, such as the fluorinated butane, HFC-338mccq ($CF_3CF_2CF_2CH_2F$). These data form the basis for evaluating and improving the mixture Helmholtz model for the thermodynamic properties (Technical Highlight 3) and an extension of the ECS model for transport properties (Technical Highlight 4).

A complete revision of the Refprop database is in the review process and will be released early in 1998. In the past year, we have added new fluids, such as HFC-245fa ($CF_3CH_2CHF_2$), and incorporated new or improved models for the transport properties (Technical Highlight 4) and surface tension. We have also collected literature data on more than 75 refrigerant mixtures and used them to fit the parameters in the mixture Helmholtz energy model (Technical Highlight 3). In the international arena, NIST coordinated a comparison of refrigerant mixture models through Annex 18 of the International Energy Agency. This comparison showed the mixture Helmholtz energy model developed at the University of Idaho and NIST to have the best combination of accuracy and generality among the five models considered. We are in the process of developing a comprehensive formulation for the thermal conductivity of R134a under the auspices of the IUPAC Subcommittee on Thermophysical Properties. We also coordinated the revision of tables of refrigerant properties appearing in the 1997 ASHRAE Handbook of Fundamentals.

Publications:

Defibaugh, D.R., Carrillo-Nava, E., Hurly, J.J., Moldover, M.R., Schmidt, J.W., and Weber, L.A., ***"Thermodynamic Properties of HFC-338mccq, CF_3-CF_2-CF_2-CH_2F, 1,1,1,2,2,3,3,4-Octafluorobutane,"*** J. Chem. Eng. Data 42, 488-496 (1997).

Lemmon, E.W., ***"Evaluation of Thermodynamic Property Models for Mixtures of R-32, R-125, and R-134a,"*** IEA Heat Pump Centre, Sittard, The Netherlands (in press).

14. *Ammonia-Water Mixtures for Use in Power Cycles*

***D.G. Friend**, J.C. Rainwater, A. Nowarski (Univ. Cracow, Poland), R. Tillner-Roth (Univ. Hannover, Germany), C.D. Holcomb, J.W. Magee, R.A. Perkins, W.M. Haynes, T. Lüddecke (Univ. Hannover, Germany), S. Kiselev (Inst. Oil and Gas Res., Russia), E.B. Thorin (Royal Inst. Tech., Sweden)*

Objective: To establish standard reference thermophysical property surfaces for mixtures of ammonia and water over a broad range of temperature, pressure, and composition.

Problem: Drastically redesigned power plants have been proposed which use the binary ammonia-water system as a working fluid, and dramatic increases in efficiency have been predicted. Several companies have obtained license agreements to implement this approach. Critical design decisions and corporate risk analysis require property parameters that are not currently available. In addition to these engineering and other practical concerns, problems in the optimization of these new cycles and in the development of performance warranty protocols have not been resolved because of uncertainties in the thermophysical properties of the working fluid. This binary system is also the working fluid in some refrigeration applications, including prospective domestic heat pump and air conditioning technologies; the optimization of designs for these systems also requires reliable standard property information.

Approach: The project has required an extensive bibliographic study and evaluation of existing data; details concerning the required data and tolerances for industrial application are also needed. Experimental measurements will be obtained for selected properties at the most important state points; these include measurements of the VLE surface, density, isochoric heat capacity, thermal conductivity, and viscosity. Some apparatus modifications and development are required to perform the measurements. The modeling effort includes studies based on scaling theory to describe the high pressure region of the phase boundaries, as well as several versions of an extended corresponding states (ECS) algorithm. These must be modified to account for the behavior of this system. Additionally, a two-fluid Helmholtz energy model is being developed to describe the thermodynamic surface of the mixture.

Results and Future Plans: A report of a workshop on the thermophysical properties of ammonia-water mixtures, held by NIST and geared to industrial users of this information, was published this year. Efforts continued in the areas of data collection and evaluation, and a two-fluid Helmholtz energy model has been optimized to the available data. The ECS model now incorporates state-dependent shape factors and seems to show promise in allowing extrapolation into the high temperature regions of major interest. A set of measurements of the isochoric heat capacity has been completed, with temperatures to 523 K, for ammonia-rich mixtures. (See Technical Highlight 16 for a description of this experiment and apparatus.) Preliminary comparisons with the models indicate that further refinement of the models may be required. Work will continue on viscosity and thermal conductivity.

Publications:

Friend, D.G. and Haynes, W.M., ***"Report on the Workshop on Thermophysical Properties of Ammonia/Water Mixtures,"*** NISTIR 5059 (1997).

Nowarski, A. and Friend, D.G., ***"Application of the Extended Corresponding States Method to the Calculation of the Ammonia-Water Mixture Thermodynamic Surface,"*** Int. J. Thermophys. (in press).

Van Poolen, L.J. and Rainwater, J.C., ***"Critical-Region Model for Bubble Curves of Ammonia-Water with Extrapolation to Low Pressures,"*** Fluid Phase Equilibria (in press).

15. Database for the Chromatographic Analysis of Natural Gas

T.J. Bruno

Objective: To provide an efficient, fast, and reliable method for identifying in both the laboratory and the field the heavier components of natural gas (the C_6+ fraction, that is, species that have a carbon number in excess of 6), and natural gas treatment materials.

Problem: The design of many processes involving natural gas, as well as the custody transfer of natural gas, rely on an accurate chemical analysis of the gas composition. However, the most common analysis of natural gas at present considers only the lightest components, and inclusion of the heavier fraction into the analysis (an approach called the "extended natural gas analysis") is a complex problem. In particular, natural gas consists of upwards of 400 organic and inorganic constituents, most of which occur naturally, and some of which are introduced intentionally during processing. Moreover, the composition varies with season, with source-well history, and with short-term usage and storage history. Thus, a fast, low-cost, and reliable method is required for the efficient commerce and use of this vital natural resource.

Approach: Gas chromatography offers an economical and accurate solution to the problem of the extended natural gas analysis. In addition to being one of the most well understood and economical analytical methods available, it is very amenable to field applications. What is needed is an interactive database that can be incorporated into the control and analysis software of both laboratory and field gas chromatographic instrumentation. We have approached the problem of standardizing and automating the extended natural gas analysis through the measurement of standard chromatographic retention parameters on the most useful stationary phases available, and also on some novel developmental phases. The standard retention parameters that we have measured include net retention volumes, relative retentions, and Kovats retention indices. These parameters are corrected for instrumental variation and are, therefore, reproducible from instrument to instrument. The measurements are performed on a specially modified commercial gas chromatograph that provides highly accurate retention information. The column temperature dependence of each retention parameter is modeled with appropriate equations to allow predictions at all relevant temperatures. These models then form the heart of an interactive database that allows offline identification of peaks, and also the optimization of more complex analyses.

Results and Future Plans: The measurement of all standard retention parameters at four or more column temperatures has been completed for a series of representative C_6+ hydrocarbons on eight stationary phases. In addition, similar measurements have been completed for odorant compounds on four stationary phases. These stationary phases include the well-known methyl silicones and their more useful derivatives, porous polymer and solid adsorbent SCOT (surface coated open tubular) columns, and also some novel stationary phases that include sol/gel phases and clay phases. During the next year, we will add measurements on additional methyl silicone derivatives, and at least one modified adsorbent CLOT (coated layer open tubular) column. All of the modeled data will be entered into the database, an initial version of which has been released for testing and evaluation.

Publication:

Bruno, T.J. and Wertz, K.H., ***"Gas Chromatographic Retention Parameters: The Basis of Chromatographic Peak Identification for Extended Natural Gas Analysis,"*** Proc. Institute of Gas Technology Symposium on Natural Gas Quality, Orlando, FL (1997).

16. Adiabatic Twin-Cell Calorimeter for Isochoric Heat Capacity Measurements

*J.W. **Magee**, R.A. Perkins, D.G. Friend, and M.O. McLinden*

Objective: To establish a calorimetric apparatus to accurately measure the isochoric heat capacity of corrosive or reactive substances over wide ranges of temperature and pressure.

Problem: Calorimetric data spanning wide ranges of temperature and pressure are needed to validate predictive models for thermodynamic properties of working fluids, especially those under consideration for advanced power cycles, refrigeration cycles, and a wide variety of industrial processes. Accurate isochoric heat capacities are especially useful because they provide a sensitive test of such models.

Approach: An extensive array of techniques has been developed to measure heat capacity. Of these techniques, the adiabatic method is generally accepted to give the most accurate results. Our research group has employed the adiabatic method for heat capacity measurements for more than 35 years. Goodwin developed a low-temperature adiabatic calorimeter, which was later modified for automated measurement and control. It has been used to measure constant-volume heat capacities (uncertainty of 0.5 to 2%) for many fluids at temperatures from 20 to 345 K, and at pressures to 35 MPa. In the planning stages of this work, we recognized a need to augment our existing measurement capabilities by developing a new calorimeter that would extend the upper temperature limit to 700 K, without a compromise in accuracy.

In the adiabatic method, heat exchange between the calorimeter and its environment is eliminated as long as a temperature gradient does not exist. However, in actual practice, the maintenance of a zero temperature gradient is an ideal situation that cannot be realized. Thus, even the most carefully conducted calorimetric experiment results in some heat loss, requiring a correction to the data. Nevertheless, this correction can be minimized by automatic adjustment of the temperature of the surrounding jacket to follow that of the calorimeter. We may realize a further refinement by employing a twin calorimeter design, thus eliminating such a correction. Twin devices employ two calorimeters that are as nearly identical in construction as possible, supported in nearly identical surroundings, resulting in the same heat losses. In the present work, we combine the features of twin calorimeters with the adiabatic method, with the goal of virtually complete elimination of the heat-loss correction.

Results and Future Plans: A high-temperature adiabatic calorimeter has been developed to measure the constant-volume specific heat capacities of both gases and liquids, especially fluids of interest to emerging energy technologies. The chief design feature is its nearly identical twin-cell arrangement, which allows accurate measurement of energy differences without large corrections for energy losses due to thermal radiation fluxes. The cells were constructed from Inconel-718, a high-strength steel with excellent corrosion resistance. Operating conditions for the calorimeter cover a range of temperatures from 250 to 700 K at pressures up to 20 MPa. Performance tests were made with a sample of twice-distilled water. Heat capacities for water were measured from 300 to 420 K at pressures to 20 MPa, a range where accurate heat capacity data already exist and have been incorporated into an internationally accepted formulation. The measured heat capacities differed from those calculated with this formulation with a root-mean-square fractional deviation of 0.48%. Measurements of the heat capacities of industrially important ammonia/water mixtures have been completed.

Publication:

Magee, J.W., Blanco, J.C., and Deal, R.J., ***"A High-Temperature Adiabatic Calorimeter for Constant-Volume Heat Capacity Measurements of Compressed Gases and Liquids,"*** J. Res. NIST (in press).

17. Thermodynamic Data for Environmental Fate and Risk Analysis

***D.G. Archer**, M.W. Chase, D.R. Kirklin, R.D. Levin, and P.A.G. O'Hare*

Objective: To provide thermodynamic information necessary for prediction of movement of heavy metals through ground waters (aquifers) and surface waters, and for prediction of remediation yields in treatment methodologies.

Problem: The environmental fate of a heavy-metal contaminant in an aqueous environment is determined by the extent of many competing reactions. The competing reactions include precipitation reactions, reduction-oxidation reactions, and ion-exchange reactions with the geological materials present. The extent of reaction for these types of processes is determined by the thermodynamic properties for the reaction in the aqueous system. This is particularly true for movement of contaminants in aqueous environments because known diffusion laws predict mass flux to be dependent on concentration gradients. Prediction of the level of contamination of aquifers and surface waters, as well as the prediction of the rate of migration of contaminants through these waters, is accomplished through calculational models (simulators). Therefore, the validity of any particular simulator's calculated distribution of a noxious contaminant is heavily dependent on the validity of the thermodynamic information for the competing reactions that is incorporated into the simulator. However, much of the thermodynamic information required to execute these calculations is not of sufficient accuracy to make the calculations meaningful. This is true not only for many heavy-metal containing species but also for some common ions with which heavy metals come into contact in a typical aqueous environment.

Approach: We intend to generate accurate thermodynamic properties of heavy-metal containing species and the common ions with which these species come into contact. Examination of the status of the literature regarding these properties will be conducted. These examinations will identify the relevant measurements described in the literature as well as document previous NIST tabulations of thermodynamic properties for these chemical species. From these analyses, the measurements necessary to determine accurately the thermodynamic properties will be identified and conducted. A data-handling structure will be constructed that allows simultaneous evaluation of thermodynamically consistent properties for the desired species.

Results and Future Plans: This year, an analysis of previously reported thermodynamic properties for selected cadmium-containing compounds was prepared, as was an analysis of the thermodynamic properties of the potassium chloride + water system. (Potassium chloride is also a standard used in isopiestic measurements and for calibrating calorimeters.) An enthalpy of solution calorimetry laboratory was established this year; enthalpy of solution measurements contribute to the knowledge of how solubilities and other reactions change with respect to temperature. During the next year, analyses of the literature on the thermodynamic properties of common species containing mercury, chromium, lead, zinc, and manganese, similar to that for cadmium, will be completed. Measurements for selected species will be initiated, mass-flow calorimetry capabilities will be added, and construction of the data-handling system will be started. Also expected is initiation of a program to determine accurate thermodynamic properties of "key" substances. The "key" substances are required to extract the properties of a heavy-metal containing reactant from the measured properties of a reaction.

Publication:

Archer, D.G., ***"Enthalpy Increment Measurements for NaCl(cr) and KBr(cr) from 4.5 to 350 K. Thermodynamic Properties of the NaCl + H_2O System. 3,"*** J. Chem. Eng. Data 42, 281-292 (1997)

18. Cavity Ring-Down Technology for Kinetic and Mechanistic Studies

***J.W. Hudgens**, R.E. Huie, and A.C.R. Pipino*

Objectives: To improve the accuracy, precision, and sensitivity of optical absorption measurement protocols and to use these to measure chemical reaction rates in gas and liquid phases and at interfaces.

Problem: The development of accurate computer models of incineration, semiconductor processing, atmospheric chemistry, and solution chemistry requires accurate reaction rate coefficients for the key chemical reactions. In turn, such reaction rate measurements require accurate determinations of low concentrations of reactants and products as functions of time. For most species, optical absorption can measure concentrations very selectively, but the sensitivity is often insufficient to allow rate measurements.

Approach: We are developing cavity ring-down (CRD) optical absorbance measurement technology to meet the requirements imposed by chemical kinetics experiments in gas and condensed phases.

Results: This year, we used CRD detection to measure reactions of the propargyl radical in a slow-flow flash photolysis reactor. Our CRD studies determined the absolute absorption cross-section of propargyl radicals at 332.5 nm. Additional experiments measured the self-reaction rate coefficient for the propargyl radical and the rate coefficient for the propargyl + oxygen association reaction. Reactions involving propargyl radicals are believed to govern the production of soot in hydrocarbon flames. We also demonstrated the first application of CRD technology to measurements of condensed matter by constructing a right-angle cavity containing a fused silica Pellin-Broca prism. In this configuration, evanescent waves emanating from the internally reflecting surface of the Pellin-Broca probed the species residing on its surface. When we exposed this surface to gas-phase I_2, the CRDS signal showed that the evanescent wave was increasingly attenuated as the surface became saturated with adsorbed I_2. We found that the detection sensitivity for surface adsorbed iodine was less than 0.04 monolayer.

Future Plans: During the next year, we will use CRD spectroscopy to determine rates of gas-phase reactions that involve halogen monoxide, ethyl, methyl, peroxy, and propargyl radicals. We anticipate that the improved sensitivity obtained with CRD detection will also enable us to obtain accurate rates for bimolecular reactions between two *different* free radicals; if successful, such experiments should allow explorations of sparsely studied but important topics in chemical kinetics. We will also use our novel optical devices to study chemical reaction rates in the liquid phase.

Publications:

Atkinson, D.B. and Hudgens, J.W., ***"Propargyl Radical Kinetics Measured Using Ultraviolet Cavity Ring-Down Absorption Spectroscopic Detection: Self-reaction and Oxygen Addition,"*** J. Phys. Chem. A (in press).

Atkinson, D.B. and Hudgens, J.W., ***"Chemical Kinetic Studies Using Ultraviolet Cavity Ring-Down Spectroscopic Detection: Self-reaction of Ethyl and Ethylperoxy Radicals and the Reaction, $O_2 + C_2H_5 \rightarrow C_2H_5O_2$,"*** J. Phys. Chem. A 101, 3901 (1997).

Pipino, A.C.R., Hudgens, J.W., and Huie, R.E., ***"Evanescent Wave Cavity Ring-Down Spectroscopy with a Total-Internal-Reflection Minicavity,"*** Rev. Sci. Instrum. 68, 2978 (1997).

Pipino, A.C.R., Hudgens, J.W., and Huie, R.E., ***"Evanescent Wave Cavity Ring-down Spectroscopy for Probing Surface Processes,"*** Chem. Phys. Lett. (in press).

19. The NIST Mass Spectral Database - Fully Evaluated

S.E. Stein, A. Mikaya (Contractor), Zhu Damo (Guest Researcher), D. Tchekhovskoi (Contractor), C.L. Clifton, and W.G. Mallard

Objective: To provide the mass spectral community with a fully evaluated mass spectral database and with tested and documented search algorithms that will enable the positive identification of unknown organic compounds using gas chromatography/mass spectrometry (GC/MS).

Problem: Modern organic analytical chemistry is critically dependent on instrumental analysis. For qualitative analysis, there is no better tool than the mass spectrometer. Like many other analytical techniques, it is best used with a library of reference spectra. Even with good reference spectra, the data must be processed correctly. Robust algorithms that have been thoroughly tested to eliminate flaws are needed.

Approach: The next release of the NIST Mass Spectral Database will be fully evaluated. In particular, every one of the more than 130,000 spectra will have been assessed by at least one expert, and all questionable data by two experts. In addition, a number of advances in the algorithms for searching the database have been developed and extensively tested, both for their inherent functionality and to compare them to other search algorithms. The best algorithms are incorporated into the NIST search software.

Results and Future Plans: During FY97, a detailed examination of the data for all compounds in the database was completed. This effort is the first time such a large collection of scientific data from so diverse a set of experimenters has ever been evaluated. The data were examined for reasonable neutral losses, for air peaks, for impurities (either solvent or other related compounds), and for errors in transcription of the data from the original source. In every case where a change had to be made, agreement between at least two evaluators was required. The analysis was always conservative; if a given spectrum or spectral feature was not clearly in error, it was not changed. On the other hand, when the data were so suspect that they were impossible to repair, they were removed from the database. In some cases where there was no alternative spectrum, this meant that the compound itself was removed from the database. Again, the decision was made to emphasize the quality of the final database and not the sheer size of the database. The resulting database represents the very best collection of mass spectral data ever assembled.

To make the database more useful to the GC/MS community, work has started on the addition of retention indices to the database. The retention index is a measure of the time it takes a compound to elute from the GC column. For many compounds that might otherwise be confused using mass spectra alone, the retention index makes it possible to make a more definitive identification. An example of an important class of compounds for which retention time data are especially useful is the hydrocarbons, many of which have very similar mass spectra. The first stages of compiling and entering retention index data have begun. Tools are being developed to evaluate the data and to use the data to predict retention parameters for compounds for which experimental data are not available.

20. Automated Gas Chromatography/ Mass Spectral Decomposition and Analysis – Tools for Automating and Improving the Use of GC/MS Instruments

S.E. Stein, O. Toropov (Contractor), A. Rumiantsev (Contractor), W.G. Mallard, and J.J. Reed

Objective: To develop and test algorithms for automatically deconvoluting and analyzing GC/MS data files using a target library of compounds.

Problem: The program currently underway has been fully funded by the Defense Special Weapons Agency (DSWA) to provide a method for analyzing for chemical weapons banned under the Chemical Weapons Convention. The software implementing the algorithms must provide full blinding of the analysis process so as not to compromise the proprietary data of treaty participants. In general, the analysis of GC/MS data files for complex mixtures can be time consuming and error prone. The normal method of doing a background subtraction to extract the single component can be essentially impossible in a complex mixture because there is no background. Even in only moderately complex chromatograms, a manual subtraction can produce seriously erroneous results.

Approach: A detailed noise analysis is performed, followed by a deconvolution of each of the peaks in the total ion chromatogram based on the individual ion chromatograms. The resulting eluents are then compared to reference spectra using a series of algorithms that take into account the degree of confidence that an analyst would have in the deconvoluted peak. The identification is presented with a confidence measure. The process of extracting the distinct eluents (or components) out of a complex data file breaks down into four parts: noise perception and evaluation, component perception, signal extraction, and compound identification. The noise perception and evaluation is central to the analysis since the recognition of the difference between a "real" peak caused by a compound eluting from the column and a "false" peak caused by noise depends upon a knowledge of the nature and size of the noise. Once the noise is understood, the individual components can be extracted. The extraction of the signal involves examining the overlap of components and removing mass spectral peaks associated with a different eluent.

Results and Future Plans: The algorithm has been tested extensively using as a target library of chemical weapons agents. Over 30,000 data files have been examined to ensure that the algorithm does not produce false positives. At the same time, a number of experiments have been performed with low concentrations of target compounds similar to chemical agents to demonstrate that the algorithm is sensitive enough to detect all true positives at analytically useful concentrations. The results of these tests have shown that the algorithms used in the development of the software are robust and capable of automated and blinded analysis. Work is continuing on refining the algorithms to reduce the incidence of false identifications by making use of data other than the mass spectra. The use of retention indices is central to the further reduction of false positives. The software developed here has been adapted by the Organization for the Prohibition of Chemical Weapons (OPCW) for use in all inspections involving GC/MS instrumentation.

21. Rheometry and Structure of Complex Molecular and Macromolecular Systems

__H.J.M. Hanley__, B.D. Butler, C.D. Muzny, G.C. Straty, M.Y. Lin (Exxon Research and Engineering), and T.M. Slawecki and C.J. Glinka (NIST Center for Neutron Research)

Objective: To investigate the relationship between the structure and viscometric functions of complex molecules, macromolecular systems, colloids, and gels and to develop a metrology that combines radiation scattering with rheometry.

Problem: The flow properties of a complex system can be predicted or manipulated if the relationship between its structure (particle positional order and/or orientation) and rheological characteristics is understood. The structure can be determined by radiation scattering and can be coordinated with data measured independently from a rheometer or viscometer. The behavior, however, of macromolecular, and especially polymeric, solutions can be very sensitive to preparation history. Hence, the scattered intensities and the rheometric functions should be measured simultaneously. Our project is the first to measure scattered neutron or light intensities simultaneously with data from a modified rheometer.

Approach: We investigate the structure of a complex system using the small angle neutron scattering (SANS) spectrometers at the NIST Center for Neutron Research (NCNR), Gaithersburg, and our light scattering facilities in Boulder. The system can be studied at rest or when subjected to a shear or stress. The scattering cell is an adapted Couette cell controlled by a constant stress rheometer that is placed in the neutron or light beam. In this way, simultaneous radiation and viscometric data can be obtained. The apparatus is capable of high accuracy measurements for viscosities that can range over ten orders of magnitude, and the combination of neutron and light radiation allows us to investigate length scales of the macromolecular system of interest ranging from about 5 nm to 10 μm.

Results and Future Plans: The scattering/rheometric apparatus has recently been constructed. We have made simultaneous measurements of the viscosity and the anisotropic scattering patterns as a function of shear stress and shear rate for a 1.0% by weight solution of cetyltrimethylammonium bromide (CTAB) and sodium salicylate in D_2O. We have also completed some preliminary measurements on the structure of a gelling colloidal silica system subjected to a shear, and related the structure changes to variations in the stress and viscosity. The combined scattering/rheometric apparatus will be a valuable resource to manipulate and characterize systems prepared under a shear or stress, or influenced by a shear or stress. Industrial examples include polymer blends, gels, and oil well drilling muds.

Publications:

Straty, G.C., Muzny, C.D., Butler, B.D, Lin, M.Y., Slawecki, T.M., Glinka, C.J., and Hanley, H.J.M., ***"A Rheometric Shearing Apparatus at the NIST Center for Neutron Research (NCNR),"*** Nucl. Instr. Ind. Methods in Phys. Res. (in press).

Straty, G.C., Muzny, C.D., Butler, B.D., Lin, M.Y., Slawecki, T.M., Glinka, C.J., and Hanley, H.J.M, ***"An in-situ Rheometric Shearing Apparatus for SANS,"*** Physica B (in press).

Lin, M.Y., Hanley, H.J.M, Muzny, C.D., and Straty, G.C., ***"Simultaneous Measurements of Viscosity and Structure for Rod-Like Micelles,"*** Physica B (in press).

Hanley, H.J.M, ***"Structure of Macromolecular Systems Under Shear; Application of Neutron Scattering,"*** Colloid & Interface Sci. (in press).

22. Surface Adsorption and Surface Structure of Surfactant/Clay Complexes

H.J.M. Hanley*, B.D. Butler, C.D. Muzny, G.C. Straty, M.Y. Lin and D.G. Peiffer (Exxon Research and Engineering), and S.K. Sinha (Argonne National laboratory)*

Objective: To investigate the formation and structure of complexes formed by the adsorption of an organic macromolecule on an inorganic substrate and, in particular, complexes of surfactants with clay minerals.

Problem: Clay technology impacts such technologies as pollution prevention and remediation, enhanced oil recovery and the treatment of petroleum liquids, the manufacture of cosmetics and pharmaceuticals, and the synthesis of nanocomposites. These technologies involve the formation of clay/organic complexes, the properties of which are dominated by the nature of the clay-organic interfacial layer. Structural information, however, on the interfacial layer is relatively scarce.

Approach: Our work applies dynamic light scattering (DLS) and small-angle neutron scattering (SANS) to help elucidate the structure of the interface and of the complex itself. We work with particulate complexes prepared by adding a cationic surfactant to dilute aqueous suspensions of a clay mineral. DLS experiments are performed in our Boulder laboratory and are used to measure the scattered light intensity autocorrelation function at fixed scattering angle. Analysis of this function can provide an estimate of the effective hydrodynamic size of particles in a suspension and, in principle, their size distribution. SANS experiments are carried out using the small angle spectrometers at the NIST Center for Neutron Research, Gaithersburg. The SANS technique can also be used to obtain an estimate of the particle size and, in addition, an estimate of shape. Furthermore, SANS is a convenient technique to investigate micelles in the solutions.

Results and Future Plans: We have investigated aqueous mixtures of the synthetic clay mineral laponite and cetyltrimethylammonium bromide (CTAB) in dilute suspension. We found that the SANS intensity pattern from the suspension of the pure clay is consistent with that from discs or platelets with diameters of about 30 nm. After addition of CTAB to the clay suspensions, CTAB adsorbs on the face of the clay platelets by cationic exchange and the resulting complex contains excess CTAB in an amount corresponding to about four multiples of the clay's cation exchange capacity (CEC). The analysis of the DLS data suggested two possible stable clay platelet configurations in the suspensions: 1) free clay platelets, and 2) clay platelets with CTAB adsorbed in an amount above the CEC, but presumably enough to form a stable surfactant bilayer. Plans are to investigate the solubility of the complexes in water and to model the thermodynamics of the interfacial and solubility phenomena.

Publications:

Lin, M.Y., Hanley, H.J.M., Sinha, S.K., Straty, G.C, Peiffer, D.G., and Kim, M.W., ***"Shear-Induced Behavior in a Solution of Cylindrical Micelles,"*** Phys. Rev E 53, R4302-R4305 (1996).

Hanley, H.J.M., Muzny, C.D., and Butler, B.D., ***"Surfactant Adsorption on a Clay Mineral: Application of Radiation Scattering,"*** Langmuir (in press).

Hanley, H.J.M., Muzny, C.D., and Butler, B.D., ***"Surface Adsorption in a Surfactant/Clay Mineral Solution,"*** Int. J. Thermophys. (in press).

Lin, M.Y., Hanley, H.J.M, Muzny, C.D., and Straty, G.C., ***"Simultaneous Measurements of Viscosity and Structure for Rod-Like Micelles,"*** Physica B (in press).

23. Measurement of the Viscosity of Xenon in Microgravity

***R.F. Berg**, M.R. Moldover, and G.A. Zimmerli (NYMA, Inc.)*

Objective: To test the theory for the viscosity of a fluid closer to the liquid-vapor critical point than is possible in earth's gravity.

Problem: Near the liquid-vapor critical point, theory predicts that the viscosity increases as an inverse power-law of the temperature difference from critical temperature. The increase is due to the fluid's microscopic fluctuations and it is thought to be universal for all fluids. Near the critical temperature and density, fluids on earth stratify in gravity and the predicted viscosity increase is hidden. Thus, careful tests of the theory are impossible on earth.

Approach: We measured the viscosity near the critical point of xenon onboard the Space Shuttle, where the typical acceleration is one millionth of the earth's gravity. During the ten years preceding this measurement, we established the limits on shear rate, frequency, and temperature control required to test the theory, and we developed instruments that met these limits. Only then, was a prototype viscometer built for operation on the Space Shuttle. The prototype's development led to new understanding in diverse areas, including hydrodynamic similarity, anelasticity in solids, and internal waves in stratified fluids. It culminated in detailed and realistic science requirements for the flight experiment. NASA translated these science requirements into an engineering plan, and in collaboration with NIST, developed the flight instrument on time and under budget.

In experiments on earth, NIST showed that the novel "fly-swatter" flight instrument was capable of measuring viscosity with an uncertainty of 0.2% while operating at very low frequencies and shear rates. Additional studies indicated that the instrument was robust enough to survive the stresses of launch and that vibrations typical of those on the orbiting Space Shuttle would not compromise its accuracy. Xenon was chosen as the test fluid because its other critical properties have been well measured and because of its convenient critical temperature. The viscometer was installed into a thermostat capable of keeping the xenon sample's temperature homogeneous to within one part per billion.

Results and Future Plans: During August 1997, the Critical Viscosity of Xenon (CVX) experiment flew as part of the 11-day STS-85 Space Shuttle mission. Data from CVX were relayed to the NIST investigators at Goddard Space Flight Center for preliminary analysis. Commands were returned to CVX to optimize its performance. In microgravity, the viscosity increase was twice as large as in the best measurements on earth. The xenon's temperature was scanned through the critical temperature at rates as low as 2 K/yr. Within 1 mK of the critical temperature, the critical fluctuations caused the xenon to become viscoelastic, resulting in frequency-dependent data that could not be obtained on earth. During the next year, the analysis of the data will be completed and the results will be compared with theory.

Publications:

Berg, R.F., Zimmerli, G.A., and Moldover, M.R., ***"Measurement of Microkelvin Temperature Differences in a Critical Point Thermostat,"*** Int. J. Thermophysics (in press).

24. Hydrogen Bonding in Water at Elevated Temperatures

R.D. Mountain

Objective: To examine the temperature and density variation of hydrogen bonding in water for states ranging from ambient to supercritical conditions.

Problem: Hydrogen bonding makes the properties of water quite different from those of most liquids. One of the current, unresolved issues in the development of a description of water at supercritical conditions is the amount of hydrogen bonding present. Different experimental probes, neutron scattering and chemical shift measurements, provide conflicting answers.

Approach: An extensive set of molecular dynamics simulations of water have been performed to develop a coherent set of hydrogen bond determinations using a model that is known to provide an accurate representation of the liquid-vapor coexistence curve, including the critical point at T_c = 647 K and ρ_c = 322 kg/m^3. The temperature and density variation of the mean number of hydrogen bonds, the lifetimes of the bonds, and the degree of connectivity of hydrogen bonded molecules have been determined.

Results and Future Plans: Simulation results have been obtained for "liquid" water for temperatures between 273 K and 823 K and for densities between 1000 kg/m^3 and 300 kg/m^3. There are several changes in the degree of hydrogen bonding that take places in this part of the phase diagram. The first change is that as the temperature is increased from 273 K to 400 K, the lifetime of hydrogen bonds decreases from several picoseconds to about 1 picosecond and the four-fold coordination of near neighbor hydrogen bonded molecules breaks down.

A second change occurs as the density decreases from 700 kg/m^3 to 500 kg/m^3. In this region the connectivity of hydrogen bonded neighbors changes from a fully percolated structure to a collection of isolated, hydrogen-bonded clusters. The third change occurs at slightly supercritical temperatures, that is T~673 K with densities lower than 600 kg/m^3. Here we find physical clusters and corresponding voids with lifetimes on the order of 1 ps and sizes comparable to a few molecular diameters. The size and lifetime distributions of the above mentioned clusters and voids will be examined further using simulations and Voronoi cell analysis. These objects are significant for theories of processes in supercritical fluids as the voids can accommodate normally insoluble molecules.

Publications:

Mountain, R.D., ***"Molecular Dynamics and Hydrogen Bonds in Water,"*** NIST Internal Report 6028 (1997).

Mountain, R.D., ***"Molecular Dynamics and Hydrogen Bonds in Water,"*** Proc. International Conference on High Pressure Science and Technology (in press).

25. *Molecular Theory of Solid-Fluid Equilibrium*

J.C. ***Rainwater****, P.D. Beale (Univ. Colorado), S.G. Gay (Univ. Colorado), and D.G. Friend*

Objective: To develop a theory of solid-fluid equilibrium for pure systems and mixtures, including hydrocarbons, refrigerants, and other compounds of industrial interest.

Problem: The complete thermodynamic description of a pure fluid or fluid mixture requires knowledge of the fluid-solid boundary. Mixtures can have a variety of interesting phase diagrams, including miscible solids, single eutectics, and solid compounds with multiple eutectics. Also of interest are the solubility of solids in liquids and supercritical fluids, the crystal structure of the solid, the heat of fusion, and the volume change on freezing.

Approach: We follow the approach of P.A. Monson and co-workers of the University of Massachusetts. The solid is described by the cell model of Lennard-Jones and Devonshire, in which the free volume is calculated for a single molecule in a cage of fixed neighboring molecules within a specified lattice structure. The molecule is initially modeled as an assembly of hard spheres, and subsequently van der Waals attractive terms and quadrupole or dipole moments are added as perturbations. The liquid free energy is obtained from a simulation, and the phase boundary is determined by a double-tangent construction. This approach can be extended to more complex molecules with arbitrary geometries and multipolar interactions.

Results and Future Plans: Starting from Monson's calculations of hard homonuclear dumbbells with quadrupole moments, we have similarly studied hard heteronuclear dumbbells with dipole moments. Our first specific candidate system has been methyl chloride, which is known to freeze into an ordered crystal. We have studied the freezing of heteronuclear hard dumbbells themselves, and have mapped out a phase diagram as a function of bond length and diameter ratio. We have studied both the lattice formed at close packing and the (different) experimental lattice. It was found that, with or without van der Waals attraction and a dipole perturbation, the former lattice has a freezing transition but at a lower temperature than that of experiment. The experimental lattice has no freezing transition unless a dipole interaction is considered, and the dipole stabilizes a transition very close to the experimentally measured temperature. We also have investigated the possibility of simplifying the free volume calculation for the cell model. Present methods require a 5-dimensional Monte Carlo integral, but we have shown that the three spatial integrations can be done analytically, leaving two angular variables to integrate over by quadrature.

Upon completion of our calculations for methyl chloride, we plan to model methyl fluoride and carbon monoxide as systems of dipolar heteronuclear hard dumbbell molecules. Both systems are known to freeze into plastic rather than ordered crystals. We then plan to model isobutane as an assembly of four spheres and to calculate its much lower freezing temperature relative to normal butane. Subsequently, we plan to study a variety of molecules of three and four atoms modeled as assemblies of hard spheres of differing radii with moments as appropriate. We are also studying some fundamental approaches as alternatives to the cell model, and will continue to develop analytic spatial integration methods.

Publications:

Rainwater, J.C., ***"The Cell Model of Solid-Liquid Equilibria in Two and Three Dimensions: Analytic Spatial Free Volume Integration,"*** Int. J. Thermophys. (in press).

Gay, S.C., Beale, P.D., and Rainwater, J.C., ***"Solid-Fluid Phase Coexistence of Hard Heteronuclear Dumbbells via Cell Theory and Monte Carlo Simulation,"*** Int. J. Thermophys. (in press).

26. *Primary Acoustic Thermometry at High Temperatures*

D. Ripple (Process Measurements Division), M.R.. Moldover, and K.A. Gillis

Objectives: 1) To reduce the uncertainty in the determination of the thermodynamic temperature by a factor of 3-8 in the range from 500 K to 900 K using speed-of-sound measurements in low density argon as a primary standard, and 2) to improve the accuracy of the high-temperature fixed points (e.g., tin point, zinc point) and radiometry tied to these fixed points.

Problem: The most accurate determinations of thermodynamic temperature above 700 K use relative radiance measurements referenced to a black body near 700 K. The thermodynamic temperature of the black body is known from NIST constant volume gas thermometry (CVGT) experiments. Unfortunately, two NIST CVGT experiments differ from each other for reasons that are not well understood. The difference leads to an estimated uncertainty of 13 mK in temperatures near 700 K and 50 mK in temperatures near the gold point (1337.33 K).

Approach: We shall measure the frequencies of both acoustic and microwave resonances in a spherical, argon-filled cavity bounded by a thick, metal shell which in turn will be enclosed by a high-performance thermostat. The data will determine the speed of sound in the argon from which the thermodynamic temperature will be deduced. The temperature will be transferred to platinum resistance thermometers and then to fixed-point devices. For acoustic thermometry, the measured quantities are frequencies and the temperature. This contrasts with CVGT, which requires the measurement of pressures and temperature; thus, systematic effects will be very different in the present work and may resolve the discrepancies in the CVGT.

Results and Future Plans: A significant technical challenge was to develop electro-acoustic transducers that are compatible with the high temperatures and which neither contaminate the argon nor significantly perturb the resonance frequencies. During FY97, the resonator was reworked and transducers were installed. The pressure vessel and furnace were fabricated and assembled. During the next year, the resonator will be installed in the furnace. Both acoustic and microwave resonances will be measured. The flowing-gas concept will be tested and optimized. The acoustic transducers will be characterized at high temperatures.

27. *Advanced Refrigeration Systems for Cryogenic Applications*

***R. Radebaugh**, P. Bradley, E. Marquardt, M. Lewis, T. Kuriyama (Toshiba), J.H. Xiao (Chinese Academy of Sciences), J. Braun (Purdue Univ.), M. Hill (Univ. Colorado), and J. Gary and A. O'Gallagher (Applied and Computational Mathematics Division).*

Objective: To develop new refrigeration techniques and improved refrigerator components for the temperature range of 120 K and below and to investigate and use measurement and modeling techniques for evaluating the performance of cryocoolers and their components, such as heat exchangers.

Problem: Cryocoolers are required for many technology areas, including the cooling of infrared sensors for surveillance and atmospheric studies, the cooling of superconducting electronics and magnets, the cooling of cryopumps for clean vacuums in semiconductor fabrication processes, and the liquefaction of natural gas for clean-burning transportation fuel. The use of these and other technologies has been hampered because of problems with existing cryocoolers, such as short lifetimes, inefficiency, high cost, and excessive vibration. Improved cryocoolers would stimulate the growth of all these technology areas.

Approach: Precision moving parts in existing cryocoolers are a source of wear, vibration, and high cost. Our approach in the development of improved refrigeration processes has been to eliminate most or all moving parts while still maintaining high efficiency. We have focused much of our research on pulse tube refrigerators, which have no cold moving parts and on the ThermoAcoustically Driven Orifice Pulse Tube Refrigerator (TADOPTR), which has no moving parts in the entire system and is a joint invention of NIST and Los Alamos National Laboratory. Our studies encompass measurements and modeling of generic losses to further improve efficiencies of these cryocoolers while increasing their lifetimes and simplifying construction techniques. NIST research in this area has much industry and other government agency support to aid in the transfer of this technology to industry.

Results and Future Plans: During the past year, measurements were made of the thermal conductance of stacked stainless steel and phosphor bronze screens of several mesh sizes and porosities at various helium filling pressures. It was found that the helium gas between the stacked screens enhanced the heat conduction through the screens by several orders of magnitude compared to vacuum. The thermal conductance degradation factors were found to be 0.1 for stainless steel and 0.022 for phosphor bronze, where this factor is the ratio of the conductance through the stacked screens to that of a solid rod of the same length and total metal cross-sectional area as the screen. Almost no prior data existed for these stacked materials, but they are needed for the optimum design of regenerative heat exchangers in many types of cryocoolers, including the pulse tube refrigerator. Packed spheres will be studied in the future.

Under a CRADA with Cryenco, Inc. of Denver, we have collaborated on a redesign of a large TADOPTR for liquefying natural gas. This is the world's largest pulse tube refrigerator and has no moving parts. The new prototype has successfully liquefied natural gas at the rate of 400 L/day. Future work will involve increasing the capacity up to about 2000 L/day. Under a CRADA with Lockheed Martin of Denver, we have also measured the performance of the world's smallest pulse tube refrigerator designed for flight on the Space Shuttle in April 1998. The effect of orifice size on the lowest temperature has been measured. The system will be delivered to NASA in January 1998 for incorporation into the Shuttle.

Publication:

Lewis, M.A., Kuriyama, T., Kuriyama, F., and Radebaugh, R., ***"Measurement of Heat Conduction Through Stacked Screens,"*** Adv. Cryo. Eng. 43 (in press).

28. *Microscale Heat Transfer*

R. Radebaugh, *E. Marquardt, M. Lewis, J.H. Xiao (Chinese Academy of Sciences), M. Hill (Univ. Colorado), and J. Siegwarth*

Objective: To develop models and correlations for predicting heat transfer between fluids and solids for cases where the length or time dimensions are very small and to perform measurements to validate and improve these models and correlations.

Problem: The miniaturization of many devices such as electronics, medical probes, laser diodes, cryocoolers, etc., is hampered by the difficulty in removing heat from very small dimensions or during very short times. In most cases the heat must be transferred from a solid to some fluid. Often the fluid serves to carry the heat to another location where the heat can be dissipated over a larger region to the environment. Our knowledge of the mechanisms for heat transfer in very small dimensions is limited, and, as a result, it is difficult to properly design a device for adequate heat transfer that will not lead to overheating. In the case of oscillating heat transfer, such as in many types of cryocoolers, the system size can be miniaturized by utilizing high frequency oscillations. Difficulties in transferring heat in very short time scales limit the operating frequency and, hence, the size reduction that can be achieved.

Approach: The early stages of this program involve a review of the literature on microscale heat transfer to determine prior efforts and to find where there are the largest gaps in our ability to predict heat transfer in very small length or time scales. The scale sizes of importance to our study are in the region where the more conventional bulk or steady-state heat transfer calculations and correlations can no longer be used with any accuracy. In the case of short time scales, we are extending our prior work on regenerative cryocoolers to investigate the effect of frequency on heat transfer and pressure drop in regenerators where helium gas is the working fluid. A normalized frequency parameter, known as the dynamic Reynolds number or the Valensi number, will be used to study correlations of heat transfer and pressure drop with frequency. Existing models will be studied to verify their applicability for these cryocooler applications. In the case of heat transfer in small length scales, we are most interested in understanding the limitations to increased heat transfer density. The systems to be studied are single- and two-phase heat transfer to allow a comparison between the two mechanisms. Multicomponent fluids are also to be studied because of their ability to be in two phases over a wide temperature range, thereby enhancing heat transfer in a heat exchanger that spans a wide temperature range.

Results and Future Plans: During the past year a literature search was carried out to gain a knowledge of previous work in the area of heat transfer to fluids in small length scales. Much of the prior work has involved the use of microgrooves in silicon surfaces. The smallest dimension of these microgrooves has usually been in the range of 200 to 500 µm. A limited number of single- and two-phase heat transfer studies has been made, but no conclusions can be drawn regarding the optimum designs of heat exchangers for the maximum heat transfer density. One study showed subcooling had no effect on the critical heat flux in two-phase heat transfer. Another study investigated the effect of fluid velocity, liquid sub-cooling, fluid properties, and micro-channel geometry on single-phase heat transfer. One study that compared single- and two-phase heat transfer gave heat transfer coefficients of about 4 to 6 $kW/(m^2 \cdot K)$ for single-phase and about 12 $kW/(m^2 \cdot K)$ for two-phase. Our investigation of the literature indicates that there is much work needed to even begin to understand microscale heat transfer. Future plans include the design of experiments to measure single- and two-phase heat transfer in very small dimensions. The influence of high velocities, such as jet impingement, on heat transfer will be considered for the design of such experiments.

29. *The Thirteenth Symposium on Thermophysical Properties*

W.M. Haynes, R.A. Overfelt (Auburn University), G.R. Hardin, and R.A. Stevenson

Objective: To organize an international conference on the thermophysical properties of fluids and solids.

Purpose: The Symposium on Thermophysical Properties is a well-established series of conferences held roughly every three years since 1959. This Symposium represents the premier international conference associated with the theoretical, experimental, and applied aspects of the thermophysical properties of gases, liquids, and solids. This conference brings together leading international experts from industry, academia, and government laboratories in these areas. NIST, in conjunction with the Thermophysical Properties Committee of the ASME Heat Transfer Division, has assumed primary responsibility for organization of this conference for more than 20 years.

The Symposium consists of plenary and parallel sessions of both general and special interest. International leaders on topics of major current interest organize special sessions, comprising about 80 percent of the sessions. Invited speakers for both the plenary and parallel sessions include international experts providing lectures on the latest developments in the wide range of topics covered at this conference. The proceedings of the conference are published in major international journals.

Response: The Thirteenth Symposium on Thermophysical Properties was held in Boulder, Colorado from June 22-27, 1997. W.M. Haynes organized this conference with assistance from R.A. Overfelt of Auburn University. The conference attracted almost 600 participants from more than 35 countries with slightly more than half from countries outside the U.S. The number of participants represented an increase of more than 40% from the Twelfth Symposium.

The conference consisted of 125 sessions over 4-1/2 days with two plenary sessions. There were as many as nine parallel sessions. The final program had 584 papers, 70 percent of which dealt with fluids. Special sessions on alternative refrigerants, aqueous systems, chemical process design, molecular simulation, structure of fluids, acoustic techniques, supercritical fluids, low gravity, natural gas systems, databases, and correlations were organized by members of the Physical and Chemical Properties Division. Other special session topics included critical behavior, optical techniques, laser photothermal techniques, wetting and interfaces, polymers and polymer solutions, subsecond thermophysics, and thin films and coatings.

Plenary session lectures were given by Prof. John M. Prausnitz of the University of California at Berkeley, Dr. Costa Tsonopoulos of Exxon Research and Engineering Co., Prof. Peter T. Cummings of the University of Tennessee and Oak Ridge National Laboratory, and Prof. Michael E. Fisher of the University of Maryland. Prof. S. Peter Kezios of the Georgia Institute of Technology gave a presentation on the history of the Symposium on Thermophysical Properties. The Thirteenth Symposium established the Touloukian Memorial Lecture with Prof. Fisher giving the first in this series. This lecture was presented at the session in which the Yeram S. Touloukian Award was presented to Dr. Ared Cezairliyan (Metallurgy Division, NIST) and to Prof. William A. Wakeham (Imperial College, London, UK) in recognition of their outstanding technical contributions to the field of thermophysical properties.

Approximately 340 manuscripts were submitted for publication in the Symposium Proceedings, which consists of special issues of the International Journal of Thermophysics and Fluid Phase Equilibria. A preprint volume of all manuscripts was prepared on CD-ROM and distributed at the conference. The same information was placed on the Symposium Website http://www.boulder.nist.gov/div838/symp13/).

The Fourteenth Symposium on Thermophysical Properties to be held in Boulder, Colorado from June 25-30, 2000 will be chaired and organized by W.M. Haynes.

30. Fourth International Conference on Chemical Kinetics

***R.E. Huie** and J.W. Hudgens*

Objective: To bring together leading scientists who generate and use chemical kinetic data.

Purpose: This conference is to bring together scientists from different disciplines to discover matters of common interest in chemical kinetics. Chemical kinetics is a fundamental tool for the understanding and control of complex chemical processes, both directly by providing rate data on the elementary reactions involved, and indirectly by an improved understanding of the reactivity patterns and the thermodynamics of reactive intermediates. Many reaction types and intermediates are of key importance in a number of different areas and under widely different conditions. Often, investigators in one field are unaware of studies carried out in another field that may provide useful insights. This is particularly true if different physical phases are involved.

The conference was held July 14 through July 18, 1997. Oral sessions took place in the Red Auditorium at NIST from about 9:00 am to 4:00 pm Monday through Thursday and 9:00 am to 12:30 pm on Friday. Poster sessions were held Monday, Tuesday, and Thursday from 4:20 pm to 6:30 pm at the Gaithersburg Hilton. The Conference was also served by a World-Wide-Web site, through which conferees could obtain information about the conference, register, find out about the meeting hotel and other hotels in the area, etc. The conferees were strongly encouraged to submit their abstracts in electronic form by e-mail. These abstracts were converted to HTML format and, in this way, all abstracts for the meeting were posted on the web site and available to all the conferees well in advance of the conference. The file of conference abstracts could be searched by key word or by author, and an Acrobat file was also available for downloading. The web site also had links from the oral sessions to topical posters, to better integrate the poster presentations with the oral program.

Response: Two hundred scientists registered for the Conference. There were fifty-seven oral presentations and one hundred forty poster presentations. The book of abstracts consisted of more than 300 pages. A wide variety of subject areas were covered at the conference, including small radical kinetics, the kinetics of inorganic radicals at high temperature, reactions of unsaturated radicals, application of theory to kinetic problems, heterogeneous reactions, combustion chemistry, and environmental chemistry. The web site was intensely utilized by the conferees in advance of the meeting, which manifested itself in better communication with the conferees and allowed better preparation on their part. This heightened the success of the meeting. As a result, in the future we envision an even greater utilization of the capabilities of the World-Wide-Web in conferences such as this.

Publications:

Conference Web site:
http://www.nist.gov/cstl/div838/kinet_conf/
conference.html

Program and Abstracts, Fourth International Conference on Chemical Kinetics, NIST, Gaithersburg, MD.

31. Technology Transfer in Computational Thermochemistry

K.K. Irikura

Objective: To publicize the scope, reliability, accessibility, and economics of computational thermochemistry.

Purpose: Global competition is shrinking the timelines for industrial process scale-up (from lab to production). This has resulted is an increased reliance on computerized modeling and simulations to replace expensive, time-consuming, and hazardous experiments. Concurrently, there has been a rapid drop in the cost of computational "horsepower," allowing the development of new predictive techniques that are practical in an industrial environment. Unfortunately, the chemical engineering community is largely unaware of this impressive recent progress. This poor communication is a major hindrance to the conversion of the science into useful technology.

Approach: Encourage communication among engineers, computational scientists, and experimental scientists, building upon their common interests in thermochemistry.

Response: In cooperation with scientists from the Dow Chemical Co., we organized the first symposium on the topic of computational thermochemistry. This included a panel discussion of the needs for and applications of accurate thermochemical data, with an emphasis on prediction. The panel members represented the users of thermochemical data in areas such as chemical processing, microelectronics, academia, and the military. The four major recommendations are expected to guide work in this area. 1) A critically evaluated, consensus database of thermochemical data is needed for methods development by scientists. 2) The scientific research base should be broadened to include the accurate prediction of a wider spectrum of engineering properties such as kinetics, vapor-liquid equilibrium parameters, critical data, and the properties of molecules on surfaces. 3) Better dissemination of these techniques to the engineering and industrial community is needed, including both publicity and user-friendly software. 4) Corporate cultures should be changed to allow private (but non-proprietary) thermochemical data to be added to public resources such as databases and estimation software. In addition to the panel discussion, the proceedings of the entire symposium are summarized in NISTIR 5973, which is publicly available on-line. The symposium was also used as the nucleus of the first book on computational thermochemistry, published by the American Chemical Society. In the future, we intend to focus on recommendations 1) and 3) and to encourage others to pursue recommendations 2) and 4).

Publications:

Irikura, K.K. and Frurip, D.J., ***"Summary Report: Symposium on Computational Thermochemistry [Computers in Chemistry Division, American Chemical Society (ACS), 212th National Meeting, Orlando, Florida, August 25-29, 1996),"*** NIST Internal Report 5973 (1997).

On-line at
http://h178102.nist.gov/nist838t/groups/refdata/irikura/symposium.pdf

Irikura, K.K. and Frurip, D.J., ***"Computational Thermochemistry"*** *and* ***"Worked Examples,"*** in Computational Thermochemistry: Prediction and Estimation of Molecular Thermodynamics; Irikura, K.K. and Frurip, D.J., Eds.; ACS Symposium Series, ACS: Washington, DC, 1997 (in press).

Irikura, K.K., ***"Essential Statistical Thermodynamics"*** *and* ***"Glossary of Common Terms and Abbreviations in Quantum Chemistry,"*** in Computational Thermochemistry: Prediction and Estimation of Molecular Thermodynamics; Irikura, K.K. and Frurip, D.J., Eds.; ACS Symposium Series, ACS: Washington, D.C., 1997 (in press).

VI. Analytical Chemistry Division (839)

Willie E. May, Chief

A. Division Overview

Vision:

The Analytical Chemistry Division serves as the nation's reference laboratory for chemical measurements and standards to enhance U.S. industry's productivity and competitiveness, assure equity in trade, and provide quality assurance for chemical measurements used for assessing and improving public health, safety, and the environment. The Division's activities primarily contribute to the accomplishment of CSTL's measurement science and measurement standards goals through the efforts of its five Groups:

- Organic Analytical Methods
- Spectrochemical Methods
- Gas Metrology and Classical Methods
- Nuclear Analytical Methods
- Chemical Sensing and Automation Technology

Programs:

The skills and knowledge derived from laboratory-based research on phenomena underpinning the measurement of chemical species in a broad spectrum of matrices are applied to the development and critical evaluation of measurement methods of known accuracy, precision, sensitivity, and selectivity. This expertise in chemical measurement science is deployed in a highly leveraged manner and serves as the foundation for cross-cutting measurements and standards programs in:

- Advanced Materials Characterization
- Analytical Instrument Performance and Calibration
- Environmental Monitoring and Technology
- Forensics
- Healthcare and Food/Nutrition

Our vision is to maximize this leverage by establishing and maintaining the infrastructure for providing national traceability and assessing international comparability of chemical measurements for these and future high priority program areas with infrastructural tools such as:

- Standard Reference Materials
- NIST **T**raceable **R**eference **M**aterials (NTRMs)
- Measurement quality assurance programs in critical national areas
- Comparisons of NIST primary methods and standards with other national metrology laboratories

The need of U.S. Industry to document traceability to national measurement standards has increased significantly in the areas of 1) domestic and international trade, 2) the health and safety of the U.S. population, and 3) compliance with quality system requirements. For chemical measurements, Standard Reference Materials are the mainstay for disseminating national measurement standards and for obtaining traceability to NIST. SRMs are certified reference materials, issued under NIST trade-mark, that are well-characterized using state-of-the-art measurement methods and/or technologies for chemical composition and/or physical properties. Traditionally, SRMs have been the primary tools that NIST provided to the user community for achieving chemical measurement quality assurance and traceability to national standards. Currently, NIST provides nearly 1300 different types of SRMs and in FY97 sold nearly 40,000 SRM units to approximately 5,000 unique customers; approxi-mately 20,000 units of these represent about 850 different types that are certified for chemical composition.

NIST does not have all of the resources necessary to provide the quantities and specific varieties of SRMs (exact sample types, unique compound combinations, concentrations, etc.) needed to meet these increasing needs. The NIST Traceable Reference Materials program has been created to address this problem. A NTRM is a commercially produced reference material with a well-defined traceability linkage to existing NIST standards for chemical measurements. This traceability linkage is established by criteria and protocols defined by

NIST and tailored to meet the needs of the metrological community to be served.

Initially the NTRM concept was implemented in the gas standards area to allow NIST to respond to increasing demands for high quality reference materials needed to implement the "Emissions Trading" provisions of the Clean Air Act of 1990 (while facing the reality of constant human and financial resources at NIST). The program has been highly successful. Since its inception, ten specialty gas companies have worked with us to certify nearly 4200 NTRM cylinders of gas mixtures that have been used to produce approximately 300,000 NIST-traceable gas standards for end-users. According to Stephen Miller, Technical Director, Scott Specialty Gases, "the NTRM program has served as an excellent vehicle for production of the high quality standards - of known pedigree - required by both industry and the regulatory community in the implementation of Title IV (SO_2 emissions trading) of the 1990 Clean Air Act." The NTRM model for the commercial production of reference materials is being extended to other mature and high volume areas so that more of our resources can be diverted to address new and/or more difficult high priority measurement problems.

In addition to our efforts to define and establish our national traceability infrastructure, we are aggressively expanding our efforts to document the comparability of NIST primary methods and standards with those of other nations and metrological regions through both multilateral (CIPM Consultative Committee on the Amount of Substance) and several strategic bi- and trilateral collaborations. Our bilateral program with NMi (The Netherlands) for determining the equivalence of primary gas standards has resulted in a formal "Declaration of Equivalence." This "Declaration" is mutually recognized by the U.S. EPA and European environmental regulatory bodies as documenting the equivalence of seven NIST and NMi primary gas mixtures suites (spanning a wide range of concentrations). Collaborations for assessing the equivalence of primary standards are being established with DFM (Denmark) and OHM (Hungary) for conductivity, with PTB (Germany) for pH, with NIMC (Japan) and BAM (Germany) for elemental solution standards, and with NIMC for volatile organic compound standards.

Other federal and state government agencies continue to be important customers. During the past year, we were involved in 15 projects with 10 federal and state government agencies primarily providing them with measurement quality assurance services for environmental and health-related activities. For example in collaboration with the National Cancer Institute, we serve as an analytical reference laboratory and quality assurance center for approximately 60 laboratories world-wide involved in studies to determine the cancer preventive benefits of dietary intakes of selected micronutrients to high risk human populations. We are working with the National Oceanic and Atmospheric Administration, the Environmental Protection Agency, and over 40 laboratories involved with the measurement of organic contaminants in marine sediments and tissues as part of various marine monitoring programs. We are interacting with eight laboratories involved in the measurement of heavy metals, pesticides, and PAHs in soil, water, food, and indoor/outdoor air samples collected and analyzed as part of the EPA National Human Exposure Assessment Study. Working with the National Institute of Justice, the Division is developing methods and standards for the analysis of drugs-of-abuse in hair, in addition to developing and applying cutting-edge statistical approaches for the analysis and visualization of DNA profiling data for laboratory performance evaluation. Compliance with the Chemical Weapons Convention is a critical international issue. The Division is working with the Defense Special Weapons Agency and the Organization for the Prohibition of Chemical Weapons to develop and critically evaluate chemical measurement protocols to be used during onsite inspections of manufacturing and storage facilities.

Selected Programs Highlights:

Details concerning these and additional interactions and collaborations with other government agencies can be found in the brief group overviews and selected Technical Activity Reports that follow. These overviews and reports illustrate the synergistic relationships among the research activities in chemical measurement science based in the various groups and the standards and quality assurance activities underway in the various program areas.

Organic Analytical Methods:

Research activities in organic analytical methods are directed toward the development, critical evaluation, and application of methods for the identification and measurement of organic and organometal species - organic mass spectrometry and analytical separations techniques including gas chromatography (GC), liquid chromatography (LC), supercritical fluid chromatography (SFC) and extraction (SFE), capillary electrophoresis (CE), and capillary electrochromatography (CEC).

Recent research activities in organic mass spectrometry have focused on the development of electrospray ionization as a tool for the quantitative determination of proteins in biological matrices. A paper describing a method for the mass spectrometric determination of albumin (M_r [relative molecular mass] 65K) in serum has been published. We are establishing reference methods for important biomarkers such as troponin-I (a new marker of myocardial infarction), glycohemoglobin (an important new marker for diabetes), serum thyroxine (an important marker for thyroid function), and cortisol (a marker for endocrine function). Development of accurate methods is an important component of our ongoing collaborations with the College of American Pathologists and the Centers for Disease Control and Prevention to establish NIST traceability for measurement of important health markers. A new high resolution mass spectrometer was acquired and is providing the high precision measurements needed for our clinical standards program and will also allow us to begin certifying reference materials for environmental contaminants such as dioxins, furans, and toxaphene in environmental matrices.

Recent research activities in separation science have focused on investigations of the physical and chemical processes that influence the separation and detection of organic compounds, and the application of these techniques in the development of reference methods for the determination of these compounds in natural matrices. The results of these investigations are used to design stationary phases tailored to solve specific separations and analysis problems. Our recent efforts have focused on application of capillary electrokinetic chromatography to clinical and environmental separation problems. The combined use of CEC with C_{30} stationary phases, developed in this laboratory, has resulted in greatly improved separations of β-carotene isomers and other carotenoids of interest in health and food/nutritional studies. Our current research in chiral separations focuses on the development of CE and SFC separation strategies for optical isomers of pharmaceutical and agricultural interest. We have identified a variety of new chiral selectors for use in CE that provide advantages and alternatives to existing reagents. In addition, we have evaluated the use of pressurized fluid extraction (PFE) as an alternative to conventional soxhlet extraction of environmental samples. Benefits include higher sample throughput, reduced solvent consumption, reduced labor, and the ability to extract small samples. We are currently using the PFE approach to assess the homogeneity of several of our environmental matrix SRMs at the 1 mg - 100 mg level. Our research in organometal speciation has resulted in the first certified values for methylmercury in three mussel tissue SRMs using a method based on gas chromatography with atomic emission detection. Efforts in this area are continuing with emphasis being shifted toward arsenic speciation using coupled LC inductively coupled plasma mass spectrometry (ICP-MS).

Several new SRMs are being developed to support measurement activities in the environmental, health-care, and food/nutritional communities. Over 70 analytes including polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), chlorinated pesticides, and trace elements have been certified in a new sediment material, *New York/New Jersey Waterway Sediment* [SRM 1944]. Several environmental matrix SRMs that had been issued previously were reanalyzed to provide a much larger number of constituents with certified or reference values. These SRMs include *Urban Dust/Organics* [SRM 1649], *Diesel Particulate Matter* [SRM 1650], *Organics in Cod Liver Oil* [SRM 1588], and *PCBs in River Sediment* [SRM 1939]. Work is underway for a replacement material for *PCBs in Human Serum* [SRM 1589]. In contrast to the previous material, the PCBs present are at naturally occurring levels and were not spiked into the serum. Work has started on a new "fillet of fish" SRM that will be certified for PCBs and pesticides and also will be characterized for proximate content (proteins, carbohydrates, fat, etc.). Both the environmental and nutritional measurement communities have requested this new material. During the past year, a new *Baby Food Composite* [SRM 2383] was certified for a number of important vitamins and carotenoid compounds.

Additional information was provided for proximates, minerals, and additional vitamins. Certification is underway for a *Meat Homogenate* [SRM 1846], identified by the USDA, FDA, and the food industry as a high priority need. The canned meat homogenate will be certified for cholesterol and selected fatty acids and provide additional information for proximates and mineral content. SRMs 1846 and 2383, along with several other recently developed food-related reference materials, will be used by the food testing/ nutritional laboratory community to facilitate compliance with new nutritional labeling laws and to provide accurate labeling information to assist consumers in making sound nutritional choices. In the coming year, efforts will be directed toward providing additional information on constituents of nutritional interest for a number of existing SRMs, a major recommendation from a recent NIST workshop involving the food industry, FDA, and USDA. In the clinical area, certification was completed for SRM 1951a, *Lipids in Frozen Human Serum*, which will be used by the clinical laboratory community to establish an NIST traceability link for important heart disease risk markers such as total, HDL-, and LDL-cholesterol, and triglycerides.

Spectrochemical Methods:

Research activities in spectrochemical methods are directed toward the development, critical evaluation, and application of techniques for the identification and measurement of inorganic species using x-ray, optical, and mass spectrometries. This research is directed toward improving the accuracy and precision of spectrochemical methods, developing and applying new approaches for characterizing advanced materials, and value-assigning reference materials for inorganic constituents.

A promising research development of the past year was the demonstration of significantly improved performance capabilities of ICP-OES using an innovative calibration and data analysis approach, which yielded analytical data of unprecedented precision (0.02-0.2% relative uncertainties). The research was accomplished using a commercial ICP-OES instrument with simultaneous multi-channel detection capabilities. This new instrument calibration and data handling strategy will be evaluated for its applicability to other spectrometric techniques and analytical methodologies. Early indications are that this approach yields similar gains in precision for GC/MS data. We expect to see similar gains for any technique that demonstrates significant drift of signal response as a function of time. Additional details concerning this new and exciting research are provided in Technical Activity Report 3.

The next stage of this research will be to realize a more thorough understanding of the potential biases in ICP-OES measurements in order to establish ICP-OES as a primary chemical metrological method. However, in the short term, this demonstrated ability to make high-precision comparative measurements vs. primary chemical standards promises to impact several prominent Division measurement and standards programs - most notably our new activities directed toward the commercial production of NIST-traceable elemental solution standards for calibration of instrumentation used for inorganic analysis (spectrometric solutions). Protocols based on this new high-precision ICP-OES approach will be transferred to commercial standards producers to allow the accuracy embedded in NIST SRMs to be transferred to their products. This new technology will also be used at NIST for blind audits of the commercially produced NTRMs.

One of the first practical applications of the ICP-OES technique was to value-assign a lithium aluminate material for the isotopic composition of Li and the atom-ratio of Li:Al that was needed by the Department of Energy in its efforts to replenish the nation's critically needed supply of tritium. The ICP-OES based method developed at NIST achieved relative measurement precisions of better than 0.1% for both Al and Li; the total relative expanded uncertainty for the Li:Al stoichiometry was 0.18%. The lithium isotopic composition was determined with a relative measurement precision of 0.06% using thermal ionization mass spectrometry procedures routinely employed in the group. This material is being used as a check sample by DOE's Idaho Falls National Engineering Laboratory to determine the proficiency of laboratories wishing to perform analyses for commercial vendors of reactor target rods. No reference materials or reference methods were available to underpin this program prior to NIST involvement. Therefore, this material will serve as the benchmark reference standard and basis for providing NIST traceability for this critical national program.

Increasingly glow discharge optical emission spectroscopy (GD-OES) is used by industry for materials characterization because it is far less dependent on matrix-matched standards than other techniques that have typically been used for direct analysis of inorganic constituents in solid samples, e.g., spark-OES. Despite this potential, the use of this technique in U.S. industrial labs has lagged well behind their European and Asian counterparts because the technique has not been investigated systematically for biases and other performance characteristics. During the past year we have developed and critically evaluated a method for determining phosphorus in Cu alloys using a GD instrument that was built at NIST. In collaborative work with both academic (Clemson University) and commercial (LECO Corporation) developers of this type of instrumentation, fundamental and practical aspects of the technique were studied. The initial work with the LECO Corporation resulted in the identification of several overlapping areas of research interest and a CRADA is being established to continue these investigations. The determination of non-metals in advanced materials is another major new Division program for FY98 and the preliminary work accomplished this year indicates that GD-OES can make a significant impact in this neglected area of analysis. Technical Activity Report 11 provides additional details concerning our work in this area.

Inductively coupled plasma mass spectrometry is now a measurement workhorse for this group, and is beginning to replace thermal ionization mass spectrometry for most of our standards-related activities. We are leading the international community in the development and implementation of ICP-MS-based protocols for inorganic chemical analysis. Last year we developed and disseminated protocols for an international intercomparison study of Pb in water where ten of eleven national standards laboratories agreed to within 1% (relative) of the assigned value. In the previous study, without the NIST-developed protocol, only four laboratories agreed within the 1% interval. The group also began preliminary studies coupling an electrothermal vaporization source to the ICP-MS and will continue to explore this technique to reduce interferences and increase the accuracy of ICP-MS. This research complements ongoing efforts to improve measurement accuracy by identifying chemical and/or instrumental approaches for removing or correcting for isobaric interferences. We have procured a high resolution ICP-MS instrument and during the coming year will investigate another instrumental approach (high resolution mass spectrometry) for addressing this problem. Technical Activity Report 6 provides details concerning an application of our ICP-MS measurement capabilities in determining a new and accurate half-life for ^{190}Pt in collaboration with universities of Maryland and Colorado.

During the past year, the full range of optical, x-ray, and mass spectrometric techniques available in the group was applied to the certification of inorganic constituents in a number of reference materials including metals, sediment, soil, food, and fuel matrices. These reference materials are the principal tools for transferring NIST measurement accuracy to the nation's inorganic chemical measurement community.

Gas Metrology and Classical Methods:

Research activities within this group are focused on gas metrology, classical wet chemical methods (gravimetry, titrimetry), coulometry, ion chromatography, optical spectroscopy, and maintenance of the theoretical infrastructure for pH and conductivity measurements.

To assist the U.S. automobile industry, we are developing and evaluating new analytical measurement tools and providing standards needed to address compliance issues associated with the Clean Air Act of 1990. We are developing an infrared-based sensing device and are working with the NIST Physics Laboratory to evaluate a new Fourier Transform microwave device for real-time detection of oxygenated hydrocarbons in auto-mobile exhaust. A series of new cylinder-based gas SRMs for low emission vehicles also is being produced to support U.S. automobile manufacturers in the development of the next generation of "clean" cars. In addition, catalytic conversion technology has been developed for the on-demand generation of standard formaldehyde-in-air mixtures from methanol-in-air standards to address stability problems associated with storage of the formaldehyde mixtures in cylinders. A prototype device has been developed at NIST and is being evaluated by the auto industry.

During the past two years, we have been working with the National Institute for Child Health and Development and several private pediatric researchers who are evaluating the therapeutic value of inhaled NO in newborn patients. Initially we determined the kinetics of NO_2 formation from NO under clinical conditions. This was extremely important because NO_2 can cause pulmonary edema and other problems in the patient's respiratory system. Based on the NIST data, it was concluded that at anticipated dwell times of <0.5 second, no significant levels of NO_2 should reach the patent during treatment and this new therapeutic regime was approved by FDA this past spring. NIST primary standards and facilities were used to allow manufacturers to demonstrate the accuracy of new monitoring devices designed to measure NO and NO_2 under these high-oxygen therapeutic conditions and to support the production by a commercial specialty gas company of NTRM gas mixtures needed for calibration of these sensors. Further details of these efforts can be found in Technical Activity Report 1.

In collaborations with EPA and the Chemical Manufacturers' Association, we are developing the quantitative database of infrared spectra required for establishing FTIR-based technology as a reliable tool for real-time monitoring for airborne chemical contaminants along plant boundaries and within plant facilities. Because the spectra are being prepared using NIST primary gas standards, well-defined traceability to NIST can be established for any subsequent field measurements. More information concerning these activities and our near-term plans for release of spectra for the 20 highest priority species can be found in Technical Activity Report 2.

During FY97, 15 gas SRMs, 43 spectrometric solution SRMs, 6 conductivity SRMs, and 2 pH SRMs were completed or measured and 74 gas SRMs were recertified. While these standards are critically needed, their continuous production ties up considerable fiscal and human resources and limits our ability to address new standards needs. The **N**IST **T**raceable **R**eference **M**aterials Program was created to address this concern. In FY97, we worked with 10 specialty gas vendors to certify 61 NTRM batches. The 1400 individual gas cylinder in these certified batches will be used to produce approximately 100,000 NIST-traceable gas standards for end-users. Plans are being put in place to extend the gas NTRM model for the commercial production of spectrometric solutions standards.

Chemical Sensing and Automation Technology:

Activities in this group are directed toward the development and certification of standards for calibrating and verifying performance of chemical analysis instruments, development of standards for laboratory automation, and research on new technologies, techniques, and standards for sample preparation and analysis in forensics and analytical toxicology.

In FY97, 192 optical filter SRMs were certified and 275 optical filter SRMs were recertified. We also began a study of environmental effects on the transmittance drift of solid filters and concluded a research project on optical wedge effects in solid filter standards and cuvettes used in chemical spectrophotometry. This work resulted in a diagnostic instrument that can detect unacceptable optical wedge bias in each candidate standard solid filter. As a result of a workshop and round-robin activity we conducted for our candidate near infrared (NIR) wavelength standard [SRM 2035], we reformulated the glass and obtained a new material with additional spectral character to extend the range to the longer wavelengths needed by the pharmaceutical industry. An NTRM program for the optical filters program was initiated with a successful "Workshop on NIST Traceability in Chemical Spectrophotometry" that attracted 32 participants from pharmaceutical and chemical companies, instrument and optical component manufacturers, and government regulatory agencies. The attendees endorsed the NTRM concept and agreed that commercial production of NIST-traceable optical filter standards was desirable as long as public and regulatory agency acceptance of NTRMs is assured.

We have developed both advanced analytical and calibration approaches for the certification of four new synthetic gasoline SRMs for oxygenate content. A combined Fourier Transform-NIR and Raman approach has been developed for inclusive non-destructive testing of the ampouled SRMs. In collaboration with the University of Washington, Center for Process Analytical Chemistry, we developed mathematical algorithms for multivariate calibrations that can be used either for value-assigning individual ampoules or for identifying "outlier" ampoules for discarding prior to batch assignment.

Over the past few years there has been an explosion in the development of microanalytical systems, i.e., laboratories on a chip. Currently the fabrication of these systems is a high-technology, high-investment activity. We have initiated a program that focuses on the design and development of inexpensive devices fabricated in plastics. We have created microchannel devices by two independent imprinting techniques, wire- and silicon-template imprinting. Channels produced by both techniques show excellent device-to-device reproducibility in the physical sense. We have also demonstrated reproducible electrokinetic injections and electrophoretic separations using prototype devices with channel diameters of approximately 25 µm.

We have initiated a new sampling and analysis approach for the detection of gunpowder residues from handgun use or from a pipe bomb explosion in collaboration with the Department of Forensic Sciences at George Washington University. Organic compounds in the residues are being recovered by automated supercritical fluid extraction (SFE) and then separated and detected by micellar electrokinetic capillary electrophoresis. We are currently determining conditions for the selective and reproducible SFE recovery of gunpowder additives. We intend to develop protocols that will permit the analysis of residue samples recovered by solvent swabbing of surfaces and from nasal mucus.

In collaboration with the University of Maryland Chemistry Department, we developed a new detection approach for the environmentally harmful organic chlorination products formed in sewage wastewater processing. Liquid chromatography was combined with a detection scheme based on post-column reaction of the N-chloramines followed by electrochemical detection. The method was used to evaluate the effectiveness and rate of commercial de-chlorination processes used to remove the toxic N-chloramines. Although "inorganic" N-chloramines rapidly dechlorinate, the LC method revealed that peptide and protein-nitrogen in the sewage are slowly dechlorinated with half-lives of over 20 minutes. Our results will allow sewage process engineers to modify and monitor the treatment processing to ensure that the harmful organic N-chloramines are fully dechlorinated before discharge of the wastewater.

The development and application of cutting edge statistical approaches for the analysis and visualization of interlaboratory DNA profiling data have continued. Over the past several years we have developed a set of graphical tools called single-locus tolerance charts – standardized scattergrams of DNA profiling sizing data used for measurement quality assurance in DNA testing. This approach has been adopted by the College of American Pathologists for presentation of data that come from the Forensic Identity Series of Laboratory Proficiency Tests in which over 140 of the approximately 200 crime laboratories in the U.S. participate. In addition, the FBI has adopted NIST algorithms for screening data prior to inclusion in the national criminal sex offender DNA database (CODIS: Combined DNA Identification System) and the charting method referred to as "The NIST Ellipse" for quality assurance. Novel statistical approaches were also developed for the NIST/NCI Micronutrient Measurement Quality Assurance Program for separating the among-laboratory measurement variability as a function of analyte concentration.

Nuclear Analytical Methods:

Research activities in this group are focused on scientific issues that are the basis for improving and extending current methods and developing new nuclear analytical techniques for identification and quantitation of chemical species. This involves the full suite of nuclear analytical techniques including instrumental and radiochemical neutron activation analysis (NAA), prompt gamma activation analysis (PGAA), and neutron depth profiling (NDP), as well as the use of neutron focusing technology for analytical applications. The measurement capabilities that reside within this group provide an excellent complement to those in the Spectrochemical Methods Group in that they depend upon characteristics of the nucleus of the element rather than the electron shells, and also that they often are nondestructive and do not require sample dissolution.

NAA is a powerful reference technique in use at NIST for many years, and new developments continue to provide improvements in detection sensitivities, elemental specificity, precision, and overall accuracy which allow it to address new measurement needs. Many analytical techniques used in industry and academia rely on the analysis of very small samples (i.e., 1 mg), typically in the solid form. Unfortunately most SRMs are certified with minimum sample sizes of 100 mg-500 mg, and are therefore unsuitable for use as control materials for these techniques unless additional information is made available. We have been studying the homogeneity of existing SRMs at small sample sizes to help meet this need. Taking advantage of the sensitivity and nondestructive properties of instrumental NAA, the use of this technique for homogeneity studies of small samples has been evaluated and implemented for the determination of sampling characteristics for a number of biological SRMs and air particulate matter. The minimal analytical uncertainty associated with the instrumental NAA measurements allows extraction of the variability due to material inhomogeneity from the observed total variability in a set of measurements. This year we have demonstrated that uncertainties for a number of elements due to inhomogeneity are in the 1% (relative) range or lower when 1 mg samples of *Peach Leaves* or *Urban Particulate Matter* SRMs are analyzed. Certification of selected elements at sample sizes in the milligram range will permit the use of natural matrix SRMs for the different solid sampling techniques that are used in industry and research.

The accurate determination of speciated forms of trace elements is an ongoing and difficult problem. A new chemical separation method has been developed to measure organically bound Hg (primarily methylmercury) in tissue samples. The procedure involves distillation of the organomercury from a mixture of powdered sample, sulfuric acid, and cupric sulfate. This distillate is then bound chemically to a cysteine-loaded filter paper. The Hg bound to the paper is then determined using NAA. The accuracy of the method was confirmed using several different CRMs certified for methylmercury. This technique was used in the certification of three mussel tissue SRMs [SRMs 1974a, 2974, and 2976]. See Technical Activity Report 15 for further details.

Pioneering research is conducted within this group on the use of cold neutron beams as analytical probes using both PGAA and NDP. PGAA measures the total amount of an analyte present throughout a sample by the analysis of the prompt gamma-rays emitted immediately following neutron capture. NDP on the other hand, determines the concentrations of several important elements (isotopes) as a function of depth within the first few micrometers of the surface, by energy analysis of the charged particles emitted during neutron bombardment. Both of these techniques continue to make important contributions in the characterization of advanced materials, particularly with the enhanced sensitivities now available using the cold neutrons from the NIST reactor.

After an extended reactor shutdown, the cold-neutron PGAA and NDP spectrometers have been rebuilt to take advantage of the newly installed cold neutron source at the NIST Reactor. The new analytical instrument designs, in combination with the new cold source, have resulted in detection limit improvements of about a factor of four for both techniques. Current NDP research applications include the measurement of nitrogen profiles in thin TiN films and lithium migration in electrochromic films to assist the semiconductor industry with quality control and product design/assessment. We continue to provide cold neutron PGAA measurements for many outside users. Non-destructive, matrix-independent measurements of hydrogen by this technique have become particularly valuable in view of the difficulties of accurate determination of this element by other techniques. During the past year, we have provided measurement services for companies within the aluminum, petrochemical, computer, and other high technology industries.

Efforts continue within the group to develop and apply cutting-edge neutron focusing technology for analytical applications. The long-term goal of our research in this area is to provide three-dimensional compositional mapping of thin-film semiconductor materials. In order to realize the greater lateral resolution and higher sensitivity needed to attain this goal, we have collaborated with X-Ray Optical, Inc. in the development and testing of a monolithic lens consisting of a fused tapered bundle of polycapillaries. This new device provided a focus of ~0.16 mm at a focal length of 20 mm and showed gains in neutron current of a factor of ~60 relative to polycapillary lenses previously tested.

Future Directions:

All Division research and service projects are reviewed on an annual basis for quality, progress, and match to mission and customer needs. The chemical measurement science and cross-cutting program areas on which the Division's research and measurement service activities are focused will not change very much in the coming year. However, we will redirect some of our efforts in chemical sensing and automation technology to address analytical instrument calibration transfer and performance issues.

The Division's budget for Standard Reference Materials activities has been ~$3M for each of the past several years. During this period, the majority of our efforts have focused on renewals urgently requested by customers and few resources have remained for development of standards to address new measurement problems/needs. The gas NTRM program described previously has provided some relief and over the past two years, we have been able to initiate efforts for development of a number of new, high priority SRMs including the following that should be completed during the coming year:

- Reformulated Gasolines (Oxygenates, organic and total sulfur, and aromatics to be certified)
- Hydrogen in Titanium (Brittleness of aircraft turbine blades related to H_2 concentration)
- Zeolite Catalysts (Na, Si, Al, Fe, and trace metals to be certified)
- Aircraft Alloys (P and S to be certified; materials failure related to P and S concentrations)
- NIR Wavelength Standard (For precise calibration of spectral region of increasing industrial interest and use)
- Meat Homogenate for Nutrition Labeling (Cholesterol, fatty acids, and minerals to be certified)
- Organics in Fish Tissue (Environmental contaminants such as PCBs, pesticides, and methylmercury along with food proximates to be certified)
- Toxic Metals in Blood (Toxic metals such as Cd, Pb, total and methylmercury to be certified)

We will continue to focus more of the Division's resources on chemical measurement science and the development of primary standards with improved accuracy and uncertainty levels, and establishment of the infrastructure for commercial production of NIST- traceable secondary standards to meet day-to-day end- user needs. We will continue to pursue the establishment of MOUs with key national chemical metrology institutes for carrying out collaborative research and performing periodic intercomparisons to assess and document the comparability of primary standards and/or measurement capabilities in critical areas. Increased effort will be directed toward establishment of the chemical metrology infrastructure needed to facilitate trade and effective heath and environmental monitoring and decision-making throughout the Americas. We will work through NORAMET and the Interamerican Metrology System (SIM) to plan and conduct intercomparisons in key measurement areas for assessing the current state-of-the-practice in various countries. We will also develop and offer formal courses at NIST concerning the use of advanced chemical measurement methods for certification of reference materials. The first series of intercomparisons are being scheduled for the summer of 1998 with courses in organic analytical methods and spectrochemical methods being planned for the following fall.

The information that has been provided represents a broad range of research and service activities within the general area of chemical measurement science. This overview plus the Selected Technical Activity Reports that follow provide additional details concerning our work and reflect the high quality of our staff. This information also shows how our efforts are impacting U.S. industry's productivity and competitiveness as well as providing measurement infrastructural support for environmental quality and human health assessments.

B. Selected Technical Reports

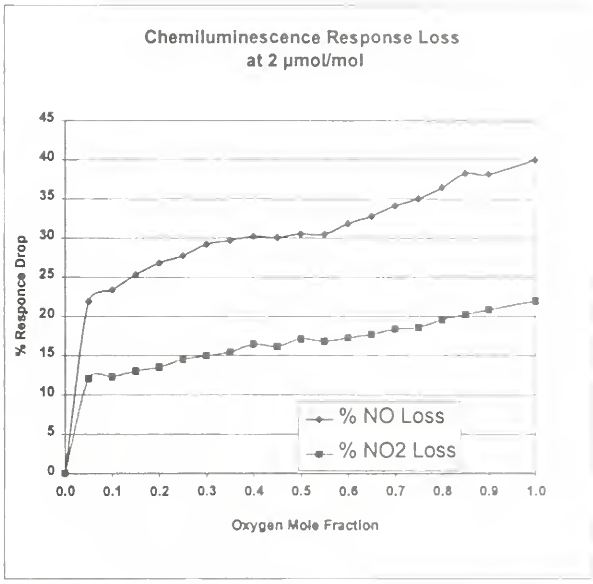
1. *NIST Supports New Inhaled Nitric Oxide Inhalation Therapy for Newborns*

***W.J. Thorn III** and P.A. Johnson*

Objective: To assist pediatric researchers and physicians at the National Institute of Child Health and Development (NICHD) and the Food and Drug Administration (FDA) in developing guidelines, accurate gas standards, protocols, and a means for evaluating medical devices needed to implement a new inhaled nitric oxide (INO) therapeutic regimen.

Problem: In a new therapy developed for infants under respiratory distress, small concentrations of nitric oxide (NO) added to inhaled oxygen have shown dramatic results as a pulmonary vasodilator in some patients. However, NO_2 can cause pulmonary edema and other problems in the patient's respiratory system and it is always present in the INO ventilator gas. It is a major contaminant in the nitric oxide source gas and NO_2 is spontaneously formed when NO mixes with oxygen in the ventilator circuit. Because of this potential for adverse effects, levels of NO and NO_2 must be continuously monitored in a typical matrix of >0.8 mole fraction of oxygen during the therapy. Instruments used to monitor NO and NO_2 under clinical conditions have been found to give inaccurate concentrations. Gas standards of known concentration are needed to properly evaluate device measurement behavior.

Approach: For two years, we have worked with both pediatric researchers and manufactures of monitoring devices on a number of metrological needs required to develop protocols and gain FDA approval for this new therapy as well as to address measurement needs during its implementation. Initially we investigated the kinetics of NO_2 formation from NO in the high oxygen clinical conditions. Based on the NIST data, it was concluded that at anticipated dwell times of <0.5 second, no significant levels of NO_2 should reach the patent during treatment and this new therapeutic regime was approved by FDA this past spring. At a workshop held at NIST last year, several of both types of instruments commonly used for NO/NO_2 monitoring – chemiluminescence-based and electrochemical-based devices – were found to measure NO and NO_2 inaccurately under the required high oxygen conditions. NIST developed primary standards to provide the accuracy base for these measurements and to support the production by a commercial specialty gas company of NTRM gas mixtures needed for calibration of these devices. In FY97 a test system developed at NIST to emulate and deliver INO ventilator circuit mixtures of known concentrations was used to evaluate the accuracy of redesigned monitoring devices in measuring NO and NO_2 and also was used to investigate possible biases due to oxygen quenching.



Results and Future Plans: A NO and NO_2 Clinical Test Gas Delivery System was assembled that utilized NIST's Volumetric Flow Calibrator to calibrate mass flows of oxygen/nitrogen mixtures which flow across gravimetrically calibrated NO_2 permeation tube SRMs. Substituting gaseous NO SRMs for nitrogen provides "known" mixtures of NO, NO_2, and O_2. At a three-day workshop, this system was used by researchers and instrument manufacturers to calibrate and evaluate the performance of instruments to accurately measure NO and NO_2 under INO clinical conditions. The redesigned NO and NO_2 electrochemical sensors performed well; however, the chemiluminescence analyzers continued to show a loss of response in high oxygen backgrounds. Because chemiluminescence is a widely used technique in clinical nitric oxide research, this response loss was evaluated. Measurements of mixtures of known concentrations of NO and NO_2 in high oxygen matrices (see figure) showed that chemiluminescence response is reduced by up to 42% in the NO mode and 24% in the NO_X mode as the oxygen mole fraction is increased. The mechanism(s) involved in this loss of response will be investigated. Understanding the causes of this bias may lead to strategies to enable accurate measurements across a wide range of oxygen fractions.

2. *Spectral Reference Database Developed to Support Open-Path FT-IR Measurement of Environmental Contaminants*

P.M. Chu, G.C. Rhoderick, F.R. Guenther, and W.J. Lafferty (Optical Technology Division, PL)

Objective: To develop a reference spectral database to support open-path Fourier transform (FT) infrared measurements of chemical emissions and hazardous air pollutant (HAP) molecules.

Problem: With the development of fast portable computers and robust instrumentation, open-path and extractive Fourier Transform (FT) infrared spectrometric techniques recently have become practical real-time chemical analysis tools. Because each molecular species has a unique spectrum, the infrared bands can be used for both qualitative and quantitative analysis of a gas sample. The EPA recently tested open-path FTIR monitoring during the remediation of several Super Fund sites and found the technique to be useful for monitoring the emission of benzene as well as other hazardous air pollutants down to nanomole/mole concentrations. A number of industries are using open-path methods to measure chemical emissions across their fence lines and inside their plants.

Recognizing the potential of FT infrared methods, the Environmental Protection Agency (EPA) is currently preparing a formal protocol (Method TO-16) for FT infrared open-path remote sensing. This new protocol will provide industry with a tool for regulatory compliance that is both cost-effective and less invasive than current practices. The success of this program is highly dependent on the availability of high-quality reference spectral data.

Approach: Primary gravimetric standards of gaseous mixtures are prepared at NIST using starting materials of assessed purity and procedures that minimize contamination. The final concentrations of these standards are verified by gas chromatography using several independently prepared calibration mixtures. Primary standards are used to benchmark the concentrations of working standards of target contaminants in nitrogen. These target compound working standards of various known concentrations are each continuously flowed through the sample cell and data averaging is initiated after a steady-state spectrum is obtained. This minimizes biases caused by sample adsorption to the cell walls. A research grade FT infrared spectrometer is used to obtain the spectra at a nominal resolution of 0.125 cm^{-1}. Spectra will be provided at a number of resolutions and apodizations to match that of field instruments. Intercomparisons of gas standards prepared by NIST and the National Physical Laboratory, UK (NPL) and intercomparisons of spectral data acquired from NIST-prepared samples by NPL as well as a number of expert laboratories in the United States will be used to assure the quality of the final data.

Results and Future Plans: Our initial work focused on examining a number of the instrumental parameters such as apodization functions, resolution, wavelength calibration, detector properties, and instrument stability. In the FT infrared data aquisition protocol developed for each contaminant, nine spectra are acquired at 0.125 cm^{-1} resolution using three different concentrations and three different path lengths. Using the known concentrations and path lengths, point-by-point absorption coefficients are calculated and tabulated on a grid of 20 points/cm^{-1}. In collaboration with EPA and industry, we prioritized the 189 HAP compounds listed in the EPA Clean Air Act Amendment of 1990. Data acquisition for the first set of 20 highest priority compounds has been completed. In the coming year, the resulting database will be published and distributed and standard reference data for the next set of prioritized compounds will be acquired.

Publications:

Chu, P.M., Rhoderick, G.C., Lafferty, W.J., Guenther, F.R., and Wetzel, S.J., ***"A Quantitative Infrared Database of Hazardous Air Pollutants,"*** Proc. of the Air & Waste Mgmt. Assoc., 89th Annual Meeting and Exhibition, Nashville, TN, June 23-28 (1996).

Chu, P.M., Rhoderick, G.C., Van Vlack, D., Wetzel, S.J., Lafferty, W.J., and Guenther, F.R., ***"A Quantitative Infrared Database of Hazardous Air Pollutants,"*** Fres. J. Anal. Chem. (in press).

3. *Methodology for High Precision ICP-OES*

M.L. Salit

Objective: To develop inductively coupled plasma-optical emission spectrometry (ICP-OES) capability for elemental analyses at the level of precision needed for Division measurements in support of SRM certifications and other programs.

Problem: ICP-OES is routinely used for elemental analysis from ng/g to mg/g mass fraction levels for nearly 70 elements of the periodic table. Modern commercial ICP-OES instrumentation is highly automated and takes advantage of solid-state detector technology thereby permitting high precision photometry simultaneously at multiple wavelengths. To make use of this commercially available, efficient technique to perform such analyses in the certification of various SRMs, particularly the elemental solution (spectrometric solution) SRMs, methodology was needed which would deliver analyses with expanded uncertainties of 0.5 % relative or better.

Approach: A commercial ICP-OES instrument with simultaneous multi-channel detection capabilities was used for this research. Such an instrument is well suited to precision analysis, particularly in assay-type applications where precise results are required, large volumes of sample are available, and significant measurement time can be expended to perform the analysis. This technology was combined with careful metrology, including an innovative calibration approach, to yield high precision methodology.

The improved methodology is based upon:

- gravimetric solution handling that includes gravimetric addition of internal standard,
- an experiment design that captures the potential sources of variability due to preparation for analysis,
- sample-to-sample differences (homogeneity), and calibrant-to-calibrant variability due to uncertainty in the calibrant materials or concentrations,
- and repeated high short-term precision internally standardized measurements over many hours (as much as 24 hours of measurement time), made possible with a new drift correction procedure that is more time-efficient and exhibits higher performance than traditional approaches.

The drift correction procedure was developed to modify and correct for systematic drift when it was observed that the very high short-term precision allowed this drift to be separated from the noise.

Results and Future Plans: Use of these advanced methodological strategies yielded analytical ICP-OES data of unprecedented precision (0.02-0.2% relative uncertainties), affording analyses with expanded relative uncertainties on the order of 1 to 2 parts-per-thousand. This has been demonstrated for more than 20 elements in single and multi-element analyses of simple solutions. Combined with developments in ICP sample input systems, ICP-OES system performance is now at a level where carefully operated commercial instruments can provide short-term precision of better than 0.5% relative and thus affords an alternative to more difficult or expensive approaches (classical methods, isotope dilution) for selected elemental analyses.

More than 1000 ICP-OES instruments of this caliber are deployed in the world and this methodology is transferable to these installations. The drift correction procedure is the element of this methodology with the greatest potential impact. Our experiments have demonstrated precision enhancement of up to 20-fold using this procedure. This promising new instrument calibration strategy is being evaluated for its applicability to other spectrometric techniques and analytical methodologies. Early indications are that this approach yields similar gains in precision for GC/MS data. We expect to see similar gains for any measurement system where the short-term noise is small compared to the drift of signal response as a function of time.

The next stage of this research will be to realize a more thorough understanding of the potential biases in ICP-OES measurements in order to establish ICP-OES as a primary chemical metrological method. However, in the short term, this demonstrated ability to make high-precision comparative measurements vs. primary chemical standards promises to impact several prominent Division measurement and standards programs.

4. *Non-Destructive Testing of Ampouled SRMs Using FT-Near Infrared and FT-Raman Spectroscopies*

S.J. Choquette *and D.L. Duewer*

Objective: To evaluate the feasibility and advantages of the use of a combined Fourier Transform Near Infrared (FT-NIR)/Raman approach for nondestructive testing of ampouled SRMs.

Problem: Many NIST SRMs are supplied in flame-sealed ampoules. Traditionally, a statistical sample of the lot is acquired, and these samples are analyzed using gas chromatographic (GC) methods. The overall uncertainty assigned to the certified material reflects the possible inclusion of outlier samples. Sources for the concentration variance are thought to include evaporation during filling of the ampoule and flashbacks during the flame sealing of the individual ampoules. As part of on-going Division efforts to improve and assure the quality of NIST SRMs, we need to assess the feasibility, advantages, and cost-effectiveness of an SRM certification approach in which the contents of **each** ampoule of the SRM pool are non-destructively analyzed, rather than having material from each of a number of randomly selected ampoules analyzed.

Approach: Last year, both FT-NIR and FT Raman techniques were demonstrated to be capable of nondestructively identifying and quantifying oxygenates in fuel within the ampoules; therefore, candidate oxygen-in fuel SRMs were chosen as a test case for evaluating the cost effectiveness and utility of this approach. (These synthetic fuel SRMs are used in support of regulations designed to reduce automotive carbon monoxide emissions.) Furthermore, with careful preparation of a suitable calibration set, the multivariate models developed could be used to predict the oxygenate concentration to within the expanded uncertainty limits of the GC method. Few SRM materials however, are issued with more than a single concentration of the desired analyte, and additional samples are usually not available for the construction of a suitable calibration set. Although it would be difficult to predict the concentration of an analyte given these constraints, it is possible to determine the chemical homogeneity of the SRM population using NIR and Raman techniques. Such a statistical model would determine the "uniqueness" of a given sample to the set. Nonconforming ampoules might have had pinhole leaks or experienced evaporation or flashback during filling of the ampoule.

The general method consists of developing an average ampoule spectra (typically from ten ampoules) and measuring the spectral standard deviation of this set. Although measurement of each ampoule is done in real time (< 30 seconds), care is taken to reduce scattering and other noise sources that might contribute to spectral variance. Each ampoule spectra is preprocessed to remove baseline fluctuation. Finally, the residual spectra, i.e., the difference between the individual and average spectra, normalized to the standard deviation of the average are plotted. A control chart can be drawn that plots the conformity spectra of each ampoule. Typical ampoule conformity spectra will fall within ± 2-3 standard deviations of the mean spectra. Nonconforming ampoules will be identified as having spectral components or regions outside these bounds.

Results and Future Plans: This method was tested with a gravimetrically prepared synthetic fuel SRM that contained ethanol, toluene, and hexane in flame-sealed ampoules. Several of the ampoules purposely were spiked with additional ethanol to give concentrations of +0.1, +0.2 and +0.3 mass % over the nominal 10.1 mass %. These samples were readily identified as outliers by this method (FT-NIR) when compared to 20 "normal" samples. In addition, samples modified with toluene to alter the nominal concentration by 0.1 mass %, were also identified, in a unique part of the spectrum, as outliers. A sample of 128 of the SRM synfuel samples were then analyzed, and of these, four were identified as having significantly different ethanol concentrations from the mean sample. Examination of these ampoules revealed two with obvious pinhole leaks. GC analysis of the suspect ampoules is currently in progress.

This approach can be used either for value-assigning individual ampoules or for identifying "outlier" ampoules for discarding prior to batch assignment. Because this method can identify nonconforming ampoules, we will attempt to extend the technique to the determination of other oxygenates (MTBE and ETBE) and olefins in the entire SRM population of 2500 ampoules of this synthetic oxygenated fuel. Automation of the process is achievable and may facilitate the routine use of this technique to assure quality of other SRM materials.

5. *Chemometric/Statistical Evaluations of DNA Analysis Techniques for Human Identification*

***D.L. Duewer**, M.K. Kline (Biotechnology Division), and D.J. Reeder (Biotechnology Division)*

Objective: To characterize the statistical properties of restriction fragment length polymorphism (RFLP) and polymerase chain reaction (PCR) measurement techniques as used in routine human identity casework practice. Knowledge of the within- and among-laboratory measurement characteristics is critical for efficient interjurisdictional exchange of information.

Problem: "DNA Fingerprinting" evidence was first introduced as evidence in a criminal trial in 1987. Today, over 100 municipal, county, state, federal, and private forensic laboratories routinely characterize samples with one or more DNA measurement technologies. Matching evidential and known-felon data collected in different jurisdictions requires quantitative knowledge of "how good" the measurements among laboratories really are. Knowing *why* measurements differ among laboratories facilitates technology improvement. NIST is an active member of the Technical Working Group for DNA Analysis Methods (TWGDAM), with the explicit challenge of supplying appropriate Standard Reference Materials, technology evaluations, experimental designs, and data analyses.

Approach: DNA technologies are rapidly evolving, requiring characterization of: 1) casework practice of established techniques, 2) interlaboratory robustness of "coming on-line" techniques and materials, and 3) the intrinsic limitations of proposed materials and methodologies. In collaboration with the Federal Bureau of Investigation and various TWGDAM laboratories, we combine retrospective analysis of routine control data with results from prospective multi-laboratory studies and experiments using our own analytical resources.

Results and Future Plans: The interlaboratory reproducibility of RFLP measurements has been quantitatively described. We have used this quantitative understanding to document that the observed small differences between measurements made on pristine and weathered samples are not measurement artifacts but reflect changes in the electrophoretic mobility of the DNA itself. We have developed quality control charts for use within forensic laboratories and for multi-laboratory performance evaluations.

PCR technologies are replacing the sample-intensive RFLP techniques. We have shown that the apparent electrophoretic size of these DNA fragments depends on experimental parameters. A multi-laboratory study of one commercially available PCR kit confirmed our results. All study participants returned appropriate qualitative results relative to known alleles, but in the absence of standard allelic calibrants the quantitative results were unacceptably variable.

We are completing our characterization of RFLP measurements and incorporating this knowledge into the statistical procedures used to evaluate "DNA Fingerprint" comparisons. We are currently designing experiments for validation of multiplex PCR systems.

Publications:

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Duewer, D.L., Currie, L.A., Reeder, D.J., Leigh, S.D., Liu, H.-K., and Mudd, J.L., ***"Interlaboratory Comparison of Autoradiographic DNA Profiling Measurements. 4. Protocol Effects,"*** Anal. Chem. 69 (10), 1882-1892 (1997).

6. *Reference Measurements Support More Accurate ^{190}Pt Half-Life Determination and Novel Geochemical Applications*

*E.S. **Beary**, R.J. Walker (U. Maryland), and J.W. Morgan (U. of Colorado)*

Objective: To make high accuracy measurements of platinum in geologic and meteoritic samples using isotope-dilution inductively-coupled-plasma mass spectrometry (ID-ICP-MS) in conjunction with a collaborative effort to evaluate and apply a Pt-Os radiogenic dating system.

Problem: Geologists use long-lived radioactive isotopic systems such as uranium-lead and rubidium-strontium to date rocks and study geologic processes. A rhenium-osmium system currently is being studied intensively by geologists since the development of a negative thermal ionization mass spectrometric (NTIMS) procedure has enabled high precision isotopic measurements of picogram to nanogram amounts of osmium. The isotope ^{190}Pt is also radioactive, decaying into ^{186}Os. Simultaneous application of the rhenium-osmium and platinum-osmium systems would be useful to geologists, since these link three similar elements. Study of the platinum-osmium system has been difficult because ^{190}Pt has an extremely long half life, previously poorly defined as 650 ± 45 billion years based on reported literature data ranging from 470 billion to 690 billion years, and is rare in nature (0.0124 atom %).

Approach: An ID-ICP-MS method was developed recently at NIST for the very precise determination of the platinum group elements (PGEs) in automobile catalysts. As part of a collaboration with the University of Maryland and Colorado State University, this technique was used to study the PGEs osmium and platinum in unique geologic and meteoritic samples. Two groups of samples were analyzed for which extensive rhenium-osmium data already exist: nickel-copper-PGE ores from Noril'sk, Siberia, and IIAB iron meteorites. Refractory by nature, the PGEs are extremely resistant to dissolution. Samples were prepared either by alkaline fusion or Carius tube digestion. The application of the Pt-Os isotope system requires precise measurement, in the same aliquot of sample, of the concentrations of Pt and Os and of the ratio of the daughter isotope (^{186}Os) relative to a reference isotope of osmium (^{188}Os) that is not affected by radioactive decay. The osmium concentrations were determined by isotope dilution and the isotopic compositions were measured by NTIMS at the University of Maryland. The University of Maryland-Colorado State University team has no comparable capability for platinum measurements, however, and ^{190}Pt was determined at NIST using ID-ICP-MS.

Results and Future Plans: The platinum concentrations ranged from 500 ng/g to 160 µg/g in the Noril'sk ores and from 10 µg/g to 40 µg/g in the meteorites with 0.8% relative reproducibility for replicate samples. Method platinum blanks were negligible for most samples. Osmium concentrations ranged from 0.8 ng/g to 600 ng/g in the Noril'sk ores and from 50 ng/g to 65 µg/g in the meteorites. The ^{186}Os/^{188}Os ratios were measured with a relative reproducibility of 0.05%; osmium concentrations were measured with a relative reproducibility of 0.1 % (both 2s).

These measurements allowed the first precise isochron to be demonstrated for the Pt-Os isotopic system. The ratio of the natural concentrations of osmium and platinum plotted versus the amount of ^{190}Pt daughter product (^{186}Os) would normally be used to determine the age of rocks. However, because the ^{190}Pt half-life was previously poorly defined, in this study rocks of well-known ages

(Noril'sk ores, 0.2512 ± 0.0003 Ga; meteorites, 4.537 ± 0.008 Ga), were used to determine a more accurate and precise ^{190}Pt decay constant (1.54×10^{-12} y^{-1} ± 1%) which translates to a ^{190}Pt half life of 450 ± 7 billion years.

The feasibility of using the Pt-Os dating system for samples with even modest Pt/Os ratios was demonstrated. In addition, the University of Maryland-Colorado State University team has shown that these precise Pt and Os measurements can be used to probe interactions between the earth's core and mantle. The coupled Re-Os and Pt-Os isotope systems promise to be very useful in studying other fundamental geochemical processes.

Publication:

Walker, R.J., Morgan, J.W., Smoliar, M.I., Beary, E., Czamanske, G.K. and Horan, M.F., ***"Applications of the ^{190}Pt-^{186}Os Isotope System to Geochemistry and Cosmochemistry,"*** Geochim. Cosmochim. Acta 61, 4799-4808 (1997).

7. The Measurement of Water in Hydrocarbon Mixtures by the Karl Fischer Method

S.A. Margolis

Objective: To investigate sources of variation and bias in measurement of water in various oils by the Karl Fischer method and provide reference materials to provide accuracy benchmarks for such measurements.

Problem: The measurement of trace levels of water in oils impacts a large number of industrial groups including the electric power industry (insulating oils), light and heavy industry and the military (hydraulic oils), and the oil industry (crude oil). Accurate moisture measurements are essential in monitoring initial and ongoing suitability of the oils required for efficient operation of machinery. ASTM-sponsored collaborative studies using ASTM-approved methods reveal an unacceptable level of variation (~20 % to 50 %) in the reported moisture in oil determinations. Identifying and assessing the parameters that contribute to this variation and bias in the measurement of water in refined, synthetic, and crude oils can lead to method modifications and/or redesigned instrumentation that result in more comparable measurements in this critical area.

Approach: Karl Fischer titration is the method of choice for determining low levels of moisture in liquids. Most commercial testing laboratories use coulometric-based instrumentation for this titration, but the amperometric-based technique is also used. In previous studies, we identified the lack of dissolution of petroleum-based oils prior to analysis as being an important source of bias in moisture in oil determinations. In current work, the key observation that led to the development of a successful approach to evaluating sources contributing to the interlaboratory variation of the measurement of water in oils was that the titratable water in oil samples decreases about 50 % after the solution in the titration vessel undergoes a transition from a homogenous to a heterogeneous solution. This occurs as additional aliquots of oil are added to the titration vessel (to provide the sample quantity required for sensitivity needs). In addition, the observation that the measurement of water in water saturated octanol (WSO) was unaffected by the transition to a heterogeneous solution indicated that the compatibility of the sample composition with the particular measurement system (in particular, the reagents used) was an important factor in the observed bias. Using this approach, results of moisture determinations using various methods/ modifications, solvents, titrants, oils, and instruments were compared and evaluated. Furthermore, by using WSO as a standard, the accuracy and linearity of the response of representative instruments could be assessed.

Results and Future Plans: The sources of systematic bias that have been identified using the above approach include: (a) two distinct types of inaccurate factory instrument calibration that resulted in low water titers (by 5 to 15%); (b) decreased water titers as a result of incorrectly setting the operator-adjustable settings and titrant selection; and (c) variable titers as a function of the instrument and titrant used. The optimum conditions for obtaining the maximum water titer using the amperometric method for a range of oil composition types entail use of a vessel solvent of chloroform:methanol 6:1 v/v titrated to dryness that results in an increase in the quantity of sample that can be added before the vessel solution become heterogeneous. Studies in progress indicate that the optimum conditions for coulometric titration are more dependent upon the composition of the oils. As expected, the higher the molecular weight of the component hydrocarbons and the viscosity of the oil, the higher the percentage of chloroform required to preserve the homogeneity of the vessel solvent and the complete solubility of the oil in the titration vessel. In the future composition studies will be extended to include motor oils, hydraulic oils, crude oils, and other oils of industrial importance.

In addition to SRMs already provided by NIST with certified values for water in mineral oil, transformer oil, and methanol, a new SRM, *Water Saturated Octanol* is being certified that is needed for calibration and/or evaluation of instrumental bias and variability as described above.

Publication:

Margolis, S., ***"Sources of Systematic Bias in the Measurement of Water by the Coulometric and Volumetric Karl Fischer Methods,"*** Anal. Chem. 69, 4864-4871 (1997).

8. Composition Mapping with a Neutron Probe from a Monolithic Lens

***H.H. Chen-Mayer**, G.P. Lamaze, and D.F.R. Mildner*

Objective: To increase NIST capabilities for performing neutron depth profiling (NDP) of advanced materials.

Approach: NDP is a non-destructive technique for determining the near-surface distribution and concentration of certain light elements in materials (such as B in Si). By using a focused neutron beam, we can add the capability for lateral spatial resolution for three-dimensional compositional mapping to NDP. Two types of neutron focusing lenses have been proposed for NDP: a multifiber lens which consists of over 1000 polycapillary fibers, and a monolithic lens with many tapered channels fused in a solid piece. Compared with a multifiber lens, a monolithic lens has less dead space at the entrance, is more compact, and can provide a smaller focal spot, although currently the total number of neutrons captured is lower, limited by the size of the entrance of the lens. We are developing and evaluating new NDP procedures incorporating a monolithic neutron lens.

Results and Future Plans: We have demonstrated experimentally the potential for adding new techniques to the measurement capabilities of NDP. A higher intensity neutron beam, focused onto a smaller spot, allows NDP to provide three-dimensional compositional mapping information. Using a prototype monolithic lens installed in the NDP chamber for testing, the neutron current density has been increased by a factor of 9 within an area of 0.12 mm diameter (FWHM of the Gaussian distribution of the focused beam) at the sample position. A preliminary test, in which the charged particle response was measured as a sample (boron in glass) with compositional variation was moved across the focused beam, demonstrated that the spatial resolution for this particular sample is within 0.25 mm.

We have set up an automated scanning routine for the NDP system to search for the maximum charged particle response. The sample (a thin ^{10}B surface deposit) is defined by an aperture of 200 μm x 200 μm, and scanned over an area of 0.25 mm^2 with a 0.05 mm step size. The distribution of the charged particle intensity of the peak nearly follows concentric rings, representing a symmetrical focused beam and charged particle response. The ratio of the charged particle count rate with the lens to that without the lens is 3.6 over the sample area. A sample size matching that of the FWHM of the beam would have given the expected factor of 9. For an extended sample with lateral concentration variation, the scanning mechanism can be used readily. In that scenario, the aperture is kept stationary and the sample is scanned across the beam.

A new alignment system being developed contains a charge injection device camera with vacuum compatibility, which provides a spatial resolution of 12 μm (pixel size) and an 8 bit dynamic range for the neutron intensity. Together with the new vacuum compatible motion stages, the alignment system will enable a position sensitive measurement without breaking the vacuum. Furthermore, the lens can be retracted out of the beam for measurements on the same sample with normal NDP geometry. We plan to scan samples with lateral non-uniformity, such as a full size semiconductor wafer, and perform measurements on elements other than B, such as Li and N, in various matrices.

Publications:

Chen-Mayer, H.H., Mildner, D.F.R., Sharov, V.A., Ullrich, J.B., Ponomarev, I.Yu, and Downing, R.G., ***"Monolithic Polycapillary Neutron Focusing Lenses: Experimental Characterizations,"*** In: Proc. Intl. Sym. On Advances in Neutron Optics and Related Research Facilities, J. Phys. Soc. Japan 65 Suppl. A 319-321 (1996).

Chen-Mayer, H.H., Lamaze, G.P., Mildner, D.F.R., and Downing, R.G., ***"Neutron Depth Profiling Using a Focused Neutron Beam,"*** In: Proc. 5th Intl. Conf. on Application of Nuclear Techniques (SPIE), Neutrons in Research and Industry 2867, 140-143 (1997).

9. *Determination of Low-level Sulfur in Aerospace Superalloys*

***W.R. Kelly**, R.D. Vocke, Jr., and T.L. Quinn*

Objective: To provide support to the U.S. aerospace industry's need to measure accurately the sulfur content in superalloys at 1 μg/g and below.

Problem: The U.S. aerospace industry is the leader in R&D spending on new technologies and is the nation's leading net exporter of manufactured goods. The most critical components of jet engines are the so-called "hot parts" with the high pressure (HP) turbine being one of the most critical. The inlet temperature to the HP turbine sets the upper limit on the power and efficiency of a turbine-based power source. Currently, turbine blades are cast using high temperature superalloys. These alloys are non-ferrous metals that are high in nickel, with moderate amounts of chromium, cobalt, and other refractory elements. The turbine blades are hollow, permitting forced air cooling, while some are also coated with a ceramic thermal barrier. These features permit the operating temperature in the HP turbine to be close to the melting point of the alloy.

Metallurgists believe that the difference between sulfur concentrations of 0.5 and 1 μg/g sulfur/g in a superalloy determines the acceptability of turbine material. Specifically, the protective oxide coating on the surface of the turbine blades may fail if the sulfur content of the metal substrate exceeds the 1 μg/g level. The instrumental techniques used in the steel and metals industries are almost exclusively combustion based. Accuracy is dependent on calibration using external standards. The aircraft industry and their supporting foundries have asked the Division to measure the sulfur content of some of their new and most technologically advanced superalloys and to certify one or more low sulfur superalloys as an SRM.

Approach: The determination of sulfur as the arsenic sulfide molecular ion by isotope dilution thermal ionization mass spectrometry is currently the only method with the required sensitivity and accuracy to address this problem. Below 5 mg/g, the chemical blank becomes the dominant source of uncertainty and the ultimate limitation to accuracy. The blank problem is being minimized by using a least squares approach to the experimental design which allows validation of the blank in relation to its associated samples. A blank and three samples of different mass are processed together and the resultant data linearly regressed. The residual standard deviation of the intercept represents the standard deviation of the blank, ~ 0.05 mg S. SRM 131e, *Low Alloy Steel*, was recertified last year using this approach. The resulting certified value of 4.34 µg/g ± 0.10 µg/g (95 % confidence interval) has a much lower uncertainty than the 1991 consensus-based certified value of 4 µg/g ± 2 µg/g.

Results and Future Plans: Preliminary measurements on nine different superalloy materials submitted by the foundries have confirmed the efficacy of this approach. Superalloy material with S concentrations as low as 0.5 µg S/g has been analyzed with expanded uncertainties near 0.1 µg S, absolute. From this pool of materials, a candidate SRM has been identified as suitable for certification. Results of these developments have been presented at the two most recent meetings of the Consortium on Casting of Aerospace Alloys. This new SRM will be used as a quality assurance tool in the production and material qualification of superalloys used in producing next-generation jet engines.

10. Fabricating Plastic Microfluid Systems for Use in Analytical Chemistry

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Objective: To develop simplified methods for the design and fabrication of microfluid networks suitable for use in micro-chemical analysis systems.

Problem: Over the past few years there has been an explosion of interest in the development of microanalytical systems based on microfluidics. Arrays of microfluid channels fabricated in silicon, glass or plastic substrates constitute microfluid networks. An important challenge in developing the first generation of microanalytical systems is in the successful design and fabrication of fluid networks. The vision is that these networks will be incorporated into whole systems that include integrated detection elements, fluid manipulation components (pumps, valves, etc.), and sampling capabilities creating an independent unit that will function as a laboratory on-a-chip. Although the projected goals seem attainable, the field is still very young and issues in fabrication remain to be addressed. Currently, the fabrication of microfluid arrays is a high technology, high investment process. Microfluid channels are most often produced in silica- or silicon-based substrates using photolithographic techniques to define the arrays, and wet-chemical etching to fabricate the arrays in planar substrates. Although batch processing of the microfluid networks is conceivable by these methods, the etched arrays produce only the bottom portion of the channel requiring an additional step to seal and complete the channels. The sealing process for silica channels is typically performed by high temperature annealing now a low-yield process. Due to these and other fabrication constraints, the emerging technology known as microfluidics is not readily accessible to researchers in the analytical chemistry community.

Approach: A new concept has been recently developed in our laboratories for the fabrication of microfluid networks in plastic substrates. Microfluid channels have been fabricated using two approaches: wire imprinting and silicon template imprinting. Wire imprinting was performed by using small diameter wire to create an impression into plastics softened by low temperature heating. The resulting devices are limited to simple linear channel designs but are easily fabricated in the analytical laboratory. Devices with more complex microchannel arrangements were fabricated by imprinting the plastic substrates using an inverse 3-dimensional image of the network micromachined on a silicon wafer. The two imprinting methods have their own unique advantages. The wire-imprinting method provides a low-cost solution for the fabrication of simple useful devices for academic or industrial research purposes. Imprinting fluid circuits using a silicon template involves an initial investment, since the master is micromachined in silicon. However, the overall result is cost-effective production of microfluid devices with potentially complex microfluid designs. The imprinting techniques are simple and inexpensive when compared to other methods of microanalytical device fabrication. By introducing simple network fabrication methods, the possibility exists for rapid growth in basic microfluidics research in both the academic and industrial communities.

Results and Future Plans: Microanalytical devices, fabricated in our laboratory using wire- and silicon-template-imprinting methods, were characterized using interferometry and scanning electron microscopy. The channels prepared by both techniques show excellent device-to-device reproducibility in both the width and depth of the imprinted sealed channels. Using electroosmotic pumping to control fluid movement in the plastic channels, we have demonstrated reproducible electrokinetic injections and electrophoretic separations using prototype devices with channel diameters of approximately 25 µm. In recent months, we have begun to explore the use of liposomes as microreactors in these devices. This initiates the second and more important phase of this analytical research: the introduction of suitable novel chemistries that will help to broaden and demonstrate the scope of applicability of the use of microfluid devices in analytical chemistry.

11. Error in Glow Discharge Optical Optically Induced Analytical Emission Spectrometry

M.R. Winchester

Objective: To improve the reliability of glow discharge optical emission spectrometry (GDOES) for chemical analysis.

Problem: GDOES has been used for many years for the elemental analysis of materials directly in the solid state. Although the technique traditionally has been applied to the analysis of electrically conductive materials such as metals and alloys, its applicability recently has been extended to electrically non-conductive materials such as ceramics, glasses and polymers, as well as to the depth-resolved analysis of thin films.

Despite the relatively widespread applicability and use of the technique, the optical systems used to measure optical emission from the glow discharge device have in some respects remained in a state of developmental infancy. Specifically, the optics used to transfer emission from the device to the spectrometer usually consists of only a single lens, which images the discharge onto the entrance slit. The suitability of this simple-minded approach for application in analytical GDOES has met with little, if any scrutiny.

In a recent paper, Hoffmann and Ehrlich [Spectrochim. Acta 50B, 607 (1995)] reported that sample material did not mix thoroughly in the gas phase in their glow discharge device. As they pointed out, this suggests that the use of a single lens to image the discharge onto the entrance slit may induce analytical error when the sample is chemically heterogeneous.

Approach: To investigate the existence and severity of this type of optically-induced error, the behavior of GDOES with two samples known to be chemically heterogeneous was evaluated. The first was a synthetic sample consisting of a brass surface with a 1-mm diameter implanted steel plug. Since this sample is not realistic in terms of its severity of heterogeneity, a second sample was also employed. This sample was a brass disc that had been rejected previously as a standard reference material, owing to a small Pb heterogeneity.

Results and Future Plans: Studies with both samples indicated the presence of optically-induced analytical error. The error demonstrated for the synthetic sample was about 35%, indicating that the error can be large. In two trials, the error associated with the more realistic sample was between 1% and 2%. Though relatively small, this level of error is of concern in quantitative GDOES analyses.

Elimination of the optically induced error was attempted with the use of an alternative optical transfer method. This method, suggested in the previous publication, utilizes two lenses to transfer emission from the discharge device to the entrance slit. The alternative approach successfully eliminated the error for both the synthetic and "real-world" samples. These results suggest that the two-lens system should be routinely employed in analytical GDOES. However, important studies remain to be done. Specifically, the use of the two-lens method should be characterized in terms of analytical figures of merit, including signal-to-noise ratios, signal-to-background ratios, sensitivities, and limits of detection for various elements and samples.

Publication:

Winchester, M.R., ***"Optically Induced Analytical Error in Glow Discharge Optical Emission Spectrometry,"*** *Appl. Spectrosc.*, **50(2)**, 245-251 (1996).

12. Mass Spectrometry as a Tool for the Characterization and Standardization of Clinical Immunoassays: Characterizing Antibodies by LC/MS

D.M. Bunk

Objective: To develop techniques for the structural characterization of monoclonal antibodies using liquid chromatography (LC) coupled with electrospray ionization mass spectrometry (ESI-MS).

Problem: Monoclonal antibodies are used with increasing frequency in medicine as both pharmaceuticals and in clinical diagnostic testing as the functional elements in immunoassays. When they are used as pharmaceuticals, antibodies are thoroughly tested and characterized. But this is not necessarily the case when they are used in immunoassays. During the development of a clinical immunoassay, the binding strength and specificity of binding of the monoclonal antibody to its target molecule, the antigen, are thoroughly evaluated. However, little structural characterization of the antibody is performed. Structural diversity of an antibody used in an immunoassay can have a pronounced impact on the outcome of the assay, limiting its accuracy. The amino acid and carbohydrate sequencing techniques used to characterize antibodies used as pharmaceuticals are very slow, labor-intensive techniques that are not suited for the mass production of immunoassay reagents. Techniques needed to provide rapid structural information for quality control of antibodies do not exist. Mass spectrometry has been applied only to a limited degree to the characterization of antibodies, but has the promise to provide faster, detailed, and accurate structural information.

Approach: To date, the mass spectrometry performed on antibodies has been done on intact molecules. With the complexity of antibody structures, e.g., multiple crosslinked protein chains, attached carbohydrates, variations in amino acid sequences, the information provided by mass spectrometry of intact antibodies does not provide sufficient structural detail. Fortunately, there are a number of established procedures for antibody fragmentation that provide fragments small enough for structural characterization. These procedures include enzymatic fragmentation, enzymatic deglycosylation, and affinity chromatography. By combining these fragmentation procedures with mass spectrometric analysis, the fragments of the antibodies can be thoroughly characterized and the structure of the antibody can be "pieced" together. In particular, ESI-MS was used because of its ability to be coupled to separation techniques such as LC.

Results and Future Plans: As observed from the earliest stage of this research, enzymatic digests of monoclonal antibodies produce a very complex mixture of antibody fragments. Part of this complexity is due to the heterogeneity in the antibody structure, a common feature of glycoproteins, and part is conceivably due to the distribution of cleavage sites of the digestive enzyme used. Some of the fragments in these mixtures exhibit very poor chromatographic behavior by reversed-phase LC that interferes with their characterization by LC/MS. Therefore, the initial stage of this research was aimed at improving the separations that could be obtained from antibody fragment digest, in particular, separations using reversed-phase LC. Differences in chromatographic column chemistries (C_4, C_8, and C_{18} columns) and the influence of temperature were studied. Elevating the column temperature improved both the chromatographic peak shape and separation from interferences of the two major classes of antibody fragments, the fragment that contains the binding sites of several molecules involved in immune response (F_c fragment) and the fragment to which the antigen binds (F_{ab} fragment). In fact, a dramatic improvement was observed in the case of the F_{ab} fragment. Little difference was observed in the chromatography of these antibody fragments using different column chemistries, a behavior consistent with the reversed-phase LC of other proteins.

Next, a digestion scheme was implemented that would produce fragments of distinct regions of the antibody molecule. LC/MS analysis of these fragments revealed a high degree of heterogeneity in their molecular masses. Following removal of the carbohydrate chains attached to the F_c fragments, less heterogeneity was observed in the F_c mass spectra. Thus the carbohydrate was implicated as the major source of structural heterogeneity. The pattern of observed molecular masses of these fragments could then be correlated with the isotype of the antibody. With additional study, LC/MS could be used to rapidly isotype antibodies with more accuracy than the immunological methods currently used.

13. Development of Methods for the Separation of Chiral Compounds

__K.W. Phinney__, B.C. Nelson, and L.C. Sander

Objective: To establish the measurement infrastructure to support the development of reference materials with chiral information.

Problem: The separation and quantification of enantiomers is an analytical requirement for the development of chiral drugs and agrochemicals, the provision of data needed for regulatory approval of these materials, and monitoring of their production. Many enantiomeric separations of chiral compounds have been performed by liquid chromatography (LC) on chiral stationary phases (CSPs). However, each CSP resolves different compounds, and the analyst must often evaluate several CSPs through a trial and error process before identifying the appropriate one for the desired separation. As a result, the analyst must have a collection of expensive CSPs to solve various separation problems. In addition, the low efficiency of these stationary phases limits their utility for complex samples such as pharmaceutical formulations or biological samples. Peak resolution in chiral LC is often not sufficient to allow accurate determinations of enantiomeric purity when one enantiomer is present in large excess.

Approach: In previous work in this area, we developed and demonstrated the applicability of coupled achiral/chiral columns with supercritical fluid chromatography for the separation of structurally related chiral compounds. We are expanding our capabilities to include the use of capillary electrophoresis (CE), that have several potential advantages compared to LC for chiral separations, including ease of changing chiral selectivity, low sample and reagent consumption, and increased efficiency. In CE, chiral separations are generally performed by adding a chiral selector to the running buffer solution. Native and modified cyclodextrins have been the most widely used chiral additives in CE. In particular, sulfated cyclodextrins have shown considerable enantioselectivity in CE. Other sulfonated carbohydrates, including heparin, dextran sulfate, and chondroitin sulfate have also been utilized as chiral selectors. We investigated pentosan polysulfate, a semisynthetic pentasaccharide, as a new chiral additive for enantiomeric separations in CE. The pentosan polysulfate used in this study had an average molecular mass of 3000 Daltons and a maximum of two sulfate groups per monosaccharide residue. Therefore, in terms of molecular weight and degree of sulfonation, pentosan polysulfate has properties intermediate between the sulfated cyclodextrins and polysaccharides such as chondroitin sulfate. Based on the success of other sulfated carbohydrates, it seemed likely that pentosan polysulfate would also exhibit enantioselectivity in CE. A variety of cationic and neutral pharmaceutical compounds were used to probe chiral recognition. The sodium salt of pentosan polysulfate was used to improve the aqueous solubility of the chiral selector.

Results and Future Plans: Compounds enantioresolved using pentosan polysulfate as the chiral additive included antihistamines, anti-malarials, and anesthetics. Chiral resolution of three pharmaceutical compounds is shown in Figure 1. Although the concentration of the chiral additive did influence selectivity, changes in pH had a much greater impact on chiral selectivity. The presence of

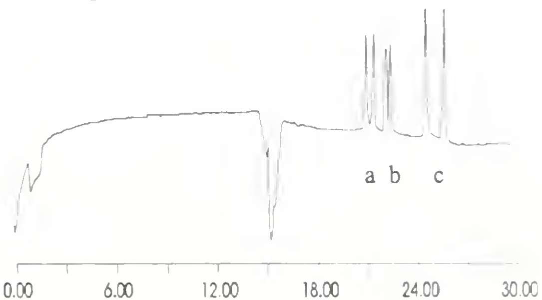

Figure 1. Separation of enantiomers of (a) doxylamine, (b) bupivacaine, and (c) tetramisole

a basic site near the chiral center seemed to improve chiral recognition. Compounds having basic sites further away from the chiral center had reduced resolution or were not resolved. For some analytes, the observed chiral selectivity exceeded that reported for other carbohydrate-based chiral additives. Future studies will involve clarifying the chiral recognition mechanisms for pentosan polysulfate and utilizing this information to identify additional ionic carbohydrates likely to yield successful enantioseparations in CE.

14. Near Infrared Transmission Wavelength Standards

S.J. Choquette and J.C. Travis

Objective: To develop a near infrared standard for wavelength validation of both dispersive and Fourier transform spectrometers.

Problem: Near infrared (NIR) spectroscopy is an analytical tool that can perform nondestructive, qualitative and quantitative chemical analysis with little, if any, sample preparation. As a consequence, the technique is being increasingly used in pharmaceutical, chemical and agricultural industries. Because the technique relies exclusively upon complex multivariate statistical methods to perform analytical determinations, instrument performance checks are much more critical than for traditional spectroscopic methods. Currently, NIST does not provide wavelength calibration materials for this spectral range. Lack of a relevant standard is significantly impeding progress in the implementation of NIR methods in the pharmaceutical industry.

Approach: Three years ago, NIST and The Center for Process Analytical Chemistry (CPAC) at the University of Washington initiated a study to produce an NIR transmission wavelength standard. At the time NIST offered optical transmission standards that covered the UV-visible and mid-infrared spectral regions, but lacked coverage in the 800 nm to 2500 nm range. The initial goal was to develop a wavelength standard that would cover the short wave NIR: 800 nm to 1600 nm. This proposed wavelength range would cover the most common types of detectors used at the time for NIR spectrometers, namely silicon and germanium. Several glass materials were investigated for suitability, and a mixture of 1 mole % -2 mole % each of Yb_20_3, Sm_20_3 and Nd_20_3 incorporated into a La_20_3 base glass was chosen as a candidate wavelength standard. This mixture, when incorporated into a 1 mm to 2 mm thick glass filter, produced resolved absorbance peaks in the wavelength range from 800 nm to 1600 nm.

In February of 1997, a round robin exercise was initiated to introduce these candidate filters to our potential SRM customers and to solicit feedback on the physical geometry of the filter, wavelength coverage, and ability of end users to locate the peak positions with various conventional dispersive and Fourier transform instruments. Twenty-three filters were sent to a variety of users including the major NIR instrument vendors, bulk chemical and polymer industry, pharmaceutical industry, NIR consultants, academics, and researchers at the Food and Drug Administration.

Results and Future Plans: Our initial results (1996) indicated that with the appropriate peak-picking algorithms, the precision for locating the peaks for a sample of 20 filters was better than 0.1 cm^{-1}. The results of the round robin indicated that users with either dispersive or Fourier transform instruments were capable of locating the certified absorbance peaks to within the desired precision (~0.5 cm^{-1}). However, as a result of the participation by the pharmaceutical industry and FDA, it was determined that this candidate filter formulation would not be adequate for validation of dispersive spectrometers that cover the wavelength region from 1000 nm to 2500 nm. A new formulation was developed that includes holmium oxide. The inclusion of this oxide introduces additional absorbance peaks in the visible region and at 2000 nm and therefore will be suitable for use with dispersive as well as with Fourier transform instruments.

Future work will examine laminating a polymer sheet to this filter to extend the wavelength coverage to 2500 nm.

15. *Mercury and Arsenic Speciation in Environmental SRMs*

M.K. Donais, S.E. Long, E.A. Mackey, M.M. Schantz, D.A. Becker, and ***S.A. Wise***

Objective: To develop analytical methods for the determination of organomercury and organoarsenic species in environmental matrices and to implement these methods in the certification of organometals in environmental matrix Standard Reference Materials (SRMs).

Problem: The biological pathway, toxicity, and fate in the environment of many trace elements are determined by the chemical form or species. For example, it is well known that the organically bound form of mercury, methylmercury, is more toxic than the free metal and many international agencies have set limits for environmental exposure, weekly dietary intake, and input of methyl mercury into the environment. Reference materials with certified values for element species are greatly needed for use in the development and validation of methods for the determination of element species and for quality control, once analytical procedures have become routine.

Approach: To address the above-mentioned needs, we have been involved in the development of analytical methods for the determination of methylmercury and arsenic species. Two independent methods for the determination of methylmercury were developed and used to provide certified concentration values for selected environmental SRMs.

Results and Future Plans: We recently certified the content of methylmercury and total mercury in three mussel tissue SRMs: SRM 1974a Organics in Mussel Tissue (*Mytilus edulis*) (Frozen); SRM 2974, *Organics in Freeze-Dried Mussel Tissue*; and SRM 2976, *Trace Elements in Mussel Tissue.* For the measurement of methylmercury, we applied two recently developed methods based on: 1) liquid-solid extraction under acidic conditions and size exclusion chromatography followed by gas chromatography with atomic emission detection and 2) distillation of organomercury compounds from a mixture of powdered sample, sulfuric acid, and cupric sulfate followed by binding of the organomercury compounds to cysteine fixed onto filter paper which was then subjected to neutron activation analysis (NAA) for mercury determination. The methylmercury results from the two NIST methods were combined with results from two other laboratories, which used analytical methods that were independent from the NIST methods, to provide certified methylmercury values for all three mussel materials. These three materials are the first natural matrix environmental NIST SRMs with certified values for metal species.

For the determination of arsenic species we are developing a method based on liquid chromatographic (LC) separation of the arsenic species followed by detection with inductively coupled plasma mass spectrometry (ICP-MS). Our initial efforts focused on development of the LC separation for the arsenic species of interest: arsenobetaine (AsB), arsenocholine (AsC), arsenic (III), arsenic (V), monomethylarsonic acid (MA), and dimethylarsinic acid (DMA). After development of the separation method, LC was coupled with ICP-MS and the system was evaluated using extracts from two certified reference materials (CRMs): *TORT-1 Lobster Hepatopancreas from the National Research Council, Canada*, and SRM 2976, *Trace Elements in Mussel Tissue.* This approach will be used in the coming year to provide values for arsenic species in several marine SRMs.

Additional work involving the determination of arsenic species in environmental samples was accomplished through collaboration with scientists from the Institute of Analytical Chemistry in Graz, Austria. Total arsenic content was determined by NAA at NIST and arsenic species concentrations were determined by LC-ICP-MS at Graz in marine mammal liver tissues from the National Biomonitoring Specimen Bank. For the 14 marine mammal liver specimens analyzed, AsB was the predominant arsenic species, ranging from 70% to 95% of the total arsenic content, with small amounts of AsC, DMA, and MA quantified. The new NIST procedure for determination of speciated As will be used in the coming year to verify the AsB value provided by the Austrian team.

Publications:

Donais, M.K., Saraswati, R., Mackey, E.A., Demiralp, R., Porter, B.J., Vangel, M., Levenson, M., Mandic, M., Azemard, S., Horvat, M., Emons, H., and Wise, S.A., ***"Certification of Three Mussel Tissue Standard Reference Materials (SRMs) for Methylmercury and Total Mercury Content,"*** *Fres. J. Anal. Chem.*, **358**, 424-430 (1997).

Mackey, E.A. and Becker, D.A., ***"Determination of Methylmercury in Two Mussel Tissue Standard Reference Materials (SRMs) by Pre-Irradiation Separation and Neutron Activation Analysis,"*** *Analyst*, (In Press).

Goessler, W., Rudorfer, A., Mackey, E.A., Becker, P.R., and Irgolic, K.J., ***"Determination of Arsenic Compounds in Marine Mammals with High Performance Liquid Chromatography and Inductively Coupled Plasma Spectrometry as an Element Specific Detector"*** *Applied Organometallic Chem.* (Submitted).

16. Standards for Hydrogen in Titanium Alloy

***R.M. Lindstrom** and R.L. Paul*

Objective: To test a direct-reaction method for preparing reference materials for hydrogen in titanium.

Problem: Hydrogen is one of the chief contributors to brittleness in metals; its control in manufacturing processes is crucial. Measurement methods in industrial use are calibrated with working standard materials, few of which are traceable to fundamental parameters. As a result there may be a method-dependent bias. Therefore, a series of metal standards of known hydrogen concentration are needed.

Approach: A procedure has been demonstrated for doping titanium alloy specimens with a known amount of hydrogen. In the reversible reaction

$Ti + H_2 = TiH_2$ ($\Delta G_f^0 = -19.2$ kcal/mol),

the equilibrium lies far to the right at low temperature ($P_{eq}(H_2) = 4 \times 10^{-12}$ kPa at 25 °C) and far to the left at high temperature ($P_{eq}(H_2) = 1.5 \times 10^4$ kPa at 900 °C). Reaction is rapid at 300 °C. This gettering reaction with hot titanium is in common use in geochemistry for separating hydrogen from oxygen and nitrogen (which react irreversibly) and from noble gases. Massive hydrides are prepared industrially by the same direct reaction process for hydrogen-based energy storage and nuclear applications.

Results and Future Plans: In a typical preparation, ten weighed specimens of about 1 cm^2 were cut from a 1-mm sheet of Ti(90%) Al(6%)V(4%) alloy, degreased with acetone, and oven dried. They were degassed by heating above 900 °C in vacuum (pumping to 10^{-3} Pa). The samples were reweighed and half were removed as a blank. After evacuating the system, a measured pressure of hydrogen gas in a calibrated volume at a measured temperature was introduced, the samples heated to above 600 °C (where $P_{eq}(H_2) = 2 \times 10^2$ kPa), and the closed system cooled again. At the end of the doping the system pressure was 10^{-5} times the starting pressure, showing that all the gas was absorbed in the metal. The accuracy of the hydrogen concentration determined from the doping preparation is limited by that of the pressure measurement, which enters the equation both from the doping pressure and the volume calibration. While a complete error analysis is yet to be done, the bias from this source appears to be less than 0.5% relative. The amount of H in duplicate 100-mg specimens of doped metal samples and blanks was measured by cold-neutron prompt-gamma activation analysis (PGAA). The PGAA net results (after subtracting the blank corresponding to the same lot of starting material) and H added during the doping of three sets materials at different target levels are given in the following table. The uncertainties given are one standard deviation from propagated counting statistics alone, which is the dominant contributor.

These results demonstrate our capability for doping metal samples with hydrogen materials at predetermined target levels. This direct-reaction method appears to be straightforwardly scalable to 1 kg quantities of metal, and in FY98 we plan to prepare and certify a Hydrogen in Titanium SRM.

Sample ID	H added, µg/g	H found, µg/g (1 s)
7/28	306	294 (11) 305 (10)
8/1	208	194 (11) 218 (11)
8/14	92	100 (11) 101 (11)

Publication:

Paul, R.L., ***"Hydrogen Measurement by Prompt Gamma-ray Activation Analysis,"*** Analyst, 122, 35R-41R (1997).

17. Long-term Stability of Cryogenically Stored Specimens in the National Biomonitoring Specimen Bank

E.A. Mackey, R. Demiralp, K. Fitzpatrick, B.J. Porter, and R.R. Greenberg

Objective: To evaluate the stability of trace element composition and integrity of the tissue specimens stored in the National Biomonitoring Specimen Bank (NBSB) at NIST to assess the adequacy of the NBSB storage protocols for these materials.

Problem: The NBSB was initiated in 1979 as a multiagency collaboration to archive environmental and biological specimens for future retrospective analyses. Sampling, processing, storage, and analysis protocols were developed for a variety of specimens including human liver, fish tissues, mussels/oysters, sediment, and marine mammal tissues (liver, kidney, blubber, and muscle). Studies requiring the use of samples from the NBSB often require determinations of selected trace elements. It is the responsibility of the curators of the NBSB to demonstrate that the storage protocols used ensure specimen stability for intended use.

Approach: Long term stability of trace element content of specimens stored under standard NBSB conditions was evaluated by comparing results of current analyses of selected specimens with results of previous analysis of these specimens. Similar evaluations were made to evaluate the adequacy of storage protocols used for selected fresh frozen SRM and other QA materials. Typically, the NBSB specimens are stored in freezers that are cooled with liquid nitrogen at approximately -150 °C. Fresh frozen SRMs and other quality assurance materials are stored in electric freezers maintained at -80 °C. Subsamples of human liver tissues originally deposited into the NBSB in 1980 and stored since that time at -150 °C, additional subsamples of the same livers stored at -80 °C, marine mammal liver tissues banked in 1987 and stored at -150 °C, and a QA pilot whale liver tissue homogenate collected and banked in 1990 and stored at -80 °C were analyzed and the results compared with the results of initial analysis at the time of banking of different subsamples of the same tissues.

For the purpose of analytical quality control and to obtain additional information on long-term stability of freeze-dried biological reference materials stored at room temperature, analyses of duplicate portions of SRM 1577a, *Bovine Liver,* (originally certified in 1982 and re-certified in 1987), and SRM 1566a, *Oyster Tissue,* (certified in 1989) were included in these analyses. All samples were analyzed for Ag, As, Ba, Cd, Co, Cr, Eu, Fe, La, Mo, Rb, Sc, Sb, Se, Sm, Sn, and Zn using instrumental neutron activation analysis.

Results and Future Plans: No significant differences were observed in the determined elemental concentrations of aliquots of samples that had been stored as a function of storage temperature or, in general, with time. A comparison of results of analysis of subsamples of human liver tissues stored at -80 °C with those stored at -150 °C shows no significant differences in determined trace element concentrations as a function of these storage temperatures. Likewise, results from analyses of the QA pilot whale liver tissue homogenate show that this material is stable in terms of selected trace element concentrations at -80 °C. In the comparison of the FY97 analyses with the analyses made at the time of the banking of the selected samples, no overall systematic changes with time were observed. The results were in agreement within the total uncertainty of the method for 28 of the 30 elemental determinations in the banked northern fur seal liver tissue samples and for 40 of the 48 values for the human liver samples.

Results of analysis of the freeze-dried materials, SRM 1577a and SRM 1566a, that were stored at room temperature for 15 y and 8 y respectively, showed no deviation from the certified values. A previous stability study by Zeisler, et al. [*Fres. Z. Anal. Chem.*, **332**, 612-615 (1988)], indicated that the As content in SRM 1577 decreased over time. In this study, it was not possible to determine whether As is stable in SRM 1577a because the levels present in this material are below the INAA detection limit of 0.08 mg/kg for this matrix. The results of the FY97 determinations of As in SRM 1566a Oyster Tissue were within the certified range that resulted from measurements made in 1988-1989.

These studies demonstrate that the NBSB storage protocols currently in use ensure the stability of banked tissue samples in terms of their elemental composition. We will continue to monitor banked tissue and sediment samples for concentrations of both organic and inorganic components in on-going stability studies.

18. Chemical Microhomogeneity of Natural Matrix SRMs

R. Zeisler and M.M. Schantz

Objective: To develop and implement analytical procedures for precise quantitative determinations of trace elements and organic compounds in small samples with the aim of assessing the chemical microhomogeneity of SRMs at milligram sample mass.

Problem: As analytical techniques become more sensitive, they can utilize ever smaller samples to determine natural and pollutant constituents which are investigated in biological and environmental materials. Concurrent with this development, new procedures are being widely used in industry, regulatory monitoring, and enforcement that utilize small size solid subsamples for analysis from which to infer the concentrations in the bulk sample, or to assess the spatial distribution of selected determinands in smaller subsamples of the bulk sample. One advantage of these procedures is the reduction or elimination of sample preparation processes that are labor intensive and generate chemical waste. Unfortunately, these solid sampling techniques are confronted with two major problems: 1) the accuracy of many of these techniques is affected by the matrix composition, i.e., standards for calibration and quality assurance must match the analyzed samples as closely as possible, and 2) few natural matrix SRMs have been certified at the required small sample sizes. Direct application of most existing SRMs for QA purposes in solid sampling procedures, i.e., analyses of samples having masses ≤1 mg, is often impossible if their homogeneity has not been demonstrated at the needed sample sizes. The use of newly developed procedures at NIST may allow the issuance of natural matrix SRMs with demonstrated homogeneity at the small sample sizes suitable for techniques such as solid sampling.

Approach: Statistical models (e.g., the Ingamells sampling constant and the Kurfürst homogeneity factor) describing chemical homogeneity of mixed component natural materials have been developed in the past. The best analytical methods for the determination of the input parameters to these models are those with small analytical uncertainty for a considerable number of components, and with a sufficiently large dynamic range. Instrumental neutron activation analysis (INAA) and pressurized fluid extraction, followed by analysis using gas chromatography/mass spectrometry, have been selected to provide the necessary analytical data for elemental and organic determinands, respectively, in these initial studies.

Results and Future Plans: The small sample capabilities of INAA were initially surveyed by determining trace elements in air particulate matter deposited on filter material; INAA produced highly precise data on several sets of test samples, with sample masses of 0.7 mg, 1 mg, and 3 mg. Then quantitative determinations in small sample sizes of SRM 1648, *Urban Particulate Matter*, SRM 1547, *Peach Leaves*, and two intercomparison materials prepared for small sample techniques, lichen (IAEA-338) and Shanghai bovine liver, were made at 1 mg to 2 mg sample sizes. For the polycyclic aromatic hydrocarbons, samples (1 mg - 400 mg) of SRM 1649, *Urban Dust/Organics*, and samples (5 mg - 100 mg) of SRM 1650, *Diesel Particulate*, were extracted and analyzed using PFE followed by GC/MS. The results were within the certified range for these compounds. The Ingamells sampling constants (i.e., the sample size of which the uncertainty due to sample heterogeneity is 1%) ranged from 40 mg to 400 mg for SRM 1649 and 40 mg to 60 mg for SRM 1650.

The homogeneity values determined from the analytical data show that the investigated materials have generally satisfactory chemical homogeneity properties for use in solid sampling procedures. No significant heterogeneity of SRM 1648 was observed at the investigated sample size for the elements studied. Not unexpectedly, SRM 1547 shows a possible inhomogeneity for the determination of Al at the investigated sample size; an exogenous fraction of alumina-silicate based material had been previously reported in this SRM. The two new preparations of Lichen and Bovine Liver for candidate reference materials for microanalytical techniques comply with the initial goal in their preparation that uncertainty due to sampling should not exceed 5% relative for a sample size of 5 mg. The data indicate that air jet milling of biological materials, especially if repeated up to three times as in the case of the Lichen, will result in very homogeneous samples. The homogeneity of SRM 1649 and SRM 1650 were demonstrated at the 1-mg and 5-mg sample size, respectively, for polycyclic aromatic compounds. In the future, the chemical microhomogeneity of SRMs of differing matrix (such as the existing mussel tissue and marine sediments), of various SRMs for additional chemical classes of organic compounds, and at even smaller sample sizes will be evaluated.

19. Development of Food- and Nutrition-Related SRMs

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Objective: To develop several natural-matrix Standard Reference Materials (SRMs) for selected vitamins, carotenoids, fatty acids, cholesterol, trace elements, and other nutrients.

Problem: The Nutrition Labeling and Education Act (Public Law 96-359) requires that specific nutritional information be provided on all processed foods sold in the U.S. In a recent study by the U.S. Food and Drug Administration, the accuracy of label information ranged from 98% to 54% for nutrients for which labeling is required. As more food-matrix SRMs become available, label accuracy should improve when the food and nutrition communities employ these SRMs in their analyses. Food-matrix SRMs are needed to validate analytical methods and for quality assurance when assigning concentration values to in-house control materials. At present there are still only a few SRMs for "comprehensive" nutrient measurements, although there are several SRMs available for nutritive inorganic constituents.

Results and Future Plans: NIST is actively working to provide an increased array of SRMs certified for such important nutrients as vitamins, cholesterol, fatty acids, and minerals as well as for toxic trace elements. Two such SRMs were certified in 1996: SRM 1544, *Fatty Acids and Cholesterol in Frozen Food Composite*, and SRM 1846, *Infant Formula*. In 1997, NIST certified two additional SRMs for selected nutrients: SRM 1548a, *Typical Diet*, and SRM 2383, *Baby Food Composite*. SRM 1548a is a freeze-dried composite of a large variety of foods representing the total daily diet consumed by an individual in the U.S. Concentration values in this SRM are provided for a number of dietary components including proximates, major and minor inorganic nutrients, and toxic trace elements. Values were assigned using results from several outside laboratories as well as NIST measurements. SRM 2383, another food composite, is a material with high levels of selected vitamins and carotenoids. Based on an NIST-specified mixture of individual food components, the material was prepared and packaged by Gerber Products Company in the form of a typical baby food (i.e., the SRM is approximately 60% water by mass). Concentration values were assigned based on values from NIST, from an interlaboratory exercise involving seventeen member laboratories of the National Food Processors Association's (NFPA) Food Industry Analytical Chemists Subcommittee (FIACS), and from an interlaboratory comparison involving sixteen additional outside laboratories that participate in a Micronutrients Measurement Quality Assurance Program run by NIST.

The nutritional measurements community identified a canned meat homogenate as a high priority for reference material development because of its high protein and high fat content. NIST is currently working on value-assigning SRM 1546, Meat Homogenate, for proximates, cholesterol, individual fatty acids, water-soluble vitamins, and minerals. Again, value assignment will be based on values from NIST and from an interlaboratory exercise involving approximately twenty member laboratories of NFPA FIACS and several additional collaborating laboratories. A meeting with representatives of the food industry, USDA, and FDA was held October 24, 1997 for discussion of additional food-related SRM needs.

Publication:

Sharpless, K.E., Schiller, S.B., Margolis, S.A., Thomas, J. Brown, Iyengar, G. V., Colbert, J.C., Gills, T.E., Wise, S.A., Tanner, J.T., and Wolf, W.R., ***"Certification of Nutrients in Standard Reference Material 1846: Infant Formula,"*** J. AOAC Intl. 80, 611-621 (1997).

20. Quality Assurance Activities in Support of Health-Related Measurements

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Objective: To provide measurement quality assurance (QA) support for laboratories performing health-related measurements.

Problem: Inaccuracy in health-related measurements raises overall health care costs, results in misdiagnoses, and leads to inaccurate conclusions in clinical studies. Health care costs represent over 13% of the U.S. GNP and have been increasing at twice the rate of our national economy in recent years. Measurements represent about 20% of the cost of health care, and approximately one-third of these measurements are performed for non-diagnostic purposes, such as retesting, error prevention, and detection limitations.

Approach: NIST has a long-term relationship with the College of American Pathologists (CAP) who sponsors three research associates at NIST to work with NIST scientists on development of accurate methods and reference materials to support accuracy in clinical analyses. In addition, a collaboration was initiated this year between NIST and the American Association for Clinical Chemistry (AACC) to mutually develop new reference materials deemed of high priority by the AACC Standards Committee. NIST works with the National Cancer Institute to provide measurement quality assurance (QA) to over 60 laboratories measuring serum levels of potential chemopreventive agents in clinical trials. Interlaboratory studies, reference materials, and workshops continue to be used to document and improve the accuracy of the measurements in these studies.

Results and Future Plans: Blood cholesterol and triglycerides are important markers of heart disease risk. The accurate measurement of blood cholesterol levels by many routine clinical laboratory systems can be a significant problem because the lyophized serum reference materials and controls used to monitor these systems often produce biased results relative to fresh human serum. The National

Committee for Clinical Laboratory Standards, in conjunction with NIST, CAP, the Centers for Disease Control (CDC), and the clinical manufacturers, has developed a protocol for preparing a fresh frozen serum reference material that does not produce biased results versus fresh serum. A material was prepared, extensively tested on the major systems used in clinical laboratories for cholesterol measurements, and was value-assigned at NIST using definitive methods for cholesterol and triglycerides. CDC provided data from their reference methods for HDL- and LDL-cholesterol and triglycerides. This new material is available from NIST as SRM 1951a, *Lipids in Frozen Human Serum*. In FY98, NIST will work with CDC and the Mayo Clinic to apply the NIST-developed cholesterol definitive method to the measurement of HDL- and LDL-cholesterol in this important material.

Troponin-I is a protein that is released into the blood when heart tissue is damaged. Because elevated levels of troponin-I correlate extremely well with a recent myocardial infarction, physicians are now using troponin-I measurements as a diagnostic tool. Unfortunately, different measurement systems for troponin-I produce widely different results. In one large study, the mean resulting from measurements made with one system was more than 20 times the mean from another system. This analyte was identified by the AACC Standards Committee as their highest priority for development of a reference material. NIST is investigating the use of liquid chromatography/electrospray ionization mass spectrometry and capillary electrophoresis for the accurate measurement of troponin-I.

Work is underway on the third renewal of SRM 968, *Fat-soluble Vitamins, Carotenoids, and Cholesterol in Human Serum*. This SRM was developed through the activities of the micronutrient QA program and is widely used by laboratories world-wide making these types of measurements. The certification process will involve a combination of measurements from NIST and QA participants. Round-robin exercises will continue to be an important part of the QA program effort as will tutorial sessions and workshops for the participants that will be held periodically in conjunction with important national meetings.

Publication:

Duewer, D.L., Thomas, J. Brown, Kline, M.C., MacCrehan, W.A., Schaffer, R., Sharpless, K.E., and May, W.E., ***"ANIST/NCI Micronutrients Measurement Quality Assurance Program: Measurement Repeatabilities and Reproducibilities for Fat-Soluble Vitamin-Related Compounds in Human Serum,"*** Anal. Chem. 69, 1406-1413 (1997).

21. Quality Assurance Activities in Support of Environmental Measurements

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Objective: To provide measurement quality assurance (QA) support for laboratories performing environmental measurements.

Problem: Decision-making based on inaccurate measurements and/or data of unknown quality can have significant economic and/or health consequences. Natural matrix SRMs representative of different types of environmental samples and intercomparison studies are needed to assist in the validation of analytical methods and for the assessment and documentation of the quality of environmental analytical measurements.

Approach: To address the above-mentioned needs, we have been involved in the development and certification of several environmental matrix SRMs during the past year including: 1) organic and inorganic constituents in marine sediment and tissue matrices; 2) certification of additional organic contaminants in existing SRMs, and 3) lead in various household matrices. Two certification modes were used for these SRMs. The marine environmental SRMs were certified using various combinations of NIST and outside laboratory measurements. The lead reference materials were certified based solely on NIST measurements.

NIST also provides other activities in support of several national environmental monitoring activities. Since 1986 we have worked in cooperation with the National Oceanic and Atmospheric Administration (NOAA) and the Environmental Protection Agency (EPA) to assess the interlaboratory and temporal comparability of data for organic contaminants from laboratories involved in the NOAA National Status and Trends (NS&T) Marine Monitoring Program and the EPA Environmental Monitoring and Assessment Program (EMAP). In 1993 we initiated a quality assurance activity in support of the EPA National Health Exposure Assessment Survey (NHEXAS), which is intended to provide critical information about the magnitude, extent, and causes of human exposures to environmental contaminants so that informed decisions can be made regarding environmental health risks. In the above programs, NIST provides QA support, including the development of needed SRMs and other control materials, coordination of interlaboratory comparison exercises, evaluation of the interlaboratory data, analysis of sample splits with the participating laboratories, and coordination of workshops to discuss the results of these activities.

Results and Future Plans: We recently completed the certification analyses for a new highly contaminated marine sediment material, SRM 1944, *New York/New Jersey Waterway Sediment*, which has certified values for PAHs, PCBs, chlorinated pesticides, and trace elements at levels approximately 10 times higher than previous marine sediment SRMs. Certified values were determined for approximately 60 organic contaminants, e.g., polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), and chlorinated pesticides, and 10 trace elements. Material was processed and analyses initiated for the renewal of SRM 1566a, *Oyster Tissue*. Analyses are in progress for 23 elements and an additional 11 elements plus methylmercury are scheduled to be measured in the coming year.

Several environmental matrix SRMs that had been issued previously were reanalyzed to provide certified and reference values for a large number of organic contaminants. SRM 1649, *Urban Dust/Organics*, and SRM 1650, *Diesel Particulate Matter*, which were issued in 1982 and 1985, respectively, with certified values for only 5 PAHs, were reanalyzed using improved analytical procedures to provide certified values with significantly lower uncertainties for over 25 PAHs in each material as well as for 29 PCB congeners and 8 chlorinated pesticides (SRM 1649 only). SRM 1588, *Organics in Cod Liver Oil*, and SRM 1939, *PCBs in River Sediment*, which were issued in 1989 and 1990, respectively, with certified concentrations for PCBs and pesticides, were reissued with certified values for about 40 constituents in SRM 1588 and 20 PCBs in SRM 1939 compared to 15 and 3, respectively, in the original materials. Work is in progress on the replacement material for SRM 1589, *PCBs in Human Serum*. The original SRM 1589 was human serum spiked with Aroclor 1260 at the 100 ng/g total PCB level. For the new serum material, we will certify natural levels of individual PCB congeners (0.1 ng to 2.0 ng/g each).

Several years ago NIST, in cooperation with EPA, HUD, and USGS, embarked on a program to develop a series of SRMs designed to assess lead contamination in indoor and outdoor environments. The planned series includes powdered paints, paint films, soils contaminated with lead-based paints, and dusts. This effort is now nearing completion, with three new SRMs and one new RM issued in the past year. The new reference materials are: SRM 2580, *Powdered Paint, Nominal 4% Lead*; SRM 2581, *Powdered Paint, Nominal 0.5 % Lead*; SRM 2583, *Trace Elements in Indoor Dust, Nominal 90 mg/kg Lead*; and RM 8680, *Paint on Fiberboard, Nominal 1 to 2 mg/cm^2 Lead.* Measurement are now complete for two new lead paint contaminated soils, SRM 2586 and SRM 2587, and work has begun on a new dust with a nominal 1% lead concentration, SRM 2584.

For the NOAA NS&T and EPA EMAP QA program, NIST efforts focus on improving the comparability of measurements for over 60 organic contaminants in marine bivalve tissue, sediment, and fish samples. Current participants in these annual interlaboratory exercises represent a number of multi-laboratory monitoring programs and include over 40 federal, state/municipal, university, private sector, and international laboratories. We have documented that regular participation in interlaboratory comparison exercises and periodic workshops to discuss the exercise results coupled with the use of SRMs and other benchmark materials lead to improved laboratory measurements. Results from these intercomparison exercises are used by program managers in conjunction with other mechanisms such as performance on analysis of SRMs to assess the quality of data being provided by these laboratories for their programs

22. *Development and Maintenance of NTRM Programs in Critical Areas*

F.R. Guenther*, J.D. Fassett, G.W. Kramer, W.E. May, and R.L. Watters, Jr.*

Objective: To establish and maintain programs in selected critical areas to provide a well-defined traceability linkage for commercially produced reference materials to existing NIST standards for chemical measurements.

Problem: Increased requirements for quality systems documentation for trade and effective decision-making regarding health and safety have increased the need for demonstrating "traceability-to-NIST". Standard Reference Materials (SRMs) are certified reference materials issued under NIST trademark that are well-characterized using state-of-the-art measurement methods and/or technologies for chemical composition and/or physical properties. Traditionally, SRMs have been the primary tools that NIST provided to the user community for achieving chemical measurement quality assurance and traceability to national standards. The demand for reference materials traceable to NIST has begun to outpace our ability to produce SRMs in many areas. NIST does not have all of the resources necessary to provide the quantities and specific varieties of SRMs (exact sample types, unique compound combinations, concentrations, etc.) needed to meet these increasing needs.

Approach: The NIST Traceable Reference Materials program has been developed to increase availability of NIST-traceable reference materials, increase leverage of NIST resources, and free NIST resources for new SRMs. An NTRM is a commercially produced reference material with a well-defined traceability linkage to existing NIST standards for chemical measurements. This traceability linkage is established via criteria and protocols defined by NIST and tailored to meet the needs of the metrological community to be served.

Results and Future Plans: The NTRM concept was developed in 1992 to address the immediate need for a large number of gas standards of known pedigree for implementation of the "Emissions Trading" provision of the Clean Air Act of 1990. Program procedures and protocols are described in "The NIST Traceable Reference Material Program for Gas Standards" [NIST SP 260-126 (1996)]. The Cylinder Gas NTRM program has been well accepted by all parties – the specialty gas industry, the regulatory community and end-users of gas standards – and has proven to be an excellent model for leveraging limited NIST resources for maximum impact. Since its inception, 10 specialty gas companies have worked with us to certify nearly 4200 NTRM cylinders of gas mixtures that have been used to produce approximately 300,000 NIST-traceable gas standards for end-users.

In another high volume production area, NIST currently provides 95 spectrometric solution SRMs (used to calibrate atomic spectrometric instrumentation) with the need to reissue 40 to 60 of these each year. Maintaining availability of these materials in a production mode with sales of >3600 units/year for a large customer base is becoming increasingly difficult and is using resources needed to address other chemical metrological needs. Thus, the NTRM model for the commercial production of reference materials is being extended to this and other mature and high volume areas currently including:

- Elemental solutions for the calibration of istrumentation used for inorganic analysis (spectrometric solutions),
- optical filters, and
- metal alloy standards.

The approach used in the current cylinder gas NTRM program in which material from selected cylinders in each commercially produced batch are benchmarked at NIST against NIST primary standards will not be practical with the anticipated number of batches of commercial material in these new areas. Therefore, these programs will include NIST NVLAP accreditation of commercial producers of reference materials that can demonstrate their capabilities and competence in preparing and value-assigning NTRMs in the specified areas according to NIST-established criteria. The proficiency testing component of these accreditation programs will include sample audits by NIST of selected commercial NTRM batches.

During the past year, we have met with reference materials producer groups from the optical filter, spectrometric solution, and metal alloy communities. Program protocols are being developed for each area. The spectrometric solutions and optical filter NTRM programs are targeted to begin in June 1999 and the metal alloy NTRM program is scheduled to begin in September 1999.

23. NIST-Traceable Proficiency Testing of Environmental Testing Laboratories

R.M. Parris and W.E. May

Objective: To establish a system under which private sector companies and interested states can be accredited by NIST to provide NIST-traceable proficiency testing (PT) that meets the needs of EPA and States to those laboratories testing drinking water and wastewater for regulated chemical, microbial, radiological, and toxicological parameters.

Problem: Since the 1970's, EPA has conducted semiannual proficiency testing (PT) to assess the competence of over 6,000 public and private sector laboratories to conduct analyses required by the Clean Water and the Safe Drinking Water Acts. At the end of 1998, the cost-free provision of these services will be phased out and replaced by a multiprovider system in which interested states and private companies will provide these PT services on a fee-basis. Mechanisms and tools to provide appropriate government oversight of these programs are needed.

Approach: In a new government-private sector partnership, NIST is working with the EPA, States, and other public and commercial entities to establish appropriate oversight of this new effort to externalize and improve the nation's environmental laboratory PT programs. Under this new arrangement:

EPA will –
- provide NIST with three-year support to develop a program for private sector/state provision of PT studies
- work with States and NIST to assure that the program developed for 1) preparing, value-assigning and distributing PT samples and 2) evaluating the quality of the Environmental Testing Laboratory data is sufficient to support national/state clean water needs

NIST will –
- develop and manage program for accrediting private sector water PT study providers
- establish and maintain SRMs to support the program
- conduct blind sample audits of the commercially supplied PT samples on an ongoing basis as part of our QA responsibility for the program.

PT Study Providers will [following NIST-developed protocols] –
- develop, manufacture, value-assign, and distribute PT samples
- score results of Environmental Testing Laboratory analyses
- report data to EPA, NIST and the States
- maintain accreditation through NIST NVLAP

Results and Future Plans: A Federal Register Notice announcing the externalization of the EPA water performance evaluation studies with NIST accreditation of private sector study providers was published June 12, 1997. Extensive discussions and many meetings among the various stakeholders have ensued as the roles/requirements of the program are being delineated and concerns addressed. A NIST handbook describing the technical requirements of this accreditation program has been drafted and will be presented for comment at a public meeting on January 16, 1998. NIST has begun producing primary benchmark materials such as Standard Reference Materials (SRMs) for those parameters not covered by existing SRMs to assist suppliers in value-assigning their PT samples and establishing the infrastructure needed to audit the commercially supplied PT samples.

To avoid a lapse in the availability of appropriate PT studies, the Analytical Chemistry Division, Ionizing Radiation Division, National Voluntary Laboratory Accreditation Program, and the Standard Reference Materials Program are working together to set up this infrastructure in a timely manner. This will allow the first class of private sector and state water PT providers to become NIST-accredited by January of 1999.

24. Intercomparisons of NIST's Primary Methods and Standards with Other National Metrology Laboratories

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Objective: To assess and document international comparability for chemical measurements among the world's national chemical metrology laboratories and to link such comparability to the U.S. and North American systems of chemical measurement traceability for improved accuracy in chemical measurements.

Problem: The need for demonstrating comparability and traceability of chemical analysis data is becoming recognized worldwide. The identification of global trends in the state of the biosphere and the evaluation of the effects of trace elements in the environment are only possible on the basis of reliable data. A significant proportion of industrial production and international trade is also dependent on analytical chemical measurement. The uncertainty in the validity and/or lack of recognition of many of these measurements leads to a considerable amount of repeat measurement, particularly by regulatory agencies on imported products. This is expensive and impedes the free flow of international trade.

Approach: The Analytical Chemistry Division is a key participant in efforts of the International Committee for Weights and Measures (CIPM) and its Consultative Committee on Amount of Substance (CCQM) to address the issues of chemical measurement comparability and traceability. The CCQM has begun to assess chemical measurement comparability through strategically selected intercomparisons among national chemical metrology laboratories. The Division is using the assessment exercises conducted through the CCQM for selecting partners for strategic bi- or trilateral collaborations to determine and document the comparability of NIST primary methods and standards with those of other nations and/or metrological regions.

Results and Future Plans: This past year, the CCQM organized an intercomparison on the determination of 4,4'-DDE in isooctane using gas chromatography-isotope dilution mass spectrometry (GC-IDMS). Two unknown solutions were provided, one at about 50 times the concentration of the other. These unknown solutions were analyzed at NIST using the prescribed GC-IDMS protocol as well as two methods developed at NIST for measuring chlorinated pesticides, one involving gas chromatography/mass spectrometry and the other using GC with electron capture detection. The results from the GC-IDMS measurements were in good agreement with those of the two GC methods for chlorinated pesticides used at NIST for routine analyses. Ten laboratories from around the world submitted results to the CCQM. For the more dilute solution six of the ten laboratories had mean values within one percent of the gravimetric value, while all ten were within one percent for the more concentrated solution. The NIST IDMS mean was indistinguishable from the reference gravimetric value for the more dilute solution and 0.43% higher than the gravimetric value for the more concentrated solution.

The CCQM has formed three working groups: 1) gas analysis, 2) organic analysis, and 3) inorganic analysis. These groups are identifying the next key intercomparisons to be undertaken, taking into account measurement issues important for international trade and global science. The Division participates in all three working groups and is the lead organization for the inorganic area.

The first strategic bilateral program with the National Measurement Institute (NMi) of The Netherlands (representing the European Union) for determining the equivalence of primary gas standards has resulted in a formal “Declaration of Equivalence”. This “Declaration” is mutually recognized by the U.S. EPA and European environmental regulatory bodies as documenting the equivalence of seven NIST and NMi primary gas mixtures suites (spanning a wide range of concentrations). In previous years the carbon dioxide, carbon monoxide, ethanol, oxygen, propane, nitric oxide, and sulfur dioxide PSMs have been shown to be equivalent. During the past year we have worked to establish equivalence in natural gas standards and have continued efforts to address a bias of 2% observed between NIST and NMi primary standards for hydrogen sulfide. Additional collaborations for assessing the equivalence of primary standards are being established with DFM (Denmark) and OHM (Hungary) for conductivity, with PTB (Germany) for pH, with NIMC (Japan) and BAM (Germany) for elemental solution standards, and with NIMC for volatile organic compound standards.