U.S. Department of Commerce
Technology Administration

National Institute of Standards and Technology
Chemical Science and Technology Laboratory

... at a glance

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NISTIR 6388

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The National Institute of Standards and Technology

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... at a glance

September 1999

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

National Institute of Standards and Technology

http://www.nist.gov/

Raymond Kammer, NIST Director
Karen Brown, Deputy Director

An agency of the U.S. Department of Commerce's Technology Administration, NIST's mission is to promote U.S. economic growth by working with industry to develop and apply technology, measurements, and standards. It carries out this mission through four major programs: the Measurement and Standards Laboratories; the Advanced Technology Program; the Manufacturing Extension Partnership; and, the Baldrige national Quality Program. Each program addresses different components of the technology pipeline.

NIST's seven discipline-based Measurement and Standards Laboratories work at all stages of the pipeline from advancing basic science and pioneering new measurement methods to the development of standard test methods, materials, and data to ensure the quality of commercial products. The seven NIST Laboratories are: Electronics and Electrical Engineering Laboratory (EEEL), Manufacturing Engineering Laboratory (MEL), Chemical Science and Technology Laboratory (CSTL), Physics Laboratory (PL), Materials Science and Engineering Laboratory (MSEL), Building and Fire Research Laboratory (BFRL) and, Information Technology Laboratory (ITL).

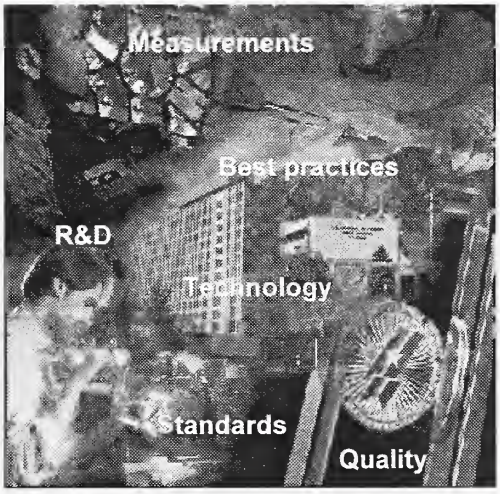
The Advanced Technology Program (ATP) helps fill the gaps that often exist between basic research advances and commercialization by providing cost-shared funding to industry for development of high-risk, "enabling" technologies with broad commercial potential.

The Manufacturing Extension Partnership (MEP) uses a nationwide network of centers to help smaller manufacturers adopt technologies and business practices that can improve their competitiveness in the global marketplace.

Finally, the Baldrige National Quality Program provides information to companies of all sizes on how to continuously improve their products, services, and processes through effective business and quality management.

Helping America Measure Up

NIST strengthens the economy and improves the quality of life by working with industry to develop and apply technology, measurements, and standards through …



- 3300 employees
- $760 million annual budget
- 1200 industrial partners
- 2000 field agents
- 1550 guest researchers
- $1.4 billion co-funding of industry R&D
- national measurement standards

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www.cstl.nist.gov

Chemical Science and Technology Laboratory

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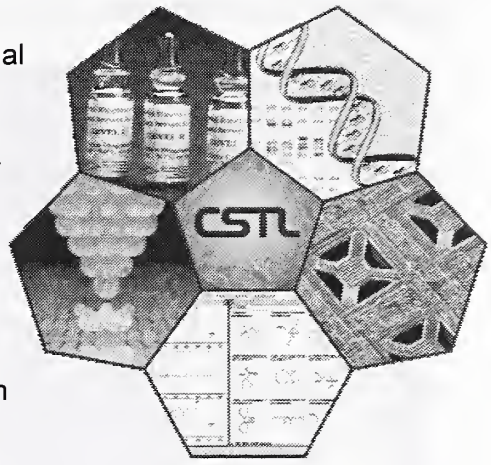


Since its creation by Congress in 1901, NIST, then the National Bureau of Standards (NBS), has been the source of measurements and standards on which industry, commerce, scientific institutions, and all branches of government depend. Reflecting the importance of chemical measurements and standards to our country, the Chemistry Division was one of the first established by the founders of NBS.

Today, the Chemical Science and Technology Laboratory has the most comprehensive array of chemical, physical, and engineering measurement capabilities of any group working in chemical science and technology.

Mission:

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. As the Nation's Chemical 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.

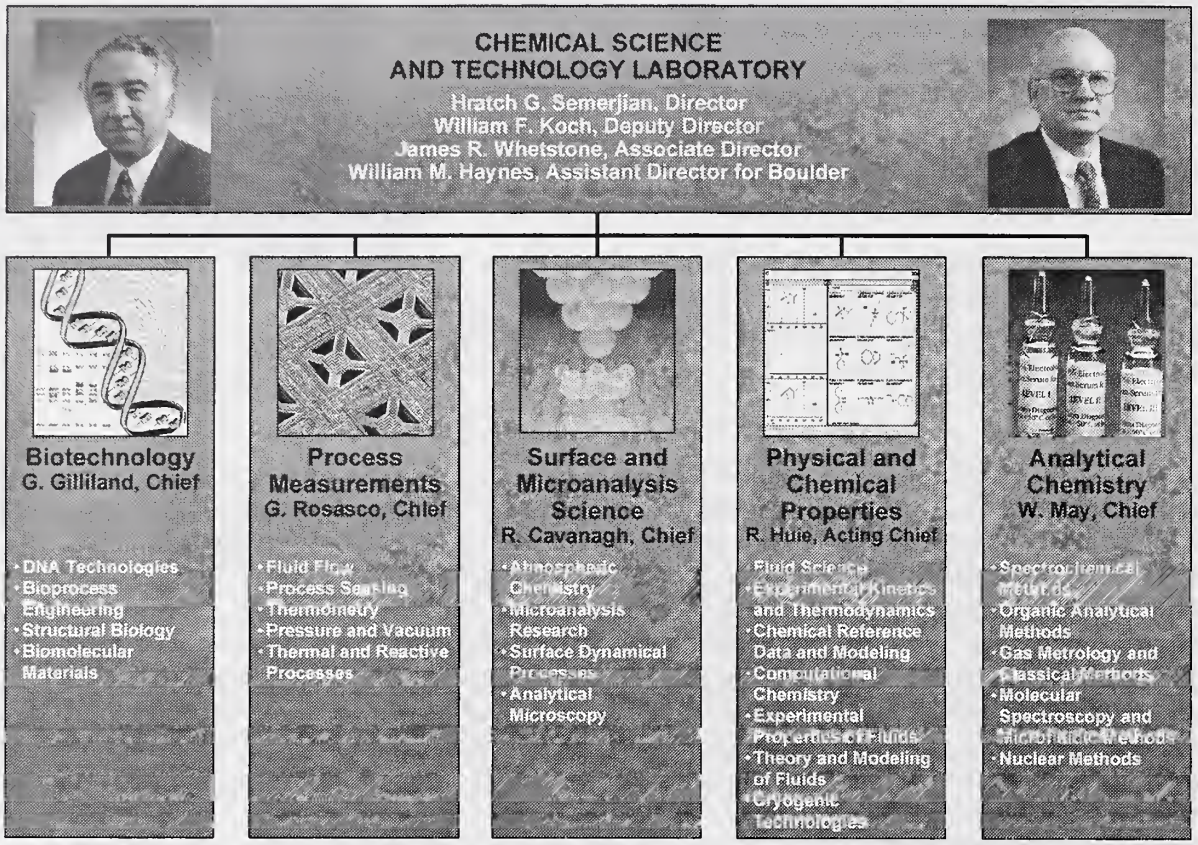
Measurement Science: Address current, and anticipate next-generation, measurement needs of the nation by performing cutting-edge research in measurement science.

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 communities. 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 programs. 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, as well as the Center for Advanced Research in Biotechnology (CARB) in Rockville, Maryland and the Marine Environmental Health Research Laboratory (MEHRL) in Charleston, South Carolina.



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Measurement Standards

... supporting emerging technologies and the nation's measurement infrastructure

NIST provides a wide variety of measurement, standards, and data services and programs to help U.S. industry improve its international competitiveness, commercialize new technology, and achieve total quality in all facets of business operations. CSTL maintains and disseminates measurement standards for chemical, biomolecular, and chemical engineering measurements by developing Standard Reference Materials, (SRM®) and providing calibration services.

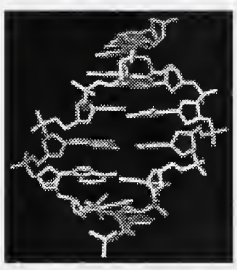
SRM® CSTL partners with the NIST Technology Service's Standard Reference Materials Program to provide scientists and engineers in industrial and academic research with internationally accepted SRMs for critical technical decision-making. NIST pioneered, and continues to lead, in the development of certified reference materials used for quality assurance. NIST provides more than 1,200 different SRMs certified for specific chemical composition or physical properties. CSTL provides technical leadership for most of the chemical and compositional standards produced by NIST.

SRMs are used for three main purposes: to help develop accurate methods of analysis (reference methods); to calibrate measurement systems; and to assure the long-term adequacy and integrity of measurement quality assurance programs. NIST SRMs also legally constitute part of the National Measurement System infrastructure of the United States and, as such, are essential transfer mechanisms for national as well as international measurement traceability. SRMs are available for: engine wear materials, environmental materials, ferrous and non-ferrous metals, food and agriculture, fossil fuels, gas mixtures, geological materials, high-purity materials, health/clinical/industrial hygiene, microanalysis, optical and thermophysical properties, and others. The complete list of available SRMs can be found on the following web site.

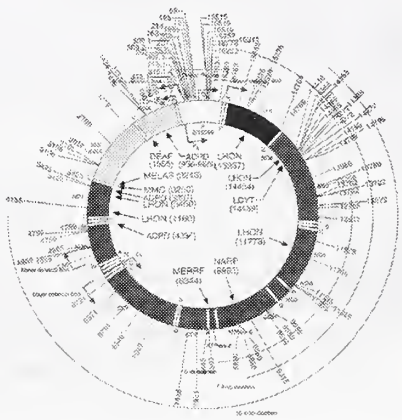
http://ts.nist.gov/ts/htdocs/230/232/232.htm

Chemical and Compositional Standards Development

CSTL assumes a proactive and leadership role in identifying chemical standards needs to support the U.S. measurement infrastructure. Currently there are new standards in production or recently available in four major areas: **Health** - *Toxic Metals in Blood and new DNA standards*; **Food** - *Meat Homogenate for Nutrition Labeling, and Mineral Oil Refractive Index*; **Environmental** - *Fish Tissue, Reformulated Gasoline, and Sediments*; and **Industrial Applications** - *Hydrogen in Titanium Alloy, Zeolite Catalyst, Aircraft Alloys, NIR Wavelength Standards, Particles in Oil, and Arsenic Implant in Silicon.*

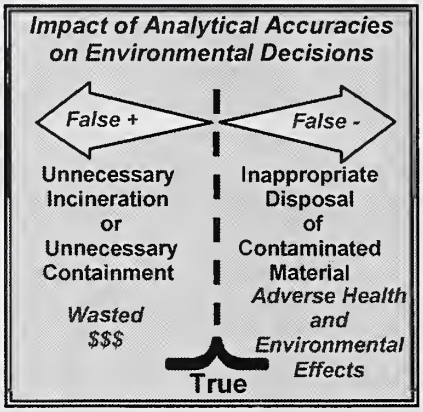


The newly released *Mitochondrial (mt) DNA Standard, SRM 2392,* was produced under the technical leadership of CSTL's Biotechnology Division. This SRM is used in quality control, in sequencing, forensic identification, medical diagnostics and mutation detection. The SRM includes extracted DNA and all information for performing: PCR amplification process, cycle sequencing steps, gel separation, data analyses to determine DNA sequence, and materials to assess the accuracy of the results. In addition, sequences of 58 sets of unique primers are also included to allow any area or all mtDNA to be amplified and sequenced.



New Sediment SRM Enhances Accuracy of Environmental Measurements and Provides Accuracy Base for Reliable Decision-making

SRM 1944, NY/NJ Waterway Sediment has recently been released by NIST/CSTL. It was produced in collaboration with the NY District Army Corp of Engineers and certified in collaboration with Environment Canada. SRM 1944 is a mixture of marine sediment collected near urban areas in New York and New Jersey. All of the constituents for which certified, reference, and information values are provided in SRM 1944 were present in the sediment material before it was processed.



SRM 1944 provides certified and reference values for over 150 organic and inorganic constituents of environmental concern. The SRM is for use in evaluating analytical methods for the determination of selected polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyl (PCB) congeners, chlorinated pesticides, and trace elements in marine sediment and similar matrices. SRM 1944 is the first NIST material characterized for selected dibenzo-p-dioxin and dibenzofuran congeners. In addition, reference values are also provided for total organic carbon, total extractable material, and particle-size characteristics.

Quantity of dredged material for disposal: > 4 x 10^6 m^3 per year
- **Disposal costs:**
  - For unrestricted disposal: **$30 M per year**
  - For containment: **$150 M to $600 M per year**
- **Testing costs per federal project: $1 M per year**

U.S. Army Corps of Engineers - New York District

NIST/CSTL Produces First Standard Reference Material for the Fluid Power Industry

Industry experts estimate that up to 85 % of hydraulic system wear problems can be traced to contamination of the fluid by solid particles. Particle counting is a mainstay of contamination control in hydraulic, automotive,and aerospace applications. To improve precision and accuracy in particle counting, the fluid power industry requested the development of a series of SRMs/RMs to replace and improve upon an existing reference material that has been used for over 25 years.

Fluid power industry has $13B market in the U.S. with $1.1B in exports

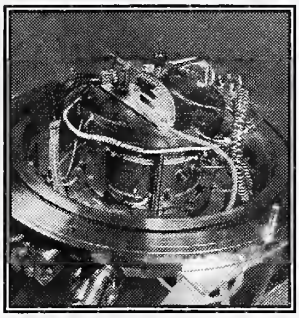
With the release of ***SRM 2806 Medium Test Dust in Hydraulic Fluid, RM 8631 Medium Test Dust and RM 8632 Ultrafine Test Dust***, together with revisions to document standards from the International Organization for Standardization (ISO) and the National Fluid Power Association (NFPA), improved accuracy and reproducibility of the particle count data can be realized.

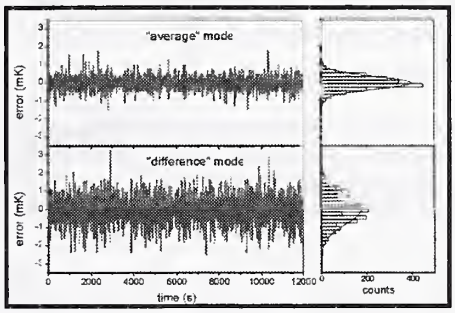
SRM 2806 consists of a silica mineral dust suspended at known concentration in clean hydraulic fluid. Certified values for the cumulative number of dust particles per unit volume of hydraulic oil for particle sizes from 1 µm to 30 µm are provided, and for particle sizes greater than 30 µm reference values are given. RM 8631 Medium Test Dust consists of dry dust taken from the same lot as the dust in SRM 2806, and is provided with reference values from 1 µm to 50 µm. Reference values from 1 µm to 20 µm are provided with RM 8632 Ultra Fine Test Dust.

Physical Standards Development

New Physical Standards under development in CSTL are in the following core areas: **Temperature** - *Implementation and Dissemination of ITS 90, Thermodynamic Temperature Measurements, and Primary Acoustic Thermometry*; **Pressure** - *New Partial Pressure Standards (CRDS), and the Comparison of International Pressure Standards*; **Flow** - *Standards for Measuring Low Flow-Rates of Gases, Reduced Uncertainty in Primary Mid-range Standards, and High Temperature Gas Flow Calibration;* **Humidity** - *Standards For Low Concentration Of Water Vapor In Gases*; **Density** - *New Liquid Density Standards*.

The New Low Frost-Point Humidity Generator Extends NIST's Calibration Services by Three Orders of Magnitude

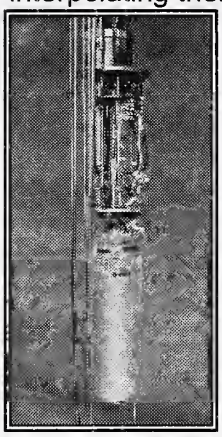




The low frost-point humidity generator was developed in response to demands for a standards grade generator that could provide calibration services for ppb-level hygrometers. This gravimetrically based primary standard has an operating range of 11 nmol/mol to 30 mmol/mol in humidity concentration. Mole fraction of water vapor is calculated from temperature and pressure measurements. The output precision is dominated by saturator temperature stability (data shown in graph). The unique temperature control system gives mK level stability and set point repeatability. For example a variation of ± 2 mK at -70 ºC produces ± 0.3% change in mole fraction of water vapor. Using this system, during 4 days of operation at -99 ºC the measured saturator temperature remained constant to within 0.5 mK. This novel, precision generator extends the range of low level humidity standards by 3 orders of magnitude to provide a standard for measurement of trace moisture levels (nmol/mol) in process gases widely used in the semiconductor industry.

NIST First to Realize the International Temperature Scale (ITS90)

The Temperature Standards program realizes, maintains, and disseminates the International Temperature Scale of 1990 (ITS-90) over the temperature range from 0.65 K to 1234.93 K. NIST is currently the only National Metrology Institution in the world to realize and disseminate ITS-90 over it full range. The ITS-90 defines temperatures in terms of a set of procedures involving interpolating thermometers, specified mathematical equations, and certain reproducible physical phenomena, known as thermometric fixed points. Specifically, temperatures are defined by the specified vapor-pressure/temperature relations of liquid helium (0.65 K to 5 K), interpolating gas thermometry (3 K to 24.5561 K), and Standard Platinum Resistance Thermometers (13.8033 K to 1234.93 K) calibrated at specified fixed points.



Industries with an interest in these services include: aerospace, chemical, pharmaceutical, defense-related, distilleries, electronics, instrument manufacturers, secondary calibration facilities, and utilities. The temperature scale is disseminated through calibrations, measurement quality assurance programs, SRMs, and workshops. These promote national consistency of temperature standards and measurements in the U.S. scientific and industrial communities.

CSTL partners with the NIST Calibration Program, and provides calibration services in the following areas: *Air Speed; Flow Measurement at Cryogenic Temperatures; Fluid Flow; Humidity; Laboratory Thermometers; Low Pressure, Vacuum, and Leaks; Ozone; Pressure; Resistance Thermometry; Thermocouples, Thermocouple Materials, and Pyrometer Indicators; and Volume and Density (Hydrometers).* **NIST calibration services** link the makers and users of precision instruments to the basic and derived units of the International System (SI) of measurements. As one of the cornerstones for ensuring the consistency of measurements in the United States and internationally, this measurement transfer system is a critical factor in controlling manufacturing, assembly processes, and marketing as well as assuring the quality of manufactured goods. Users of these services send transfer standards to NIST where they are calibrated according to a measurement process that is stable, predictable, and statistically controlled. Currently, NIST provides more than 500 different calibrations, special tests, and measurement quality assurance programs in seven major measurement areas.

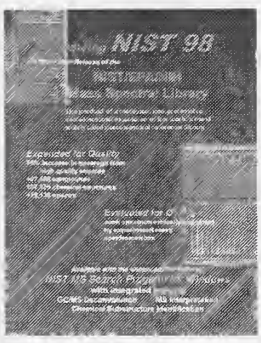
Chemical and Process Information

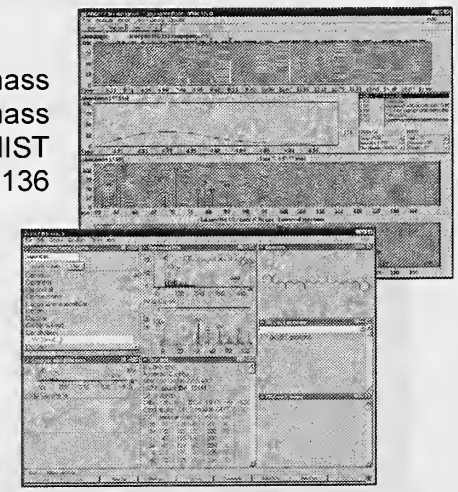
...assuring that U.S. Industry has access to accurate and reliable data and predictive models

NIST DATA The NIST **Standard Reference Database** (SRD) series has grown to over 50 electronic databases in chemistry, physics, materials, building and fire research, software recognition, and electronics. Versatile interactive databases provide easy access to high quality NIST data. Many databases are now available via the World Wide Web. Through this program CSTL provides SRDs for Analytical Chemistry, Atomic and Molecular Physics, Biotechnology, Chemical and Crystal Structure, Chemical Kinetics, Industrial Fluids and Chemical Engineering, Materials Properties, Surface Data, and Thermodynamics and Thermochemistry.

http://www.nist.gov/srd/

The NIST Mass Spectral Database - new release is the world's most widely used mass spectral library

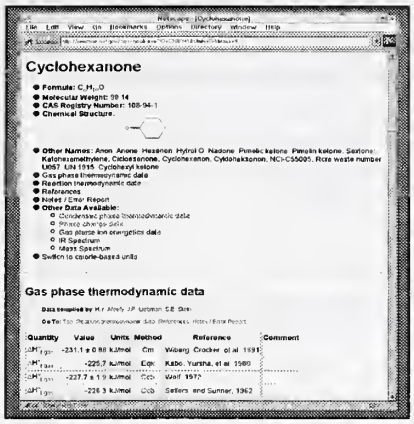


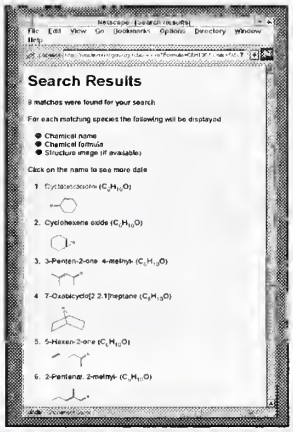


CSTL led the efforts to provide the mass spectral community with a fully evaluated mass spectral database. The major new release, NIST 98, is a database of mass spectra with 129,136 evaluated spectra for 107,886 compounds. Structures are provided for 107,829 compounds, replicate spectra for 13,205 compounds. The data are largely for full spectra with a mean of 93 peaks/spectrum and a median of 78 peaks/spectrum. Each of the spectra has been evaluated by at least one expert, and all questionable data by two experts. Over the last few years a number of advances in the algorithms for searching the database have been developed and tested. Work is underway to add retention indices to the database. An example of an important class of compounds for which these data might be particularly useful is the hydrocarbons, many of which have very similar mass spectra.

The NIST WebBook - provides Internet access to a complete set of chemical data

http://WebBook.nist.gov/





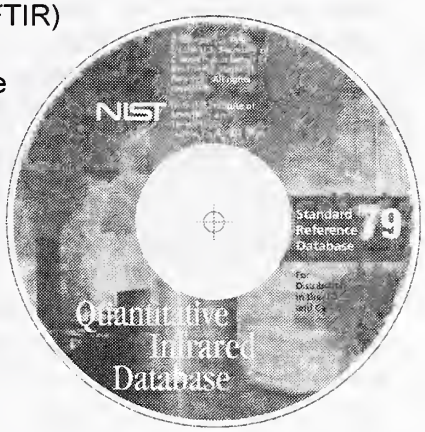
The rapid growth of the World Wide Web has been phenomenal, and it is clear that the Web has dramatically changed the way we do science. The use of the Web as a publishing medium and as a resource for communication has been growing rapidly. The WebBook provides a quick and direct source of chemical data that is available at all times. The initial efforts are tied to an approach based on compounds rather than properties. All 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.

5,000 - 10,000 users/week,
> 40% are repeat users

In parallel with the efforts to gather and evaluate data, another major part of this effort 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).

FTIR Database - First database traceable to NIST primary gas standards

Both open-path and extractive Fourier Transform infrared (FTIR) spectrometric techniques have recently become useful real-time analytical tools due to the development of fast, portable computers and robust instrumentation. The success of the technique is highly dependent on the quality of the reference data available to quantitatively evaluate the field results and to compare measurements. NIST/CSTL has issued SRD 79, a CD in JCAMP-DX format of reference spectra of 21 of the EPA high-priority compounds. To better match field data, data may be obtained at several resolutions and apodization functions. Internet updates are available.



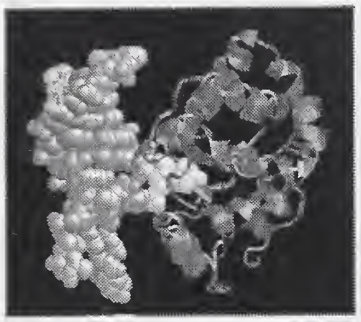
Quantitative FTIR measurements are absolute measurements of fundamental molecular properties. Therefore, this database is an excellent complement to the NIST gas standards program. It has the potential of providing user communities with a method of making NIST traceable measurements with a minimum number of SRMs or NIST Traceable Reference Materials (NTRMs).

Measurement Science

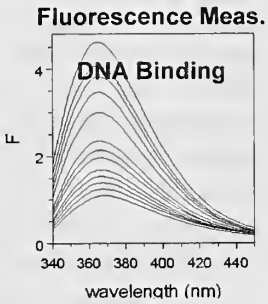
... to anticipate and address next generation measurement needs of the nation

CSTL maintains a strong basic research program in broad aspects of measurement science that positions us with the capability to provide the required measurements, standards, and data needed to support future technology development. New measurement techniques are important for a host of industries including biotechnology, heath care environmental technologies, and the chemical process industry. Many of our activities, such as protein crystallography and materials microanalysis, are at the leading edge of science and technology.

Advances in DNA Technologies - a new measurement method provides insights into DNA repair



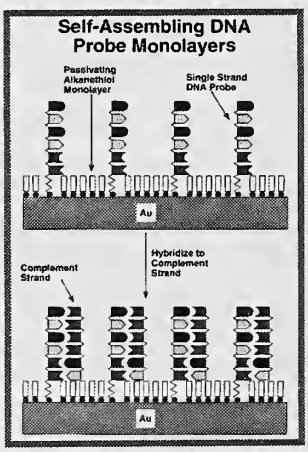
Mechanistic Enzymology of DNA Repair: DNA repair enzymes are required to maintain the integrity of the human genome against a constant onslaught of DNA damaging agents, and are important tools for the research and medical diagnostic communities. A variety of state-of-the-art approaches are being used to determine the mechanisms by which DNA repair enzymes obtain their extraordinary specificity and catalytic power. These approaches include rapid kinetic methods, NMR spectroscopy, X-ray crystallography, kinetic isotope effects, and computational techniques. The objective is to provide models and measurements to better understand the nature of enzymatic DNA repair, and provide a mechanistic basis for engineering these enzymes for new applications in the biotechnological, medical diagnostic, and manufacturing industries. These methods are having a broad impact in the areas of rational drug design, enhanced methods for determining structures of DNA and RNA using NMR, and fluorescence detection methods for high-throughput screening.



Industrial Collaborator
Codon Pharmaceuticals,
Gaitherburg, MD

New Sensor Technology - for rapid, accurate, cost-effective screening

Self-Assembled Monolayers (SAMS): Biosensors and diagnostics are being developed to perform multi-analyte measurements rapidly, accurately, and at low 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 health care, toxicology, forensics, industrial processing, and environmental monitoring.

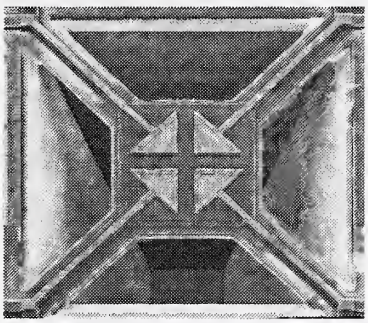


Alkanethiol SAMs impart chemical sensitivity to Au surfaces by forming stable, ordered structures with highly tunable surface chemical and physical properties. The thiol headgroup bonds strongly to the Au surface, forming a densely packed monolayer where the functional group on the opposite end of the molecule forms the SAM surface. Biologically active films are prepared by derivatizing a biomolecule of interest with a thiol group, and then

self-assembling the thiol-modified biomolecule on Au. The surface density, hybridization activity, and molecular conformation of the surface-bound DNA probes are characterized with a variety of surface-sensitive methods, including electrochemical techniques, neutron reflectivity, grazing angle FTIR, surface plasmon resonance, ^{32}P radiolabeling, x-ray photoelectron spectroscopy, ellipsometry, surface-enhanced Raman spectroscopy, scanning tunneling microscopy, and secondary ion mass spectrometry.

Micro-Hotplate Sensor Arrays

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 measurement concerns are encountered in the automotive field where engine performance and reduced emissions are issues. Meeting these demands requires a low-cost technology for the measurement of gas species, which can provide real-time, on-site analysis for the detection of reaction products, exhaust gases, leaks, etc.



Advances in microfabrication technology now make possible miniaturization of conventional conductometric low-cost metal oxide sensors in a planar array form. At NIST, a sensor array platform has been developed that uses a "micro-hotplate" as the generic device structure. The micro-hotplate has three functional layers: a heater, a thermometer/heat distribution plate, and electrical contacts for monitoring the conductivity of sensing films. Devices are fabricated using CMOS processing combined with post-CMOS process silicon micromachining, and sensor film deposition. NIST holds three patents on this technology.

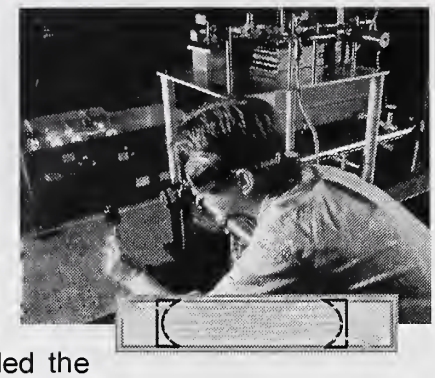
Because of their 50μm to 250μm size the elements can be heated and cooled rapidly with time constants of 1ms to 2ms over a large operating temperature range (>800 °C), This capability supports a novel sensing approach, temperature programmed sensing (TPS). The effects that produce a response signal are 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 and chemometric-based approaches are being used to optimize the generation of signatures and to analyze signals during sensing.

Collaborators:
EEEL - device design
University of MD and CPAC - response signature
MIT Lincoln Laboratories - device fabrication
DoD - Threat reduction applications
DoE - Environmental management applications

Advances in Cavity Ring-Down Spectroscopy (CRDS)

The Semiconductor Industry Association (SIA) identifies water vapor measurements as a key metrological parameters for contamination-free manufacturing of the next generation of devices. Measurement capability of 100 pg/g (ppt) are anticipated by the year 2001.

Single Mode CRDS - Quantitative Optical Measurements of Gas Partial Pressures: 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 that underpin measurement accuracy and reliability. Traditional techniques for generating low partial pressure standards for 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.



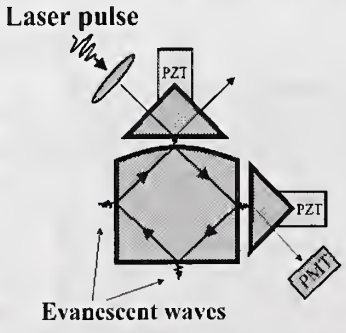
The objective of this research is to develop quantitative high-sensitivity optical measurements and to establish a new primary standard for low-levels of gaseous contaminants. **Cavity ring-down Spectroscopy (CRDS)** has been identified as the most suitable approach. The centerpiece of CRDS is a state-of-the-art, high-Q Fabry-Perot etalon. The Q of the cavity is determined by measuring the time constant for intensity decay of an injected light pulse. The introduction of an absorbing species into the cavity degrades the cavity-Q providing a measure of the gas absorption and hence its concentration. Recent advances in the high-quality mirrors used to form the optical cavity have enabled the realization of this measurement. Using these 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.

Evanescent-Wave CRDS - a new tool for studying chemical reactions at interfaces

Evanescent wave cavity ring-down spectroscopy (EW-CRDS), has been developed as a fundamentally new measurement capability for characterization of interfaces and thin films. In contrast to conventional CRDS, which employs narrow-spectral-bandwidth mirrors and is applicable only to the gas-phase, EW-CRDS employs a miniature, monolithic, total-internal-reflection (TIR)-ring cavity of regular polygonal geometry with at least one convex facet to induce stability. Evanescent waves generated by TIR probe absorption by matter in the vicinity of the cavity. Optical radiation enters and exits the resonator by photon tunneling, which permits precise control of input and output coupling. Furthermore, the broadband nature of TIR circumvents the narrow bandwidth restriction imposed by dielectric mirrors in conventional gas-phase cavity ring-down spectroscopy. The use of evanescent waves in spectroscopy is the basis for the well-established technique known as attenuated total reflectance (ATR). Yet conventional ATR lacks the sensitivity required to address many key problems in interfacial science and technology.

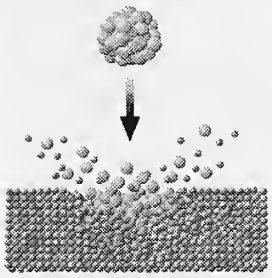
EW-CRDS combines the advantages of cavity ring-down and ATR spectroscopies to achieve a synergistic new technology that exceeds existing optical absorption techniques in sensitivity by many orders of magnitude and may ultimately achieve single molecule detection.

A theoretical model for the EW-CRDS TIR-ring cavity technology has been developed that incorporates all of the design variables related to cavity size and stability, as well as the electrodynamic details of evanescent wave absorption and photon tunneling. The model permits optimum cavity designs to be identified. A square, TIR-ring cavity has been fabricated from ultra-high-purity fused silica. This cavity permits a wide variety of processes occurring in and on thin films to be studied in the near-UV to the near-IR. Since the chemical response of a surface is established over a much shorter length scale (≈1 nm to 5 nm) than the evanescent wave decay length, the surface response of a semi-infinite medium is obtained. Experiments on the adsorption of iodine as a model system to study EW-CRDS sensitivity has demonstrated a detection limit of <100 μg/g (ppm) of an iodine monolayer. Reaction of I_2 to form I_3^- in the presence of adsorbed water can be observed and quantified. Furthermore, by measuring the ring-down time for the s- and p-polarization components separately, the average orientation of adsorbed molecules can be extracted with unprecedented sensitivity.



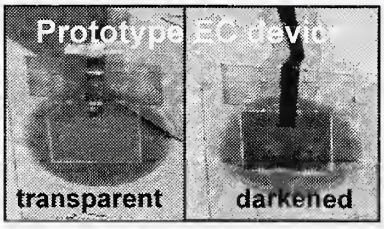
Novel Depth Profiling Methods

Secondary Ion Mass Spectrometry (SIMS) for Depth Profiling with Polyatomic and Cluster Primary Ion Beams - characterization of ultra-shallow dopant profiles in advanced semiconductor devices and biological tissues



A modified hot filament duoplasmatron ion source has been constructed for generation of SF_5^+ polyatomic primary ion beams. An evaluation of this novel primary ion beam species for ultra-shallow depth profiling has been conducted on a variety of test samples including low energy B implants in silicon, B and Ge delta-doped test structures in silicon and a Ni/Cr depth profiling Standard Reference Material. Most experiments have been conducted using the SF_5^+ ion beam at 3.0 keV impact energy and an incidence angle of 52° with and without oxygen backfill. Results using boron delta-doped structures indicate that SF_5^+ primary ion bombardment, with oxygen backfill, gives improvements in trailing edge decay lengths (a measure of the depth resolution of a depth profile) of approximately a factor of 2 compared with O_2^+ bombardment under the same conditions (1/e decay lengths for SF_5^+ ~ 1 nm). For depth profiling of metals, the SF_5^+ primary ion beam without oxygen backfill results in a substantial reduction in surface roughness (factor of 6) giving depth profiles comparable to those obtained with O_2^+ bombardment and sample rotation. These studies are being extended by the addition of a second primary ion cluster source that will facilitate evaluation of depth profiling with a wide variety of polyatomic and metal cluster primary ion beams. In addition, we are investigating the use of SIMS as a true chemical microscope for biomolecular detection. Imaging of large molecules is anticipated to have utility in diverse fields of biotechnology, e.g., for mapping the distribution of drugs, their metabolites, and toxins in tissues and in a broad range of biological matrices. This knowledge, in turn, could yield valuable information about the biological or pharmacological roles of those compounds.

New Neutron Depth Profiling (NDP) Method for the Assessment of Lithium Mobility in Active Devices - *in-situ* measurement of Li movement in thin film electochromic coatings



Thin film "rocking-chair" type cells hold great promise for both "smart window" and rechargeable battery applications by way of reversible ion transfer. "Smart windows" and many types of lithium batteries consist of two mixed electron/ion-conducting layers separated by an ion-conducting, solid electrolyte layer. Variation in optical density or charge potential is achieved as lithium ions are transported from one layer, through the electrolyte, to the other layer. NDP provides a non-destructive method of measuring the analyte concentration as a function of the depth in the matrix material. This approach has been employed to examine the dynamic lithium distribution in active electrochromic multi-layers, and has provided insight to the correlation between the device optical density and the amount of lithium transferred between the device electrodes. Measurements made with and without the electrical bias quantify the migration of lithium as it occurs. The application of this method to lithium batteries may provide new insights into the mechanisms of charge capacity loss with cycling, lower than theoretically attainable reversible charge capacity, and maximum charging and discharging current densities.

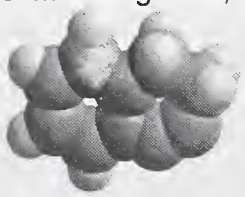
Market demand for all types of rechargeable cells is expected to grow at a compound rate of 11 percent per year, reaching a total of 2 billion cells by 2001, of which the lithium ion cell share is expected to be 440 million cells. Thus the market for lithium ion cells will soon reach about $4 billion. In spite of this rapid commercialization, much of the underlying materials science is not completely understood; such knowledge is necessary to produce better-performing and less expensive products.

New Directions

CSTL is expanding programs in the following areas to support emerging technologies into the new millennium: Information Technology and E-Commerce; Biotechnology; Measurements and Standards for Health Care; Measurements and Standards for International Trade; and, Nanotechnology. These program expansions are compatible with current and planned programs.

Information Technology and E-Commerce for the 21st Century
...computational tools and electronic dissemination of data ... essential to ensure that U.S. industry remains globally competitive

The area of **Computational Chemistry** is rapidly growing with the increased use and availability of modeling tools, and the improved accuracy of computed physical and chemical properties.



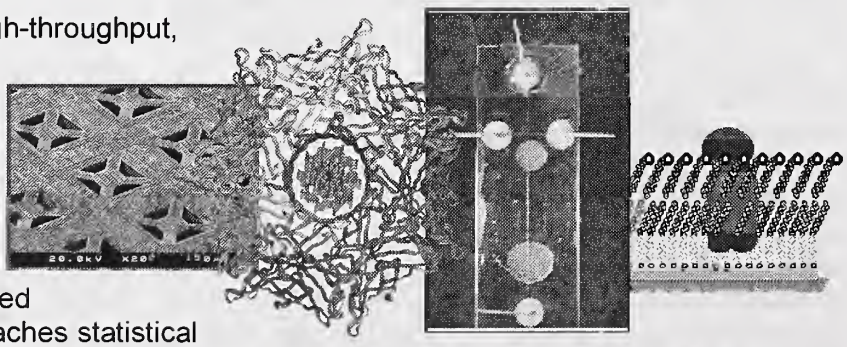
This development is driven by the industrial need for reducing the cost and time for product development, coupled with the increasing cost of making experimental measurements. However, along with the modeling tools, there is a need for benchmark data for process design, chemical identification, environmental fate and risk analysis, and data dissemination *via* the internet.

The CSTL/NIST role is to develop the infrastructural technology for the evaluation and dissemination of chemical process information and data, as well as supplying standards for interoperability in clinical and analytical laboratories. In accordance with the Technology Vision 2020, the following technical areas have been identified for increased focus in CSTL: accurate predictions of thermo-chemical/physical/kinetic properties of gases, liquids, solids and multiphase mixtures; reliable methods for modeling chemistry in condensed phases and at interfaces; methods for determination of large, complex structures (such as proteins) from sequence information; methods for combining computational chemistry with fluid dynamics for modeling reacting flows; accessible databases with evaluated data and "data on demand" from predictive models; and reliable computer architectures and scalable, portable codes for MPP (massively parallel processing).

Applications for Computational Chemistry in Chemical Processing
- **New Bioprocesses**
- **Catalyst Design**
- **Improved Reaction Pathways**
- **Product Development - (polymers and pharmaceuticals)**
- **Efficient Process Design**
- **Materials Design**
- **Polymer Processes**

Combinatorial Approaches - for a competitive edge, U.S. industry must reduce R&D Cycle time with higher quality and performance

Better ... Faster ... Cheaper



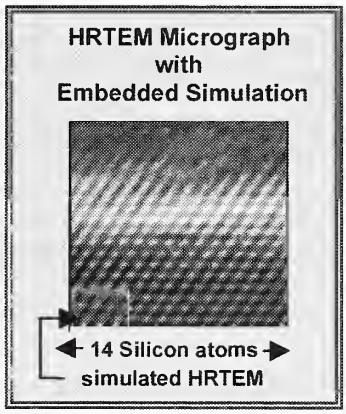
Combinatorial Chemistry - high-throughput, parallel-synthesis chemistry for materials and pharmaceutical discovery. It is an integral combination of experimental design and validation, synthesis and processing, screening mechanisms, and informatics. To obtain the desired benefits of combinatorial approaches statistical tools, computational/molecular modeling, automation, sensors and analytical systems, and databases need to be developed. CSTL has core efforts in the areas of modeling tools and benchmark data, Standard Test Data, and has expanded programs in the area of nanosampling and nanosensing.

Nanotechnology - measurement capabilities and devices approaching the atomic scale

Nanoscale Chemical Characterization: The program objectives are to push the measurement envelope and provide infrastructural tools for the measurement communities to determine the chemical composition of various samples, at increasing spatial resolution and decreasing 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 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, photon, and X-ray probes. These measurement tools can be applied across a broad range of problems in the private and public sectors such that the "microspatial" relationship of chemical species can be correlated with specific macroscopic properties of high technology materials or electronic devices as well as to determine the effects of individual manufacturing steps on a system or product.

Measurement Capabilities and Devices for:

Semiconductors
Optoelectronics
Storage Technology
Medicine
Catalysis
DNA Diagnostics



High Resolution TEM (HRTEM) is being developed to support industrial production of ultra thin layers for future devices cited in the SIA National Technology Roadmap. Sub-nanometer resolution has been accomplished on NIST CM 300 FEGTEM - 0.2 nm point-to-point. This method has projected applications for ultra-thin amorphous SiO_2 films grown on Si substrates.

New Measurements and Standards Needs

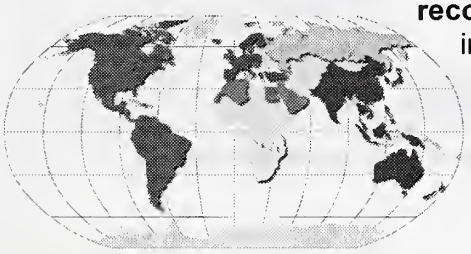
Standards and Measurements to Reduce Health Care Costs: Research activities by CSTL's organic mass spectrometry team have focused on the development of techniques for characterization and quantitative determination of proteins in biological matrices. Reference methods for important biomarkers such as troponin-I (a new marker of myocardial infarction), glycohemoglobin (an important new marker for diabetes), and serum thyroxine (an important marker for thyroid function) are being developed. Techniques have been developed for the chemical characterization of purified troponin-I preparations, thus providing a means for comparing structure with results from field studies involving immunoassays. An isotope dilution GC/MS method for cortisol (a marker for endocrine function) has been developed and is undergoing testing. 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.

Next Generation Health Status Chemical Markers

- Troponin I (coronary heart disease)
- Glycated hemoglobin (diabetes)
- Prostate-specific antigen
- p53 DNA (breast cancer)

Measurement specificity is critical for accurate diagnosis

International Trade - ensuring global measurement comparability and world-wide recognition with key comparisons: U.S. trade success in the international marketplace relies in part on overcoming technical measurement barriers and creating a globally accepted measurement and standards infrastructure, with vertical (national, regional) and horizontal (international)



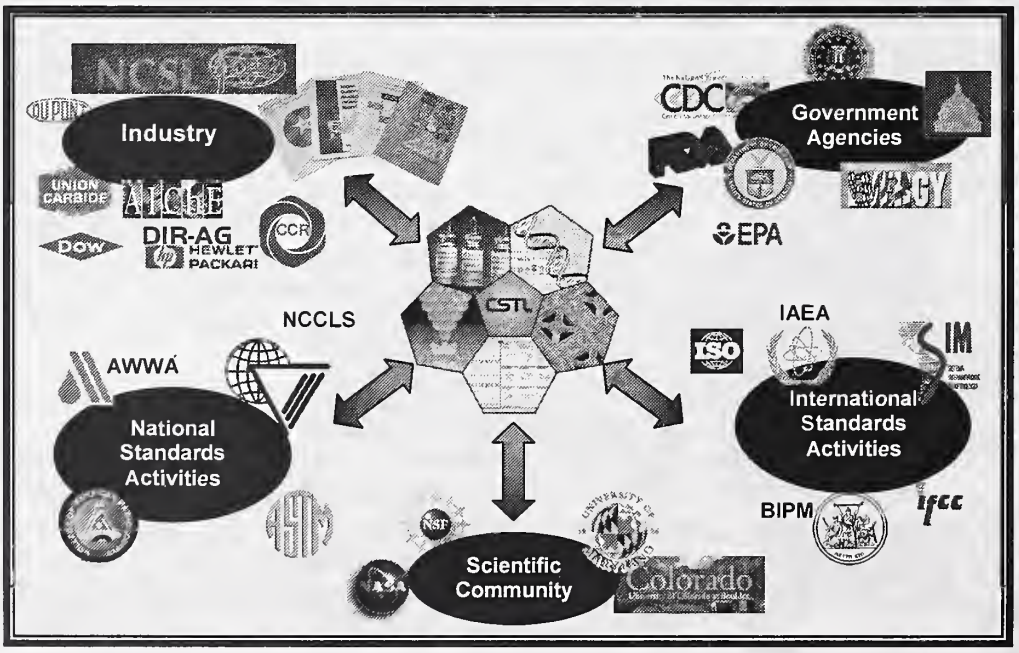
relationships. CSTL is working to harmonize key international standards through bilateral and multilateral comparisons of chemical and physical measurements, provide technical training, and influence international standards organizations through membership. As a member of technical committees of the International Committee for Weights and Measures (CIPM), CSTL is responsible for providing the links between chemical (and selected physical) measurements in the United States and for the International System of Units (SI). World-wide traceability of chemical and physical measurements is ensured through a highly leveraged system of key Standard Reference Materials, primary methods of chemical analysis, and primary physical standards. CSTL activities in this international arena positively impact the automotive, environmental, pharmaceutical, petrochemical, agricultural, chemical, and instrument manufacturing industries.

BIPM//CCQM Key Comparisons - chemical measurements
Health - Clinical diagnostic markers, trace elements in bio-fluids
Food - Pesticide residues, toxins in food, trace elements in drinking water
Environment - Waste water, primary gas standards, contaminants in sediments
Advanced Materials - Semiconductors, alloys, catalysts, polymers and plastics
Commodities - Sulfur in fossil fuels, natural gas, cement, ore composition
Forensics - Ethanol in air, drugs of abuse
Analytical Applications - Solution standards, purity of materials, pH standards

Partnering to Meet the Needs of the Future

Interactions help CSTL assess industrial and government agency needs and set CSTL program directions

CSTL staff have extensive ties to industry and also participate widely in national and international committees and professional organizations. These activities take many forms including: meetings of users of CSTL products, committees of national and international standards organizations, the Council for Chemical Research (CCR), the International Organization for Standardization (ISO), the American Society for Testing and Materials (ASTM), the National Committee for Clinical Laboratory Standards (NCCLS), and the National Conference of Standards Laboratories (NCSL). CSTL also interacts with government interagency planning committees, such as the National Science and Technology Council committees on biotechnology and environmental technology and the Calibration Coordination Group (CCG) of the U.S. Department of Defense (DoD). In addition to industrial collaborations, CSTL collaborates with other technical laboratories within NIST. These efforts provide an additional means for determining and meeting customer needs.



The Protein Data Bank

The single most comprehensive international repository for the processing and distribution of 3-D structure data of biological macromolecules determined experimentally by Nuclear Magnetic Resonance (NMR) and X-ray crystallography

The Protein Data Bank (PDB) is an international repository for macromolecular structure data. This structure data is very important for medical research, drug design and advanced manufacturing. In 1997 the RCSB (see box below) was formed and proposed the following:

- ***To provide a user interface that is powerful and easy to use for both deposition of structures and for more powerful querying of the deposited, annotated data;***
- ***To reprocess legacy data to increase the integrity and uniformity of the data; and,***
- ***To convert the existing PDB to a relational database system with an underlying architecture based on a dictionary accepted by the structural community.***

Research Collaboratory for Structural Bioinformatics (RCSB)

- **Rutgers, Department of Chemistry State University of New Jersey**
- **San Diego Super Computer Center at the University of California**
- **NIST/CSTL Biotechnology Division**

Currently, the new data system is in place and the RCSB annotators are processing all of the new depositions. The new query system, ***Searchlight***, has been released to the public and has had a positive review. The new PDB managed by the RCSB has had a smooth transition, by focusing the strengths and experience of the three RCSB organizations and overcoming the potential problems of having a complex database distributed over large geographical distances. NIST has garnered the experience and resources of CSTL's Biotechnology Division and Technology Service's SRD Program with support from the ITL computer services to create this unique CSTL project.

Metabolic Engineering for Industrial Ecology

Shifting away from petroleum-based feedstocks toward using renewable feedstocks such as glucose to synthesize a variety of valuable products (dyes, polymers, and flavor compounds) via non-polluting biochemical processes

Metabolic engineering, also referred to as biocatalysis, is a major activity within the Bioprocess Engineering Group in CSTL. This group is focused on the development of measurement methods, databases, and generic technologies related to the use of biomolecules and biomaterials in manufacturing.

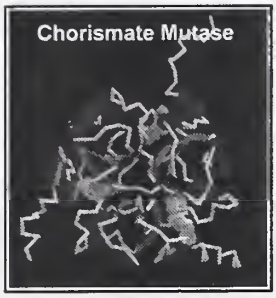
Future Plans:
NIST Chorismate Metabolism Database with all known information for species:
- **Genes**
- **Enzymes**
- **Reaction pathways**

Industrial Contacts and CRADAs:
- **Life Technologies, Inc.**
- **Amgen, Inc.**
- **Molecular Probes, Inc.**
- **BioSpace International, Inc.**
- **Dow Chemical Co.**

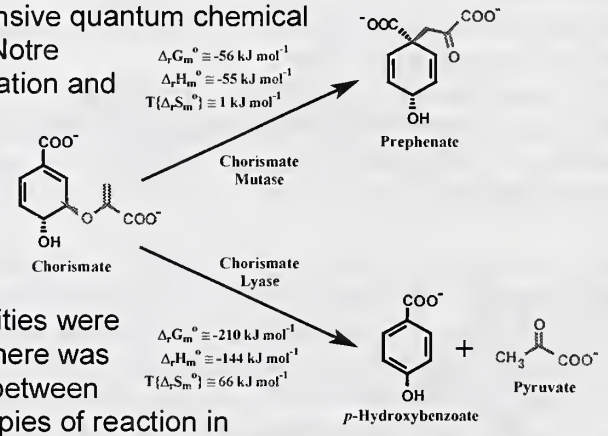
The combined use of equilibrium and calorimetric measurements coupled with thermodynamic modeling calculation enables the characterization of the thermodynamics of enzyme-catalyzed reactions of interest to biochemistry and biotechnology. The information obtained allows for the prediction of the position of equilibrium of a variety of biochemical reactions over wide ranges of temperature, pH, and ionic strength. When possible, the thermodynamic information is correlated with the structures of the substances in the reactions and complemented with the results of

computational and estimation methods. Classes of reactions that have been studied include the isomerization, hydrolysis, and phosphorylation of sugars, and ammonia and water elimination reactions. A series of comprehensive reviews of the thermodynamics of enzyme-catalyzed reactions are accessible on the Web as the NIST Enzyme Catalyzed Reaction Thermodynamics Standard Reference Database.

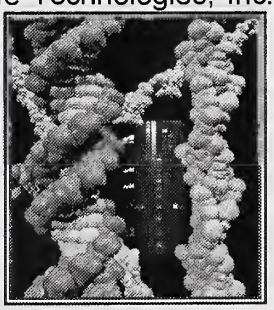
http://ibm4.carb.nist.gov:8800/enzyme/enzyme.html



Recent research has focused on reactions in the chorismate metabolic pathway that has been a focal point of interest because of its potential industrial importance (glucose feedstock). The thermodynamics of a major portion of this pathway have been characaterized by studying the reactions catalyzed by tryptophan synthase, prephenate dehydrogenase, prephenate dehydratase, chorismate lyase, chorismate mutase, glutaminase, and tyrosine aminotransferase. In the case of two of these reactions, the microcalorimetry measurements, which are shown in the figure, were complemented by extensive quantum chemical calculations by scientists at the University of Notre Dame and at UCLA. The effects of water solvation and solvent polarization were accounted for by using a Self-Consistent Isodensity Polarized Continuum Model. The quantum chemical calculations yielded values of absolute and relative energies for these substances both in the gas phase and in aqueous solution. The structures and thermodynamic reaction quantities were also obtained. In the case of both reactions, there was a reasonable accord (difference 10 kJ mol^{-1}) between calculated and measured values of the enthalpies of reaction in aqueous solution. Thus, while the experimental values are still considered to be definitive, the relatively good agreement has served to lay a basis for the extension of quantum mechanics to other biochemical reactions. Completion of the thermodynamic investigations are expected in 1999, and thus obtain a relatively complete picture of the thermodynamics of this pathway that is a source of aromatic amino acids.



Electrophoretic DNA separations are being done in collaboration with Life Technologies, Inc. (Rockville, MD). Electrophoresis is a high-resolution separation technique that has proven difficult to scale up. A recent approach to the scale-up of electrophoresis has been the development of reversible electrophoresis gels. This technology allows high resolution electrophoretic separation or isolation of target DNA in the gel phase, followed by gel phase "reversal" back to solution and subsequent release/recovery of target DNA. These reversible gels are based on the carbohydrate polymer gellan gum (Figure). A patent based on this technology is being filed by NIST/CSTL/Life Technologies, Inc. Also, some of the new commercially available selective membranes are being examined for their potential to perform the same electrophoretic trapping of circular DNA that we observed in several polymeric gels.

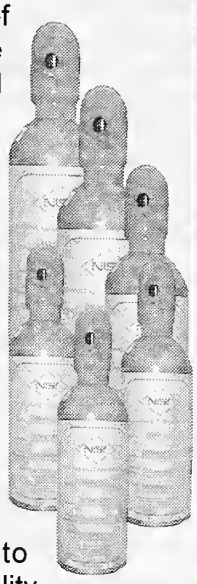


Chromatography is the workhorse of industrial separations, but improvements in productivity (throughput) and cost are needed to expand its usefulness. We are making measurements on the selectivity, capacity, and throughput of new types of chromatography columns (continuous beds) and membrane modules. In collaboration with Amgen, Inc. (Thousand Oaks, CA), chromatographic parameters are being measured using model proteins and industrially relevant feedstocks.

Leveraging Resources

The NIST Traceable Reference Materials (NTRM™) program: a new paradigm to meet increasing industrial needs

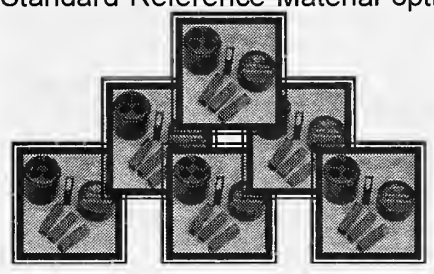
The NTRM concept was originally developed for gas standards: The NTRM program was created to address the problem of increasing needs for Reference Materials with a well-defined linkage to national standards. An NTRM is a commercially produced reference material with a well-defined traceability linkage 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. The NTRM concept was implemented initially 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. 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 [SO2 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 to more effectively deliver an increasing number of NIST-traceable standards to end users.



NIST has met the reference materials needs of U.S. industry and commerce for nearly 100 years. While our reference materials program has focused primarily on U.S. requirements, it is clear that these materials address international measurement needs as well. As demonstration of quality and "traceability" for chemical measurements have become increasingly global issues, the need for internationally recognized and accepted certified reference materials (CRMs) have increased correspondingly because their use is often mandated in measurement and quality protocols of analytical testing laboratories. Coupled with the fast pace of technological change and greater measurement needs, the demand for additional quantities and additional specific varieties of reference materials has mushroomed.

The Gas Metrology Team partnered with 10 specialty gas companies to create more than 5,600 different NTRM cylinder gas standards which were used by the partnering companies to produce approximately 400,000 NIST-traceable gas standards resulting in $100M in revenues.
From 1999 Hammer Award Citation

Reference Materials for Chemical Spectrophotometry: Molecular absorption spectrophotometry in the ultraviolet-visible spectral region is a mature quantitative analysis tool that is widely used in the chemical and pharmaceutical industries. The absorption measurement is sufficiently robust that frequent expensive chemical calibrations are not required as long as the instrument can be shown to be functioning properly. For this purpose, NIST certifies a suite of Standard Reference Material optical filters for verifying the absorbance accuracy and calibrating the wavelength axis of chemical spectrophotometers. The use of these filters is widely specified by such regulatory and standards organizations as the U.S. Food and Drug Administration, the U.S. Pharmacopoeia, and the American Society for the Testing of Materials. The demand placed by regulatory and quality control pressures has resulted in the formation of a NIST - NTRM program to leverage the NIST measurement capability through the commercial production,



certification, and sale of reference materials with a well-defined NIST heritage. CSTL's second-generation Reference Spectrophotometer is currently being used to certify SRMs and will be used to qualify and periodically validate transfer spectrophotometers for the NTRM program.

The first NTRMs for chemical spectrophotometry will be on the market in early 2000, and will be modeled on NIST SRM 930e and SRM 1930, neutral density glasses certified at five wavelengths in the visible spectral region and spanning absorbances between 0.3 and 2.0. The expanded uncertainties will be kept close to those of the corresponding NIST standards by reducing the NTRM certification period to one year, which will be compatible with the renewal cycle of many industrial QC protocols. Other NTRM filter reference materials will follow for wavelength calibration and UV absorbance verification. For all of these reference materials, the certifying laboratories will be accredited through the NIST-based National Voluntary Laboratory Accreditation Program (NVLAP) and will maintain periodic intercomparison measurements with the National Reference Spectrophotometer in the Analytical Chemistry Division of NIST.

Other NTRM Programs Planned

- **Elemental Solutions**
  Implementation planned for 2001
- **Metals (under development)**
  pilot partner identified
  draft protocol prepared

NIST/EPA Proficiency Testing (PT) Program: In a government-private sector partnership, NIST's CSTL and NVLAP, the EPA, state and local governments, and private sector laboratories are working together to establish a proficiency testing (PT) system for waste water and drinking water for regulated chemical, microbial, and radiochemical parameters.

EPA –

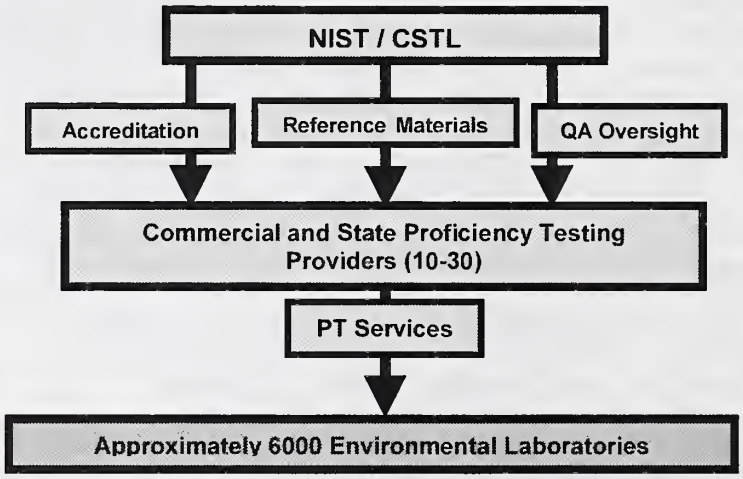
- provides NIST with support to develop a program for private sector/state provision of PT studies
- works with states and NIST to assure that the program developed for 1) preparing, value-assigning and distributing PT samples and 2) evaluating the quality of the Environmental Testing Laboratory data is sufficient to support national/state water program needs

NIST –

- develops and manages program for accrediting private sector water PT study providers
- establishes and maintains SRMs to support the program
- conducts 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 –

- develop, manufacture, value-assign, and distribute PT samples
- score results of Environmental Testing Laboratory analyses
- report result to participants, EPA, NIST, states, and appropriate accrediting authorities
- maintain accreditation through NIST/ NVLAP



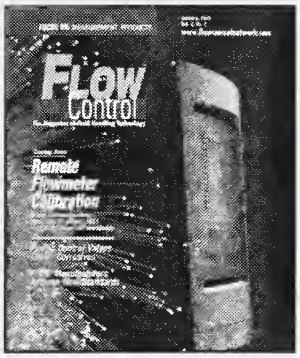
A NIST handbook describing the technical requirements of this accreditation program was drafted, presented for comment at a January 16, 1998 public meeting, and subsequently issued as a revised document. NIST NVLAP is accepting applications for accreditation in this new field, Providers of Proficiency Testing, for the provision of chemistry and microbiology PT studies as described in EPA's "National Standards for Water Proficiency Testing Studies: Criteria Document" (US EPA, August 20, 1998 Version). NVLAP program designations for providers of radiochemistry PT studies will be added after the EPA requirements for these studies have been delineated by US EPA in its criteria document.

NIST has begun producing primary benchmark materials, including SRMs, for those parameters not covered by existing SRMs to provide the infrastructure needed by NIST to audit the commercially supplied PT samples and to assist providers in value-assigning their PT materials.

Sharable Resources - Telepresence

Telecalibration

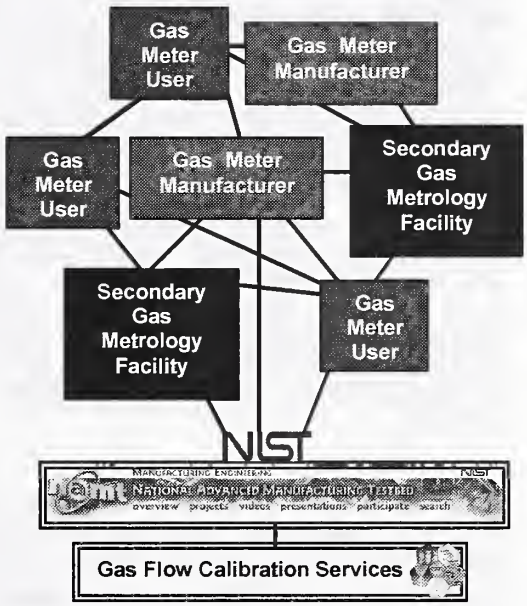
Utilizes IT to expand calibration services via telepresence for remote calibration, traceability and accreditation of U.S. metrology laboratories



January, 1999 issue, Vol. V, No. 1
www.flowcontrolntetwork.com

Every year in the U.S. gas flow meters are used to make determinations of trillions of dollars in goods destined for consumption here and abroad (e.g., Americans use natural gas at the rate of $2.2 billion per day and this gas is metered some five to seven times between the well head and the consuming burners). Gas flow meters are used extensively by industry as process control monitors in applications that range from the measurement of power plant emissions to the control of oxygen flow for premature children in intensive care units. Trying to assure the quality of these important measurements, NIST provides gas flow measurement standards and meter calibration services to U.S. industry, other government agencies and academia for a gamut of gases, for widely ranging conditions for flows from 1 slm to 8.5 x 10^4 slm (standard liters per minute).

Even though NIST provides calibration services over the better part of five decades in flow, U.S. industry has critical needs for gas measurement traceability at much higher flow rates (ranging from 1 x 10^8), and at a wide range of working pressures from 100 Kpa to 6,000 Kpa (1 atm to 60 atm), and for a large number of gas species. The construction of facilities capable of handling such large flow rates at NIST is all but impossible due to capital and space constraints. However, a small number of secondary metrology laboratories in the U.S. are capable of calibrating sensors at flow rates larger than those attainable by NIST. One such facility is the Colorado Engineering Experiment Station Inc. (CEESI), in Nunn CO, which provides calibrations at flow rates as large as 2.7 x 10^5 slm (although plans are underway for a CEESI facility in Iowa capable of flowing as much as 4.3 x 10^7 slm – the largest facility of its kind in the world).



Current Partners
DANIEL CEESI

NIST MEL/ NAMT (National Advanced Manufacturing Testbed) information infrastructure is being used to expand the range of NIST gas flow calibrations by making the facilities at CEESI available to us over a wide-area high-speed network. As envisioned, this project calls for the installation of NIST instrumentation at CEESI's so called "Primary A" facility in Nunn, CO. This instrumentation will then be accessed using Web-based technology by NIST personnel to provide NIST-certified calibrations outside NIST's Gaithersburg campus.

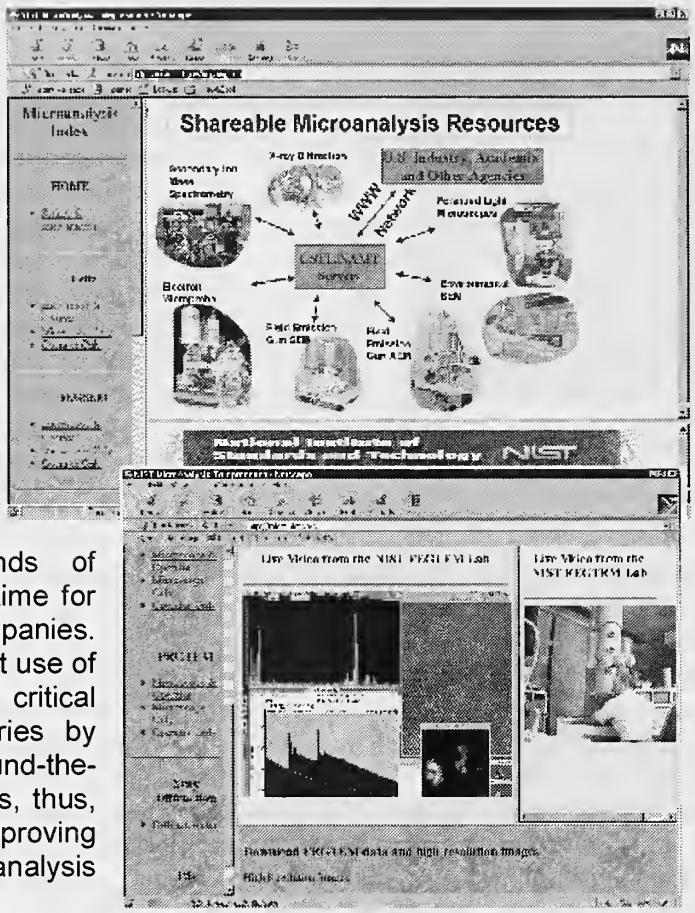
This pilot project will demonstrate the feasibility of using information technology to expand NIST's calibration services via telepresence in U.S. secondary calibration laboratories. In addition, it will expand NIST's gas flow calibration capabilities by initially allowing NIST/CSTL to calibrate meters in flows 3 times larger than those used at present, with the possibility of expanding to flows 500 times larger in the near future. Also, it would be the first implementation of the "portable primary" standard concept considered as the way of the future in flow meter calibrations.

http://www.mel.nist.gov/namt/projects/gas.gasov.htm

Telepresence Microscopy and Microanalysis

Remote sensing provides industrial and academic clients with access to NIST's broad range of state-of-the-art equipment and expertise

Telepresence microscopy and microanalysis is the remote sharing and/or operation of microscopes and microprobes. The chemical microstructure of material specimens is critical to materials science and technology, semiconductor device development, quality measurements and process control, and failure analysis and evaluation. NIST/CSTL microanalysis customers need quick access to advanced microscopy and microanalysis instrumentation and expertise. This access is especially critical to small start-up firms requiring quality measurements of nanoscale dimensions and of material chemistry properties. Demands of process control make rapid turn-around time for analysis a high priority for these companies. Telepresence is enabling the more efficient use of expensive, scarce resources and critical personnel at industrial central laboratories by providing remote, instantaneous, around-the-clock access to critical production facilities, thus, providing "just-in-time" analysis and improving communications within the service analysis industry.



Special Features

- **Real-time analysis with dramatic impact on speed and quality of communications**
- **Links technical experts with process engineers**
- **Provides total networking capability from designer to manufacturer to user**
- **Provides small businesses with state-of-the-art technologies**
- **Dramatically improves efficiency of larger business through improved communication**
- **Remote and instantaneous analysis promotes rapid understanding and process improvement**
- **Direct and immediate feedback for intercomparisons - national and international**

NIST/CSTL researchers are establishing remote communications with microanalysis customers from NIST labs via inexpensive teleconferencing hardware/software that utilize World Wide Web-based technology. Specifically it allows for "over-the-shoulder" remote monitoring of NIST analysis experiments. This method specifically targets small enterprises that account for a large percentage of the industrial community working in these areas. Researchers are also developing the hardware and software necessary for remote control of the leading-edge instrumentation at NIST labs by utilizing high bandwidth networking technology capabilities. In addition, CSTL researchers seek to gain critical research experience in telepresence operation by solving actual problems found daily within industry. Ultimately, standards and standard data will be created that validate telepresence microscopy and microanalysis.

http://www.mel.nist.gov/namt/projects/tele/tele1.htm

Integrated NIST Programs Impact Industry

..selected joint ATP/CSTL ventures from ATP's Chemistry and Life Sciences Office

CSTL supports ATP's vision to "bridge the gap between the laboratory and the marketplace" through proactive participation in ATP's intramural program. The focus areas featured below are all funded through the Chemistry and Life Sciences Office of NIST/ATP. The industries having joint ventures with NIST's ATP are listed in the boxes below, and some details of selected CSTL/ ATP related projects are provided.

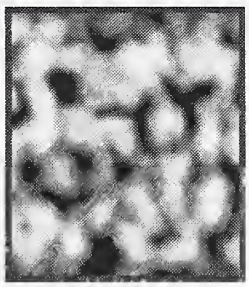
Catalysis and Biocatalysis Technologies

To develop the tools, abilities, and theoretical insight to identify, design, and implement new catalytic and biocatalytic processes and catalyst manufacturing techniques of major economic importance to chemical producers and other catalyst users.

Joint Ventures in Catalysis and Biocatalysis-Industry Particpation

Genencor International, Inc.
Phillips Petroleum Co.
General Electric Company
ABB Lummus Global
B.F. Goodrich/3M Co.
Amoco Corporation
W.R. Grace/Cryovac
Maxygen, Inc.
Thermatrix, Inc.
Henkel/GE
Dyax Corporation

Selected CSTL Projects:



Nanoscale Catalyst Characterization Tools: The objective for this intramural research is to develop diagnostics suitable for nanoscale probing of the crystallographic, compositional, and topographic structures of catalysts and products of novel catalytic reactions. Key technical milestones are: the use of AFM/NSOM (Atomic Force Microscopy/ Near-Field Scanning Optical Microscopy) techniques to probe spatial/ chemical dynamics of multi-component organic and polymer films on oxide surfaces; the use of vibrationally resolved NSOM to examine the reactivity of nanostructured surfaces as a function of the composition of the gases that are in contact with the specimen; expanded study of the effect of heating on internal surfaces of rutile particles; and investigation of the variations in pore size within and between mesoporous samples with different chemistries and conditions of formation.

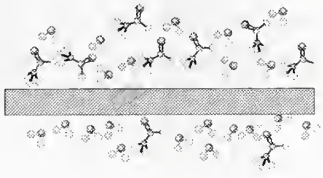
Practical Methods for Molecular Simulation: The long-term goal is to develop validated models, based upon physical and chemical principles, that predict the bound conformation of noncovalent complexes and the standard free energy of binding. Such models will be of value in a range of applications, including protein-engineering, and the structure-based design of medications. A novel method of computing configuration integrals forms the basis of the approach to computing binding affinities. The energy hypersurface of ligands in protein binding sites is also being studied. A prototype database on noncovalent binding is currently in preparation.

Membrane Technology

Joint Ventures in Membrane Technology-Industry Participation

Facilichem
Praxair/WJA
Cargill/Osmonics
Praxair
Baxter
Amoco
Air Products
BP/Praxair
GelTex Pharm.
Aphios
Mycogen

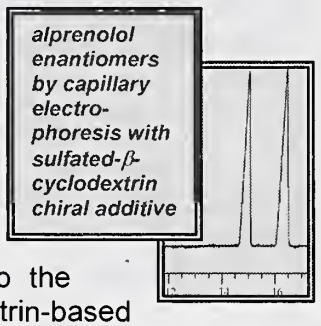
To develop the combination of materials science and manufacturing technology advances needed to create new families of membrane materials and process technologies for advanced high-selectivity, high-throughput chemical separations (including concentration and purification), producing feedstocks for areas as diverse as pharmaceuticals and medical diagnostics, automobile parts, consumer electronics, clothing, and alternative fuels.



Infrastructure for Development of Selective Membrane Platforms: CSTL supports the development of new membrane

materials and structural forms that provide exquisite control of chemical selectivity, while maintaining high flux (productivity) by providing: (1) advanced techniques for quantifying multicomponent transport in solid materials; (2) development of an improved metrology for obtaining pore statistics for pores in the 0.5 nm - 1000 nm range; and (3) a critically reviewed and annotated database.

Chromatographic and Electrophoretic Techniques to Investigate Chiral Recognition: Large-scale separations are a growing priority in the pharmaceutical industry. In some instances, production scale separations are being used to isolate the desired enantiomer from a racemic (50:50) mixture. This work utitizes capillary electrophoresis as a tool to study the interactions of cyclodextrin-based chiral selectors with several groups of optically active compounds of pharmaceutical interest. Slight structural differences among families of analytes resulted in disparities in chiral recognition and provided insight into the structural features needed for successful chiral resolution with cyclodextrin-based chiral selectors. The chiral additives can also be immobilized on a support material for liquid chromatographic studies. Understanding chiral recognition mechanisms will facilitate the development of chiral selectors that possess the degree of selectivity necessary for preparative scale separations.



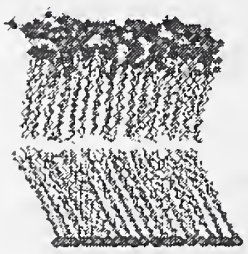
Selective Preparative Separations of DNA Using Membranes and Electric Fields: Technology that utilizes membranes with applied electric fields to rapidly and selectively purify circular DNA from crude samples has been developed. Selective membranes are being developed that will be able to process large numbers of samples, important for large-scale sequencing and gene discovery projects. Circular DNA such as plasmids and bacterial artificial chromosome DNA must be purified in large number for these projects.

Tissue Engineering

To enable dramatic advances in the development and use of biocompatible materials, with or without a cellular component, to replace damaged or defective tissues and organs. The program concentrates on four key areas: biomaterials, cellular components (including large-scale culturing techniques and genetic or environmental manipulation), manufacturing processes, and implantation and transplantation technologies.

Joint Ventures in Tissue Engineering-Industry Participation

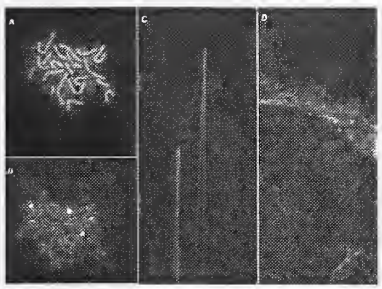
Automated Cell Tech.
Cytomatrix
Osiris Therapeutics
Alexion
Advanced Tissue Sci.
Acorda Therapeutics
Multi-Cell Assoc.
Life Science Holdings
Alexion Pharm.
Integra LifeSciences
Ethicon
CyroLife



Biomimetic Membranes for Tissue Engineering: A hybrid bilayer membrane (HBM) system consisting of both natural (phospholipids) and synthetic (alkanethiol) components has been developed. This bilayer membrane 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 has practical applicability to industrial-scale use since it is rugged and easy to fabricate. Using impedance analysis, 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 toxin, melittin and to anesthetics. 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. This system may provide one of the few ways to achieve high-resolution structural information on membrane proteins, which, in general, are intractable to crystallography. In addition, it provides an important experimental tool

for reconstituting and studying the function of transmembrane proteins such as cell surface receptors, light harvesting proteins, transport and toxin proteins, and redox enzymes.

Biological Assessment of Ex-Vivo Engineered Tissue Reimplantation: Assays for changes in the length of human telomeres are under development in CSTL for human tissue engineering applications. This program interfaces with the Biotechnology Division's Fluorescence Intensity Standards Program. Fluorescence based methods for quantitation of telomeric repeats will aid in monitoring cellular growth modulations in the transition from normal growth control to transformation, differentiation and malignancy for the biotechnology market. Figure Legend: A) DAPI-stained metaphase chromosomes (blue). B) identical cells to (A) showing in situ hybridization of T2AG3 repeats at the ends of the chromosomes. The large blotches are artifacts due to immunochemical reagents. C) Combed DNA fibers in glass slide treated with octyl silane. DNA fibers are stained with DNA-binding stain YOYO-1. D) Combed DNA treated as in (C) but on untreated glass. DNA attached in a random coil, not in linear uniformly-stretched DNA molecules.



Unpublished Data: Peter E. Barker, NIST

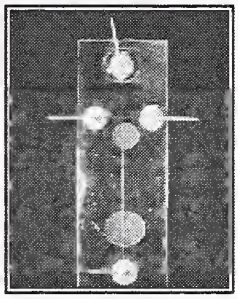
Tools for DNA Diagnostics

Joint Ventures in DNA Diagnostics - Industry Participation

Nanogram
GeneTrace Systems
Third Wave Technology
Affymetrix, Inc
Bio-Rad Laboratory
Hyseq, Inc
Genosensor
Vysis, Inc.
CuraGen
Sarnoff Corporation
Bruker Daltonics
ACCARA Biosciences
PE-Biosystems
Orchid Biocomputer
Caliper Technologies
Clinical Micro Sensors
Amersham Pharmacia

To develop compact, low-cost, automated DNA analysis technologies and equipment to enable fast, inexpensive detection and diagnosis of human, animal, and plant diseases. Other applications include personal identification, toxicology, environmental monitoring, and bioprocessing.

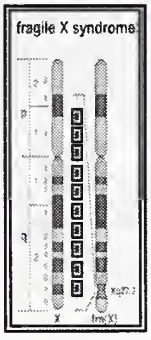
Microelements and Sensors in Plastic Microchannels: CSTL researchers are developing the technology to create hybrid microchannel devices composed of inexpensive plastic microfluid channels merged with active elements fabricated in silicon or glass for "lab-on-chip" applications.



Methods developed integrate heating and sensing elements within plastic channels by forming them on separate substrates and then bonding them together.

Hybrid devices would be less expensive than devices fabricated entirely in silicon, but would offer all of the advantages of silicon in terms of packaging, integration, and miniaturization.

Quantitative Measurement Program for Triplet Repeats Associated with Human Disease: The goal of this work is to provide the clinical community with accurate protocols and measurements for the detection of genetic disease. ***CSTL Efforts*** have been focused on the quantitation of CGG repeat element that interrupts the FMR-1 gene on the X chromosome. The interruption occurs when more than 200 copies of the triplet repeat are present. Fragile X (see figure) is the most common inherited cause of mental impairment, affecting approximately1 in 2,000 and 99% of all cases result from the expansion of the CCG trinucleotide repeat in the FMR1 gene.



Chemical Science and Technology Laboratory (CSTL) collaborates with other NIST Measurement and Standards Laboratories

Building and Fire Research Laboratory (BFRL)
http://www.bfrl.nist.gov/

BFRL is the national laboratory dedicated to enhancing the competitiveness of U.S. industry and public safety performance prediction methods, measurement technologies and technical advances needed to assure the life cycle quality and economy of constructed facilities. Its products are used by those who own, design, construct, supply, and provide for the safety or environmental quality of constructed facilities.

Major goals of BFRL are to improve the productivity of the U.S. construction industry, which now faces stiff competition from overseas firms, and to reduce the human and economic losses resulting from fires, earthquakes, winds, and other hazards. The laboratory studies fire science and fire safety engineering; building materials; computer-integrated construction practices; and structural, mechanical, and environmental engineering. Products of the laboratory's research include measurements and test methods, performance criteria, and technical data that are incorporated into building and fire standards and codes.

The laboratory conducts investigations at the scene of major fires as well as structural failures due to earthquakes, hurricanes, or other causes. The knowledge gained from these investigations guides research and is applied to recommendations for design and construction practices to reduce hazards.

BFRL/CSTL Interactions: Alternative Refrigerants (ARI, ASHRAE), Process Design Exchange Standards (PdXi), Environmental Technology Initiative, Particle Metrology

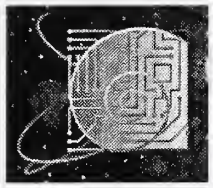
Electronics and Electrical Engineering Laboratory (EEEL)
http://www.eeel.nist.gov/

EEEL promotes U.S. economic growth by providing measurement capability of high impact focused primarily on the critical needs of the U.S. electronics and electrical industries, and their customers and suppliers.

EEEL provides the basis for all electrical measurements in the United States; practical measurement methods for the electronics, optoelectronics, and electrical industry sectors; advertised calibration services and artifact standards (Standard Reference Materials). This measurement capability underlies the development, manufacturing, marketing, and after-sales support of new products in industry. In addition, EEEL conducts research and development to advance the electrical and electronic measurement state-of-the-art. EEEL emphasizes measurement research and services that are essential to equity in domestic and international trade.

EEEL/CSTL Interactions: Semiconductor Metrology, Sensor Technology, Electron Impact Data on PFCs (perfluorocompounds) and CFCs (chlorofluorocarbon), Office of Law Enforcement and Standards (OLES), Surface Chemical Measurements (X-Ray Cal.)

Information Technology Laboratory (ITL)
http://www.itl.nist.gov/



ITL responds to industry and user needs for objective, neutral tests for information technology. These are the enabling tools that help companies produce the next generation of products and services, and that help industries and individuals use these complex products and services. ITL works with industry, research, and government organizations to develop and demonstrate tests, test methods, reference data, proof of concept implementations, and other infrastructural technologies. Because measurements create a common language for technology advancement, tools developed by ITL provide impartial ways of measuring information technology products so that developers and users can evaluate how products perform and assess their quality based on objective criteria. ITL's activities support the development and use of information technology systems that are usable, scalable, interoperable, and secure. Program activities include: high-performance computing and communications systems; emerging network technologies; access to, exchange, and retrieval of complex information; computational and statistical methods; information security; and testing tools and methods to improve the quality of software.

ITL/CSTL Interactions: Uncertainty Analysis for SRMs and Calibrations, Bioinformatics, Process Modeling, Computational Chemistry.

Manufacturing Engineering Laboratory (MEL)
http://www.mel.nist.gov/

MEL serves as a central research laboratory for manufacturing infrastructure technology, measurements, and standards. It provides industry-needed manufacturing engineering tools, interface standards, manufacturing systems architectures, and traceability. For example, the industrial measurements of length, force, mass, acoustics, vibration, and product data exchange ultimately rely on traceability to NIST/MEL.

Manufacturers employ MEL research results, test methods, software conformance tests, calibration services, and measurement tools. MEL collaborates with manufacturers on technical projects, standards development, and testbed-based research, both on an individual basis and as members of industrial consortia. In addition, MEL plays a key role in fostering inter-company cooperation and industrial adoption of strategically important manufacturing and computing hardware, equipment, and software standards.

To help U.S. manufacturers meet the challenges of changing technology in a global ecomonic environment, MEL inaugurated the state-of-the-art National Advanced Manufacturing Testbed (NAMT). Using the NAMT, research partners and NIST remotely access and share information, demonstrate manufacturing feasibility, and evaluate prototype standards. The NAMT provides the means to conduct distributed and virtual manufacturing research in advanced metrology, control, and interoperability technology. The results will create a new information technology-based manufacturing model.

MEL/CSTL Interactions: Telepresence Microscopy, Tele-Calibrations (NAMT)

Materials Science and Engineering Laboratory (MSEL)
http://www.msel.nist.gov/

MSEL provides technical leadership and participates in developing the measurement and standards infrastructure related to materials critical to U.S. industry, academia, government, and the public. MSEL's mission is to stimulate the more effective production and use of materials by working with materials suppliers and users to assure the development and implementation of the measurements and standards infrastructure for materials. Materials science and engineering programs at NIST cover a full range of materials issues from design to processing to performance.

Separate research initiatives address ceramics, metals, polymers, composites, superconductors, and the theory and modeling of materials structure and performance. This research supports efforts of U.S. industry to develop reliable, low-cost manufacturing methods for producing tailor-made materials and products with superior properties. Through laboratory-organized consortia and one-to-one collaborations, NIST's materials scientists and engineers work closely with industrial researchers. The laboratory is also strengthening its relationships with both the manufacturers of high-technology products and the major users of advanced materials.

MSEL/CSTL Interactions: Consortium on Casting of Aerospace Alloys, X-Ray/Neutron Focusing, Chemical Analysis Methods.

Physics Laboratory
http://www.pl.nist.gov/

In keeping with NIST's mission to promote U.S. economic growth, the Physics Laboratory works with industry to provide measurement services and research for developing electronic, optical, and radiation technologies. PL programs span the full range from those that respond to immediate needs of industry to those focused on the longer-term, high-risk research that anticipates future industrial challenges. PL researchers address the fundamental triad of standards, measurements, and data in an environment of vigorous and competitive research focused on gaining knowledge for potential application.

To ensure that industry derives maximum benefit from the laboratory, resources are focused on research programs and services in four strategic areas:

- Electronic and magnetic devices - developing innovative measurement methods for device characterization and electronic information and communication, including magnetic microscopy, direct-write lithography, atomic frequency standards, synchronization techniques, and information networking.
- Optical technology - providing the national basis for optical radiation measurement and developing optical measurement systems for industrial and environmental applications including length measurement, remote sensing, data transmission, and atom optics.
- Radiation applications and control - supporting the innovative, effective, and safe use of radiation by developing standards, measurement methods, and data critical for health care technology, environmental technology, industrial radiation processing, nondestructive evaluation, and the nuclear power industry.

- Fundamental physical quantities - striving to improve the definitions and physical realizations of base and derived SI units and pursue opportunities for new determinations of fundamental constants.

PL/CSTL Interactions: Surface Chemistry, Automobile Emission Measurements (AIGER), Environmental Technology Inititative, Rapid Thermal Processing, Linkage of Radiometric and Contact Thermometry in ITS 90.

Technology Services (TS)
http://www.ts.nist.gov/

TS provides U.S. industry, government, and the public with measurements, standards, and information services that promote innovation, increase competitiveness, and facilitate trade. Technology Services programs support U.S. industry to gain access to markets, realize regulatory reform, ensure the accuracy of measurements, and build strategic partnerships.

TS promotes the use and adoption of U.S. standards, measurement practices, and technology by important trading partners, and helps to reduce barriers to trade through cooperation with other departments and agencies of the federal government, state, and local governments. NIST/TS is specifically involved in efforts to establish uniform legal metrology practices, standards, codes, and specifications by: developing, producing, and distributing Standard Reference Materials; providing Standard Reference Data; providing calibration and laboratory accreditation services; promoting understanding and acceptance of the metric language of measurement; managing the Small Business Innovation Research Program (SBIR); providing information services in support of NIST; and, collaborating with NIST's Laboratories in carrying out Technology Services responsibilities.

TS/CSTL Interactions: Standard Reference Materials Program, Standard Reference Data Program, Calibration Program, Accreditation Programs.

Opportunities for Collaborations with NIST/CSTL Staff

CSTL Graduate Fellowship Program

This program represents a unique opportunity for students who have outstanding undergraduate academic records and are interested in pursuing an advanced education and research career at a world-class research laboratory. We at NIST see this program as a vehicle for adding energetic high-quality researchers to our staff, of which more than 60% are Ph.D. scientists and engineers.

http://www.cstl.nist.gov/gradfell.htm

NIST Postdoctoral Research Associateships Program

The NIST/NRC Postdoctoral Research Associateships Program provides two-year temporary appointments for outstanding scientists and engineers chosen through a national competition administered by the National Research Council of the National Academy of Sciences. These appointments provide an opportunity for the nation's best scientists, mathematicians, and engineers to engage in state-of-the-art research in association with senior research specialists on the NIST's staff, using the excellent and often unique research facilities at NIST.

http://www.nist.gov/oiaa/postdoc.htm

NSF-NIST Interaction in Chemistry and Chemical Engineering

The purpose of the NSF-NIST Interaction in Chemistry and Chemical Engineering is to provide the opportunity for faculty and graduate students who are supported on NSF grants in the Divisions of Chemistry (CHE) and Chemical and Transport Systems (CTS) of NSF to participate in research at NIST facilities.

Chemistry and chemical engineering at NIST are centralized in CSTL, one of technical operating units within NIST. As part of its mission, CSTL maintains close ties to U.S. industry, particularly the chemical industry. CSTL operates well-equipped, state-of-the-art laboratories.

http://www.nsf.gov/cgi-bin/getpub?nsf97109

http://ts.nist.gov/ts/htdocs/220.htm

NIST's Technology Services

The Office of Technology Partnerships (OTP) provides direct services to CSTL and all the NIST laboratories, principally by fostering partnerships between the laboratories and the private sector. This leverages the resources of the laboratories, and helps propel NIST technology into industry's hands fast and effectively, thereby contributing to U.S. economic growth. The OTP services described below are those that impact CSTL and its ability to work with researchers in areas of mutual interest.

NIST Industry Fellow Program

The NIST Industry Fellow Program is used for those situations where NIST may better achieve an understanding of industrial R&D, manufacturing, or other industrial issues by experiencing the ongoing activities of a host firm at that firm's location.

Cooperative Research and Development Agreement (CRADA)

The CRADA is a partnering tool that allows federal laboratories to work with U.S. industries, academia and other organizations on cooperative R&D projects. The CRADA provides flexibility in structuring project contributions and intellectual property rights, and in protecting proprietary information and CRADA research results.

NIST Domestic Guest Researcher Program

The Guest Researcher Agreement (GRA) provides the Guest Researcher access to NIST facilities and equipment while participating in NIST R&D activities (of mutual interest). If intellectual property rights or protection of proprietary information is important, the Cooperative Research and Development Agreement (CRADA) may provide a more suitable mechanism for interaction.