NATIONAL BUREAU OF STANDARDS REPORT

10 599

Progress Report

on

SOLUBILITIES OF PHOSPHATES AND OTHER SPARINGLY SOLUBLE COMPOUNDS

NBS

U.S. DEPARTMENT OF COMMERCE

NATIONAL BUREAU OF STANDARDS

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Walter E. Brown, Director
American Dental Association Research Unit
National Bureau of Standards
Washington, D. C. 20234

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1. INTRODUCTION

Rapid increases in phosphate levels in lakes and rivers near heavily populated areas have made the understanding of factors that control these concentrations a matter of great social importance. Phosphate is thought to be the nutrient which is the limiting factor in the growth of algae in most waters (1); it is possible that carbonate, under some conditions of heavy pollution, may also be a limiting substance. Solubilities of salts of these two anions have been proposed as having considerable control over their concentrations in lake waters. The same considerations do not apply to nitrogen, however, because all of its salts are quite soluble. Even though metabolic processes, such as growth and decay of organisms, are probably of primary importance in establishing the concentrations of dissolved orthophosphate and carbonate ion at any instant, particularly during warm periods, it appears reasonable that physicochemical processes such as dissolution of suspended particles and sediments, leaching of rocks and soil, and precipitation of insoluble salts have major roles in establishing over-all, long term levels.

The observation that continual entry of phosphate into a lake does not increase the phosphate level in proportion to the amount that has entered (1) clearly indicates that at least some of the phosphate is being removed by a precipitation process. The high levels of calcium frequently found in lake waters suggest that a calcium phosphate may be one of the forms by which it is removed. This alone is justification for the treatment given here on the solubilities of calcium phosphates. The emphasis here is on thermodynamic and operational points of view and on making the treatment sufficiently general so that it can be applied to sparingly soluble phosphates of cations other than calcium and to salts of other weak acids.

Much of the information described here was developed in studies (2-8) of calcium phosphates for application to systems containing tooth, bone and dental calculus; the method of approach, however, is equally applicable to other complex, multicomponent systems.

Solubilities of sparingly soluble salts is a subject that has been basic to chemistry over the years, and more recently has been treated extensively as applied specifically to minerals and limnetic solutions (9,10). One might wonder what more can be said on the subject. However, the treatment given here differs from others in the emphasis that is placed on how to interpret data for a multicomponent system in terms of a four component system. This should be useful in the interpretation of data collected under natural conditions. Also, stress is placed on considerations which are vital for making measurements on solubilities of other salts, such as those of iron which are thought to limit the phosphate concentrations under acidic conditions. There is urgent need, on the one hand for more solubility and thermodynamic data on a fairly large variety of salts and minerals. On the other hand, it should be recognized that the data must be quite accurate if one is to avoid serious misinterpretations. For example, a relatively small error in the solubility product of one compound may have a dramatic effect because it may change the identity of the compound which is thought to be most stable for some solution compositions.

The application of solubility principles even to the simple ternary system, $Ca(OH)_2$-H_3PO_4-H_2O, is far more complex than is usually thought to be the case. Much of this complexity goes back to the fact that orthophosphoric acid is both a weak acid and a polybasic acid; but there are other complicating factors, including those caused by the presence of ions other than calcium and phosphate, by the presence of more than one solid phase, and by the formation of ion pairs and complexes. It is possible to treat each of these factors provided it is adequately understood, but we have found it desirable, both conceptually and experimentally, to start out with the simplest system first and then to add complicating factors. Some of these complicating factors are described next as a preliminary to examining the system in greater detail.

When the solubility of calcium phosphates is thought to be the factor that limits the concentration of a solution, attention is usually fixed on hydroxyapatite, $Ca_5(PO_4)_3OH$, as the saturating solid phase because it is the least soluble of the several calcium phosphates under the situations encountered most frequently. Actually, directing one's attention solely to this salt is an over simplification because hydroxyapatite is only one of several salts with which such a solution may be supersaturated; under these circumstances it becomes difficult to predict which will precipitate. The other sparingly soluble calcium phosphates include $CaHPO_4 \cdot 2H_2O$, $CaHPO_4$, $Ca_8H_2(PO_4)_6 \cdot 5H_2O$ and β-$Ca_3(PO_4)_2$; two others, tetracalcium phosphate, $Ca_4O(PO_4)_2$, and alpha-tricalcium phosphate, α-$Ca_3(PO_4)_2$, do not persist when in contact with aqueous solutions. Experience has shown that the two hydrated salts, $CaHPO_4 \cdot 2H_2O$ and $Ca_8H_2(PO_4)_6 \cdot 5H_2O$, are the ones that precipitate most easily, particularly at ambient temperatures, provided the degree of supersaturation with respect to hydroxyapatite is sufficiently high so that their solubilities also have been exceeded. Subsequently, these salts tend to convert to the more stable forms, sometimes going through a sequence of phases of increasing stability, but this can be a slow process. Under circumstances where one of the other salts has formed, it may not be possible to describe the composition of the solution from solubility considerations unless that salt is taken into account. This is true even though the salt is metastable with respect to hydroxyapatite and one or more of the other calcium phosphates (provided the rate of its dissolution is great compared to the rates of precipitation of the more stable salts).

Ions in the solution other than calcium or phosphate affect the solubilities of the solid phases in several ways:

(1) The most important factor is probably the acidity or basicity of these components. This comes about because the concentration of the PO_4^{3-} ion is strongly repressed by relatively low concentrations of hydrogen ions. Thus, as described later, the calcium and phosphate concentrations in a solution saturated with respect to hydroxyapatite at a pH of about 4 could be as high as 10^{-1} M. As is shown later, when several other components are present it is the net acidity (i.e., surplus of acid over base) or the net basicity of these components that is one of the dominant factors in setting the solubility of any calcium phosphate in a given solution.

(2) Both calcium and phosphate ions enter into the formation of ion pairs or complexes, between themselves as well as with other possible components. As noted later, uncertainties in the theory of ionic solutions make it difficult to be certain about the presence or absence of specific calcium-phosphate ion pairs. This uncertainty comes about because the concentrations of these ion pairs are usually quite low (less than 10 to 20% of the total calcium or orthophosphate in solution) and because it is always necessary to make extra-thermodynamic calculations to arrive at ionic activities. However, we can now have some confidence that these ions do

form pairs because extensive studies (4-10) of the ternary system, $Ca(OH)_2$-H_3PO_4-H_2O, at 5°, 15°, 25°, and 37°C have shown that the solubilities of four of the above calcium phosphates can be described accurately if it is assumed that the ion pairs, $CaHPO_4^\circ$ and $CaH_2PO_4^+$ are present in solution. In the pH range above 7 or 8, the ion pair $CaPO_4^-$ may be present in significant concentrations (11). Stable complexes are known to form between phosphate ions and a variety of multivalent cations found in natural waters (e.g., iron and aluminum); calcium ions form complexes with a rather limited number of anions found in natural bodies of water, primarily organic ions, and now, possibly, polyphosphate ions. Carbonate ions, because of their ubiquitous presence in all natural waters, must be given special consideration in this respect because there is still some uncertainty about the stability of calcium-carbonate ion pairs (12,13).

(3) The presence of other ions also increases the ionic strength of a solution, thereby affecting the solubilities, but usually in a less spectacular way that the first two effects. A high ionic strength has two effects on the equilibria: (i) the solubility is enhanced by decreases in the ionic activity coefficients, and (ii) the distribution of phosphate ions among the various species is altered because the activity coefficient of a multivalent ion such as PO_4^{3-} should be more

affected than that of, say, $H_2PO_4^-$. Evidence of the latter effect can be sought in the way the ionic strength affects relative solubility of an acid calcium phosphate (e.g., $CaHPO_4$) as compared to a more basic calcium phosphate (e.g., $Ca_5(PO_3)OH$) and in how it affects the apparent electroneutrality unbalance (see equation (12), later). Neither of these effects is large and, thus, would require very accurate data.

Finally, non-thermodynamic factors, such as rates of dissolution and precipitation, barriers to nucleation or crystal growth, ionic transport rates, and conversion of metastable solid phases into more stable solid phases, serve to make these systems difficult to handle experimentally and necessitate caution in the interpretation of results.

Recitation of these difficulties is made not to discourage the reader, but instead to stress the need for use of a valid thermodynamic treatment, a chemically and physically appropriate model, and a systematic approach which will help to clarify the concepts and avoid some of the pitfalls. This is the major objective of this chapter.

2.0. SOLID PHASES

As noted earlier there are five solid calcium phosphates that are of importance in terms of being sparingly soluble salts that are relatively stable in aqueous systems. It is generally considered that hydroxyapatite, $Ca_5(PO_4)_3OH$, is the least soluble of these salts. The other salts in order of increasing solubility under normal conditions are: whitlockite or β-tricalcium phosphate,

β-$Ca_3(PO_4)_2$; octacalcium phosphate, $Ca_8H_2(PO_4)_6 \cdot 5H_2O$; anhydrous dicalcium phosphate or monetite, $CaHPO_4$; dicalcium phosphate dihydrate or brushite, $CaHPO_4 \cdot 2H_2O$. Some investigators have tended, more or less, to disregard the fact that each of these salts has individual characteristics and that each, therefore, would have its own solubility for a given solution composition, temperature, and pressure. Thus, although $Ca_5(PO_4)_3OH$ is the most stable salt under most conditions found in nature, it becomes less stable (i.e., more soluble) than $CaHPO_4$ and $CaHPO_4 \cdot 2H_2O$ if the solution is sufficiently acid. As is described below, the pH at which the relative stability of two salts is reversed (i.e., the singular point) depends on the concentrations of other components. The apparent solubility behavior of $Ca_5(PO_4)_3OH$ in a solution more acid than the singular point, or which at some time had been more acid than the singular point, may be quite different from what one would expect for $Ca_5(PO_4)_3OH$; the formation of the more acid calcium phosphates, especially if formed as surface coatings, can lead to apparent high solubilities. This effect is accentuated by the facts that (i) the solutions tend to be so dilute that a large volume of aqueous phase is required to dissolve a relatively small amount of the more acid calcium phosphate phase, and (ii) hydroxyapatite crystal growth appears to be a slow process so that the elimination of the acid calcium phosphate by conversion to hydroxyapatite may not occur to a significant extent.

These facts have not always been taken adequately into account; the resulting apparent anomalous behavior may have led some investigators to the conclusion that the properties of calcium phosphates in general, and $Ca_5(PO_4)_3OH$ in particular, are rather variable (14-17). Actually when working with well purified materials, it was possible to show from solubility measurements (4-10) that each behaves in a quite normal fashion in terms of its solubility and thermodynamic properties.

The order of increasing solubilities of these salts listed above is true only for a limited range of pH. This is shown in Figure 1 where the negative logarithm of the calcium concentration, pCa, at saturation is plotted against pH for the five salts mentioned above (4-9, 18). A similar diagram is obtained when the negative logarithm of the total orthophosphate concentration, pP, is plotted against pH. It is important to keep in mind that these plots apply only to the ternary system (i.e., solutions which contain only calcium, phosphate and water ions). The relative solubilities (at 25°C) of the salts at a given pH are easily seen from this graph. At pH 7, the order of increasing solubility is $Ca_5(PO_4)_3OH$, β-$Ca_3(PO_4)_2$, $Ca_8H_2(PO_4)_6 \cdot 5H_2O$, $CaHPO_4$ and $CaHPO_4 \cdot 2H_2O$; below pH 4.8 the most stable salt is $CaHPO_4$, and even $CaHPO_4 \cdot 2H_2O$ is more stable than $Ca_5(PO_4)_3OH$ below pH 4.3. The pH values for various singular points for the ternary system are defined by the broken vertical lines. If one were to extend this plot to high concentrations, four other singular points would be found where the solubilities of the two monocalcium phosphates, $Ca(H_2PO_4)_2$ and $Ca(H_2PO_4)_2 \cdot H_2O$, which are found only under very acid conditions, become less than those of $CaHPO_4$ and $CaHPO_4 \cdot 2H_2O$ (19, 20).

2.1. HYDROXYAPATITE, $Ca_5(PO_4)_3OH$

The compound of greatest interest in most physiological and other natural circumstances is hydroxyapatite because this compound is a prototype of the principal crystalline material in tooth, bone and many minerals. It is the ultimate alteration product of fertilizers in soils, and undoubtedly is a factor in the precipitation of phosphates under limnetic circumstances and in sewage and waste treatment facilities. Because of the relationship between its structure and its chemical properties, the crystal structure of hydroxyapatite (21-24) is shown projected on the *c* face in Figure 2 and in a stereoscopic illustration in Figure 3. Some of the atoms in Figure 2 are shaded to show their relationship to $Ca_8H_2(PO_4)_6 \cdot 5H_2O$, described later. The stereoscopic illustration has the advantage of showing the groups of ions in three-dimensional perspective. The ellipsoid representing each atom depicts its apparent thermal motions. The unit cell contains two formula weights and consists of the following groups of ions: (i) two OH^- ions lying on the hexagonal axis at the center of the diagram. The oxygen of the OH^- ion lies about 0.3 Å above or below the plane formed by three nearby calcium ions, and the hydrogen attached to this oxygen has a strong librational motion and is even farther away from the calcium triangle; (ii) six calciums in the form of two triangles separated by half a unit cell translation plus a 60° rotation, (iii) six PO_4 groups in two triangles similar to those of the calciums; and (iv) four calciums made up of pairs located on the trigonal axes near the corners of the cell depicted in Figures 2 and 3. By keeping in mind these four sets of atoms, one can easily visualize the structure of hydroxyapatite. A closely related mineral of importance to these considerations is fluorapatite, $Ca_5(PO_4)_3F$. It differs from $Ca_5(PO_4)_3OH$ in that the OH^- ions have been replaced by F^- ions situated at the centers (i.e., in the planes) of the calcium triangles instead of being 0.3 Å away. The displacement of OH^- ions from the centers of the calcium triangles in $Ca_5(PO_4)_3OH$ introduces the possibility of disorder in the three-dimensional arrangement of these ions. This disorder probably affects the solubility of hydroxyapatite through its effects on entropy and internal energy. The disorder may be enhanced by partial replacement of OH^- by F^- or O^{2-} ions or by vacancies.

Normally one might expect all the OH^- groups in a given column to point in one direction because this gives maximum separation of protons that are on adjacent OH^- groups. On the other hand, an F^- or O^{2-} ion located in the plane of the Ca triangle can act as a center of inversion by being hydrogen bonded to the OH^- groups above and below it. This arrangement could decrease the enthalpy and increase the entropy over what might be expected from a simple solid solution, thereby decreasing the solubility significantly. Several studies on the solubilities of laboratory preparations of hydroxyapatite have shown that it is possible to describe its solubility in a straightforward manner. However, evidence is accumulating showing that enamel, which is the most crystalline of the apatites produced *in vivo*, has a variable solubility even though fluoride is present in minor amounts. This may be caused by the presence of crystal imperfections and impurities (such as carbonate), by the presence of other calcium phosphates, or by particle-size effects. Furthermore, the effects of F^- ion on the solubility of fluorapatite-hydroxyapatite mixtures are poorly understood beyond being able to say that such mixtures tend to form in the presence of F^- ion and are, therefore, more stable than hydroxyapatite alone. These uncertainties create major problems in the application of solubility principles to limnetic solutions, as they do for tooth and bone chemistry.

2.2. OCTACALCIUM PHOSPHATE, $Ca_8H_2(PO_4)_6 \cdot 5H_2O$

The structure of this salt (25) bears a special relationship to that of hydroxyapatite and is shown in projection in Figure 4 and as a stereoscopic illustration in Figure 5. The unit cell contains two formula weights. The shaded atoms in Figure 4 correspond in position very closely to those of hydroxyapatite which are shaded in

Figure 2. The presence of this layer in $Ca_8H_2(PO_4)_6 \cdot 5H_2O$ permits an epitaxial relationship with hydroxyapatite (26, 27). The resultant formation of surface layers and intracrystalline mixtures is believed to be a major factor that has led to confusion about the composition and properties of hydroxyapatite. The unshaded atoms in Figure 4 have essentially no relationship to the structure of hydroxyapatite. The water molecule (O(43) in reference 25) is of chemical interest in that this site may be only partially occupied, thus introducing possible variability into the chemical properties of octacalcium phosphate.

As a result of the similarity in the two structures, it appears that $Ca_8H_2(PO_4)_6 \cdot 5H_2O$ may participate in the nucleation and growth as a precursor to hydroxyapatite; it may act, also, as a transition layer between the hydroxyapatite crystals and the aqueous phase. It is thought (28) that a hydrated structure such as octacalcium phosphate will have a lower interfacial energy as compared to that of an anhydrous ionic structure such as hydroxyapatite. Thus, octacalcium phosphate may have an important bearing on other properties of hydroxyapatite such as (i) influencing the morphology of the crystallite, (ii) participating in the reactions with fluoride ions, and (iii) possibly stabilizing hydroxyapatite so that it can exist as very fine crystallites. The existance of hydroxyapatite in this finely divided form in most of its occurrences is one of its most important properties, giving it the characteristics of a colloid.

Additional insight into the manner in which octacalcium phosphate may complicate the chemistry of hydroxyapatite can be gained if we consider the different processes by which hydroxyapatite can be formed by precipitation from an aqueous solution. It was proposed (28) that hydroxyapatites may be formed through three mechanisms.

(1) One of these is easily carried out in the laboratory. Octacalcium phosphate is precipitated first (e.g., by hydrolysis of $CaHPO_4 \cdot 2H_2O$ or by titration of a calcium solution with a phosphate solution at room temperature and approximately neutral pH). Once formed, the octacalcium phosphate can be hydrolyzed to hydroxyapatite by boiling or by treating with an alkaline solution. In this process the larger crystals tend to become coated so that complete hydrolysis is difficult, and the gross composition tends to be intermediate to the two salts. An important aspect of this process is that it tends to occur *in situ* so that the resulting hydroxyapatite crystals have the platy or blade-like morphology of the original octacalcium phosphate. This is an important indication of the previous history of such crystals.

(2) A second and the most obvious process would be the growth of hydroxyapatite directly without an intermediary phase such as octacalcium phosphate. Under many conditions, this route is very slow or ineffectual. Many possible constituents of lakes and rivers, such as carbonate, magnesium and polyphosphate ions, seem to inhibit precipitation of hydroxyapatite.

(3) A third process might be a combination of these two and would involve the successive steps of precipitation of, say, a unit-cell thick layer of octacalcium phosphate on the (100) face of hydroxyapatite followed by its hydrolysis to hydroxyapatite; this process would then be repeated, each time converting a unit-cell thickness of octacalcium phosphate to a double unit-cell thickness of hydroxyapatite. Such a mechanism was proposed (28) because of the structural similarity described above and because direct precipitation of hydroxyapatite seems to be very difficult.

Fluoride ions would play an important role in the first and third of these processes in that they tend to accelerate the hydrolysis of octacalcium phosphate to an apatite. This process was proposed (28) as a partial explanation of why extremely small amounts of fluoride in tooth mineral can have such profound effects in reducing caries. Limnetic conditions are such that they, too, could facilitate the formation of octacalcium phosphate as an intermediary in the formation of hydroxyapatite since the growth of octacalcium phosphates seems to be preferred at lower temperatures. This mechanism and the proposed role of F^- ions could, therefore, be important factors in the kinetics of precipitation in natural bodies of water.

2.3. WHITLOCKITE, β-$Ca_3(PO_4)_2$

Like hydroxyapatite, β-$Ca_3(PO_4)_2$ is a mineral (29, 30). It is somewhat unusual in that cations smaller than calcium (Fe^{2+} and Mg^{2+}, in particular) seem either to make it more stable or to facilitate its formation in aqueous media.

For a long time the composition of this salt was in doubt because of a discrepancy between the unit cell constants and the apparent symmetry (31). Recent determinations of the structure are resolving both the uncertainty in the structure and the reason for the stabilizing effect of small cations.

Recent solubility measurements on the pure calcium salt (9) have shown that above about pH 6 (see Figure 1) this salt is second only to hydroxyapatite in its insolubility. Therefore, under suitable circumstances one might expect that it would form at least as an intermediary phase to hydroxyapatite. Special considerations should be given to this compound in those modifications of sewage or industrial-waste treatment processes in which the presence of Fe^{2+} or Mg^{2+} ions may facilitate formation of β-$Ca_3(PO_4)_2$

2.4. BRUSHITE, $CaHPO_4 \cdot 2H_2O$

Although under most circumstances, this salt is the most soluble of the five that we are discussing here, it deserves special consideration; because of crystal-growth kinetics it appears to form very readily. Therefore, it is found under many circumstances where it is metastable with respect to the other four salts. Another feature that seems to be important to both this compound and octacalcium phosphate is the presence of waters of hydration. It seems that the presence of these waters may reduce the interfacial energy of these salts when they are in aqueous systems. This would enhance the relative stability of the hydrated salts when the particles are extremely small, that is, during the nucleation and initial growth stages. Thus, it is possible that one of these salts is actually more stable than hydroxyapatite during the incipient stage of formation. In any event, it is a common experience in the laboratory to find that brushite (or octacalcium phosphate) forms initially and the more stable anhydrous salts form subsequently, either by hydrolysis *in situ*, as in the case of transition from octacalcium phosphate to hydroxyapatite, or through a dissolution step followed by a precipitation step, as seems to be the case usually in the conversion of brushite into one of the other more insoluble forms.

2.5. MONETITE, $CaHPO_4$

Although this salt is always more stable than brushite, except possibly at very high pressures and temperatures below about 5°C, it is encountered less frequently than brushite under most circumstances. This is in part due to the fact that the salt is somewhat difficult to detect by X-ray methods. Petrographic microscopy should be used when its presence is suspected because its birefringence is relatively high (33). It has a relatively low probability of occurrence under limnetic conditions for two reasons: (i) the pH range in which it is the most stable salt (about 5 to 1) is rarely encountered in lakes and rivers, and (ii) its metastability with respect to several other calcium phosphates is not compensated by a rapid rate of crystal growth as is the case with brushite.

2.6. AMORPHOUS CALCIUM PHOSPHATE

In recent years considerable emphasis has been placed on the observation that precipitated calcium phosphates frequently display no crystalline characteristics. These products are also thought (34-36) to have a composition closely approximating that of $Ca_3(PO_4)_2$ except that they contain considerable water. These materials cannot be treated according to the solubility product principles described later even though they might have a fairly fixed composition because it is unlikely that they fulfill the necessary condition of having a fixed standard free energy of dissolution per mole. There is no reason to believe that a material as ill-defined as amorphous calcium phosphate would have fixed thermodynamic properties. Whether such materials ever have significant effects on the compositions of limnetic solutions is difficult to say. It seems probable that they would nearly always be metastable with respect to all five of the sparingly soluble calcium phosphates described above, and can therefore be formed only when (i) the solution is so highly supersaturated that the reactions are too rapid for crystal growth of any of the well-defined crystalline phases or (ii) the solution is only moderately supersaturated, but crystal growth poisons are present that prevent the formation of the other phases.

2.7. CALCIUM CARBONATES

Calcite and aragonite are the two most commonly occurring anhydrous calcium carbonates. Several other anhydrous forms, including vaterite, several high pressure modifications of calcite (37, 38) and a multiply twinned type of aragonite structure, should be kept in mind as having an outside chance of being involved in some way in growth from water solutions. The two hydrated salts, $CaCO_3 \cdot H_2O$ (39-41) and $CaCO_3 \cdot 6H_2O$ (42, 43), are more likely participants in nucleation in crystal growth; they would tend to be favored by (i) properties such as interfacial energy and kinetics of crystal growth, and (ii) conditions such as low temperatures, high pressures, and growth poisons (Mg^{2+} and polyphosphates) which poison the growth of the anhydrous salts more than that of the hydrated salts.

3.0. THE LIQUID PHASE

3.1. DEFINITION OF COMPONENTS

For the sake of convenience in defining the activities or chemical potentials of the components, we have chosen to describe the ternary system with the components $Ca(OH)_2$, H_3PO_4 and H_2O. For many years the components that were chosen to describe this system were CaO, P_2O_5 and H_2O. However, in dilute solutions, the activities and chemical potentials of the oxides cannot be visualized or expressed as easily as those of $Ca(OH)_2$ and H_3PO_4, which can be defined as follows:

$$A_{Ca(OH)_2} = (Ca^{2+})(OH^-)^2, \qquad (1)$$

$$A_{H_3PO_4} = (H^+)^3(PO_4{}^{3-}), \tag{2}$$

$$A_{H_2O} = (H^+)(OH^-), \tag{3}$$

$$\mu_{Ca(OH)_2} = \mu^\circ{}_{Ca(OH)_2} + RT\ell n(Ca^{2+})(OH^-)^2, \tag{4}$$

$$\mu_{H_3PO_4} = \mu^\circ{}_{H_3PO_4} + RT\ell n(H^+)^3(PO_4{}^{3-}), \tag{5}$$

and

$$\mu_{H_2O} = \mu^\circ{}_{H_2O} + RT\ell n(H^+)(OH^-). \tag{6}$$

In this chapter, parentheses denote activities of ions, and square brackets denote concentrations.

The very useful fact that the chemical potential of any component, whether it is a weak or a strong electrolyte, can be defined in terms of an ionic product is frequently overlooked. As a consequence of this definition, the chemical potential of an acidic or basic component rises or falls as the pH is changed even though the concentration of the component is held constant. A graphic illustration of this effect is described later where the chemical potential of $Ca(OH)_2$ is shown to decrease along an isotherm even though the concentration of calcium ion is increased over a thousandfold. For this reason it is important to distinguish clearly between the concentration of a component and its chemical potential. Although these effects are generally recognized in the treatment of inorganic processes, they should be given more consideration than presently in treating metabolic processes where the driving forces for diffusion and chemical reactions also involve differences in chemical potentials.

In the ternary system, the chemical potentials are relatively easily definable quantities because the calcium and phosphorus concentrations and pH are measured directly. One then needs only to know the ionic strength to be able to use an empirical relationship such as the Debye-Hückel or the Davies equation (4) to calculate the activities of the individual ions. In these calculations, one must also use equilibrium constants for the dissociation of H_3PO_4 and for the calcium-phosphate ion pairs that may be present.

The application of the equilibrium constants obtained from the study of the ternary system to those that contain additional components is described in a later section. It is noted here, however, that in natural waters there are exceptional difficulties in defining the concentrations of the components. Phosphate, for example, occurs in various other forms such as (i) organically bound phosphate, (ii) particulate material, (iii) adsorbed on particulate material, (iv) complexed ions, and (v) possibly as polyphosphates or metaphosphates. It is only the "free" orthophosphate and the orthophosphate ion-paired to calcium (which can usually be calculated) that should be counted as affecting the solubility of a calcium phosphate salt.

The task of defining the components to be used in describing a system should not be taken lightly. Although neutral salts and non-ionizing components tend to have secondary effects on solubility and frequently can be ignored, some components may introduce new solid phases even when present in very low concentrations, which would then dominate the nature of the equilibrium. HF is an example of such a component because it forms highly insoluble fluorapatite (or fluorapatite-hydroxyapatite solid solutions). In general, it is advantageous to choose all other components as acids or bases because it is the acidity or basicity that is usually the primary factor affecting the solubility of a phosphate or carbonate salt because of its effect on the degree of dissociation of H_3PO_4 or H_2CO_3. The exception to this rule would be a constituent that forms soluble complexes or insoluble precipitates. As is shown later, the selection of the additional components as acids and bases makes it easier to treat their effects by combining them into a single variable which has been called the "electroneutrality unbalance".

3.2. SOLUBILITY ISOTHERMS

We have already mentioned some of the complications that are introduced into understanding the solubilities of the calcium phosphates because of the fact that phosphoric acid is a weak polybasic acid. For this reason, we approach the subject from a basic position. The Gibbs phase rule, when applied to a system containing three components and in which a solid phase and a liquid phase are in equilibrium at fixed temperature and pressure, allows only one degree of freedom. This fact is easily seen from Figure 6, a logarithmic plot of the concentration of calcium hydroxide against that of phosphoric acid. The compositions of the solutions that are saturated with respect to hydroxyapatite are given by the line designated $Ca_5(PO_4)_3OH$. The fact that the equilibrium compositions are described by a line (the "isotherm") is a consequence of the single degree of freedom. Thus, if the $[Ca(OH)_2]$, $[H_3PO_4]$ or pH of a saturated solution is specified, then the composition of the solution is completely fixed by the point where that composition or pH line crosses the isotherm. Along this isotherm the chemical potential of hydroxyapatite is constant even though the concentration of the components $Ca(OH)_2$ and H_3PO_4 vary over three orders of magnitude. This is true because saturation requires that

$$\Delta F^\circ_{HA} + 9\mu_{H_2O} = 5\mu_{Ca(OH)_2} + 3\mu_{H_3PO_4} \qquad (7)$$

where ΔF°_{HA} is the standard free energy of dissolution of hydroxyapatite. This relationship is a direct consequence of the assumption that the solution is saturated with respect to hydroxyapatite and, therefore, the reaction

$$Ca_5(PO_4)_3OH(s) + 9H_2O(\ell) = 5Ca(OH)_2(aq) + 3H_3PO_4(aq) \qquad (8)$$

takes place without a change in free energy. In the dilute solutions under consideration, μ_{H_2O}, the chemical potential of water, is essentially constant.

One can now visualize a hypothetical process in which the composition is changed toward the region of high concentrations and low pH's (toward the upper right along the isotherm), at all times maintaining equilibrium. In this process, five times the decrease in chemical potential of $Ca(OH)_2$ is exactly compensated by three times the increase in chemical potential of H_3PO_4. The chemical potential of $Ca(OH)_2$ is decreased during this process because the pH has a greater effect on the chemical potential of $Ca(OH)_2$ than does the concentration.

The isotherm is the line of demarcation between the region of supersaturation with respect to hydroxyapatite (above and to the left of the isotherm in Figure 6) and the region of undersaturation. In the latter region, the reaction defined by equation (8) would be accompanied by a decrease in free energy. It must be kept in mind that equation (8) is not the only reaction that can be written. Isotherms are shown in Figure 6 for other calcium phosphates which define the solution compositions where there would be no change in free energy for the dissolution-precipitation reaction for each of these salts. The fact that these isotherms have regions of positive slope in the range of concentrations of primary interest to us is an important characteristic of phosphatic systems and is a consequence of phosphoric acid being a weak electrolyte. The same situation applies to the solubilities of calcium carbonates. It accounts for the well known phenomenon that calcium carbonate dissolves when the partial pressure of CO_2

is increased. On the other hand, the slope of an isotherm for a salt formed from a strong acid and a strong base should be monotonically negative over the entire range (in the absence of complex formation). The slope of the isotherm for hydroxyapatite becomes negative when the pH reaches a value in the vicinity of pK_3 of phosphoric acid, but the phosphate concentrations are then so low and the pH's so high that this is not a range of significance except possibly when waste water is being treated with lime.

With the exception of the isotherm for octacalcium phosphate, which was calculated by use of a tentative solubility constant, the other isotherms given in Figure 6 represent experimental measurements. The isotherms for all the salts shown in Figure 6 are nearly superimposed in the range of higher concentrations and lower pH's. This is why it is necessary to use a plot of the type shown in Figure 1 to separate the isotherms for the various salts. The fact that these isotherms are nearly superimposed in Figure 6 relates to a property of phosphoric acid which can be used to give additional insight into these systems, as described in the section on the "electroneutrality surface". Next, however, we consider some of the consequences of having two solid phases in equilibrium with a liquid phase.

3.3. SINGULAR POINTS

As noted above, when a single equilibrating solid phase is present, application of the phase rule shows that the ternary system has one degree of freedom; the presence of a second equilibrating solid phase reduces the degrees of freedom by one so that the system becomes invariant (at a given pressure and temperature). This is represented in Figure 1 as the point of intersection where the isotherms of two solids intersect; the composition at the point of intersection is known as the "singular point". A total of six singular points are shown in Figure 1. The singular points, although present, cannot be seen in Figure 6 because the isotherms are so nearly superimposed. One can approximate three additional singular points by extrapolating the isotherms of $Ca_5(PO_4)_3OH$, $Ca_8H_2(PO_4)_6 \cdot 5H_2O$ and β-$Ca_3(PO_4)_2$, Figure 1, to the points where they intersect. However, the metastability of these compositions with respect to $CaHPO_4 \cdot 2H_2O$ and $CaHPO_4$ (and the ease with which $CaHPO_4 \cdot 2H_2O$ precipitates) prevents them from having more than theoretical significance. The invariance of the calcium and phosphorus concentrations and pH at the singular points is destroyed when the system contains more than three components. It is shown next that the variability in the concentrations of these components does not signify that their chemical potentials are variable at the singular point.

At the singular point, saturation with respect to two solids requires that the solubility products for both are satisfied. Thus at the singular point of $Ca_5(PO_4)_3OH$ and $CaHPO_4$, for example, we have

$$(Ca^{2+})^5(PO_4{}^{3-})^3(OH) = K_{HA} \qquad (9)$$

and

$$(Ca^{2+})(HPO_4{}^{2-}) = K_m \qquad (10)$$

or

$$(Ca^{2+})(H^+)(PO_4{}^{3-}) = K_mK_3, \qquad (11)$$

where K_{HA} and K_m are the solubility products for hydroxyapatite and monetite, respectively, and K_3 is the third dissociation constant for phosphoric acid. Simply by dividing equation (9) by the third power of equation (11) and substituting K_w for $(H^+)(OH^-)$, we have

$$(Ca^{2+})(OH^-)^2 = K_{HA}{}^{\frac{1}{2}}\left(\frac{K_w}{K_mK_3}\right)^{\frac{3}{2}} \qquad (12)$$

and by dividing by the fifth power of equation (10), we have

$$(H^+)^3(PO_4{}^{3-}) = (K_mK_3)^{\frac{5}{2}}\left(\frac{K_w}{K_{HA}}\right)^{\frac{1}{2}}. \qquad (13)$$

These equations reveal that the chemical potentials of $Ca(OH)_2$ and H_3PO_4 are fixed at the singular point at a given temperature or pressure because the addition of other components will not change the quantities on the right hand sides of (12) and (13).

The singular points are important features of the system because they represent compositions with relatively high probability. This is a direct result of the phenomenon of metastability. An example illustrates this point. Consider a solution which is saturated with respect to hydroxyapatite and which has a pH less than that of its singular point with brushite (i.e., to the left of pH = 4.3 in Figure 1). The solution will be supersaturated with respect to brushite, which, therefore, can precipitate, making the solution undersaturated with respect to hydroxyapatite. Dissolution of the basic salt, hydroxyapatite, and precipitation of the acid salt, brushite, will cause the pH of the solution to rise. This process would continue until the pH and solution composition reached the singular point. Conversely, brushite in a solution with a pH above that of the singular point would tend to cause the precipitation of hydroxyapatite; subsequent dissolution of brushite would drive the pH down; again, these processes would continue until the singular point was reached.

Relationships similar to (12) and (13) are obtainable at the singular point for any pair of calcium phosphates. The chemical potential of $Ca(OH)_2$ or H_3PO_4 would again be constant although, for each pair it would have a different value. According to equation (12), the activity of the calcium ion at the singular point would increase a hundredfold with a tenfold increase in hydrogen ion activity. These increases can be brought about only by the presence of other components (e.g., HCl, H_2CO_3, H_2SO_4) in the solution; concomitantly, the PO_4^{3-} ion activity would be decreased by the presence of these other anions. One can see these relationships better by keeping in mind that the charge of the foreign anion is balanced by a greater calcium concentration. The consequent greater calcium ion activity results in a lower PO_4^{3-} ion activity because of equations (9) and (11). Similarly, according to equation (13), the activity of PO_4^{3-} would be increased, and the activities of the calcium and hydrogen ions would be decreased, by the presence of components such as NaOH, KOH and $Mg(OH)_2$. Since the composition and pH of the singular point solution is affected by the presence of other ions, equations (12) and (13) are especially useful for estimating the pH of the singular point of a solution in which the phosphate concentration is greatly exceeded by those of other anions such as carbonate and sulfate, as is the case in many natural waters. Note the direction of these effects; an excess of added anion increases the calcium and hydrogen ion activities, and an excess of added cation increases the PO_4^{3-} activity and the pH.

Since $Ca(OH)_2$ is a legitimate solid in the ternary system, it could co-exist with hydroxyapatite to form a singular point which could be of great interest in the treatment of sewage with lime. However, this region of the system has not been studied adequately because the phosphate concentrations are too low to measure conveniently.

3.4. THE "ELECTRONEUTRALITY SURFACE"

Knowledge of the dissociation constants of phosphoric acidand the stability constants for calcium-phosphate ion pairs permits one to calculate the pH of any dilute solution for which the concentrations $[Ca(OH)_2]$ and $[H_3PO_4]$ are given. Furthermore, one can define a surface in three-dimensional space by plotting -log $[Ca(OH)_2]$ against -log $[H_3PO_4]$ in the plane of the paper, as was done in Figure 6, and the pH in the third direction. This surface can be depicted as in Figure 7 by lines of constant pH which define the contours of the surface. Although this surface is more properly called a "pH surface", it was first called (44) the electroneutrality surface for the reason that it is necessary to introduce the condition of electroneutrality,

$$[H_2PO_4^-] + 2[HPO_4^{2-}] + 3[PO_4^{3-}] + [OH]^- - [H^+] - 2[Ca^{2+}] - [CaH_2PO_4^+] = 0 \qquad (14)$$

to be able to calculate the pH at any given point. More details about this surface are given elsewhere (44).

The important feature about this surface is the presence of two steep faces where the pH contours fall very close to one another in the range of pH from about 4 to 10. The existence of these steep faces is the reason why the isotherms in Figure 6 are nearly superimposed over much of their lengths. These isotherms, like those of all other electrically neutral compositio must lie in the electroneutrality surface. In those regions where the surface is very steep, and when the surface is viewed from above as in Figure 6, the isotherms will appear nearly superimposed. When the isotherms are projected into a face that contains the pH axis, as is the case in Figure 1, the isotherms appear well separated. Diagrams similar to Figure 6 may be calculated for fixed compositions of a fourth component and for other temperatures and pressures through use of the solubility and ion-pair formation constants which have been derived from studies of the ternary system.

The two steep faces, in the pH ranges 4 to 6 and 8 to 9, are separated by a slightly flattened region at pH 7. Since pK_2 for phosphoric acid is 7.20, it is apparent that the flattening of the surface in this region corresponds to the pH where the two ions $H_2PO_4^-$ and HPO_4^{2-} have equal activities and the system has a maximum in its buffer capacity. The flat surfaces below pH of 4 and above 10 are regions that are buffered by the combinations $H_3PO_4/H_2PO_4^-$ and HPO_4^{2-}/PO_4^{3-}, respectively. Thus the steep faces occur at pH values that are intermediate to the pK values for the acid. Accordingly, the system $Ca(OH)_2$-H_2CO_3-H_2O should have a steep face at a pH of about 8.3.

The presence of the steep faces in Figure 7 is very valuable for interpreting experimental data or for designing experiments. For example, it is difficult to tell whether a solution is saturated with respect to any specific calcium phosphate from a knowledge of the calcium and phosphate concentrations alone; it is necessary to know the pH as well.

In other words, in the steep faces the calcium and phosphate concentrations are slowly changing variables, whereas the pH is the most sensitive variable, and it is the one that should be chosen if the approach to equilibrium is to be monitored. This is not true, of course, in a multicomponent system that contains a high concentration of buffer.

Another use for the type of diagram shown in Figure 7 comes from the fact that the solutions, regardless of their state of saturation with respect to the various calcium phosphate salts, are restricted in their compositions to a rather narrow region. Most solutions of interest fall in the pH range 5 to 9. Thus this is a region of fairly high probability from the standpoint of finding solution compositions, and one can use it for purposes of approximation in much the same way as one would use an isotherm. The presence of other components will displace the steep surface in a manner that will be described in a later section. However, before doing this it is necessary to consider the effects of additional components in a more general way.

3.5. MULTICOMPONENT SYSTEMS

Isotherms describing the solubility of hydroxyapatite in the presence of constant amounts of a fourth component are shown in Figure 8. For reasons given later, the amount of the fourth component is given in terms of the negative logarithm of the concentration, U(±), of this component, where U(-) represents an acid and U(+), a base. The isotherm labelled pU(O) is the same as the one given for hydroxyapatite in the ternary phase diagram in Figure 6. In accord with the phase rule, the addition of a fourth component introduces a second degree of freedom, but by restricting the concentration of that component to a given value, the degrees of freedom are again reduced to one. Thus, all solutions containing 10^{-4} mol/ℓ of, say, HCl would have compositions defined by the line pU(-) = 4 when saturated with respect to hydroxyapatite; solutions containing 10^{-3} mol/ℓ of HCl would correspond to the isotherm labelled pU(-) = 3. These isotherms lie in the region which, in the absence of HCl, would be supersaturated with respect to hydroxyapatite, thus showing that the effect of the acid, as one would expect, is to increase the solubility of hydroxyapatite. The latter two isotherms were calculated on the basis of equilibrium constants obtained from the ternary system. The position of the isotherm should not be shifted very much if, say, HCl were replaced by HNO_3 or by any other strong acid of the same normality that did not have specific interactions with calcium or phosphate ions. A similar set of isotherms, shown below that of pU(0) in Figure 8, is obtained for a series of solutions with constant concentrations of a base such as NaOH or KOH. Examples with pU(+) = 3 and 4 are shown in Figure 8. In the range of higher pH's and lower calcium and phosphate concentrations, the curves with positive values of pU(±) acquire negative slopes as do the curves with negative values of U(±). However, this portion of the phase diagram is in the range of such low phosphate concentrations that it does not have much practical significance.

According to the view presented here, it is the acidity or basicity of the other components that is important as long as they do not form significant concentrations of ion pairs and complexes. Furthermore, in the presence of several of such components, it is the excess of base over acid, or vice versa, that determines the position of the isotherm. This leads to the definition of the quantity U(±),

$$U(\pm) = \sum_i \nu_i C_i \ , \tag{15}$$

where ν_i is the valence and C_i is the concentration of the i^{th} ion, and the sum is taken over all species of ions other than calcium, phosphate, and water ions, and calcium-phosphate ion pairs. Because the solution is electrically neutral, an alternative definition of U(±) is given by

$$U(\pm) = -\sum_j \nu_j C_j \ , \tag{16}$$

where the sum is taken over calcium, phosphate and water ions (i.e., the ions present in the ternary system). This is why the quantity U(±) has been called (44) the "electroneutrality unbalance". In essence, U(±) is the measure of the excess of basic over acidic components but it takes into account only the dissociated portions of these acids and bases. Ion pairs and complexes are counted as acids or bases depending on whether their valence charges are negative or positive, respectively. For these reasons, the quantity U(±)

can be considered to be the fourth component, which, when positive, is a base and, when negative, is an acid. Its use partially ignores the effects of ionic strength on activity coefficients, but for the dilute solutions under consideration here, this would not be a major source of error. Ion pairs and complexes (other than the calcium-phosphate ion pairs) must be taken into account explicitly, and the concentrations of calcium or phosphate in these forms must be subtracted from the quantities $[Ca(OH)_2]$ and $[H_3PO_4]$ used as the coordinates in Figure 8.

The isotherms for the various values of pU(±) can be viewed as forming a three-dimensional surface in a way somewhat similar to that of Figure 7 except that the coordinate in the vertical direction would be pU(±) instead of pH. Since each point on an isotherm has a specific pH, one can define lines of constant pH on this surface. These are shown, in projection, in Figure 9, which is a duplicate of Figure 8 except that it shows lines of constant pH.

Figure 9 displays at a glance considerable information about how solubility of hydroxyapatite is affected by other components over the normal range of limnetic solutions. Compositions with pH's less than 4 are not shown because hydroxyapatite is no longer the most stable phase; above pH = 9, the orthophosphate concentrations are too low to be of much significance compared to other forms of phosphate found in natural waters. Figure 9 shows that a wide range of calcium and phosphate concentrations can be saturated with respect to hydroxyapatite at a given pH. The breadth of this range (i.e., the fanning out of the isotherms) is much greater in the dilute region of the diagram. Figure 9 also shows that the calcium and phosphate concentrations of saturated solutions are quite high in the acid region. As noted previously, the phosphate concentration at a pH of 4 is remarkably high, being of the order 0.1 M over a considerable range of values for U(±).

The lines of constant pH can be used to determine whether or not the solution is saturated even when one does not know the value of U(±) for that solution. Thus, the lines of constant pH can be used as "isotherms" when U(±) is not known or is a variable. For example, a solution undersaturated with respect to hydroxyapatite would have a pH below that shown in Figure 9 for a point defined by its calcium and phosphorus concentrations. A disadvantage of this method (as with any other method) is that either the concentrations of ion pairs and complexes must be negligible or they must be taken into account explicity in the manner noted previously.

3.6. EFFECTS OF DILUTION

The positive slopes of the isotherms in Figures 7 through 9 have an interesting effect on what happens when a saturated solution is diluted, say, by rain water which is relatively free of solutes. The slope of an isotherm over much of its length is so nearly one that even after a severalfold dilution the composition point is not far from the isotherm. The degree of undersaturation of the new solution, as measured by the ion activity product, would probably be quite low; however, as long as the composition lies on a "steep face" of the electroneutrality surface (i.e., in the pH range 4 to 10) it is likely to be near the isotherm. This is true even when the value of U(±) of the initial solution is quite large because the new composition and the newly applicable isotherm both lie in the "steep face" for solutions with the new value of U(±). This phenomenon can be explained on a physical basis. Dilution of the solution causes a decrease in the calcium concentration, but this is largely compensated by an increase in the OH^- and PO_4^{3-} ion concentrations so that the ion-activity product is not reduced as much as one might expect. On the other hand, dilution of a saturated solution with one that has a positive value of U(±) is likely to lead to a final solution that is supersaturated with respect to the salt. The reason for this is that the isotherm applicable for the final solution will have been shifted farther to the right then would be the case if U(±) of the diluent were zero or negative, and, the composition of the mixture will tend to lie to the left and above the applicable isotherm (i.e., in the region of supersaturation). This type of consideration exemplifies the use of the "generalized four-component phase diagram". Detailed calculations, based on the initial and final compositions of the solutions would also permit one to analyze the effects of dilution for any given situation, but this would be much more tedious than the use of the phase diagram, and it would be nearly impossible except when the initial and final pH's were known. These pH's would have to be known in any case where the solutions contain weak electrolytes because their contributions to U(±) vary with pH and dilution. Carbonate, of course, is such an electrolyte; sulfate and chloride, the other principal anions contributing to U(±) in most waters, are not affected by pH in the ranges found in most lake waters.

3.7. APPLICATION TO NATURAL WATERS

No effort is made here to test the application of Figure 9 to specific examples of lake water because this would require knowledge that the solution was saturated with respect to hydroxyapatite. However, it should be noted that the calcium concentration usually exceeds that of phosphate by one to two orders of magnitude. This is consistent with a large negative value of U(±) which would be supplied by the carbonate, chloride, and sulfate ions. The latter provide most of the negative charge needed to counterbalance the positive charge of the calcium ions. Large negative values of U(±) lead to high calcium and low phosphate concentrations as seen in Figure 9 when the pH is above about 6.

3.8. OTHER CALCIUM PHOSPHATES

A diagram similar to Figure 9 can be calculated for each of the other four calcium phosphates for which solubility constants are available. Because of the way the isotherms tend to superimpose, the positions of the isotherms in these diagrams would be quite similar to those in Figures 8 and 9. They would differ considerably, however, in the locations of the pH lines in Figure 9. The greater the relative solubility of a given salt, the more its lines of constant pH would be shifted toward the upper right in the diagram. Increasing the ionic strength with neutral salts, which tend to increase the solubility of the salt, would shift the pH lines in the same direction. Similarly, factors that enhance solubility of a given salt, such as small crystallite size, crystal impurities or structural defects, would shift the positions of the pH lines, but they would shift the positions of the isotherms only slightly. The effects of these structural factors on the solubility of hydroxyapatite is poorly understood, but there is reason to believe that they may be quite significant (46).

3.9. OTHER ELECTRONEUTRALITY SURFACES

The electroneutrality surface shown in Figure 7 for the system $Ca(OH)_2$-H_3PO_4-H_2O was calculated taking into account the ion pairs of $CaHPO_4{}^\circ$ and $CaH_2PO_4{}^+$, but these are of relatively minor importance over most of the achievable range of concentrations. A system such as $Fe(OH)_3$-H_3PO_4-H_2O, where complexing between the cation and the phosphate is strong, would produce a grossly different surface. The shape of this surface can be calculated provided the stability constants for the complexes are known. The electroneutrality surface for such a system may also have steep faces, but these are likely to be displaced toward lower pH's. The reason for this displacement would relate to the facts that (i) the complexing enhances the dissociation of the protons on the phosphate groups, and (ii) the inflections in the steep faces correspond approximately to the pH values half way between the first and second and the second and third dissociation constants of the acid. As noted above, the system $Ca(OH)_2$-H_2CO_3-H_2O is also likely to have an electroneutrality surface with a steep face at a pH of about 8.3. The location and slope of this face may be of considerable value in describing calcium carbonate solubility. As with the phosphate system, other ions will affect the shape of the surface for the carbonate system. The presence of other ions might be handled, as in Figures 8 and 9 for each of the calcium carbonates, by defining a quantity similar to $U(\pm)$ given here for the phosphate system. On this diagram, the lines of constant chemical potential of the component H_2CO_3 would correspond to lines of constant partial pressure of CO_2. It can be easily shown that the chemical potential of $Ca(OH)_2$ is also a constant along these lines.

3.10. CHEMICAL POTENTIAL DIAGRAMS

Figures 1 and 6 have considerable utility in that the quantities that are plotted are directly measureable. However, the presence of other components destroys their utility and it becomes necessary to use a phase diagram such as Figure 9 where one can compare the directly measured quantities (calcium and phosphate concentrations and pH) with functions (isotherms and lines of constant pH) that have been derived from theoretical considerations. There is another type of derived diagram (Fig. 10), usually called a "potential diagram", which is quite useful in multicomponent systems. Equation (7), which is valid regardless of the number of components, can be written

$$\mu_{Ca(OH)_2} = -\tfrac{3}{5}\,\mu_{H_3PO_4} + \tfrac{1}{5}(\Delta F^\circ_{HA} + 9\,\mu_{H_2O}). \qquad (17)$$

Substituting equations (4) and (5) into (17) gives

$$\log\,(Ca^{2+})(OH^-)^2 = -\tfrac{3}{5}\log\,(H^+)^3(PO_4{}^{3-}) + K. \qquad (18)$$

It can be seen from equation (18) that the chemical potential of $Ca(OH)_2$ is linearly related to that of H_3PO_4, and that the negative inverse of the slope of the line, 5/3, is the Ca/P ratio of hydroxyapatite, the equilibrating phase. Similar relationships have been derived for the other calcium phosphates (47) in a more general way. The slope and position of the line for each solid is characterized by the Ca/P ratio and its solubility product (i.e., its standard free energy of dissolution). Brushite and monetite would both have a line with a slope of one, but the line for brushite would be displaced in the direction of higher chemical potentials.

Potential diagrams (47) have proven quite useful in attempting to identify the phase that may be saturating a given solution or a series of solutions. In addition to the usual difficulties related to uncertainties as to the formation of ion pairs and complexes and whether equilibrium has been attained, this type of plot has two shortcomings: (i) it is strictly a comparison of *derived* quantities (involving ion activities which can be calculated only through the use of arbitrary conventions), and (ii) the concentrations are not shown explicitly, so that two solutions differing greatly in composition may fall on the same point in the potential plot. In spite of these shortcomings, potential plots are useful adjuncts to the other types of plots.

It is apparent in Figure 10 that the point where two lines intersect (the singular point) has constant values for the chemical potentials of $Ca(OH)_2$ and H_3PO_4 regardless of what other components may be present. This is a direct result of equations (12) and (13).

4.0. DESIGN OF SOLUBILITY EXPERIMENTS

Some rules for the design of valid solubility experiments are given in this section. One needs to make only a cursory review of the literature on the solubilities of sparingly soluble calcium phosphates to see that the results of different investigators can be in considerable disagreement. When properly carried out, solubility measurements are tedious and costly. It is important, therefore, to design the experiments carefully to avoid introducing a weakness that will destroy the value of the results. The following principles should help in this respect.

4.0.1. Phase rule considerations: The phase rule provides minimum criteria which, although frequently ignored, must be fulfilled before equilibrium experiments can be valid. The first step in the design of the experiments should be to analyze the number of degrees of freedom in terms of the components to be used in the equilibrations. Our experience has been that it is best to minimize the number of components so that the number of degrees of freedom is limited to one. In this way it is possible to plot the experimental data directly in the forms given in Figures 1 and 6. Experimental errors can frequently be detected as points that do not fall on a smooth curve. Buffers are frequently used to control the pH, but there is another way of controlling the pH range (described later) which does not introduce additional components with the concomitant uncertainty of having specific interactions with the calcium and phosphate ions. The addition of a constant amount of another component to all of the equilibrations in a given series does not, in effect, increase the number of degrees of freedom, but it may prevent the use of the electroneutrality balance as an internal check.

4.0.2. Solid phases: The first requirement is that the identity and pertinent properties of all the solid phases that can form in the system should be known. X-ray diffraction patterns and chemical analyses are necessary, but insufficient, criteria for establishing the purity of a given preparation. Both are insensitive to the presence of minor phases and coatings which could markedly alter the apparent solubility of the major phase. Examination with a petrographic microscope is essential for establishing the absence of impurities and for ascertaining that the crystals are suitable for the measurements.

4.0.3. Criteria for equilibrium: Strict criteria must be used in ascertaining that equilibrium is achieved in the solubility experiments. Whenever possible equilibrium should be approached from both supersaturation and undersaturation. The approach from supersaturation can usually be achieved by pre-equilibrating at a different temperature or by the use of a salt that is more soluble than the one under study. However, the approach to equilibrium from supersaturation does not always go smoothly; intervening precipitation of a metastable salt or a slow rate of crystal growth may preclude equilibration from supersaturation. Both of these factors appear to apply to solutions that are supersaturated with respect to hydroxyapatite. Knowledge of this type can be of practical value, however, in understanding the behavior of the system under natural conditions.

4.0.4. Monitoring approach to equilibrium: One should use the most sensitive variable to monitor the approach to equilibrium. As noted previously, changes in pH can be detected more readily than changes in calcium and phosphate concentration when the composition is on the "steep faces" of the electroneutrality surface. The same would not be true in the ranges of pH below about 4 and above about 10. In the range 4 to 10, however, relatively large changes in pH have been found to occur even when no change in calcium or phosphorus concentration could be detected. An electroneutrality surface is so easily calculated by the use of computers that it should be calculated prior to design of the experiments so that one can decide on the most sensitive variable for the purpose of monitoring. A disadvantage of the use of pH for this purpose is that it cannot be measured continuously on the solution being equilibrated because of possible contamination from the salt bridge. Continuous monitoring can be achieved, however, through the use of conductivity (48).

4.0.5. Equilibration times: Constancy in the monitored quantity should be achieved over a large range of equilibration times. It is sometimes possible to get very short equilibration times by the use of leaching columns. The comparison of these data with those obtained from long-term end-over-end rotations can provide confidence that equilibrium has been achieved. It should be recognized, however, that an approach to equilibrium that requires dissolution of one or more solid phases and precipitation of another, particularly when the liquid is in the dilute range, can be exceedingly slow and can give steady-state conditions that mimic equilibrium. Lack of equilibrium can sometimes be detected by plots of the experimental data, such as Figures 1 and 6 above, or by use of the adjustment procedure, described later, for treatment of the data.

4.0.6. Condition of electroneutrality: Since this is a condition that must be fulfilled by any chemical solution, it should be used to test the validity of the data. A non-zero value indicates either (i) an error in analysis, (ii) presence of impurities, or (iii) an incorrect calculation of the phosphate ion distribution because of the use of inappropriate phosphoric acid dissociation constants, ion-pair formation constants, or expressions for calculating ion-activity coefficients.

4.0.7. Solid-to-solution ratio: If the ratio, weight of the solid to the volume of aqueous phase, is too small, the rate of approach to equilibrium may be too slow for it to be achieved in a reasonable length of time. This problem becomes especially important if difficulties with preventing growth of micro-organisms are likely to limit the equilibration time. On the other hand, high solid-to-solution ratios are likely to lead to two types of difficulties: (i) small amounts of impurities -- either as foreign ions or as secondary solid phases -- may exert a disproportionate effect on the equilibrium composition, and (ii) the amounts of desorption of calcium and phosphate ions from the surface may be large compared to that obtained from dissolution of the crystalline portion of the sample. Although, in theory desorption and resorption of ions from surfaces should not affect the equilibrium constants derived from the experiment, these processes do alter the apparent stoichiometry of the reaction. These effects can be of relatively large magnitude when working with insoluble salts in the dilute region of the phase diagram.

4.0.8. Stoichiometry of the reaction: Another internal check on the validity of the experimental results is the requirement that the solid should dissolve stoichiometrically. Desorption reactions, as noted above, can invalidate the use of this as a check, but these can be minimized by a preliminary equilibration with the solution to be used in the final equilibration or by the use of the leaching-type technique (10). Hydrolysis (i.e., conversion of a metastable salt under study to one that is more stable) will alter the apparent stoichiometry of the reaction. However, hydrolysis does not necessarily vitiate the results. The composition of the solution may still be adequately representative of equilibrium with respect to the metastable phase provided the latter phase is present in preponderant amounts so that its rate of dissolution exceeds greatly that of precipitation of the more stable phase.

4.0.9. Metastability: For the reason cited above, it is possible to study metastable equilibria provided favorable equilibration conditions are chosen and other precautions cited here are taken into account to verify that the results represent equilibria. In many phase-diagram studies it is possible to mix the components together in almost any form that will give the desired final composition and then to wait long enough for final equilibrium to be attained. Equilibria involving dilute solutions, however, tend to be slow, and one must start with the solid phase to be studied, whether it is the stable or the metastable one, and use experimental techniques that facilitate rapid equilibrium. Sufficiently large solid-to-solution ratios and continuous stirring are particularly important.

4.0.10. Range of concentrations studied: The range of compositions studied should be as large as possible within the limitations provided by the accuracy in the analyses, on the dilute side, and uncertainties in treating the data (i.e., calculation of activity coefficients) on the concentrated side. Another possible limiting factor is metastability with respect to other salts in the system. When the supersaturation with respect to the more stable salt becomes too great, then its rate of formation becomes excessive.

A broad range of concentrations is necessary if one is to distinguish between the effects related to the solubility product of the salt and those due to ion-pair formation. This can be seen by considering a potential plot such as that given in Figure 1. Unless ion-pair formation is properly taken into account, the line would not be linear. This lack of linearity would not be detected if the range of chemical potentials that is covered by the experimental data is too narrow. It is fortunate that ion pairs such as $CaHPO_4^{\circ}$ and $CaH_2PO_4^+$, which differ by the dissociation of a hydrogen ion, will usually have their most significant concentrations in different pH ranges of the phase diagram, thus making it possible to detect their presence if the pH range is sufficiently broad. In the system $Ca(OH)_2$-H_3PO_4-H_2O it is possible to achieve a broad range by equilibrating the solid with various initial concentrations of H_3PO_4. In this way, concentration ranges of more than three orders of magnitude can be covered (4, 6, 7). In a multicomponent, buffered system, a similar range of chemical potentials can be achieved by use of a large range of Ca/P ratios in the solutions, and in the system $Ca(OH)_2$-H_2CO_3-H_2O, varying the partial pressure of the CO_2 achieves the same purpose as varying the initial concentration of H_3PO_4.

The apparent concentration of the ion pair $CaH_2PO_4^+$ is greatest in the low pH range where no difficulties are encountered with metastability or measurement of the calcium and phosphate concentrations, but the high ionic strengths of the solutions make calculation of ionic activities uncertain. The concentration of $CaHPO_4^\circ$ in solutions saturated with respect to $CaHPO_4 \cdot 2H_2O$ or $CaHPO_4$ is assumed to be constant throughout the range. However, its concentration becomes significant only in the higher part of the pH range when the total calcium and phosphorus concentrations are small because of the reduced solubility of the salt. Analytical errors and metastability with respect to the more basic calcium phosphates tend to be the limiting factors in this range.

4.0.11. The equilibrium model: The model to be used for treatment of the data entails selection of (i) dissociation constants for the acid, (ii) stability constants for the ion pairs or complexes, (iii) an expression for calculating individual ion activities, and (iv) standard values for the thermodynamic properties of ions and components and their variations with temperature. Decisions have to be made as to whether the reaction is taken to be stoichiometric, how to weight the measured variables, and whether the condition of electroneutrality is to be used as a condition function.

The greatest difficulty is encountered with the choice of types of ion associations to be used in the model. The following species have been included (4,6-7,11,49-52) in descriptions of calcium-phosphate equilibria: $CaHPO_4^\circ$, $CaH_2PO_4^+$, $CaPO_4^-$, $H_5(PO_4)_2^-$, $H_4(PO_4)_2^{2-}$, $H_3(PO_4)_2^{3-}$, $CaH_3(PO_4)_2^-$, $CaH_2(PO_4)_2^{2-}$, $CaH(PO_4)_2^{3-}$, $Ca(PO_4)_2^{4-}$, and

$Ca_2H_2(PO_4)_2^\circ$. The relatively low concentrations of the ion pairs and other ionic associations in this system make it difficult to select the appropriate species to be used in the model. The same appears to be true of the system $Ca(OH)_2$-H_2CO_3-H_2O. The situation can best be described by some examples. The maximum ion-pair formation found (4) in the solutions saturated with respect to $CaHPO_4 \cdot 2H_2O$ in the pH range 3.6 to 7.7 was about 25% of the calcium. Hydroxyapatite (5) being the most insoluble salt over much of this pH range, provides an example of the other extreme. Generally, formation of the ion pairs $CaHPO_4^\circ$ and $CaH_2PO_4^+$ in solutions saturated with respect to hydroxyapatite is not very significant, never exceeding 3.5% of the calcium. There are two qualifications: (i) In the low pH range (below 5), the solubility of hydroxyapatite approaches that of $CaHPO_4 \cdot 2H_2O$ and, therefore, these solutions may contain significant concentrations of the $CaHPO_4^+$ pair. (ii) When the Ca/P ratio of the solution is high, as is the case with many natural waters, the fraction of the phosphate in the form of ion pairs may be quite large even though their absolute concentrations are low.

Possible errors in the dissociation constants for phosphoric acid and uncertainties in the use of expressions for calculating ionic activity coefficients further confound the problem of selecting ion pairs for the model because one can never be certain that some of the apparent formation of ion pairs is not attributible to errors from these sources.

It should be kept in mind also, that equilibrium constants such as those for dissociation of phosphoric acid and ion pairs, were derived from systems which are likely to differ grossly in composition from the one being studied, and a totally different mathematical treatment may have been used in deriving these constants. Although some consolation may be taken from the fact that the constants are sometimes "limiting law" values, frequently they are not, and at other times the extrapolations are so great that specific ionic interactions may limit their accuracy for use in other systems. Consideration, therefore, should be given to refining the values for such constants using the solubility data from the system being studied and keeping in mind the empirical character of the calculations.

In general, one should avoid the temptation provided by the fact that the fit of experimental data to a mathematical model can always be improved by including more equilibrium species in the model. However, the number of such equilibria should be kept to a minimum to be realistic. In spite of the large number of species (cited earlier) which have been suggested as having sensible concentrations in the dilute range of the system $Ca(OH)_2$-H_3PO_4-H_2O, it is found (4-10) that the pairs, $CaHPO_4{}^\circ$ and $CaH_2PO_4{}^+$ sufficed to describe the data in the pH range from about 4 to 7. The pair $CaPO_4{}^-$ (11) may have to be included in the higher pH range. Considerable help in reaching the decision concerning the minimum number of ion pairs was provided by the adjustment procedure for treating data described below. There are specific reasons for questioning the reliability of constants derived for ion associations involving more than one calcium and one phosphate.

Solubility studies and potentiometric (pH) titrations are the two methods that are most commonly used to determine stability constants for ion pairs and complex ions. Reference is made later to the advantage given by having the additional constraints provided by the conditions of saturation and stoichiometric dissolution. Titration studies (51) used in studying calcium phosphate ion association have led to the conclusion that multiple ion groups were present. However, calculations show that some of the solutions used in these studies were highly supersaturated. Before the stability constants for multiple groupings such as $CaH_3(PO_4)_2^-$ and $Ca_2H_2(PO_4)_2^\circ$ derived from these studies can be fully accepted, it is necessary to show that the supersaturation did not lead to formation of a colloidal precipitate that went undetected. Supersaturation in a titration experiment is likely to give more difficulty than is given by the same phenomenon in the study of the solubility of a metastable solid; the presence of a large amount of equilibrating solid tends to overcome the effects due to precipitation of small amounts of the more stable phase, and the longer equilibration times used in solubility measurements tend to reveal any changes taking place in the solution. In selecting an expression for activity coefficients, one should be aware of the deficiencies in the two that are most often used. On the one hand, there are thermodynamic strictures (53) against the use of the Debye-Hückel equation to calculate activity coefficients of ions of different valencies; on the other hand, there is an apparent physical unreality in the Davies equation (54) which requires the use of the same activity coefficient for all ions of a given valence. As a result, one should keep in mind the more conservative view that the primary objective is to treat the data in a way such that the derived constants have transferral value from a laboratory system to the one in which they are going to be applied. That is, one should seek to achieve maximum cancellation of errors through the use of a uniform treatment and compatible constants. A step has been taken in this direction by assembling an internally consistent set of thermodynamic values for the calcium phosphates which is based on solubility measurements (55).

4.0.12. Treatment of data: Now that the use of computers permits sophisticated treatment of large blocks of data, there is little justification for point-by-point calculation of the equilibrium constant, followed by calculating an average value and a standard deviation of the average from the individual constants. We have found most satisfactory (4, 56) the use of a generalized least-squares procedure in which the various equilibrium expressions, the electroneutrality and the stoichiometry of the reaction (when possible) for the model are introduced as constraints, the variations of which are to be minimized. Estimates of the experimental errors enter into the weighting scheme as part of the calculation of the errors of the derived constants. One of the most useful features of the output is the list of adjustments that would have to be made in the experimental data to minimize the deviations in the constraints imposed by the model. Consistently large adjustments reveal that the model is inadequate or that systematic errors, possibly due to lack of equilibrium, are present in the data.

One might anticipate intuitively that the more restrictive an experimental model, the more reliable the constants that one can derive from the data. It was possible to test this hypothesis (4) through the use of the adjustment procedure. Incorporation of the condition functions based on electroneutrality and congruent dissolution into the mathematical model significantly decreased the standard deviation of the adjustment and thus increased the reliability of the derived constants over those obtained when these condition functions were omitted. Similarly, the use of the solubility data as compared to titration data, has the advantage of introducing one or two extra constraints which should increase the reliability of the dissociation or stability constants derived from the data. The only constraints applicable to titration data are the dissociation equations and the electroneutrality expression.

A computer program has been reported (57) for handling titration-type data for the calculation of ion associations. This program was not designed to take into consideration the condition functions related to saturation and stoichiometric dissolution, nor was it explicitly stated whether the condition function for electroneutrality had been included.

4.0.13 Reporting of results: Although it should not be necessary to make this admonition, the fact is that two types of deficiencies frequently appear in the reports on solubilities of sparingly soluble salts. The primary data, concentrations of all components and pH, are not always given along with the derived equilibrium constants and/or graphs. The absence of primary data implies a lack of esteem for the data, and it prevents the re-evaluation of the data at a later time when a more appropriate model may be available. Another questionable practice is to list the logarithms of the constants for a given set of experiments rather than the constants themselves. It is not always recognized by the reader that constancy in pK is far less significant than constancy in K. Finally, some estimate should be given of the variation in the derived product that may be caused by errors or by junction potentials in the pH measurements. Very frequently the error in pH, which is a logarithmic quantity, is the greatest source of variation in the derived constants. In the adjustment procedure described above, this error is taken into account automatically, otherwise it may show up only in the actual variations of the derived equilibrium constants.

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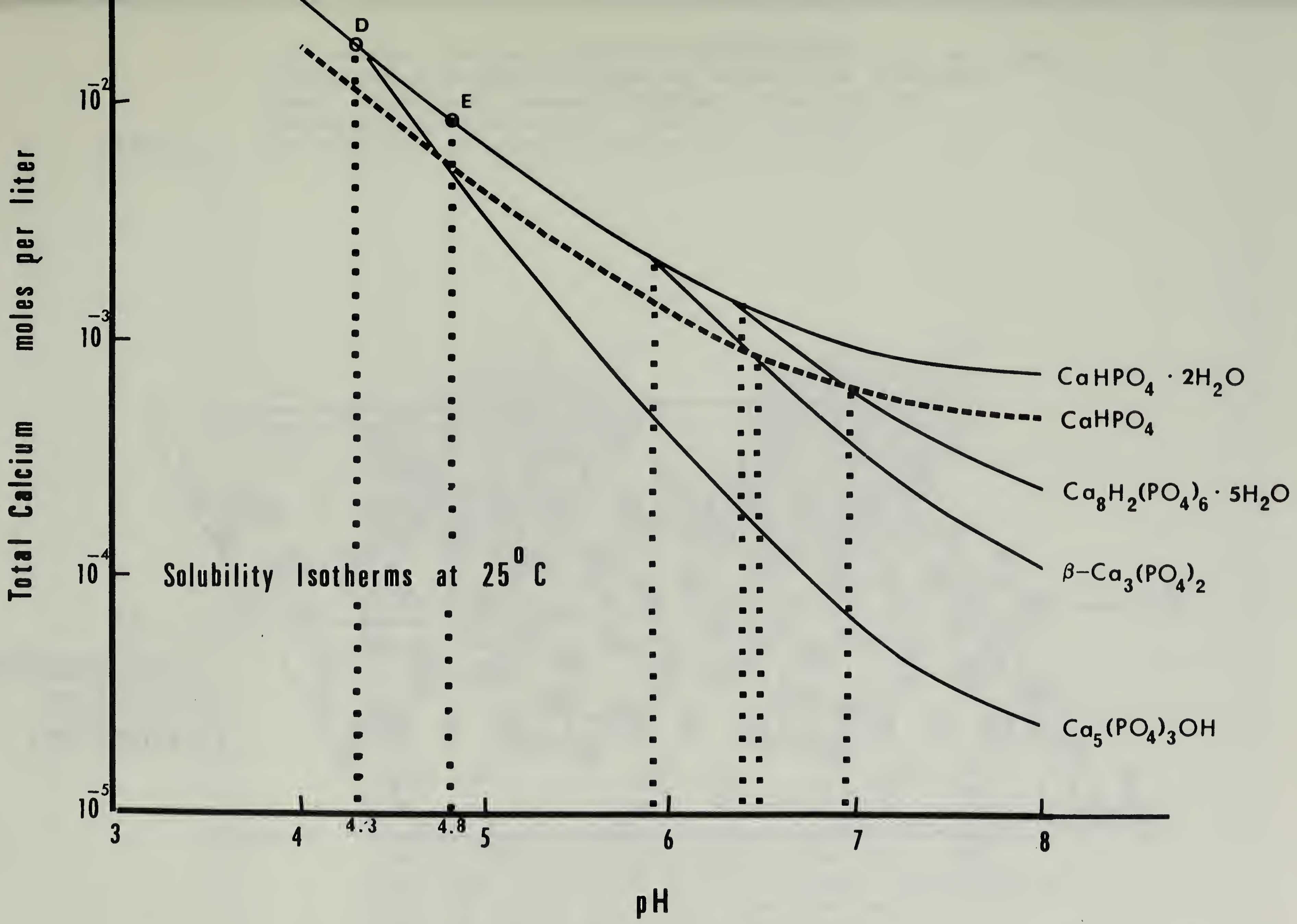

Figure 1: Calcium concentrations and pH values of solutions saturated with respect to various calcium phosphates in the ternary system, $Ca(OH)_2$-H_3PO_4-H_2O at 25°C. (Reproduced courtesy Clinical Orthopaedics, No. 44, 1966).

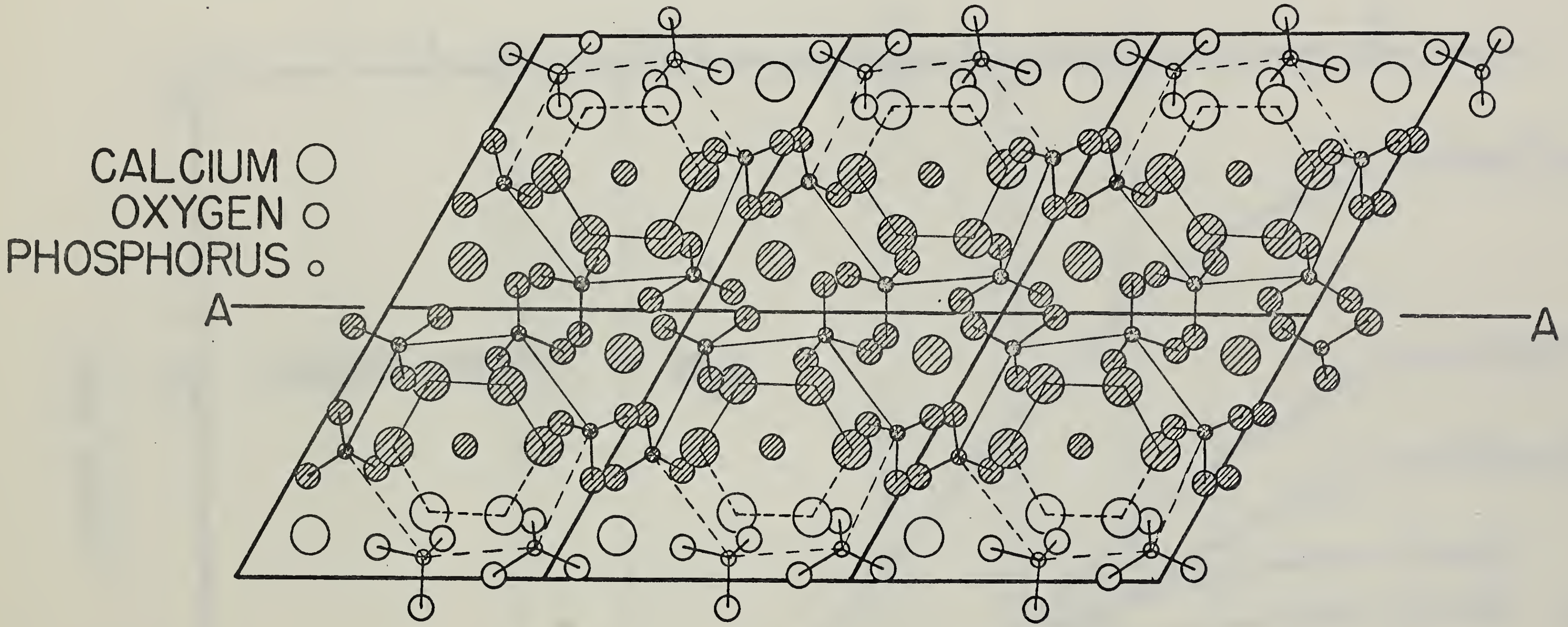

Figure 2. The structure of hydroxyapatite, $Ca_5(PO_4)_3OH$, projected into the *c* face. Six unit cells are shown. The line, A-----A, defines a plane of compatibility with the structure of octacalcium phosphate. (Reproduced courtesy Clinical Orthopaedics, No. 44, 1966).

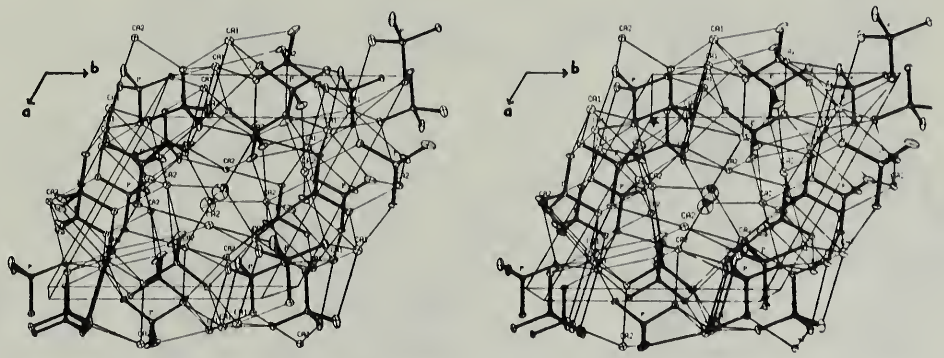

Figure 3. A stereoscopic drawing of the structure of hydroxyapatite as viewed approximately down the *c* axis. The atoms are denoted by their thermal ellipsoids so that the larger ellipsoids near the center of the diagrams (which have large librational motions) represent hydrogens and the smaller ones are the oxygens of the OH group.

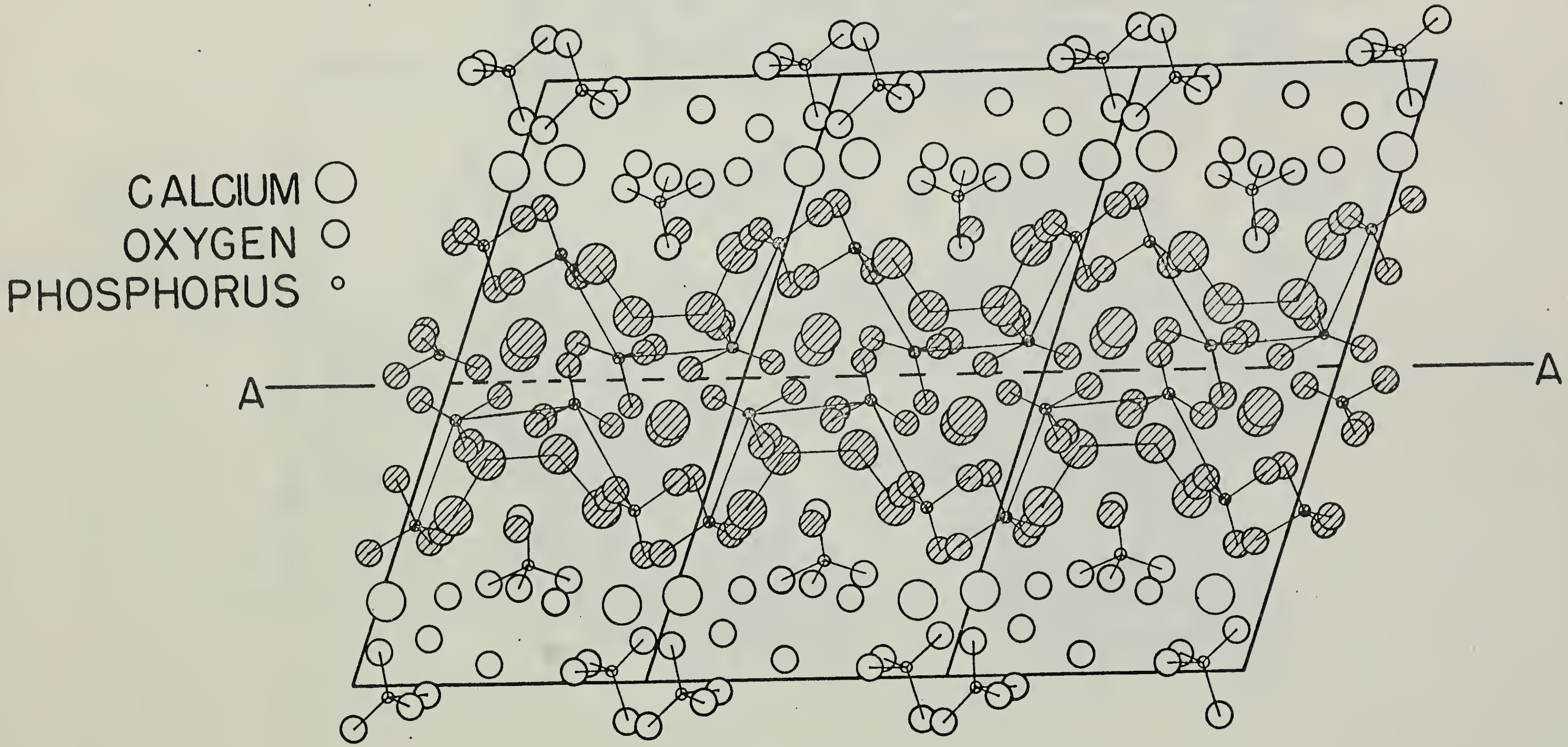

Figure 4. The structure of octacalcium phosphate, $Ca_8H_2(PO_4)_6 \cdot 5H_2O$ projected into the *c* face. Three unit cells are shown. The line, A----A, defines a plane of compatibility with the structure of hydroxyapatite.

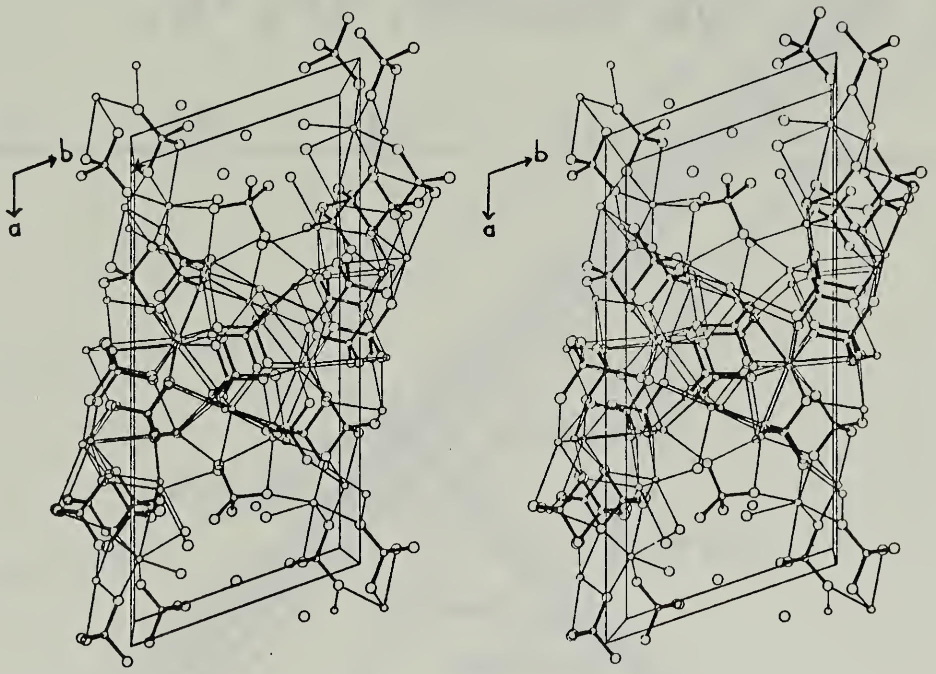

Figure 5. A stereoscopic drawing of the structure of octacalcium phosphate as viewed approximately down the *c* axis. The PO_4 groups are defined by the heavy lines and the calciums by circles that are smaller than those for the oxygens.

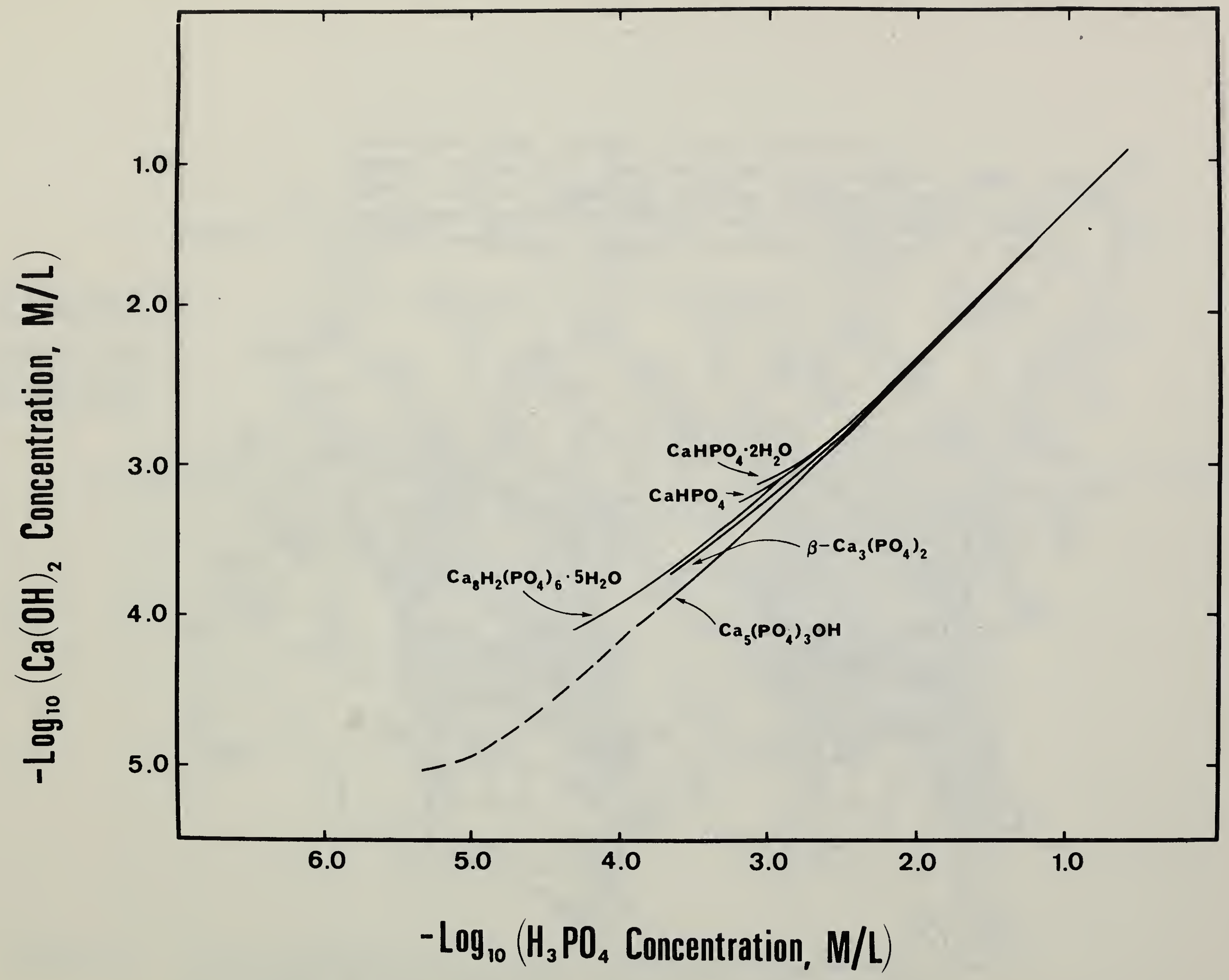

Figure 6. The phase diagram for the ternary system, $Ca(OH)_2$-H_3PO_4-H_2O at 25°C showing solubility isotherms for the salts $Ca_5(PO_4)_3OH$, β-$Ca_3(PO_4)_2$, $Ca_8H_2(PO_4)_6 \cdot 5H_2O$, $CaHPO_4$, and $CaHPO_4 \cdot 2H_2O$. The coordinates are the negative logarithms of the concentrations of $Ca(OH)_2$ and H_3PO_4. Broken lines represent calculated points.

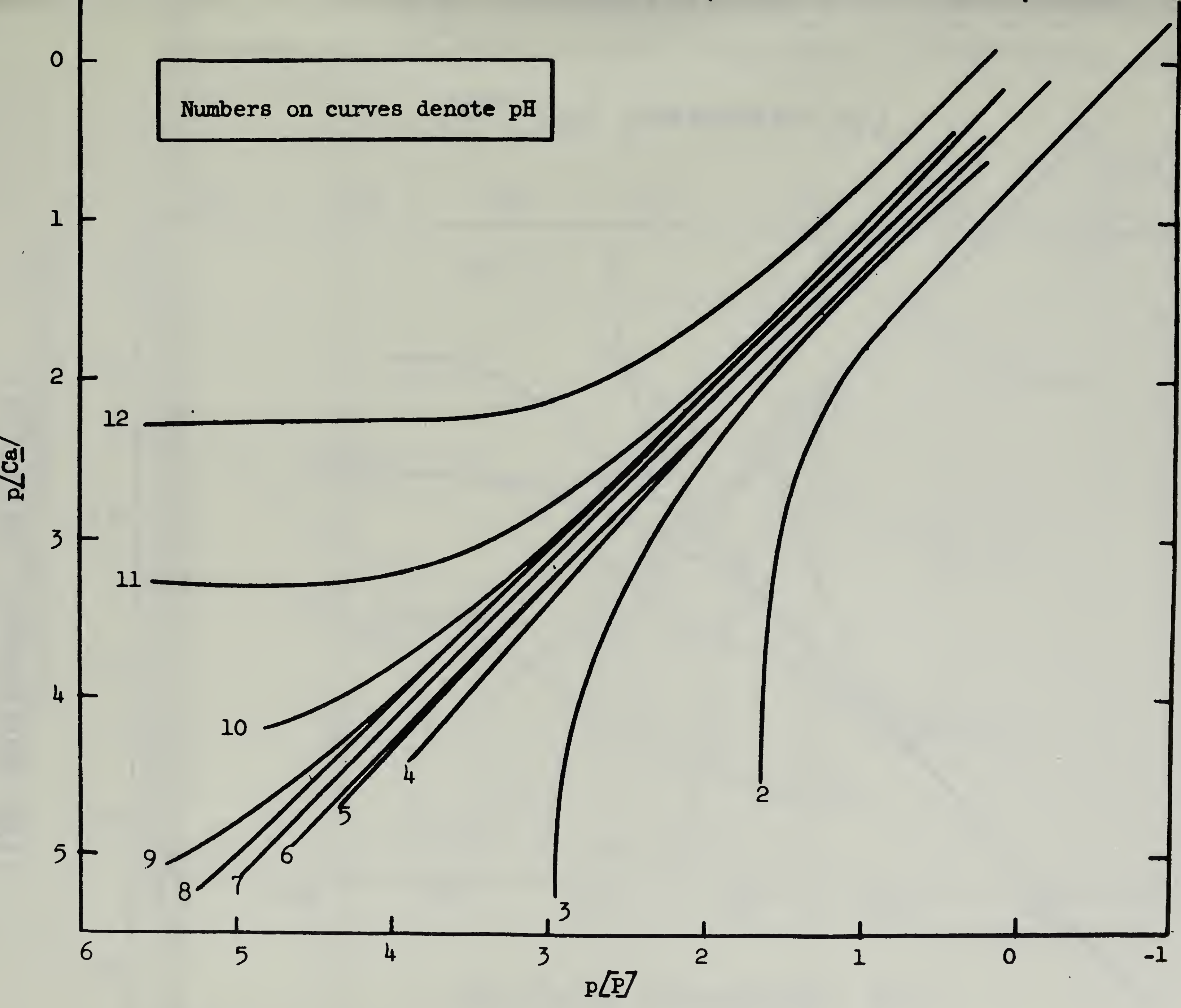

Figure 7. The electroneutrality surface for the ternary system, $Ca(OH)_2$-H_3PO_4-H_2O. The lines of constant pH represent contours of a surface in three-dimensional space in which pH is the vertical coordinate.

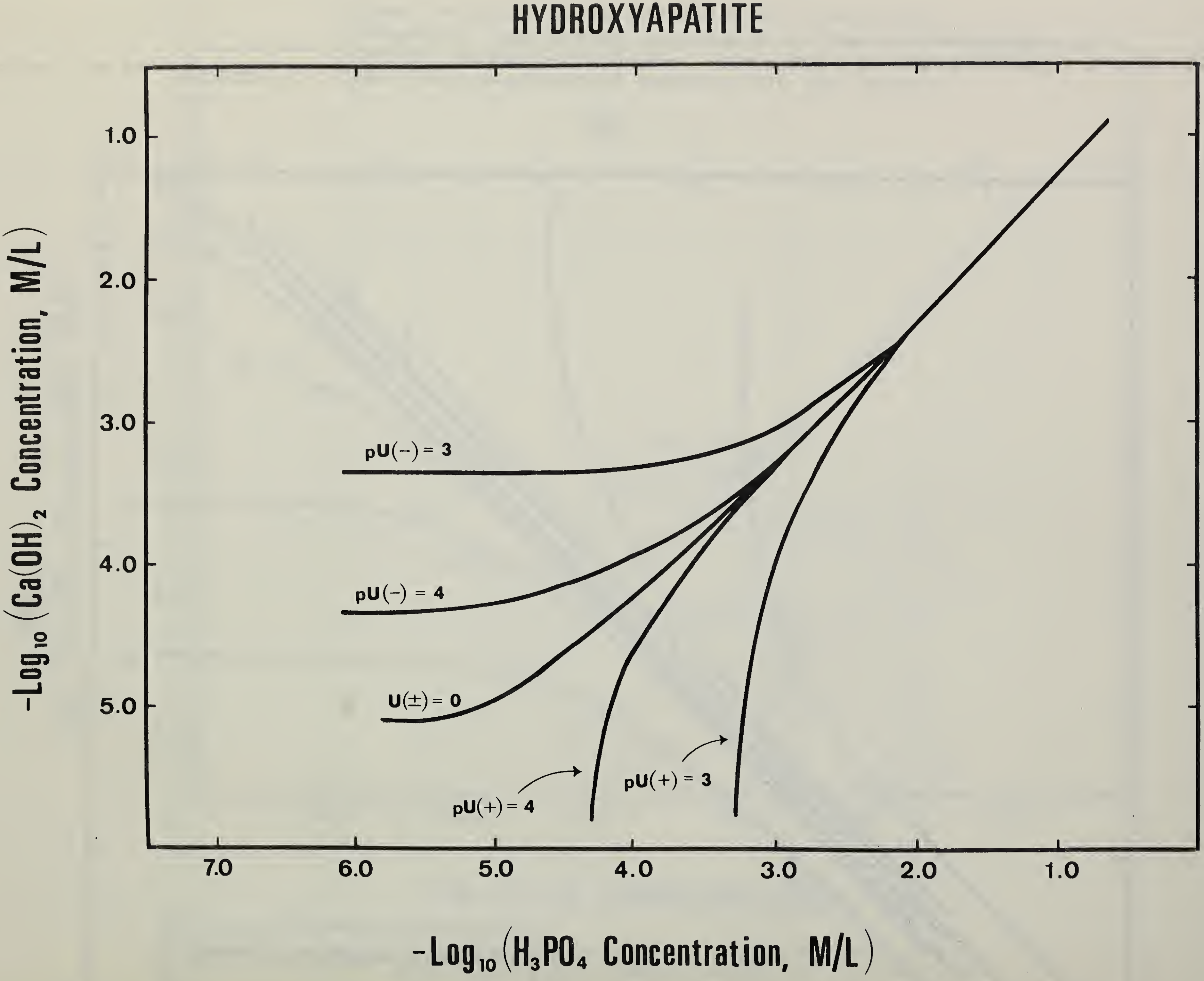

Figure 8. Calculated solubility isotherms for hydroxyapatite at 25°C in the "generalized four-component system", $Ca(OH)_2-H_3PO_4-H_2O-U(\pm)$. The concentrations of acid or base, $U(\pm)$, is defined by equations (15) and (16).

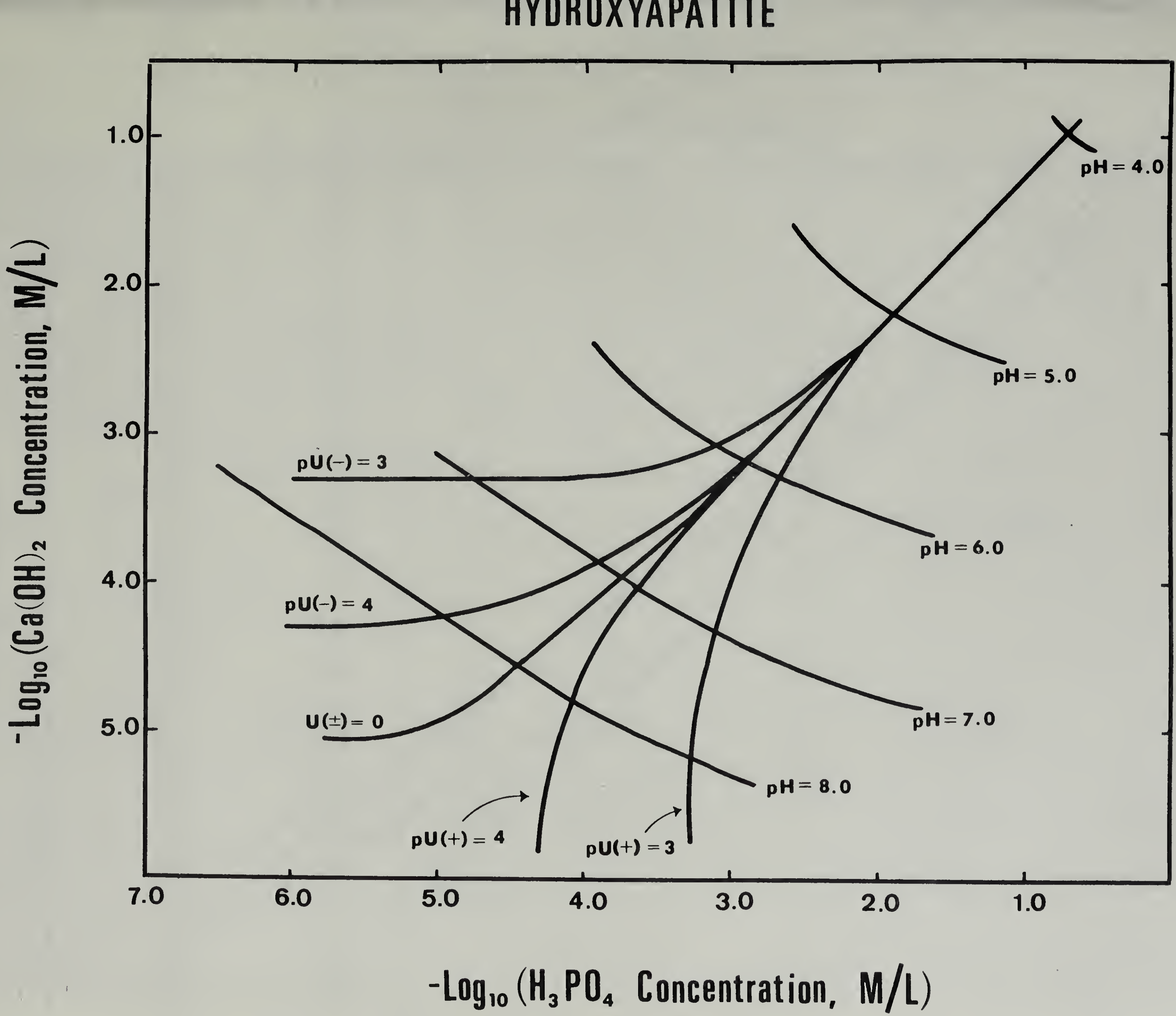

Figure 9. A repeat of Figure 8 showing lines of constant pH.

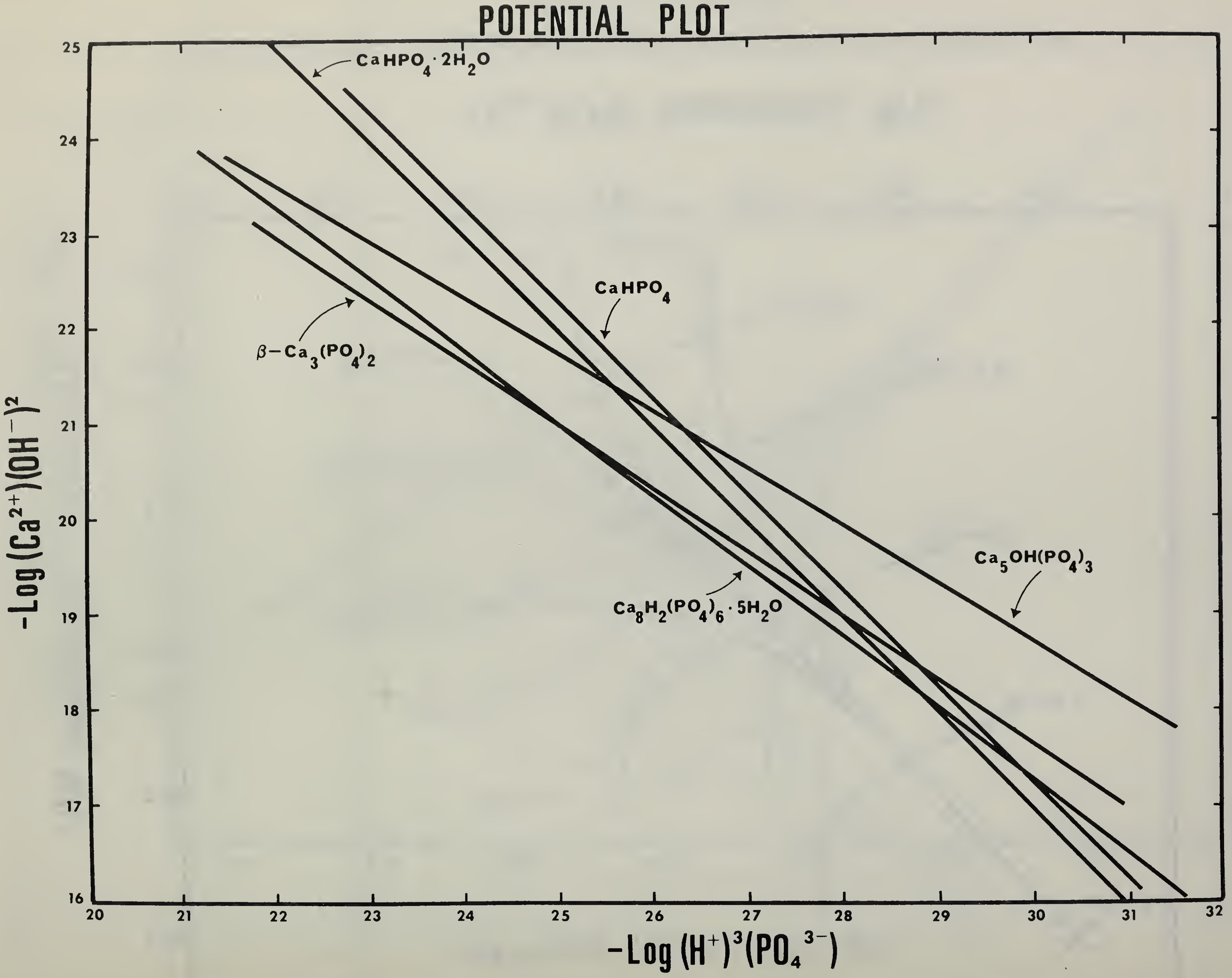

Figure 10. A "potential diagram" for calcium phosphates. The coordinates, the negative logarithms of the activities of the components $Ca(OH)_2$ and H_3PO_4, are proportional to the chemical potentials of these components.

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