Dissolution and Reprecipitation in Model Systems of Porous Hydroxyapatite

Studies of the attack of gel-stabilized suspensions of hydroxyapatite show dissolution at the boundary of the solid region and reprecipitation within this region. The results are apparently consistent with a theory which assumes that porous solid dissolution is diffusion-controlled but constrained by nonlinear solubility products.

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Introduction

Diffusion and reaction in porous solids are most completely analyzed for the special case of an irreversible, first-order chemical reaction. When the diffusion and reaction occur at comparable speeds, the analysis leads to the concept of an effectiveness factor, measuring the reduction in reaction caused by diffusion. When the diffusion is much slower than the chemical reaction, the analysis leads to concepts like the shrinking core model, in which chemical kinetics are unimportant.

In this work we are concerned with a different special case, that in which the chemical reaction is not irreversible and first order, but reversible and nonlinear. We will limit our concern to the special case where diffusion is much slower than the nonlinear reaction. However, the reversibility of this reaction will lead our investigation in a radically different direction than that of the shrinking core model.

As a focus for the work, we will emphasize the chief mineral in teeth, a nonstoichiometric calcium phosphate similar to hydroxyapatite. Pure hydroxyapatite is often given the formula $Ca_5(PO_4)_3OH$, but those assigning this formula to biological materials caution that the calcium-to-phosphorous ratio can vary by as much as two. Indeed, the name "apatite" itself reflects chemical frustration, for it is based on the Greek verb meaning "to deceive."

When teeth are immersed in an acid solution, their hydroxyapatite will dissolve. This dissolution, a step in the formation of dental caries, is a complex process (Lazzari, 1976). Part of the complexity comes from the fact that dental enamel is not completely solid, but contains about 15 vol. % voids filled with a gel of protein, lipid, and water. During dissolution, acid, dissolved calcium, and dissolved phosphate all can diffuse into these voids.

Dissolution of pure, porous hydroxyapatite can produce three different regions in the tooth (Featherstone *et al.*, 1979; Featherstone, 1983). First, at the surface of the tooth, mineral dissolves. Second, slightly below the surface, mineral reprecipitates, producing a region that may contain more mineral than was present in the original tooth. Third, still further below the surface, mineral again dissolves (Featherstone *et al.*, 1985, 1986). Similar effects have occasionally been reported in other minerals, including those used in ancient monuments (Rossi-Manaresi, 1976).

In this paper we report studies that attempt to explain the reprecipitation occurring slightly below the tooth's surface. Past efforts to explain this effect are not completely satisfying. Those that assume some type of microbial intervention cannot explain why the effect occurs *in vitro*. Those which assume a solubility of hydroxyapatite that is different within the tooth than in the bulk can fit the data, but include an assumption that cannot be independently checked. Those that assume kinetically controlled dissolution or the reprecipitation of different crystals than those which dissolve are good possibilities (Christofferson *et al.*, 1978; White and Nancollas, 1977; Featherstone *et al.*, 1979; Koutsoukos *et al.*, 1980). They are, for us, less complete than the explanation given below.

Theory

Our explanation is based on a new theory of dissolution of porous solids (Cussler, 1982; Cussler *et al.*, 1983; Fogler and Rege, 1986). This theory is similar to others for phase separations in alloys (Kirkaldy and Brown, 1963); for fog (Toor, 1971a, b); and for spontaneous emulsification (Ruschak and Miller, 1972). It assumes that many dissolutions are diffusion-controlled, so that any chemical reactions within the solid are near equilibrium. As an example, we consider the dissolution

$$\text{solid} + \nu H^+ = M + \text{water} \qquad (1)$$

where ν is a stoichiometric coefficient and M represents the dissolved species produced. We assume that everywhere within the

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porous solid,

$$[M] = K[\mathrm{H}^+]^{\nu} \tag{2}$$

where K is a solubility product of this solid. We then write the continuity equations for the metal ions and the acid

$$\frac{\partial[M]}{\delta t} = D\frac{\delta^2[M]}{\partial z^2} + r \tag{3}$$

$$\frac{\partial[\mathrm{H}]}{\partial t} = D\frac{\partial^2[\mathrm{H}^+]}{\partial z^2} - \nu r \tag{4}$$

where D is the diffusion coefficient, assumed equal for all species, and r is the dissolution rate. We then insert Eq. 2 into Eq. 3, use Eq. 4 to eliminate $\partial[\mathrm{H}^+]/\partial t$, and rearrange to obtain:

$$r = -\left[\frac{\partial^2[M]}{\partial[\mathrm{H}^+]^2}\right]\left\{\frac{D\left(\frac{\partial[\mathrm{H}^+]}{\partial z}\right)^2}{1+\nu\left(\frac{\partial[M]}{\partial[\mathrm{H}^+]}\right)}\right\}$$

$$= -[\nu(\nu-1)]\left\{\frac{D[M]\left(\frac{\partial \ln[\mathrm{H}^+]}{\partial z}\right)^2}{1+\nu^2\left(\frac{[M]}{[\mathrm{H}^+]}\right)}\right\} \tag{5}$$

Note that everything in braces in Eq. 5 is positive, so that the sign of r is controlled by the term $\nu(1-\nu)$. If $\nu < 1$, r is positive and the theory predicts dissolution. If $\nu > 1$, r is negative and the theory predicts reprecipitation within the porous solid. This theory predicts the correct results of sixteen of seventeen systems studied to date (Cussler *et al.*, 1983; Kopinsky, 1985).

We want to apply this theory to porous hydroxyapatite. To do so, we must recognize that this mineral can show different chemical equilibria depending on the local pH. If this pH is less than 2.1, then

$$\mathrm{Ca_5(PO_4)_3OH + 10H^+ = 5Ca^{++} + 3H_3PO_4^- + H_2O} \tag{6}$$

If calcium and total phosphate are stoichiometrically related, we can write the solubility equilibrium

$$[\mathrm{Ca^{++}}] = K[\mathrm{H}^+]^{10/5+3} \tag{7}$$

Thus ν is 10/8, greater than one. Eq. 5 then becomes

$$r = -\left\{\frac{5D[\mathrm{Ca^{++}}]\left(\frac{\partial \ln[\mathrm{H}^+]}{\partial z}\right)^2}{16+25\left(\frac{[\mathrm{Ca^{++}}]}{[\mathrm{H}^+]}\right)}\right\} < 0 \tag{8}$$

Since r is always negative, hydroxyapatite will precipitate under these conditions.

On the other hand, if the pH is between 2.1 and 7.2, the dissolution is

$$\mathrm{Ca_5(PO_4)_3OH + 7H^+ = 5Ca^{++} + 3H_2PO_4^- + H_2O} \tag{9}$$

If calcium and total phosphate are stoichiometrically related, then

$$[\mathrm{Ca^{++}}] = K[\mathrm{H}^+]^{7/(5+3)} \tag{10}$$

Thus ν is now 7/8, less than one. Thus

$$r = +\left\{\frac{7D[\mathrm{Ca^{++}}]\left(\frac{\partial \ln[\mathrm{H}^+]}{\partial z}\right)^2}{64+49\left(\frac{[\mathrm{Ca^{++}}]}{[\mathrm{H}^+]}\right)}\right\} > 0 \tag{11}$$

Thus r is always positive, and Eq. 11 predicts dissolution at this higher pH.

The implications of this theory for hydroxyapatite are summarized schematically in Figure 1. In this figure, the interface between bulk solution and solid is shown schematically by the vertical line. Bulk acid solution is to the left of the line; porous solid is to the right.

The acid dissolves the porous solid at this interface. This dissolution produces a maximum of dissolved calcium and phosphates near the interface. From this maximum, both calcium and phosphates diffuse to the left, into the bulk acid, and to the right, deeper into the solid's pores. Acid also diffuses into the pores. Near the surface but within the solid, this simultaneous diffusion of calcium, phosphates, and acid leads to reprecipitation of the original solid, as described by Eq. 8. Farther into the pores, at higher values of pH, the diffusion of acid and dissolved solids results in dissolution, as described by Eq. 11. As a result, a porous hydroxyapatite that has a constant original concentration should develop an eroded surface, a depleted core, and an intermediate region where there is a higher solid concentration than was originally present.

In the following sections of this paper we test these predictions for dilute hydroxyapatite suspensions stabilized within

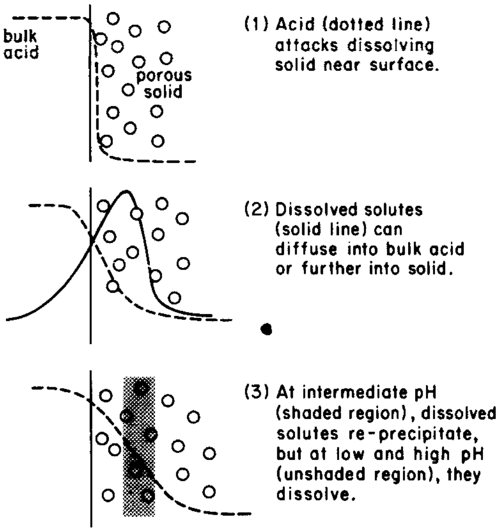

Figure 1. Dissolution of porous hydroxyapatite.

Bulk acid on the left is diffusing into the porous hydroxyapatite on the right. The acid dissolves solid at the surface, producing a maximum in dissolved calcium and phosphates. These dissolved solutes diffuse both into the bulk acid and into the solid's pores. Within the pores, they may reprecipitate under conditions outlined in this paper.

gels. We describe how these experiments were made, and then report the results. Finally, we explore how these experiments elucidate the dissolution and reprecipitation of this particular porous material.

Experimental Method

Because the experiments are described in great detail elsewhere (Kim, 1985), only a synopsis is given here. The porous solids used in this work consisted of dilute suspensions of hydroxyapatite (Bio-Gel HTP, Biorad Labs) suspended in aqueous gelatin (100 Bloom type B, Fisher). These gels were challenged by solutions of hydrochloric acid (Fisher) or lactic acid (Fisher), which in some cases contained sodium dihydrogen phosphate (Baker) or calcium chloride (Mallinckrodt). Other chemicals used in analysis were a universal pH indicator (pHydrion, VWR), ammonium molybdate (Spectrum), sulfuric acid (Mallinckrodt), ascorbic acid (Eastman), and sodium hydroxide (Fisher). All these materials were reagent grade.

The experiments involved three steps: making the gel-stabilized suspensions, cutting them into slices, and analyzing the slices. The gel suspensions were made in 6 cm^3 disposable syringes that had both ends cut flat. The syringes contained a close-fitting steel piston. They were filled with a suspension of 0.5 g hydroxyapatite powder (particle diameter: 53–63 10^{-6} m) in 10 g gelatin, ten drops of pH indicator, and 50 g doubly distilled water.

Each test syringe was dropped into a stirred Erlenmeyer flask containing 250 mL of acid solution at the desired concentration. After a known time, the syringe was removed and clamped in a microtome (American Optical Model 880). The gel was forced out of the syringe with the piston and cut into slices about 0.05 cm thick. The slices were weighed and set aside.

The mineral composition of each slice was determined as follows. The slice was dissolved in 5 cm^3 of concentrated HC*l* and diluted with 30 cm^3 of water. Total calcium concentrations were measured by atomic absorption spectrophotometry (Buck Model 200), and total phosphate concentrations were measured by UV-visible spectrophotometry (Perkin-Elmer Model 139) as the phosphomolybdate (Fogg and Wilkinson, 1958). The pH of the slices was measured differently. The slice of sample gel was placed in a 25 mL graduated cylinder and soaked with 8 cm^3 distilled water. After more than 30 min of soaking time, we measured the hydrogen ion concentration with a Coleman model 39 pH meter. These direct measurements of pH were always consistent with those inferred from the pH indicator. In addition, the acid solution and the gelatin were analyzed for calcium, phosphate, and pH before each experiment.

These measurements give the total concentrations of calcium, phosphate, and hydrogen ion in the system. We are more interested in the concentrations of dissolved calcium, dissolved phosphate, and undissolved hydroxyapatite that are present in each slice. To calculate these new concentrations from our measurements, we need to know the equilibrium constants in Eqs. 7 and 10. We used the literature values of $10^{21.3}$ $(mol/L)^{-2}$ and $10^{15.0}$ mol/L, respectively (Avnimelech *et al.*, 1973; Chuong, 1973; Moreno *et al.*, 1975).

Results

The experiments made in this work study the dissolution of porous solids modeled as gel-stabilized suspensions. The results are best presented in three groups: those showing the homogeneity of the original suspensions; those giving the measured total concentrations; and those reporting the calculated concentrations of dissolved ions and of solid. The homogeneity of the suspensions before the addition of acid is illustrated in Figure 2, which shows the calcium concentration vs. position in two of the gel suspensions. Because the calcium concentration is constant within 10%, the hydroxyapatite concentration is as well. As a result, the gel-stabilized suspensions do show the step function in solids needed for these experiments.

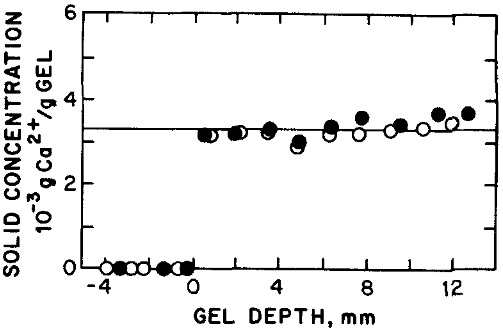

Figure 2. Initial hydroxyapatite concentration within gel suspension.

Open and closed circles are two independent experiments. Concentration of calcium outside of the suspension is zero, but jumps to a constant value within the suspension. Thus the concentration profile of hydroxyapatite is initially a step function, as assumed in the theory used here.

The concentrations of total calcium, of total phosphate, and of pH are reported vs. position *z* and time *t* in Figures 3–5. In these figures, the data are plotted vs. position/ $\sqrt{time}$ because such a plot superimposes the data. Plots *vs.* the cube root of time (Arends and Christofferson, 1986) do *not* superimpose our data. The superposition vs. (distance/ $\sqrt{time}$) is common in free-diffusion problems, and is the basis for the Boltzman transformation for diffusion in an infinite slab (Cussler, 1984). Its use here is empirical. For simpler chemical equilibria than those involved here, one may show that this superposition is theoretically justified (Kopinsky, 1985).

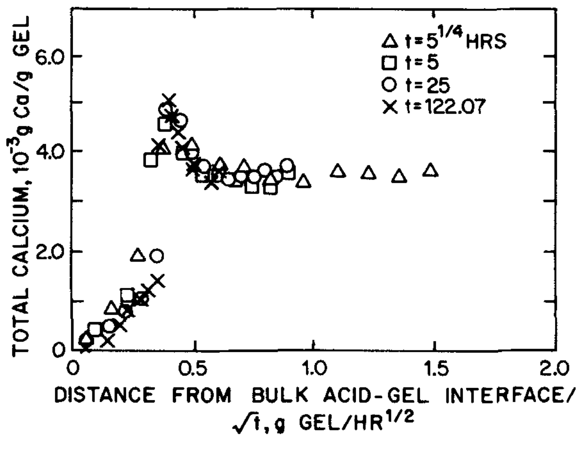

Figure 3. Total calcium concentration.

A gel-stabilized suspension containing 0.83 wt. % hydroxyapatite is attacked by excess 0.1 M HCl. Total calcium concentration measured is near zero in the bulk acid at zero distance, and reaches a constant value characteristic of hydroxyapatite at large distance.

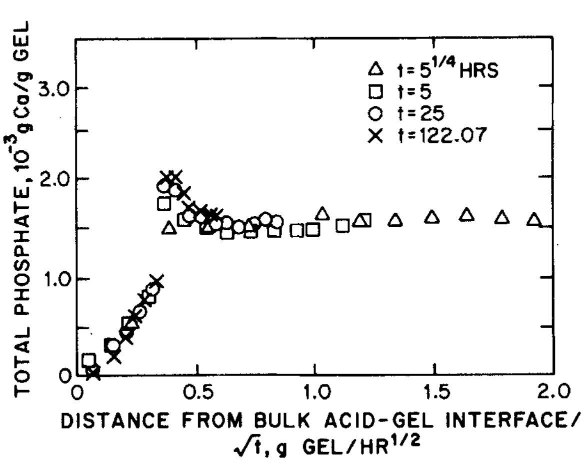

Figure 4. Total phosphate concentration.

Experiments under the same conditions as in Figure 3. Total phosphate concentration is given as a function of position and time. The maximum shown includes reprecipitation of additional solid caused by dissolution at the boundary of the solid region.

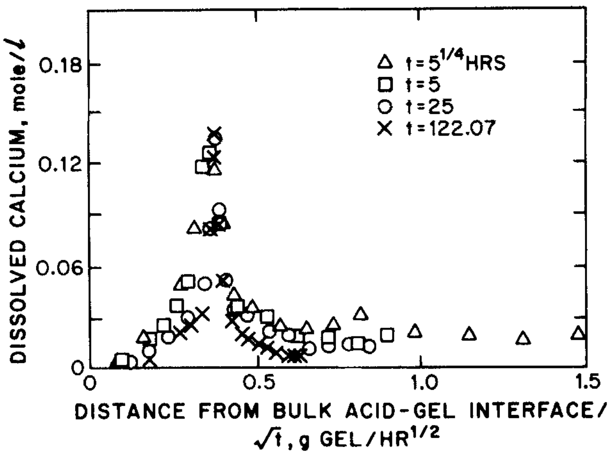

Figure 6. Dissolved calcium vs. distance and time.

Data represent the calcium ion dissolved in solution, and hence differ from those in Figure 3, which are the total of dissolved calcium and calcium in solid. The maximum at the boundary of the solid region is produced by dissolution.

The variations of total calcium and phosphate are complex. They are zero at the gel interface, where any dissolved solutes are greatly diluted by the stirred bulk acid. They rise to a sharp maximum, which is located just within the region of suspended solid. They then fall, asymptotically approaching the limit of homogeneous solid originally present in the gel. The variation of pH is simpler, beginning at the value present in the 0.1 M bulk acid, rising sharply at the solid boundary, and then approaching the value in the original gel. We were surprised at how low the pH in the gel is; it is unaltered by the presence of hydroxyapatite.

The concentrations of dissolved calcium and of total dissolved phosphate calculated from these data are shown in Figures 6 and 7. The phosphate concentration in Figure 7 is the sum of H_3PO_4 and $H_2PO_4^-$; the relative importance of these two is of course controlled by the pH. The calculated concentrations are again plotted vs. position/ $\sqrt{\text{time}}$ to superimpose the data. Both dissolved calcium and phosphate concentrations show a sharp maximum at the moving boundary of the suspended solid region located at about 0.3 g gel/h$^{1/2}$. At smaller distances, the dissolved species are diffusing into the bulk acid; at greater distances, they are diffusing deeper into the suspended solid, where they may reprecipitate.

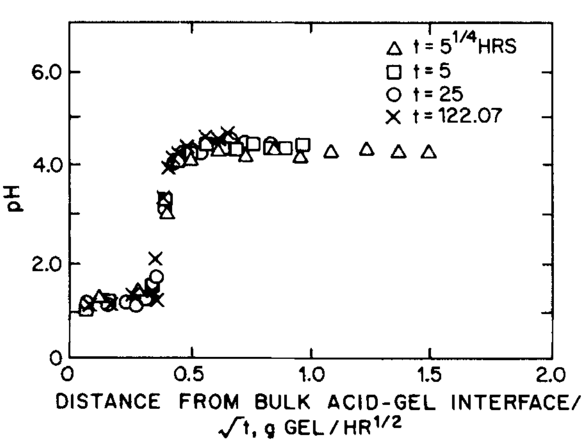

Figure 5. Acid concentration during dissolution.

pH measured vs. position and time under same conditions as in Figures 3–4. Measurements by titration are within experimental error of those found using a pH indicator (Kim, 1985).

That they do reprecipitate is shown in Figure 8. Here, the concentration of the solid is zero at small values of $z/\sqrt{t}$. It reaches its initial value at large values of this quantity. At intermediate values of $z/\sqrt{t}$ the solid concentration reaches a maximum, exceeding the concentration of solid that was originally present. By comparing Figure 8 with Figures 6 and 7, we see that this maximum in solid is located within the solid, at larger values of $z/\sqrt{t}$ than the solid boundary where the maxima in Figures 6 and 7 are located. The maximum in solid shown in Figure 8 represents reprecipitation of solid.

We also found reprecipitation under other chemical conditions (Kim, 1985). We found it when the solid was attacked with solutions of (0.1 M HCl + 0.1 M NaH_2PO_4), of (0.1 M HCl + 0.1 M $CaCl_2$), and of (0.1 M HCl + 0.1 M NaH_2PO_4 + 0.1 M $CaCl_2$). We could not measure any maximum for attack with 0.01 M HCl or with 0.1 M lactic acid. We occasionally saw a

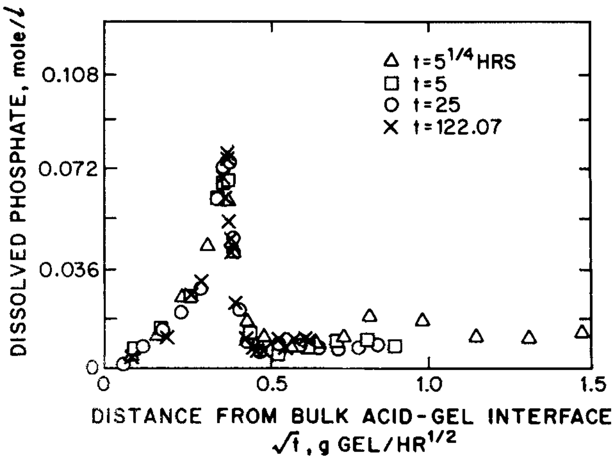

Figure 7. Dissolved phosphates vs. position and time.

Like the dissolved calcium shown in Figure 6, the dissolved phosphates are low in the bulk acid and well within the gel-stabilized suspension. They also show a high value at the boundary of the solid region.

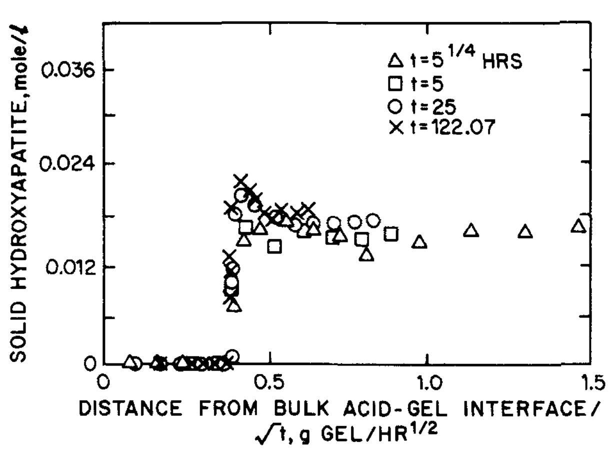

Figure 8. Solid concentration vs. position and time.

The initial solid concentration profile shown in Figure 2 is changed into the profile shown here by the dissolution. At small distances, solid concentration is zero; at large distances, it approaches the value in the original suspension; at intermediate distances, it shows the reprecipitation predicted by Eq. 6.

tendency toward a minimum in solid concentration far within the solid region, which would be consistent with the dissolution at higher pH implied by Eq. 11. However, this apparent minimum was within the error in our original distribution of solid and hence is not proven.

Discussion

The results presented above show reprecipitation within gel-stabilized suspensions of hydroxyapatite. This reprecipitation is predicted at lower pH by Eq. 8. The results above do not prove or disprove dissolution far within the suspension. Such dissolution is predicted at higher pH by Eq. 11.

We want to reexamine the predictions in the light of these results. The dissolution theory assumes that all solutions are ideal, an assumption that we continue to believe is a valid first approximation. It assumes no supersaturation, which seems reasonable because solid is always present in the solid region. This means that the effects observed here occur under different conditions than those encountered for Liesegang rings (Kai *et al.*, 1982; Venzl and Ross, 1982). The dissolution theory assumes that all diffusion coefficients are equal, which certainly is not true. However, numerical calculations with unequal diffusion coefficients show little effect (Kopinsky, 1985).

The theory makes two more serious assumptions. The first is that the diffusion is one-dimensional, unaffected by the local geometry of the suspension. This is equivalent to the assumption that

$$\frac{\ell^2}{4Dt} \ll 1 \tag{12}$$

where ℓ is the distance between the particles. For our suspensions, ℓ is about 0.02 cm, D is near 10^{-5} cm^2/s, and t is at least an hour, so this inequality easily holds. The second serious assumption is that the dissolution is diffusion-limited, that any chemical reactions have half-lives that are much faster than the characteristic diffusion time of one or more hours. While the ionic reactions certainly vary widely, those here are expected to be fast, at least in 0.1 M HCl.

As a result, we expect this theory to hold under the conditions used in our experiments. We believe that the reprecipitation observed is due to the diffusion and nonlinear chemical reaction described in the first section of the paper. This reprecipitation is interesting because it is counterintuitive. After all, dissolution is not expected to do anything but dissolve. The suggestion that it can cause dissolution in some regions and reprecipitation in others is unexpected and hence interesting. At the same time, we are not sure why the expected subsurface dissolution does not appear. It may be there, but be too small to measure. It may be inhibited by the relatively low pH of the gel. It may be due to chemical reactions too slow to reach equilibria.

These results may have implications for dental caries (Lazzari, 1976). As implied in the introduction, dental caries begin when the tooth is attacked by microbially generated acid. The acid causes demineralization near the tooth surface, remineralization slightly below this surface, and occasional demineralization still farther below the surface. If remineralization is equivalent to reprecipitation of hydroxyapatite, then the theory and experiments given in this paper explain this effect. This explanation is consistent with known chemistry and is without recourse to any biochemical or microbiological intervention.

The results have implications for diffusion and reaction in porous solids. When the reaction is reversible and nonlinear, it can occur in one direction in some regions of the system and in the opposite direction in other regions. Such unexpected behavior signals unexplored richness in a classical chemical engineering field.

Acknowledgment

This work was largely supported by National Science Foundation Grant Nos. CPE80-25304 and CPE84-08999. Other support came from the Celanese Corporation.

Notation

D = diffusion coefficient
$[i]$ = molar concentration of species i
K = equilibrium constant
ℓ = distance between particles, Eq. 12
r = dissolution rate
t = time
z = position
ν = stoichiometric coefficient, Eq. 1

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Manuscript received Aug. 11, and revision received Oct. 27, 1986.