Role of adsorbed fluoride ions on the dissolution of synthetic hydroxyapatite

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The dissolution kinetics at 37 °C and for constant pH values of 5.0 and 6.0 are studied for calcium hydroxyapatite (HAp) equilibrated at pH 7.0 in the presence of 1 or 10 ppm of F^-. Experiments are realized using an automatic setup which allows a continuous record of proton uptake and calcium or fluoride activities in solution using specific electrodes. It is shown that the presence of fluoride ions affects the dissolution kinetics in two ways. Their presence at the HAp interface reduces the final solubility of HAp, but accelerates the initial dissolution rates. Both observations are fully interpreted using the HAp dissolution model recently developed. According to this model, apatite dissolution is auto-inhibited by the adsorption at the solid interface of calcium ions forming a cationic semi-permeable layer. Adsorbed fluoride ions interact with this natural cationic layer, decrease its ionic capacity and accelerate the dissolution process.

1. Introduction

Hydroxyapatites $Ca_{10}(PO_4)_6(OH)_2$ (HAp) have been investigated and used as tooth replacement [1], bone substitution [2], jaw augmentation [3] and middle ear reconstruction [4] because of HAp's biocompatibility owing to their similarity with natural tooth and bone minerals. Several investigations [5, 6] also demonstrated that coating metal implants with a HAp layer enhances implant performance because of the establishment of rapid significant interfacial attachment. Fluoride is also thought to be an essential trace element present in saliva and plasma, and is required for normal dental and skeletal development [7]. At a fluoride intake level of 1.5–4 mg/day, dental caries are significantly reduced [8]. Simonen and Laitinen [9] reported a decrease in hip fracture in a fluoridated community compared with a neighbouring non-fluoridated community. Numerous studies [10] have been devoted to the determination of the role of fluoride ions in enamel caries as well as in the dissolution process of synthetic hydroxyapatites. In this respect, the solubility reducing effect of fluoride ions for hydroxyapatite has been extensively described, but the mechanism by which fluoride ions act is far from clearly understood [11]. Recent analyses [12] demonstrated that fluoride ions present in solution, rather than included in the lattice, had the strongest influence on apatite dissolution.

The effect of fluoride ions can, however, only be clearly interpreted when the apatite dissolution and the surface fluoride interaction mechanisms are well

understood. Despite the fact that these aspects have been extensively investigated in the two last decades, both aspects have been the aim of an experimental and theoretical work in our group. Based on a careful experimental approach [13], we have recently proposed a quantitative model [14, 15] for the dissolution of HAp. In this model the dissolution process is auto-inhibited by the rapid formation at the solid interface of a semi-permeable layer due to the strong adsorption of the ions liberated by the acidic attack. The adsorbed ions play a similar role to the fixed charges within an ionic membrane and restrict strongly the diffusion of the ions liberated by the dissolution. We demonstrated that the driving force is the degree of saturation of the bulk solution with respect to HAp. Uptaken proton fluxes J_H and released calcium fluxes J_{Ca} during dissolution were simply expressed by a first-order law

$$- J_H = RJ_{Ca} = RP^OCa(a_S - a)/(1 + k) \quad (1)$$

with

$$P^OCa = DS/\varepsilon \quad (2)$$

in which R (depending on pH) corresponds to the number of protons needed for the release of one calcium P^OCa is the mass transfer coefficient in the Nernst layer adjacent to the solid interface and in the absence of any chemical reaction. D is the diffusion coefficient of calcium ions in water, S the specific surface area of apatite and ε represents the thickness of the Nernst layer. a_S is the saturated calcium activity at the solid interface and a the calcium activity in the

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bulk solution. The $(1 + k)^{-1}$ factor characterizes, comparatively to the Nernst layer, the permeability reduction due to the semi-permeable membrane. Equation 1 clearly demonstrates a process controlled by two different parameters: the degree of saturation of the bulk solution with respect to HAp (given by the term $a_S - a$) and the permeability of calcium ions through the ionic membrane described by the term $(1 + k)^{-1}$. When a congruent HAp dissolution occurs then the calcium a_S value corresponds to the calcium activity a in the solution at equilibrium. In the quantitative proposed model k is pH dependent and a function of the calcium adsorption characteristics [14] (number of adsorption sites and binding energy).

In this paper, the dissolution kinetic of a synthetic HAp are studied for constant pH values and with the presence of fluoride ions in the solution. We used the same experimental setup, as for previous studies [16]. This equipment allows us to follow the proton uptake and the calcium or fluoride activities in the solution continuously over time. The effect of two initial fluoride concentrations (1 and 10 ppm) were evaluated since the adsorption of these ions on the apatite interface have previously been studied under the same experimental conditions [17].

2. Materials and methods
Experiments were realized at 37 °C, with 10 mg HAp platelets (160–200 μm, Ca/P = 1.63) (Biogel HTP, Bio-rad Laboratories, Richmond, USA), having a specific surface area of 45 m² g^{-1} in a reactor containing 50 ml of solution, in the presence of 8×10^{-2} M KCl and at a stirring speed of 1000 rpm. The reactor included a water tight cover, an argon bubbling system, a combined pH electrode, a calcium electrode (Orion Research, type 93-20) and a fluoride electrode (Orion Research, type 94-09). The equipment comprises two Mettler pH-stat units (type DL-21) linked to a microcomputer [16]. The pH and F$^-$ and Ca^{2+} concentrations within the bulk solution were followed versus time. In a series of preliminary experiments, the behaviour of electrodes was carefully checked [17]. All salts employed (KCl, CaF$_2$, KF, HCl, KH$_2$PO$_4$) were of analytical grade. For a typical experiment HAp powder is first equilibrated for 2 h at pH 7 in the presence of none, 1 ppm (5.26×10^{-5} M) or 10 ppm (5.26×10^{-4} M) fluoride ions. Then, pH is decreased to the dissolving pH value (5.0 or 6.0) by rapid acid addition, and maintained constant. For the kinetics lasting over 5 h, proton uptake and calcium or fluoride activities in solution were followed continuously versus time. For all the selected conditions 10 mg of HAp represented a large excess with respect to the activities present in solution at the end of the dissolution period. Thus, the calcium activities (a_S) at dissolution equilibrium could be measured in similar experiments after 12 h of reaction (time after which both proton uptake and calcium activity remained unchanged). The following values of $a_S = 7.64 \times 10^{-4}$ M and 5.61×10^{-4} M were, respectively, determined in the presence of 1 or 10 ppm of fluoride at pH 5.0, whereas at pH 6.0 these values were, respectively, 1.79×10^{-4} M and 1.58×10^{-4} M. Kinetics were quant-

itatively analysed up to a conversion of 30%, a percentage for which the shape of HAp platelets remained unchanged [13].

3. Results and discussion
3.1. Fluoride adsorption onto HAp
In order to analyse quantitatively the dissolution kinetics in the presence of fluoride, it is first necessary to know precisely the behaviour of these ions before and during the dissolution process. Figs 1 and 2 give the variations of the adsorbed fluoride amounts on HAp in the initial presence of 1 (Fig. 1) or 10 ppm (Fig. 2). Each figure describes the fluoride adsorbed during the equilibrium step (up to 120 min) at pH 7.0 and during the following dissolution stage at a constant pH of 5.0. Uptaken amounts of fluoride (G_{F^-}) were calculated by depletion from bulk activities. In the presence of 1 ppm fluoride (Fig. 1), a plateau with
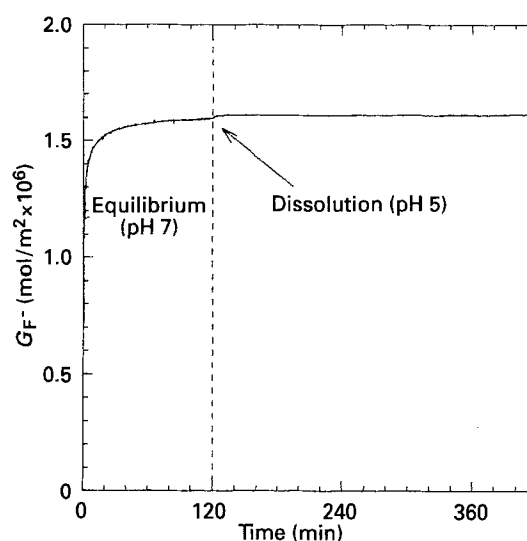

Figure 1 Kinetics of fluoride adsorption G_{F^-} onto HAp before and during acid dissolution at pH 5.0. Initial fluoride added was 1 ppm. Arrow indicates passage from equilibrium to dissolution step by HCl addition.
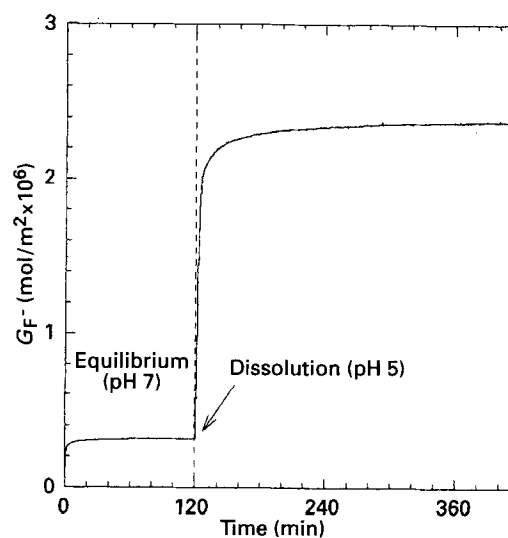

Figure 2 Kinetics of fluoride adsorption G_{F^-} onto HAp before and during acid dissolution at pH 5.0. Initial added fluoride was 10 ppm. Arrow indicates passage from equilibrium to dissolution step by HCl addition.

an adsorbed amount of 1.6×10^{-6} mol m^{-2} is rapidly reached. The subsequent decrease of pH to 5.0 (arrow) does not induce any further evolution in the uptaken amounts. These data confirm our previous results [17] and correspond to Langmuir-adsorption. It was also earlier shown that for these conditions the main adsorbed ions are $H_2PO_4^-$ and F^- (fixed in a ratio of 1.5) together with some calcium ions. When 10 ppm of fluoride (Fig. 2) are initially added, the adsorbed amount becomes 10 times higher (23.8×10^{-6} mol m^{-2}) as soon as pH is decreased from 7 to 5. This large increase corresponds to a precipitation of CaF_2 at the HAp surface [17]. The solubility limit for CaF_2 in our experimental conditions is 4×10^{-4} M, a value not very different from the fluoride concentration (5×10^{-4} M) reached at equilibrium. The ability for supersaturation of CaF_2 solutions explains why one observes an important activation of the CaF_2 precipitation only after pH decrease, which leads to a strong increase of the interfacial calcium and phosphate activities. In similar conditions, the previous studies showed that Ca^{2+}, F^- and $H_2PO_4^-$ were absorbed at the interfaces in the ratios $Ca^{2+}/F^- = 0.4$ and $H_2PO_4^-/F^- = 1$.

3.2. Dissolution kinetics

Figs 3 and 4 show the proton uptake (a) and calcium release (b) kinetics for experiments lasting 5 h at pH 5 (Fig. 3) or pH 6 (Fig. 4) in the presence of 0, 1 and 10 ppm of initially added amounts of fluoride. Analysis of the kinetic curves show two characteristic fluoride effects. First, a well-known property, the presence of fluoride ions in solution decreases the total proton amount necessary to attain the final equilibrium and the higher the fluoride concentration present in solution, the lower the amount of protons consumed to reach equilibrium. The same observation is also valid for the released calcium amounts and is confirmed by the important decrease of the saturating calcium activities (see section 2). Secondly, the initial dissolution rates are accelerated by fluoride addition and increase with the amount of fluoride added. This
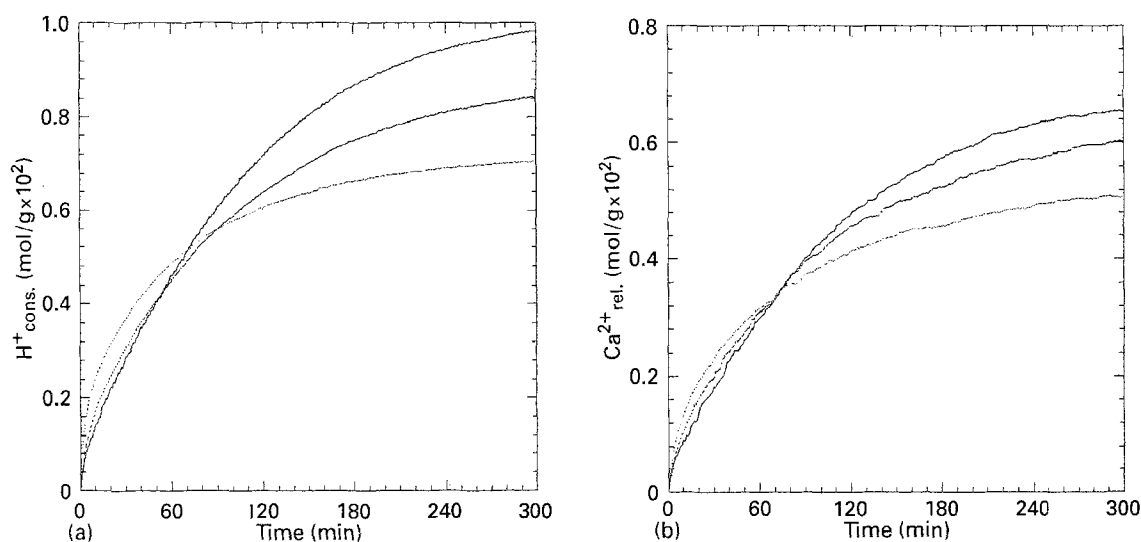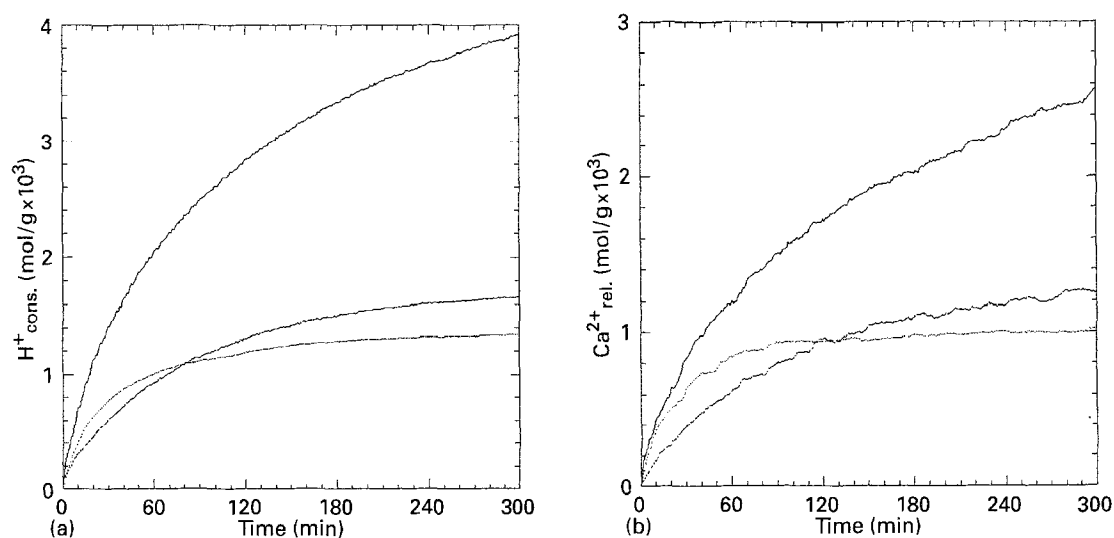

Figure 3 HAp dissolution kinetics at pH 5.0 (with and without the presence of fluoride ions). (a) and (b) correspond, respectively, to the proton uptake and calcium release curves. (— [F^-] 0 ppm; – – – [F^-] 1 ppm; ..... [F^-] 10 ppm).

Figure 4 HAP dissolution kinetics at pH 6.0 (with and without the presence of fluoride ions). (a) and (b) correspond, respectively, to the proton uptake and calcium release curves. (— [F^-] 0 ppm; – – –[F^-] 1 ppm; ..... [F^-] 10 ppm).

acceleration is particularly well observed at pH 5.0 (Fig. 3a and 3b).

In order to check the congruency of the dissolution kinetics and to verify that the dissolution process is in agreement with the chemical reaction, the ratios $R = Q_H/Q_{Ca}$ between the amounts of protons consumed and calcium released were analysed at each pH value (Fig. 5). It is observed that, after about 2–3 h, the theoretical values are attained ($R_{th} = 1.392$ and 1.327 at pH 5 and 6, respectively). However, the deviation from congruency ($R > R_{th}$) at the beginning of the dissolution process is important. This was also observed in the absence of fluoride ions and interpreted as an accumulation of calcium at the interface [18].

The experiments can be interpreted by considering relation 1 and evaluation of the concentration gradient ($a_S - a$) which can be easily calculated knowing the a_S values (see section 2) and the calcium activity given by the calcium electrode. For the evaluation of k we have also to estimate P^OCa obtained by taking [13] for the diffusion coefficient of calcium ions $D = 1.34 \times 10^{-5}$ cm^2 s^{-1} and for the thickness of the Nernst layer $\varepsilon = 5 \times 10^{-3}$ cm. The variation of the rate reduction factors $1/(1 + k)$ up to a conversion percentage of 30% are given in Figs 6 and 7 and show that these factors are higher in the presence of fluoride ions, and increase when the fluoride concentration is increased. The effects, particularly important in the early dissolution stages, tend to decrease with time and vanish after long dissolution periods. These observed evolutions reflect the initial acceleration noticed for the dissolution kinetics in the presence of fluoride ions. However, in order to understand the dissolution properties resulting from fluoride adsorption onto the HAp surface, we have to remember that according to our model, the transport properties at the HAp interface are regulated by the adsorbed calcium ions. The efficiency of the barrier, as in the case of ionic membranes, increases with the amount of calcium ions and the valence of the anions present [19]. This explains also why at pH values above 5,
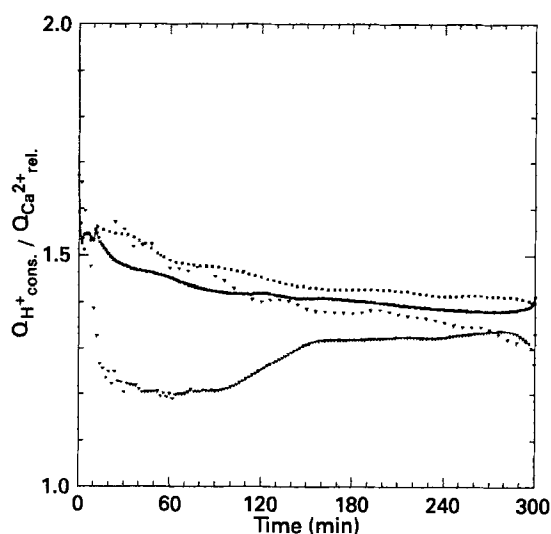

Figure 6 Variations of kinetics rate reduction factors $(1/(1 + k))$ versus time calculated according to Equation 1 for the experiments given in Fig. 3 (pH 5.0). (— 0 ppm; ——— 1 ppm; ..... 10 ppm).
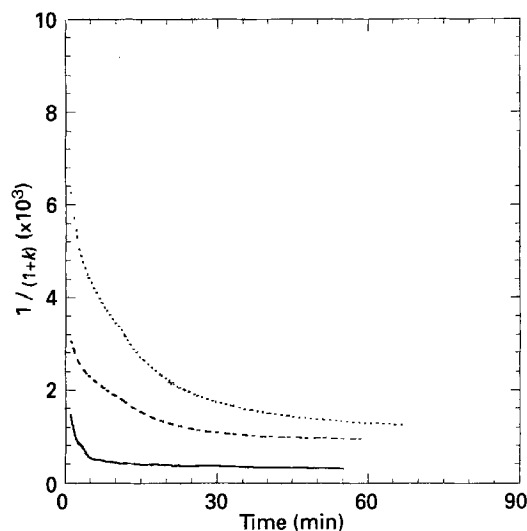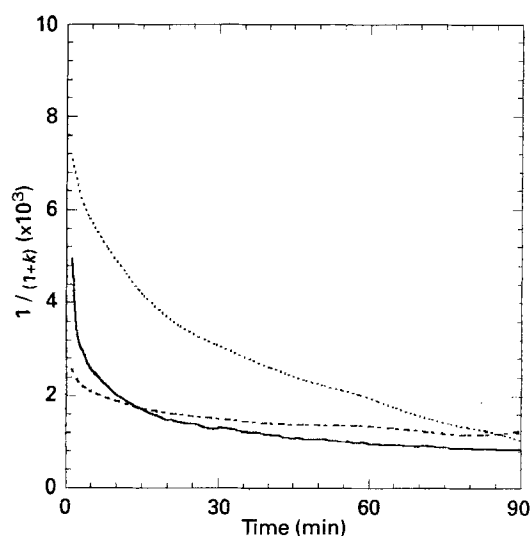

Figure 7 Variations of kinetics rate reduction factors $(1/(1 + k))$ versus time calculated according to Equation 1 for the experiments given in Fig. 4 (pH 6.0). (— 0 ppm; ——— 1 ppm; ..... 10 ppm).

where HPO_4^{2-} ions appear in solution, the permeability increases with pH.

It was shown (Fig. 1) that F^- ions are adsorbed at the HAp surface and adsorbed fluoride leads to a decrease of the cationic capacity of the ionic interfacial membrane. In the presence of 10 ppm fluoride (Fig. 2), the effects is even stronger since an important amount of the neutral CaF_2 species is formed at the solid interface. Thus, in the presence of fluoride ions, the permeability of the interfacial membrane increases leading to an increase of the dissolution rate. With the progress of the dissolution kinetics, the calcium concentration in solution increases and, as a consequence, the amount of calcium ions adsorbed at the HAp surface also increases. With dissolution time, the interface becomes more positively charged and recovers its natural semi-permeability.

The present study demonstrates the ambiguity of the role of fluoride ions in the dissolution process of HAp. Even when the global fluoride effect is positive

Figure 5 $R = Q_H/Q_{Ca}$ ratios versus time for experiments realized in the presence of fluoride for kinetics from Figs 3 and 4. (— pH 5, 10 ppm F$^-$; .... pH 5, 1 ppm F$^-$; .... pH 6, 1 ppm F$^-$; .... pH 6, 10 ppm F$^-$).

with respect to dissolution inhibition, since the presence of these ions leads to the attainment of lower solubility equilibrium, these ions possess also detrimental properties because their presence at the interface decreases the natural self-inhibiting power of HAp. In particular, high fluoride concentrations have to be avoided in order to prevent CaF_2 deposits which strongly increase the permeability of the HAp interface.

References

1. C. DE PUTTER, K. DE GROOT and P. A. E. SILLEVIS SMITT, *J. Prosth. Dent.* **49** (1983) 87.
2. K. DE GROOT, *Med. Progr. Technol.* **9** (1982) 129.
3. M. S. BLOCK and J. N. KENT, *J. Oral. Maxillofac. Surg.* **43** (1985) 3.
4. C. A. VAN BLITTERWIJK, J. J. GROTE and W. KUIJPERS, in *Biomaterials in otology*, edited by J. J. Grote (Martinus Nijhoff: Boston, USA, 1984).
5. K. DE GROOT, R. G. T. GEESINK, C. P. A. T. KLEIN and P. SEREKIAN, *J. Biomed. Mater. Res.* **21** (1987) 1375.
6. K. A. THOMAS, J. F. KAY, S. D. COOK and M. JARCHO, *ibid.* **21** (1987) 1395.
7. C. COOPER, C. A. C. WICKHAM, D. J. R. BARKER and S. J. JACOBSEN, *J.A.M.A* **166** (1991) 513.
8. G. BOIVIN and P. J. MEUNIER, in "The metabollic and molecular basis of acquired diesease", edited by R. D. Cohen, B. Lewis, K. G. M. M. Alberti and A. M. Desman (Bailliere Tindall: London, 1990).
9. O. SIMONEN and O. LAITINEN, *Lancet* **24** (1985) 432.
10. IADR/ORCA, in International Symposium on Fluorides, Pine Mountain, Georgia. *J. Dent. Res. (Spec. Iss.)* **69** (1990) 505.
11. J. M. TEN CATE, *ibid.* **69** (1990) 614.
12. D. J. WHITE and G. H. NANCOLLAS, *ibid.* **69** (1990) 587.
13. J.-M. THOMANN, J.-C. VOEGEL and Ph. GRAMAIN, *Colloids and Surfaces* **54** (1991) 145.
14. *Idem., J. Colloid. Interface Sci.* **157** (1993) 369.
15. S. MAFE, J. A. MANZANARES, H. REISS, J.-M. THOMANN and Ph. GRAMAIN, *J. Phys. Chem.* **96** (1992) 861.
16. J.-M. THOMANN. P. GASSER, E. F. BRES, J.-C. VOEGEL and Ph. GRAMAIN, *Comput. Method Program Biomed.* **31** (1990) 89.
17. P. GASSER, J.-C. VOEGEL and Ph. GRAMAIN, *Colloids and Surfaces* **74** (1993) 275.
18. Ph. GRAMAIN, J.-M. THOMANN, M. GUMPPER and J.-C. VOEGEL, *J. Colloid. Interface Sci.* **128** (1989) 370.
19. F. HELFFERICH, in "Ion exchange" McGraw-Hill (New York, 1962) p. 339.