

First principles model of the transformation of hydroxyapatite into brushite and growth of brushite

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Keywords: precipitation, calcium phosphate, hydroxyapatite, brushite, particle growth

Topic: Process Modelling, Simulation and Control

Abstract

In this paper, a dynamical first principles model of the precipitation of hydroxyapatite (HAP) into brushite and growth of brushite is developed. The process itself is challenging since it consists of multiple phases and there exists strong nonlinear and dynamic effects between the variables. However, our objective was to build a comparatively simple and reliable model to explain the dynamical behaviour of the process. Based upon a databank of laboratory measurements of the calcium concentration in solution (on-line) and the particle size distribution (off-line) an unified model of the process for a gamma of initial concentrations of the reagents was derived as a system of ordinary differential equations of time. The performance of the model is examined with respect to prediction quality of the time trajectories of mass of calcium in solution and the average (in mass) particle size.

1 Introduction

The precipitation of calcium phosphate was studied by various authors under different conditions. Depending on the temperature, the level of supersaturation, pH and initial concentration of reagents, one can obtain different calcium phosphate phases. One of them is the dicalcium phosphate dihydrate (DCPD) known also as brushite. In a previous work (Ferreira et al., 2003) the overall process of DCPD precipitation was thoroughly discussed and the process evolution was divided into five stages:

- 1) Precipitation of HAP, its growth and pH stabilization are essentially due to the consumption of calcium not yet dissolved into the solution.
- 2) The calcium is completely dissolved, and consequently the HAP growth is responsible for the pH decrease.
- 3) Formation of the first nuclei of brushite.
- 4) Two species, brushite and HAP, coexist in the solution
- 5) Brushite becomes the most stable specie in the solution and a transformation of HAP into brushite occurs. Brushite growth is stabilized.

The experiments have shown that the last two phases are particularly challenging because we are faced not only with a precipitation phenomenon to model with its traditional difficulties but the concurrent phenomenon of chemical species transformation (HAP to brushite) has to be accounted as well. In this paper a dynamical analytical model with respect to these two stages is proposed. The issue of dynamic modelling of the dual nature of brushite particle growth has not been directly addressed by the existing models, which was the main motivation for the present study. In fact, to the best of our knowledge, there are no previous publications considering this problem comprehensively.

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The present work is based on several contributions in different fields. Modelling of the general crystallization kinetics has been established by Randolph and Larson, 1988. The mechanisms that govern the formation of brushite are investigated in Ferreira et al., 2003. Models that combine analytical and data-driven approach to approximate the batch crystallization phenomenon have been developed in Georgieva et al., 2003.

The paper is organised as follows. In section 2 the experimental procedure of brushite precipitation is briefly discussed. In section 3 a mathematical dynamical model of the process is introduced and the main theoretical motivations are stated. Finally in section 4 the model is evaluated by simulations and the results for optimisation and validation data are illustrated.

2. Experimental procedure

Experiments were performed in a batch reactive crystallization cylindrical tank made of glass, with 100mm in diameter and 250mm in height, and a thermostat bath maintained at 25°C. The reactive crystallization of Brushite was carried out by mixing equal volumes, 0.5 dm³, of equimolar calcium hydroxide (Riedel-de Haën, 96%, 31219) and orthophosphoric acid (Pronalab, 85%) aqueous solutions. The concentrations of these solutions were changed from 50 to 300 mol.m⁻³. In the batch system, orthophosphoric acid aqueous solution was added before mixing the calcium hydroxide.

Off-line measured particle size distributions and on-line collected data related to the calcium concentration, pH, temperature and conductivity were obtained. The calcium concentration was measured with a selective electrode of calcium. Laboratory experiments with various initial concentrations of reagents (0.05, 0.1, 0.2, 0.3, and 0.4 M) were repeated a number of times and for each experiment at different time moments suspension samples were taken out, filtered, dried and analysed by scanning electron microscopy (SEM) and characterised by X-ray diffraction. As a result, a database with the evolution of the particle size distribution along time was recorded.

3. First principles model

Process modelling involves the following assumptions: (i) the suspension is well mixed in the whole tank volume; (ii) the suspension volume is constant during the precipitation process.

Mass balances

The mass balance equations include mass of calcium in solution (M_c), mass of HAP (M_{HAP}), mass of brushite (M_B), with respective molar weight ratios (q_{m1}, q_{m2}), as follows

$$\frac{dM_c}{dt} = -q_{m1} J_{crys} \quad (1)$$

$$\frac{dM_{HAP}}{dt} = -K_{HAP} (M_{HAP})^2 \quad (2)$$

$$\frac{dM_B}{dt} = J_{crys} + 10q_{m2} K_{HAP} (M_{HAP})^2 \quad (3)$$

$$q_{m1} = \frac{mm_C}{mm_{HAP}}, \quad q_{m2} = \frac{mm_B}{mm_{HAP}} \quad (4)$$

M_{HAP} is defined as a monotonically decreasing function, which corresponds to the experimentally observed HAP dynamical behaviour.

Population balance

The difficulty in precipitation modelling is essentially on the accurate description of the kinetics involved. This particular kinetics model involves some simplifying assumptions that were experimentally confirmed by the SEM images: (i) during the last two phases of DCPD precipitation

the number of crystals does not change significantly; (ii) agglomeration and breakage phenomena are negligible and therefore were not considered for modelling, (iii) growth rate is independent on crystal size. For the evolution of the CSD the approach of Randolph and Larson, 1988 is adopted and the population balance is represented in terms of the number-size density function $n(L)$

$$\frac{\partial n(L)}{\partial t} + \frac{\partial(Gn(L))}{\partial L} = 0 \quad (5)$$

The general population balance expression assumes some form of birth and dead functions of the particle distribution, which means the right hand side of the equation (5) would be different from zero. However, since the brushite precipitation is considered as a consequence of HAP particle transformation it follows that at the beginning of the process, the total number of particles exists already. The model has to represent the transformation of a certain number of HAP particles into approximately the same number of brushite particles and their growth. Therefore, nucleation phenomenon is not explicitly accounted, while particle's dead phenomenon is substituted by particle transformation.

In order to recover the evolution of the particle size distribution based on the moments, the first five moments are included as part of the model. Applying subsequent transformations, the following set of ordinary differential equations represents the required moments of $n(L)$

$$\frac{d\mu_0}{dt} = 0 \quad (6)$$

$$\frac{d\mu_i}{dt} = iG\mu_{i-1}, \quad i = 1,2,3,4 \quad (7)$$

Eq. (7) reflects the general assumption for absence of secondary nucleation. The number of crystals (μ_0) is assumed constant. This statement is experimentally grounded since the periodical SEM analysis of the particle size distribution along time confirmed that the number of the crystals has not changed significantly.

Particle growth due to the supersaturation of calcium in solution.

The main kinetic parameter that reflects the mechanism of particle growth consuming the calcium in solution is the linear growth rate (G),

$$G = \frac{k_a R_g}{3\rho_B k_{vB}}, \quad (8)$$

which is a function of the specific growth rate (R_g), that was considered to be of second order with respect to the relative supersaturation.

$$R_g = K_g \left(\frac{C - C^*}{C^*} \right)^2 \quad (9)$$

Particle growth due to the transformation of HAP into brushite

Invoking general relations between the mass (m), the volume (V) and the linear size (L) of a particle

$$m = \rho V, \quad V = k_v L^3,$$

the expression for L can be rearranged as

$$L = \left(\frac{m}{\rho k_v} \right)^{\frac{1}{3}}$$

Hence, the linear size of a HAP particle (L_{HAP}) and a brushite particle (L_B) with an equal mass ($m_{HAP} = m_B = m$) is going to be

$$L_{HAP} = \left(\frac{m}{\rho_{HAP} k_{vHAP}} \right)^{\frac{1}{3}}, \quad L_B = \left(\frac{m}{\rho_B k_{vB}} \right)^{\frac{1}{3}}.$$

Then a relation between the two particles can be derived as

$$L_B = \left(\frac{\rho_{HAP} k_{vHAP}}{\rho_B k_{vB}} \right)^{\frac{1}{3}} L_{HAP} = k_L L_{HAP}, \quad (10)$$

where

$$k_L = \left(\frac{\rho_{HAP} k_{vHAP}}{\rho_B k_{vB}} \right)^{\frac{1}{3}} > 1 \quad (11)$$

is a proportional parameter that can explain the observed effect of particle growth due to the transformation of a HAP particle into a brushite particle. In this particular case $k_L = 1.4205$. Transforming a unit mass of HAP specie into brushite species results into an enlargement of the particle size quantified by (10-11).

According to Randolph and Larson, 1988, the average (in mass) particle size (AM) is a ratio of the third and the fourth moments

$$AM = \mu_4 / \mu_3 \quad (12)$$

Note, that (17) represents the crystal growth only due to the supersaturation of calcium in solution. Numerical simulations of the model with AM calculated by (17) led to a significant discrepancy between the experimental and simulated crystal size distribution. In order to take into account the enlargement of the crystal size due to the transformation of HAP into brushite (15), the different density of the two species has to be considered explicitly. A possible way to handle the problem is to introduce a weighting factor of (12) in the form

$$AM = P \frac{\mu_4}{\mu_3}, \quad (13)$$

where P is a function of the parameter k_L as follows

$$P = \frac{k_L M_B + M_{HAP}}{M_B + M_{HAP}}. \quad (14)$$

The motivation behind the expression (14) is based on the discrete form of computing the average (in mass) particle size as

$$AM = \frac{\sum_{i=1}^p L_i M_i}{\sum_{i=1}^p M_i}, \quad (15)$$

where p is the number of different particle sizes considered, known also as classes, M_i and L_i are the total mass and the respective particle size of class i . At each discrete time of the HAP-brushite transformation process, the total mass of particles from class i consists of mass of brushite (M_{Bi}) and mass of HAP (M_{HAPi}),

$$M_i = M_{Bi} + M_{HAPi} \quad (16)$$

and respectively we may express

$$L_i M_i = L_{Bi} M_{Bi} + L_{HAPi} M_{HAPi} \quad (17)$$

Assuming equation (10) for each class it follows

$$L_{Bi} = k_L L_{HAPi} \cdot \quad (18)$$

Hence, taking into account (16-18), equation (15) is modified as

$$AM = \frac{\sum_{i=1}^p L_{HAPi} (k_L M_{Bi} + M_{HAPi})}{\sum_{i=1}^p (M_{Bi} + M_{HAPi})} \quad (19)$$

Finally, equation (14) is a first-order approximation of the time integral of (19). Two model parameters (K_{HAP} and K_g) were adjusted based on data set for two experiments with different initial concentrations of reagents (0.1 and 0.3 M) following a classical non-linear regression. The final values of the optimised parameters and the values of constant parameters are given in Table1.

Table1 Values of constant and optimised model parameters

mm_B [kg/mol]	mm_C [kg/mol]	mm_{HAP} [kg/mol]	ρ_B [kg/m ³]	ρ_{HAP} [kg/m ³]	k_a	k_{vHAP}	k_{vB}	K_g	K_{HAP}
0.172	0.04	1.004	2304	3156	4.75	0.5236	0.25	$0.2 \cdot 10^{-5}$	0.323

4. Results and discussion

The analytical model introduced in section 3 is evaluated for its ability to predict process behaviour for various initial concentrations of reagents (0.05, 0.1, 0.2, 0.3, and 0.4 M). Some of the results are depicted in Fig. 1 and Fig.2. In the figures on subplots a), c) and d) data for the main system states (M_c , M_{HAP} and M_B) are denoted by dashed line. On subplots b) stars denote data for AM . The time trajectories of M_c (a) and AM (b) serve as direct indicators of the model quality since measurements for them are available. The mass of HAP and brushite are not directly measured variables but they are readily determined on the basis of available measurements. Thus, the plots of M_{HAP} (c) and M_B (d) are indirect indicators confirming the model reliability. Data from experiments with initial concentrations of reagents 0.1 and 0.3 M were used to optimize the model parameters, therefore it is not surprisingly that the model variables closely matches the observed data for these experiments.(see Fig.1). However, more valuable are the results depicted on Fig.2 where the model was tested on new 'unseen' validation data corresponding to the experiment with initial concentration 0.5 M.

6. Conclusions

A general dynamical model of the precipitation of DCPD is introduced in this paper. The last two stages of the overall precipitation process are considered, i.e. the transformation of HAP into DCPD (named as brushite) and the growth of brushite. Results obtained demonstrate a good agreement between the first principles model and the available experimental data for a number of different initial concentrations of reagents.

Acknowledgement: This work was partially developed in the Laboratories of the Research Unit Instituto de Sistemas e Robótica Porto, financed by the Portuguese Foundation for Science and Technology.

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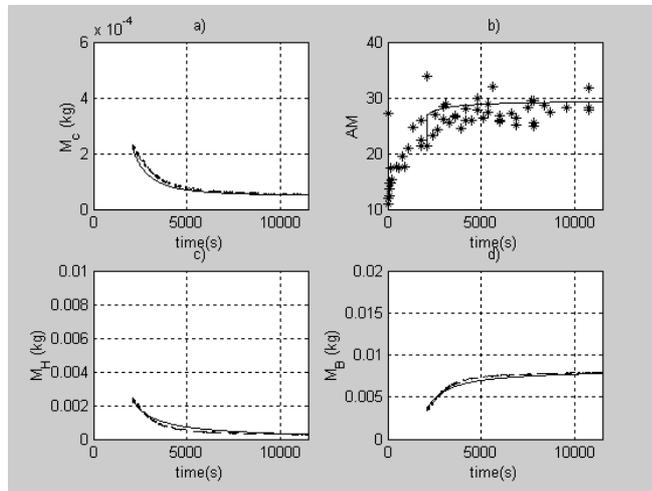
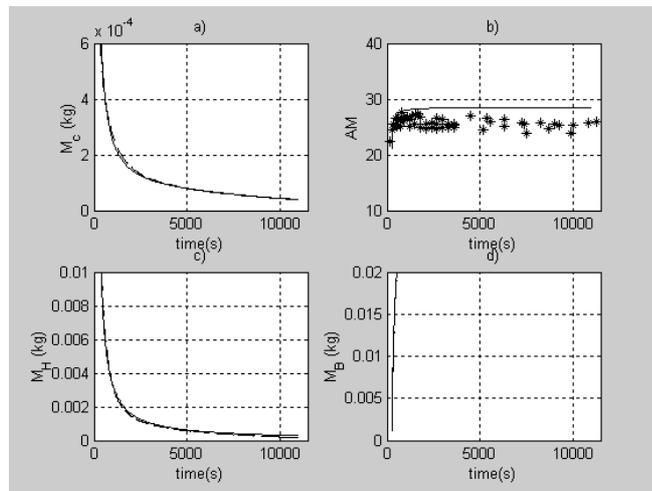


Fig.1 Data points (dashed line/stars) and model curves (solid line) along time for a) mass of calcium in solution, b) the average size AM [μm]; c) mass of HAP; d) mass of brushite. Initial concentration of reagents 0.1 M (model fitting data)

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2.2. Initial concentration of reagents 0.5 M

Fig. 2 Data points (dashed line/stars) and model curves (solid line) along time for a) mass of calcium in solution, b) the average size AM [μm]; c) mass of HAP; d) mass of brushite.(model validation data)