

# Solid particles formation from solutions, an intellectual and industrial meeting point and challenge

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## Abstract

In this paper we will attempt to summarize a number of experiences and ideas concerning the problem of the formation of nanometric and micrometric solid particles from solutions. We will present the scope of the problem, some new advanced in techniques to produce and control the formation of solid particles, a description of a number of formation mechanisms of particles from solution, together with an analysis of the influence of the surface energy created in the nucleation process on the aggregation behavior of the nuclei formed. A new heuristic model on the aggregation mechanisms of particles, based on the action of impurities is proposed.

Key words: Precipitation, particles formation, aggregation, oxides, hydroxyapatite

## Resum

En aquest article presentem un recull d'experiències i idees sobre el problema de la formació de partícules sòlides nanomètriques i micromètriques a partir d'una solució. Presentem l'estat de la qüestió, alguns avanços en tècniques de precipitació, una descripció dels mecanismes de formació de partícules a partir d'una solució, amb una anàlisi de la influència de l'energia superficial formada en el curs de la nucleació sobre el procés d'agregació de nuclis. Es presenta un model d'agregació de partícules basat en la influència de les impureses.

The formation of solid material is a main concern in fields of science such as astrophysics or biology, chemistry, geology, and especially in recent times materials science. The theories proposed for the formation of sideral powder in the first few seconds following the Big Bang, the crystal formation and the slow gathering of cells to form complex living structures coincide with the theories of the association of matter driven by thermodynamic disequilibria and some kind of ordering laws. Just what these disequilibria are and what the mechanisms that create the mentioned order are, are central questions that remain open and are also found in such distant fields as geology and chemical engineering.

The production of uniform particles in size and shape is a fascinating area of research, which finds many applications of technological interest in fields as diverse as ceramics, pigments, catalysis, etc.[1,2]. Significant progress has been made in recent years particularly in the preparation of a large number of inorganic colloids by precipitation [3,4]. However, an important question that still needs to be satisfactorily explained in these colloidal systems is the determination of the precise mechanism of particle formation. It should be pointed out that the formation of monodispersed

colloids is very restrictive concerning the different parameters that rule it, such as pH, nature and concentration of the salt, temperature, time of aging, etc. Matijevic and co-workers (1-4) have illustrated this sensitivity in many systems. Hence, it can be argued that the production of monodispersed particles is a *controlled process*, where the *sensors and actuators* are components of the system acting through regular laws. These regular laws must be related to the specific interaction taking place within a solution, i.e., the equilibria between the solution components, the identification of the growth units, and the interactions between solid surfaces and solution components.

In this paper we will try to summarize a number of experiences and ideas generated on the problem of formation of nanometric and micrometric solid particles from solutions. We will present the scope of the problem, some new advanced in techniques to produce and control the formation of solid particles, and a few proposals of interpretation.

## The precipitating system

Precipitation of crystals from solutions is the most widespread method of crystallization both in nature and in industry. Examples are the precipitation of carbonates, sulfates, halides, sulfides, etc., in oceans, and most of the commodities used by the chemical industry, such as salt, sugar, cop-

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per sulfate, etc. Major problems encountered by the pharmaceutical and fine chemicals industry, such as the control of polymorphism, crystal size distribution and morphology, are related to a precise control of the precipitation conditions.

A solution is a homogeneous system formed by a reaction of at least two components, the crystallizing substance (solute) and the solvent. However, this distinction is not clear in some cases, e.g. in the crystallization of hydrates from aqueous solutions or in the flux growth of solid solutions. A solution is homogeneous because there are interactions between its components on the molecular scale that make it more stable than their pure mechanical mixture. The two main factors that must be known in order to control a precipitation process are: 1) the conditions of equilibria between the crystal and the solution, and 2) the building of the thermodynamic driving force for crystallization.

Depending on the main type of bond responsible for the cohesion in the solid state, we classify crystals into four types: ionic, covalent, van der Waals (molecular crystals) and metallic. This classification is useful because it indicates the kind of interaction inside a crystal that must be broken to form a solution, and also gives us an idea of the energy associated with dissolution or crystallization from solutions. The basic condition to form a solution is a lowering of the Gibbs free energy of the solution with respect to the mixture of pure solute and solvent. The formation of a solution is generally accompanied by some heat exchange, but this exchange is one or two times lower than the energy needed to break the solid bonds (lattice energy). Consequently, this heat must be provided by the heat liberated during the interaction between solute and solvent (solvating energy), which is proportional to the dielectric constant of the solvent. Therefore, to form a solution, the interactions between solute and solvent species (hydration energy) must *essentially* be of the same magnitude as the energies of the bond responsible for the crystal cohesion (crystal energy).

## The driving force for precipitation

Dissolution and precipitation of crystals are chemical reactions that can be described as phenomena of ligands exchange [5]. The driving force for the process, i.e., the balance of free energy ( $\Delta G$ ) between the supersaturated solution and the products of precipitation (saturated solution and crystal), is provided by the differences in the heat and entropy contributions of reactants and products. In real solutions, the heat contribution to a dissolution process in a solution is represented by the partial molar heat of solution of the solute in a slightly undersaturated solution, which is considered as equal –but of the opposite sign– to the heat of crystallization under low supersaturation.

The entropy contributions to the crystallization process merit our attention (6). The entropy changes of an isothermal and isobaric process in a closed system (exchanging heat with the surroundings),  $\Delta S_{\text{SYS}}$ , Eq. (1), consist of two parts: the internal entropy change ( $\Delta S_I = -\Delta G/T$ ), which is

always positive due to spontaneity, and the entropy exchange with the surroundings ( $\Delta S_E = \Delta H/T$ ), which can be, either positive (endothermic processes) or negative (exothermic processes).

$$\Delta S_{\text{SYS}} = \Delta S_I + \Delta S_E \quad \text{Eq. (1)}$$

In all circumstances,  $\Delta S_{\text{SYS}} > \Delta S_E$

The free energy difference between the final state (saturated solution and the crystal) and the initial state (supersaturated solution) of a reaction of precipitation from an ionic solution of the type:



is given by :

$$\Delta G = G_{\text{SAT.}} + G_{\text{S.}} - G_{\text{SUP.}} = \Delta H - T(\Delta S_I + \Delta S_E) < 0; \quad \text{Eq. (2)}$$

Where subscript  $_{\text{SUP.}}$  indicates supersaturated solution,  $_{\text{SAT.}}$  indicates saturated solutions and  $_{\text{S.}}$  indicates solid.

The precipitation of crystals from aqueous solution (or any other solvent) can be analyzed from the point of view of enthalpy and entropy contributions to the processes, i.e., *the balance between the contributions of end products and reactants*. The enthalpy contribution to the process comes from the energy balance produced in breaking and creating bonds in the solute-solvent, solute-crystal and solvent-solvent interactions. Three situations may arise:

- I) If the solute-solvent interaction is weaker than the solute-crystal plus solvent-solvent, the process of crystallization is exothermic ( $\Delta H < 0$ ). This is the case of crystallization of salts with positive solubility coefficient with temperature.
- II) If the solute-solvent and solute-crystal plus solvent-solvent interactions are equivalent, the process takes place without heat exchange ( $\Delta H \approx 0$ ), corresponding to an ideal solution system or salts with little or no change of solubility with temperature.
- III) If the solute-solvent interaction is stronger than the solute-crystal plus solvent-solvent, the process of crystallization is endothermic ( $\Delta H > 0$ ). This is the case of salts with a negative solubility coefficient with temperature.

With respect to the entropy balance we can also consider five situations:

- A)  $\Delta S_I > 0, \Delta S_E < 0, \Delta S_{\text{SYS}} < 0$
- B)  $\Delta S_I > 0, \Delta S_E < 0, \Delta S_{\text{SYS}} \approx 0$
- C)  $\Delta S_I > 0, \Delta S_E < 0, \Delta S_{\text{SYS}} > 0$
- D)  $\Delta S_I > 0, \Delta S_E \approx 0, \Delta S_{\text{SYS}} > 0$
- E)  $\Delta S_I > 0, \Delta S_E > 0, \Delta S_{\text{SYS}} > 0$

If we analyze the formation of a crystal from a supersaturated solution in accordance with the above considerations, we

may gain an insight into the type of crystals and their growth units related to the contributions to the driving forces for the precipitation process. The following combinations for the creation of the driving force ( $\Delta G < 0$ ) can arise:

1. Situation IA:  $\Delta H < 0$ ,  $\Delta S < 0$ ,  $\Delta H < T \Delta S$

This system is peculiar. It is an exothermic process which means there is little interaction between solvent and solute, i.e. the solute components could be water-structure-breaking substances. The entropy of the supersaturated solution is higher than that corresponding to the saturated solution in spite of the internal entropy increase. This seems to be the case of crystallization of salts formed by soft acids and soft bases, or structure breaking systems, such as KI aqueous solution, which has an exothermic heat of crystallization of  $9.121 \text{ KJ.mol}^{-1}$ , positive solubility with temperature [7] and positive enthalpy of ion-pair formation [8], but  $\text{K}^+$  is a hard acid and  $\text{I}^-$  is a soft base, both being structure breakers [9].

2. Situation IB:  $\Delta H < 0$ ,  $\Delta S \approx 0$ ,

This situation corresponds to an exothermic process with equal but opposite contributions of internal and surrounding entropies. As in the proceeding case, the driving force for the process is the enthalpy balance, but we are on the borderline of the soft-hard interactions, as in the case of NaBr [10]. The exothermic character of this crystallization [11] must be due to higher lattice energy than solvating energy.

3. Situation IC:  $\Delta H < 0$ ,  $\Delta S > 0$ ,

This case corresponds to an exothermic process due to the great affinity between the solute components, where there is a net entropy gain after crystallization due to a higher increase in the internal entropy. This situation corresponds to a hard acid-hard base interaction, but with release of part of the water (hard ligand) of the solvating shells. This is perhaps the case of crystallization of hard-hard hydrates such as  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$  (10,11).

4. Situation IID:  $\Delta H \approx 0$ ,  $\Delta S > 0$ ,

This situation corresponds to crystallization from ideal solutions (i.e. very dilute system where  $\Delta H \approx 0$ ) or to the crystallization from solutions or hard-hard anhydrous crystals such as NaCl, NaF,  $\text{NaNO}_3$  (10,11). The driving force for crystallization is the entropy gain of the system due to the release of solvating water.

5. Situation IIIE:  $\Delta H > 0$ ,  $\Delta S > 0$ ,  $\Delta H < T \Delta S$ ,

This situation represents an endothermic process due to the energy needed to remove the solvating water of cations and anions, this energy being higher than the lattice energy. The driving force for the process is an enormous entropy gain, which exceeds the enthalpy balance. This situation corresponds to a hard acid-hard base interaction or to extreme cases of competition between the hard base  $\text{H}_2\text{O}$  and the anions of the electrolyte, and implies a release of all or most of the solvating water. An example of this case is the crystallization of anhydrous crystals such as  $\text{Na}_2\text{SO}_4$  or  $\text{Li}_2\text{CO}_3$  (11) or  $\text{MgSO}_4 \cdot \text{H}_2\text{O}$ .

The driving force for crystallization from solution, the excess free energy, can be expressed as the ratio of the actual ionic product of the solute to the solubility product, or as the ratio between the values of the solute activity of the supersaturated and saturated solutions. The non-equilibria existing in a supersaturated solution only involve the equilibria between the growth units and the crystal and not other equilibria existing between the rest of solution components, whose equilibrium constants depend only on temperature at constant pressure. We can assume that, in order to restore equilibrium, the reactions between the solution components produced as a consequence of the change of composition due to crystallization occur at a much faster rate than the rate of crystallization. Therefore, all other equilibria existing in the solution are quickly reached and the entire process is controlled by the slowest step of crystallization.

### The question of the growth units

A critical analysis of the results of growing crystals from solutions agrees quite well with the statement of Nielsen (61): «the very clear correlation between ion pair formation, solubility and interfacial tension, may be taken as evidence that these phenomena are very closely related and are caused by nearly the same forces». We might add the corollary that the nature of growth units (g.u.) also depends upon the equilibria associated with the above mentioned phenomena, because only those crystals whose growth units are present in a solution can grow from it.

There exist certain ambiguities in what we call a growth unit. They can constitute the elemental part of the crystal structure which reacts with the solvent in the interface during the dissolution process and incorporates into the crystal through the reactions in the growth sites (kinks) during the growth process, without a great conformational change, as in the case of dissolution or growth of most of the organic molecular crystals from organic solvents solutions, or in the crystallization of hydrates from water solution.

In the case of dissolution or growth of ionic crystals, the growth units are species present in the solution (i.e. solvated ions, ion pairs, polynuclear cluster, etc.) able to react in the growth site to produce elemental part of the crystal structure, and reaction products such as solvent molecules. In this case we can expect some conformational changes of the chemical species previous to their incorporation to the crystal lattice, such as a progressive dehydration, or the breaking apart of polynuclear species.

In the case of oxides dissolution or growth, the situation is more complex: The surface structure (composition, relaxation, adsorption layer, kinks and ledges concentration, etc.) strongly determines the nature of the species able to be incorporated to the crystal. It is very unlikely that the growth units would be formed in the bulk solution; instead, some sort of surface-catalyzed process must take place between the arrival of chemical species to the surface and their conversion to form the growth units incorporating into the crystal.

In any case, the definition of the growth unit should be based on a careful analysis of the crystal lattice and its interactions with the solution through the interface. In principle, the criterion of minimum free energy of the evolving system must necessarily be used to define the growth unit. Consequently, enthalpy and entropy considerations must be taken into account.

The question we must deal with here is the relationship between complex formation in the solution and crystal growth. In terms of solution chemistry, the crystal is an enormous polymer formed by the aggregation of «monomers», g.u., which may or may not be complex formations, with the peculiarities of having a periodical order and a surface. The equilibrium between a solid and a solution is characterized by a solubility curve, which represents the result of the various equilibria taking place in the solution. The precipitation of the solid is simply the result of the presence of its growth units in a concentration high enough to exceed its equilibrium constant or solubility product. However, a situation could arise in which the components of the solid growth units form other complexes in the solution with different equilibrium constants in which case the solubility of the solid will depend on the relative values of the equilibrium constants. This type of interaction may describe salting-out and salting-in effects.

Merino et al (13) described a very good example of how the solution composition and the mass-action law alone can define some of the growth units taking part in the precipitation of Al-silicates from aqueous solutions. These authors established different equilibria between the Al-octahedrally-coordinated-with-water-or-OH<sup>-</sup>-complex, the tetrahedrally-coordinated complex [Al(OH)<sub>4</sub>]<sup>-</sup> and the free hydroxyl ions in the solution. They obtained a sharp dependence of the concentration of the tetrahedral complex with respect to the total Al concentration with pH. The transition between predominantly octahedral to predominantly tetrahedral aqueous Al takes place at about 5.5 to 6.5 pH at 25°C, and at 4 to 5 pH at 100°C. By the mass-action law, crystals of silicate growing from aqueous solutions should incorporate tetrahedral Al for Si proportionally to their concentration in the solution. This argument has been very elegantly used by J. García-Carmona (unpublished Thesis, Autonomous University of Barcelona, 1997) to predict the domains of precipitation from water solution of several zeolitic aluminophosphates, with different ratio of tetrahedrally (T) to octahedrally (O) coordinated Al in the crystal structure. (Fig. 1).

The case of precipitation of AgBr from the reaction of AgNO<sub>3</sub> and NaBr or KBr reported by Matijevic et al. (14) is a fine example of the arguments stated above. In Fig. 2, we can see that the precipitation is not a function of concentration only. The surpassing of the solubility product depends on the changes in the activity coefficients of the solution components or, in other words, on the formation constants of complexes other than the growth units. In the above example, the formation of soluble AgBr<sub>2</sub><sup>-</sup>, AgBr<sub>3</sub><sup>2-</sup> and Ag<sub>2</sub>Br<sup>+</sup>, Ag<sub>3</sub>Br<sup>2+</sup> complexes avoid the formation of the insoluble growth unit AgBr<sup>0</sup>.

The contribution of complex formation to the energy balance of the precipitation processes, or the equilibrium be-

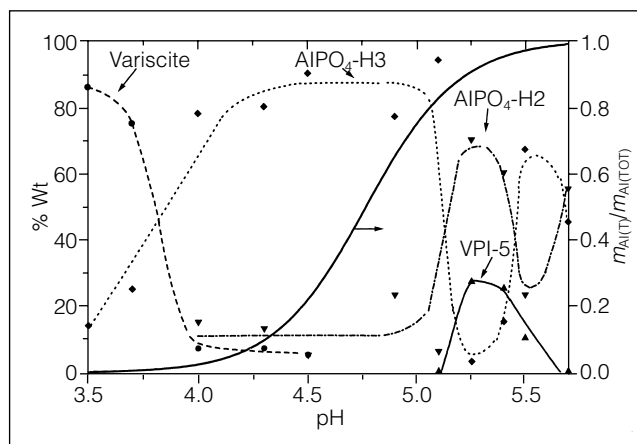


Figure 1. Percentage in weight of several AlPO<sub>4</sub>-hydrates as a function of the pH of the gel precursor. The ratio of Al coordinated tetrahedrally, Al(T), with respect to the total Al in the crystal structure (T+O) is: Variscite, 0; AlPO<sub>4</sub>-H3, 1/2; AlPO<sub>4</sub>-H2 and VPI-5, 2/3.

tween solids and solution, has been summarized by Nancollas (15): «Complexes formed through the predominantly electrostatic interactions between hard ions are entropy stabilized; the enthalpy changes are usually small and endothermic reflecting the energy required for the removal of coordinated solvent molecules from the co-spheres of the ions. Soft or covalent interactions, on the other hand, are always characterized by exothermic enthalpy changes. The accompanying entropy terms become increasingly negative with increasing softness of the interacting acid-base species». As a result, the driving force for the formation of hard-hard complexes is the increase in entropy, whereas for soft-soft complexes it is the exothermic enthalpy (16). In general, high values of  $\Delta H$  and  $\Delta S$  in the complex formation indicate a trend towards mainly an inner sphere complex with increasing temperature (17).

If the association constant increases with the temperature

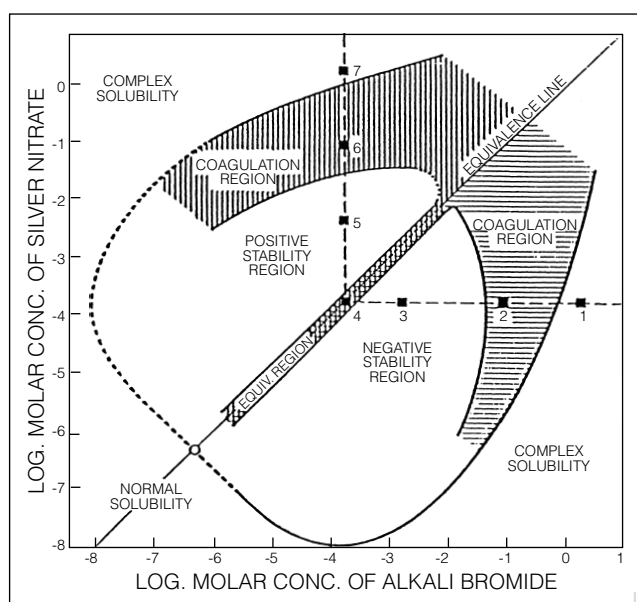


Figure 2. Precipitation body of AgBr from the reaction of AgNO<sub>3</sub> with KBr. From (14).

and the solubility does likewise, as in the cases of the solids  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$  and  $\text{MgSO}_4 \cdot 6\text{H}_2\text{O}$  and the soluble complex  $\text{MgSO}_4^0$  ( $\text{Mg}^{++} + \text{SO}_4^{=} \rightleftharpoons \text{MgSO}_4^0$ ) (Fig. 3), the associated species described by this association constant cannot be growth units. This is so because if a saturated solution is heated to a higher temperature, the crystal in contact with it will dissolve, while the solute components will form more associated species. According to the Le Chatelier Principle, this divergence in behavior with respect to temperature excludes ion pairs as growth units. Therefore, the growth units in the precipitation of  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$  will be hydrated ionic species. By contrast, at high temperatures, in the stability field of  $\text{MgSO}_4 \cdot \text{H}_2\text{O}$  solubility decreases with temperature, that is, if we heat a saturated solution the solid will precipitate but the formation of ion-pairs will also increase. We may, thus, suppose that the associated species act as growth units (5).

The Cd-halides provide another striking example of the relationship between the complexing behavior (8,14) and the solubility of salts (7):  $\text{Cd}^{2+}$  and  $\text{I}^-$  are, respectively, soft donor and soft acceptor. Therefore, a tendency to form pairs may be expected. In deed, we observe that the association constants between them are high and the process of association is exothermic. Since solubility increases with temperature, we may conclude that ion-pairs or other complexes are the growth units (Fig. 4).

In the case of Cd and Br the situation is different (Fig. 5). due to the soft-borderline character of the ions: The solubility of the two stable solids increases with temperature, but the association behavior is not clearly temperature dependent. At low temperatures there seems to be an exothermic process, but at high temperatures it may also have an endothermic character depending on the cumulative association constant chosen. The solid precipitated at low temperature is  $\text{CdBr}_2 \cdot 4\text{H}_2\text{O}$ , indicating a stronger affinity of Cd for  $\text{H}_2\text{O}$  than for Br. However, at high temperatures anhydrous  $\text{CdBr}_2$  precipitates and in this case we must accept one of the following mechanisms: either the growth units are the exothermically formed complexes,  $\text{CdBr}^+$  or  $\text{CdBr}_3^-$ , or the growth is controlled by the dehydration of solvated Cd.

The Cd-Cl is a clear soft-hard interaction. The complex formation in solution is an endothermic process, its association constant increases with temperature and so do the solubility curves of the two stable solids,  $\text{CdCl}_2 \cdot 5/2\text{H}_2\text{O}$  and  $\text{CdCl}_2 \cdot \text{H}_2\text{O}$  and  $\text{CdCl}_2 \cdot \text{H}_2\text{O}$  (Fig. 6). Therefore, in accordance with our model, the growth units are solvated Cd and Cl ions and not the Cd-Cl complexes formed in solution. The internal entropy gain of the system is not very high because the solvent released during precipitation is used to solvate the ions produced through the displacement of the equilibrium of ion pairs.

### Formation mechanisms of uniform particles in solution

Early papers explained the formation of monodispersed colloids by the LaMer model (18), according to which all the

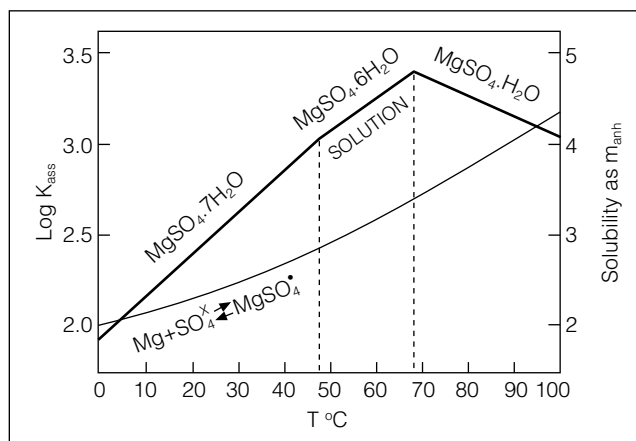


Figure 3. Phase diagrams of the system  $\text{MgSO}_4\text{-H}_2\text{O}$  from 0 to  $100^\circ\text{C}$ , and evolution of the  $\text{Mg-SO}_4$  association constant.

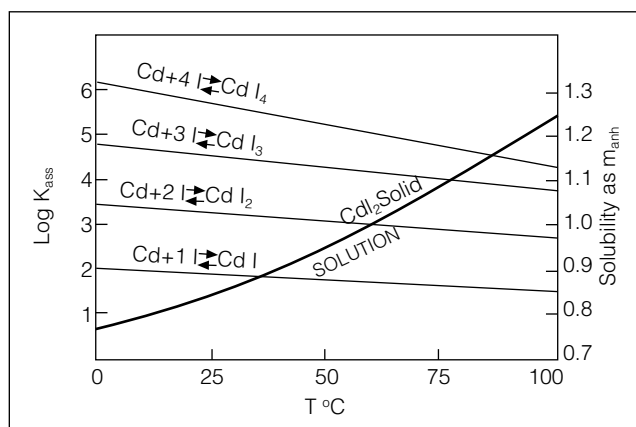


Figure 4. Phase diagrams of the system  $\text{CdI}_2\text{-H}_2\text{O}$  from 0 to  $100^\circ\text{C}$  and evolution of the association constants of the Cd-I complexes.

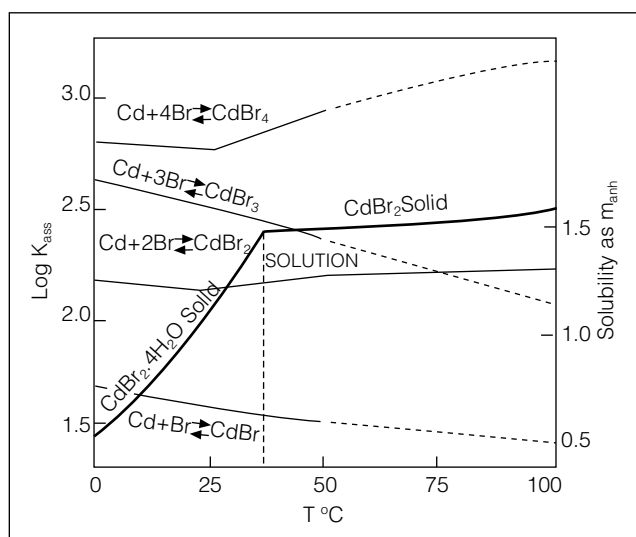


Figure 5. Phase diagrams of the system  $\text{CdBr}_2\text{-H}_2\text{O}$  from 0 to  $100^\circ\text{C}$  and evolution of the association constants of the Cd-Br complexes.

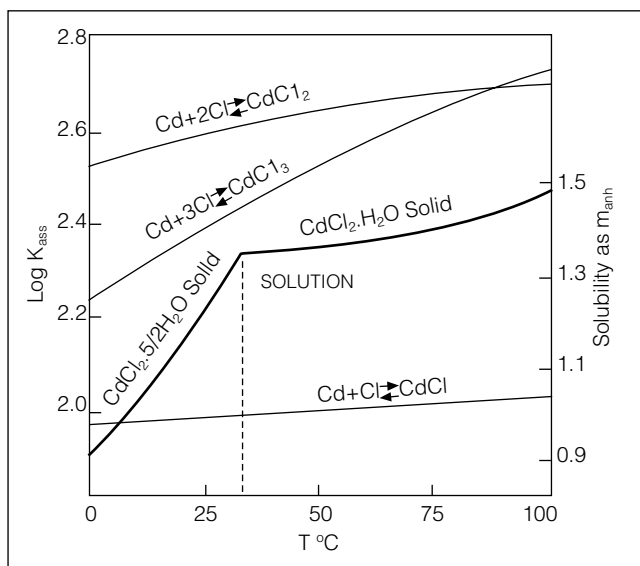


Figure 6. Phase diagrams of the system  $\text{CdCl}_2\text{-H}_2\text{O}$  from 0 to  $100^\circ\text{C}$  and evolution of the association constants of the Cd-Cl complexes.

particles must nucleate at the same time to grow to the same size. However, this is not always the case. Since the pioneer work in  $\alpha\text{-FeOOH}$  by Murphy et al (19), who observed that rod-shaped particles of  $0.1\ \mu\text{m}$  were formed by aggregation of spheres of about  $30\ \text{\AA}$ , several other colloidal particles have been known to form by aggregation of smaller subunits (primary particles) (20-26).

This aggregation process has to be ordered and controlled, since a disordered and uncontrolled aggregation in a dispersed system would result in polydispersed particles of variable morphology. The reason why these primary particles aggregate in an ordered way, or continue to grow from the solution complexes, is not yet known. The final explanation must lie in the balance of forces between particles acting in typical colloidal systems (DVLO theory), the equilibria between the system components—especially the subsystem solid surface-solution—, and, perhaps some unknown contributions that influence the formation of particles with anisometric shapes (25,26).

The mechanisms of formation of monodispersed colloids can differ considerably depending on experimental conditions which explains why only small variations in the system can produce particles with very different shapes and sizes. To understand this, let us briefly review the formation mechanisms of several well established monodispersed inorganic colloidal systems paying special particular attention to those particles formed by an aggregation process.

#### Nucleation and growth by diffusion

Until recently, most of the experiments for the preparation of «monodispersed» particles were based on the LaMer model, which was initially developed to explain the formation of uniform spherical sulfur particles (18). In essence, this model implies that monodispersed particles are formed when the system is kinetically controlled by the diffusion of the solute within the solution. When the initial solution reaches critical supersaturation, a short single burst of nuclei results. The

nuclei then grow uniformly, by diffusion of solutes, toward the surfaces giving the final uniform particles.

Recently, it has been widely argued that LaMer's approach is only applicable in a limited number of cases (25,27). More over, it has been found, that separating the nucleation and growth steps of the process is not an essential feature in the formation of monodispersed particles. In fact, it some cases where the concentration of the solution has been measured through out the process, it was found to be supersaturated respect to the solid during most of the reaction period (28), and successive nuclei burst were produced continuously. In this case, a broad range of particle sizes would be expected and, in fact, were observed. But after a time, final monodispersed particles were formed. It has been suggested that particle uniformity is achieved through a self-sharpening growth process where the small particles grow more rapidly than the bigger ones (29). This was observed during the process of formation of  $\alpha\text{-Fe}_2\text{O}_3$  spherical particles ( $0.15\pm 0.02\ \mu\text{m}$ ) from  $0.02\ \text{mol dm}^{-3}$   $\text{FeCl}_3$  solutions aged at  $100^\circ\text{C}$  for 2 days. A simplified diagram of the formation of these particles is shown in Figure 7. Electron diffraction patterns obtained from individual particles indicated that they were single crystals of hematite.

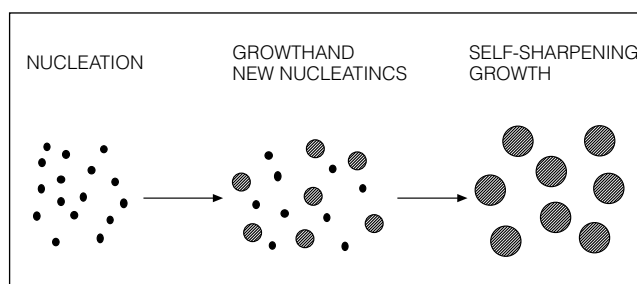


Figure 7. Formation mechanism of amorphous spherical particles by unidirectional aggregation of tiny spheres (primary particles).

Sugimoto et al. (30) have been able to produce pseudocubic particles of  $\alpha\text{-Fe}_2\text{O}_3$  with a diameter of  $1.65\ \mu\text{m}$  by a different procedure, which present x-ray diffraction patterns of polycrystalline particles. Under the electron microscope these particles show that well-defined faces are not always a proof of single crystal character. The differences in crystallinity between the cubic and spherical  $\alpha\text{-Fe}_2\text{O}_3$  particles are in agreement with the observations of Kandori et al (31), who found that the spheres were single crystals while the cubes were polycrystals. It should be noted that the formation mechanism of  $\alpha\text{-Fe}_2\text{O}_3$  cubic particles has not yet been described but would necessarily be different to that of the spheres mentioned above.

#### Aggregation of nuclei

It is a known fact that colloidal particles tend to associate into larger structures, but electrostatic repulsion between them usually prevents aggregation. There is now however evidence that in many cases aggregation between nuclei, or small particles at a certain size (primary particles), is an important mechanism in the formation of many monodispersed solids.

In Table 1, we have classified different systems in which an ordered aggregation has been clearly observed, usually by electron microscopy. The aggregation processes have been divided according to the morphology and crystalline structure of the resulting particles, non-directional (amorphous or polycrystalline spheres) or directional. A directional aggregation process has to occur in order to produce single crystal particles even for solids whose crystalline structure belongs to isometric systems (cubic). However, the directional aggregation does not always results in monocrystalline particles (21).

#### Non-directional aggregation

Amorphous silica (Fig. 8) and amorphous titania particles prepared by hydrolysis of alcoholic solutions of metal alkoxides have shown to be formed by the aggregation of even smaller primary particles (nuclei) (Fig. 9).

Thus, in the case of  $\text{SiO}_2$ , electron micrographs obtained during particle formation show the coexistence of large spheres with rough surfaces and vast quantities of tiny particles, which are apparently aggregating (28). This model of particle formation has recently been questioned by measuring the growth of silica on seed particles with a bimodal size distribution, where it was found that the growth rate of the particles was independent of their size (32).

Monosized spherical titanium oxide particles of 0.2-0.5  $\mu\text{m}$  in diameter prepared by controlled hydrolysis of titanium were found to be composed of primary particles of 6-10 nm in diameter (20). On aging, a cementation mechanism inside the aggregates was observed giving particles with smoother surfaces (33).

In some cases, non-directional aggregation results in uniform particles, which are polycrystalline (Table I). This is the case of  $\text{CeO}_2$  in which aggregation produces spherical particles composed of tiny subunits (21) or equiaxial  $\text{SnO}_2$  particles of 50 nm, which appear to be composed by elongated tiny crystallites of about 5 nm (22).

#### Directional aggregation

By far, the most interesting case is the formation of particles by directional aggregation processes (Table I). Mur-

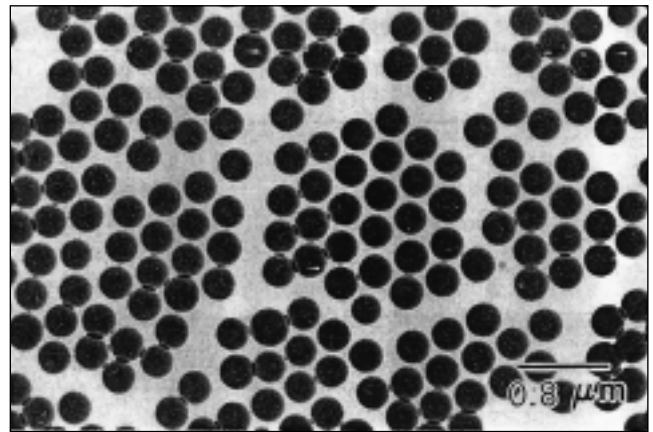


Figure 8. Transmission electron micrograph of amorphous spherical particles formed by unidirectional aggregation of tiny spheres (primary particles).

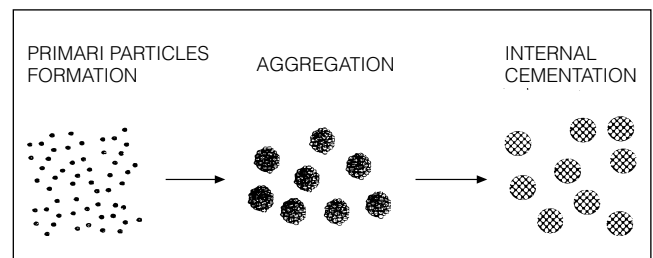


Figure 9. Proposed aggregation mechanisms for the case of Fig. 8.

phy et al (19) reported in the preparation of  $\alpha\text{-FeOOH}$  (goethite) by hydrolysis of ferric salts in homogeneous solutions the first example in which monodispersed solids were formed through this mechanism. They show that the primary particles (nuclei) in the hydrolysis of ferric perchlorate solutions were spherical polycations of about 3 nm in diameter, which finally give  $\alpha\text{-FeOOH}$  rod particles 100 nm in length (18). Although structural information of the particles was not reported, it appears that the  $\alpha\text{-FeOOH}$  rods were monocrystals. It is obvious that a directional aggregation took place in order to produce such a kind of particles. Directional aggregation has also been observed in the reactive precipitation of Hydroxyapatite by mixing two reactants solutions.

Table 1. Monodispersed colloids formed by an aggregation process.

	Crystalline Character	Solid	Primary particles (shape, size)	Final particles (shape, size)	References
Undirectional	Amorphous	$\text{SiO}_2$	Spheres, 30 Å	Spheres, 0.3 $\mu\text{m}$	7
		$\text{TiO}_2$	Spheres, 100 Å	Spheres, 0.5 $\mu\text{m}$	8
	Polycrystalline	$\text{CeO}_2$	Spheres, ~30 Å	Spheres, 0.05 $\mu\text{m}$	9
		$\text{SnO}_2$	Rods, ~50 Å	Spheres, 0.06 $\mu\text{m}$	10
Directional	Polycrystalline	$\text{CeO}_2$	Spheres, ~600 Å	Hexagonal platelets, 2 $\mu\text{m}$	9
		$\text{CeO}_2$	Plates, ~1000 Å	Rods, 0.5 $\mu\text{m}$	9
	Monocrystalline	$\alpha\text{-FeOOH}$	Spheres, 30 Å	Rods, 0.1 $\mu\text{m}$	6
		$\text{Fe}_3\text{O}_4$	Spheres, 100 Å	Spheres, 0.5 $\mu\text{m}$	11
		$\alpha\text{-Fe}_2\text{O}_3$	Ellipsoids, 300 Å	Ellipsoids, 0.6 $\mu\text{m}$	12
		$\text{ZnO}$	Spheres, 5000 Å	Prisms, 2 $\mu\text{m}$	13

### Precipitation by hydrolysis

Another case reported in the iron oxide system is the formation of monocrystalline  $\text{Fe}_3\text{O}_4$  by aggregation of small tiny particles of about 10 nm in diameter (24). Even in this case, in which the solid has cubic symmetry, some directional aggregation is required in order to produce monocrystals.

A striking example has been recently reported in the preparation of  $\alpha\text{-Fe}_2\text{O}_3$  ellipsoidal particles (axial ratio  $\approx 6$ ) (25) formed after 6 days of aging at  $100^\circ\text{C}$  of a solution of  $1 \times 10^{-3} \text{ mol dm}^{-3} \text{ FeCl}_3$ , in the presence of  $4.5 \cdot 10^{-4} \text{ mol dm}^{-3} \text{ KH}_2\text{PO}_4$ . It should be noted how a small amount of  $\text{KH}_2\text{PO}_4$  (approximately one phosphate group per 50 iron cations) can undergo such a great change in particle morphology, i.e. from spheres (Fig. 7) to ellipsoids (Fig. 10). A representation of the proposed formation mechanism, based on the electron microscopy observations carried out at different time intervals, is outlined in Fig. 11. As shown in this chart, after nucleation, phosphate groups adsorb on surface planes parallel to the  $c$  axes of the nuclei, which results in the growth of anisometric primary particles. These primary particles, of about 30 nm in diameter, aggregate in a directional and ordered manner through their  $c$  axes with phosphates desorption from the surface, producing the final ellipsoidal particles. Both the primary particles and the final particles are monocrystalline, as illustrated for the latter in Fig. 10. This indicates that during the aggregation process real bonds at the interface of the primary particles are formed, producing an intraparticle sintering (34). Here, it can also be speculated that as the anisometric primary particles grow, an increasing magnetic force is originated as a consequence of this anisometry (25,35) which could determine the ordered and directional aggregation that gives rise to the formation of the final particles.

An analogous case to that of the  $\alpha\text{-Fe}_2\text{O}_3$  ellipsoids has been observed in the formation of prismatic particles of  $\text{ZnO}$

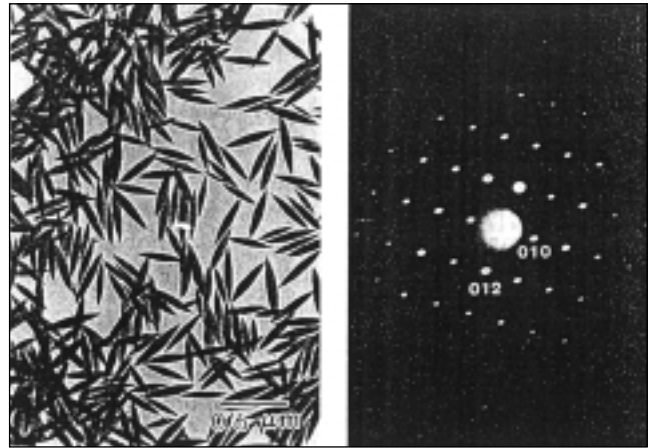


Figure 10. Transmission electron micrograph of ellipsoidal  $\alpha\text{-Fe}_2\text{O}_3$  particles formed by aggregation and electron diffraction pattern of a single particle showing its monocrystalline character.

in  $\text{Zn}(\text{NO}_3)_2$  solutions ( $0.05 \text{ mol dm}^{-3}$ ) aged at  $100^\circ\text{C}$  for 30 min (26). The primary particles observed were monocrystalline spheres of  $0.5 \mu\text{m}$  in diameter. On aging, every two spheres coupled through their  $c$  axes forming embryonic rod particles. Finally, the latter develop perfect faces, giving prisms of  $0.5 \times 2 \mu\text{m}$  in length. These final particles are also single crystals with the  $c$  axis in the direction of the longest particle dimension. Although the reason why the particles begin to couple at a certain size ( $\approx 0.5 \mu\text{m}$ ) is not evident, this directional aggregation could be related to the net polarization that takes place in the  $c$  direction of  $\text{ZnO}$  crystals, which is responsible for their pyroelectric behavior.

### Continuous precipitation by mixing reacting solutions.

#### The case of hydroxyapatite

Hydroxyapatite (HA),  $\text{Ca}_5\text{OH}(\text{PO}_4)_3$  is the principal inorganic constituent of human hard tissues such as bones and

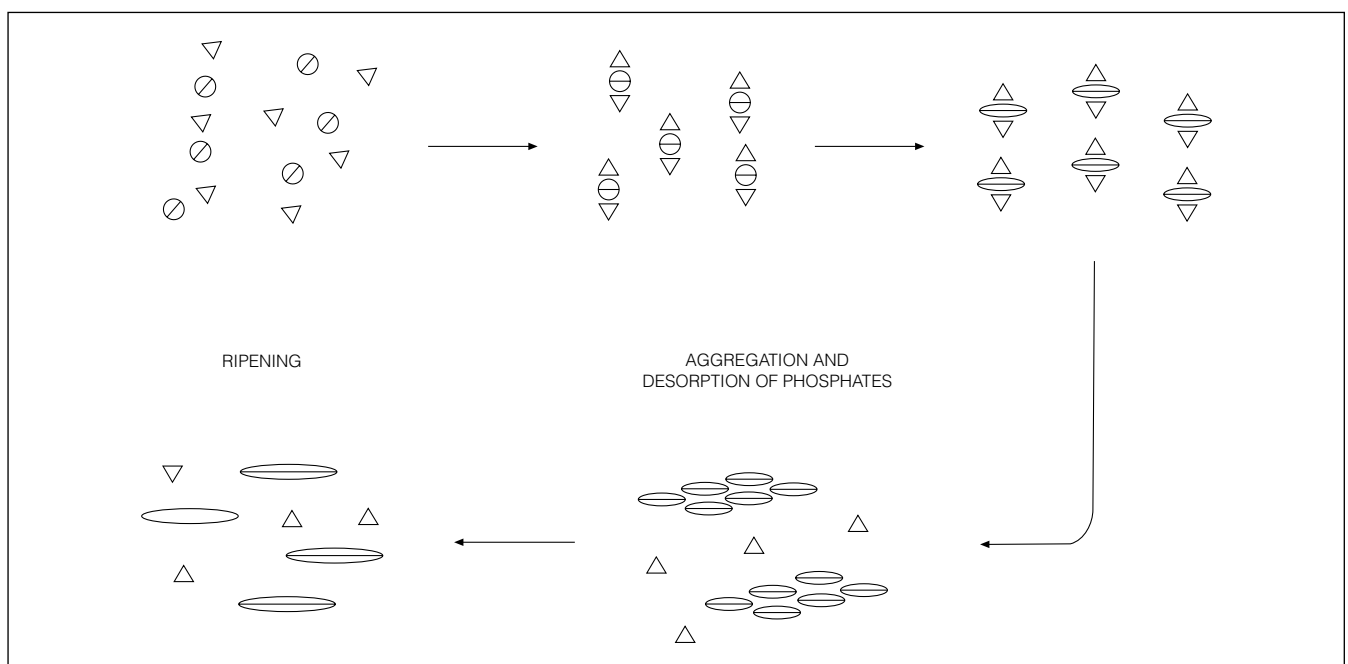


Figure 11. Proposed mechanism of formation of  $\alpha\text{-Fe}_2\text{O}_3$  ellipsoidal particles by an aggregation process directed by a phosphate impurity.



teeth. It crystallized in the hexagonal system, and its equilibrium crystal morphology is a combination of prism and bipyramid. The habit most frequently observed is typically prismatic. The HA particles in the human body are also prismatic with crystal sizes varying from 130x30 nm in the teeth enamel to 20x4 nm in the dentine and bones (36). The preparation of nanosized HA is, –an interesting target in technologies using restorative biomaterials with HA–, is to mimic the sizes present in the human body.

HA has been synthesized in batch and continuous precipitation systems (37,38). Abundant literature exists dealing with the crystallization pathways of HA at 37 °C, resulting in a general consensus on the existence of precursors of the ACP type and OCP type. However, at higher temperatures (>85°C) the direct precipitation of HA or a very rapid transformation of the precursors into HA is observed. The crystal size distribution obtained in the precipitation at high temperature ranges from submicrometer to several micrometres. However, a microscopic analysis of the samples shows the polycrystalline character of the elemental particles, indicating a process of particles formation by aggregation rather than by crystal growth.

In Mixed Solutions Mixed Products Removal (MSMPR) reactors, used for continuous crystallization, the crystal size distribution (CSD) depends on the nucleation and growth kinetics as well as the residence time distribution within the crystallizer. Under steady-state conditions the population balance is given by (39):

$$\frac{d[G(L)n(L)]}{dL} + \frac{n(L)}{\tau} = 0 \quad \text{Eq. (3)}$$

where  $n(L)$  is the differential population density of crystals of size  $L$ , –the number of particles of size  $L$  to  $L+dL$  in a unit volume–,  $G(L)$  is the linear rate of growth and  $\tau$  is the mean residence time within the crystallizer. For size-independent growth rate, the semilogarithmic plot of population density vs. size yields a straight line with the slope  $-1/G\tau$  and the intercept  $n^0$ , the nucleation population density, related to the nucleation rate  $B^0=n^0G$ . The nonlinearity in  $\ln n(L)$  vs.  $L$  plots for MSMPR crystallizers may result from: (i) secondary nucleation in a small finite size range, (ii) size-dependent growth rate, (iii) growth rate dispersion, and (iv) particle agglomeration (40).

We have performed several experiments of precipitation of stoichiometric HA in a 450 ml. MSMPR reactor at 358 K, constant pH=9 and residence time of 30 min., by mixing solutions of  $\text{CaCl}_2$  and  $\text{K}_2\text{HPO}_4$ , the composition of which was maintained at the molar ratio  $\text{Ca/P} = 1.67$ . There are a number of interesting features related to the precipitation of HA in continuous reactors:

- 1) The yield of solids decreases with the increase of the initial concentration, but it is always higher than 80%.
- 2) The Ca/P ratio of the products is the stoichiometric ratio, 1.67
- 3) The residual thermodynamic supersaturation in the steady state of a continuous reactor is higher than  $10^{18}$ ,

which is extremely high in terms of the chemical potential of the solution.

The analysis of the CSD of HAP in the range of detection of the size analyzer (Coulter LS instrument), i.e. from 0.1 to 1000  $\mu\text{m}$ , using the plots of the population density data  $n(L)$  versus  $L$ , Fig. 12, shows an initial rise from  $L=0.1$  to around  $L=1$   $\mu\text{m}$ , followed by a decrease with a positive deviation from linearity and some minor maxima.

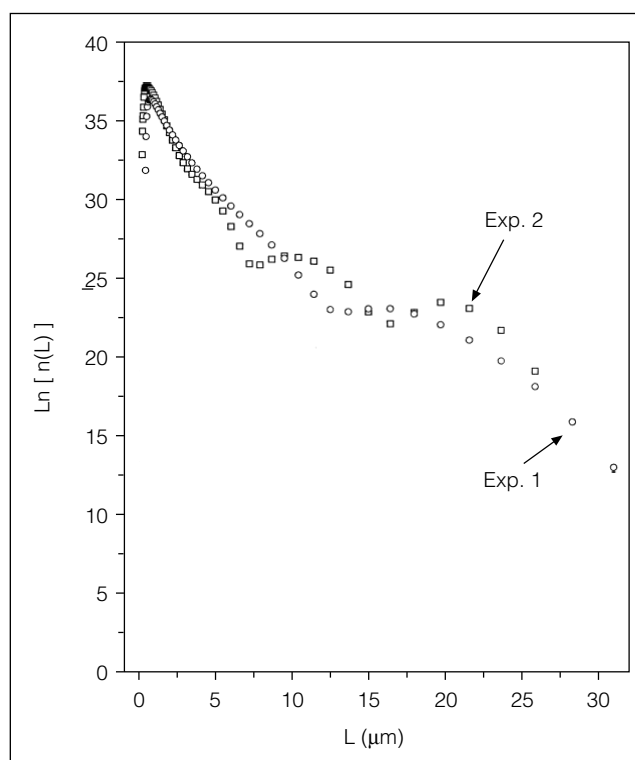


Figure 12. Plot of the logarithm of the population density function  $n(L)$  vs.  $L$  for two runs of hydroxyapatite precipitation in a continuous MSMPR reactor.

In principle, the analysis of these plots, without including the initial rise, could indicate a mechanism of particle formation dominated mainly by nucleation, growth and aggregation in the micrometer size range, with discrete sizes of the aggregates. The absence of individual particles with  $L > 1$   $\mu\text{m}$  in length, as observed in the micrograph of Fig. 13, seems to have little effect of the crystal growth.

However, the initial increase in the  $\ln n(L)$  vs.  $L$  plot (Fig. 12) could very likely reflect aggregation in the nanometric/colloidal range, yielding the so-called primary particles (or primary aggregates). The peculiar shape of this plot suggests that the particles formed by nucleation (not observed by the Coulter analyzer) tend to aggregate in an orderly manner, preserving the prismatic habit, and forming primary aggregates. These aggregates continue to agglomerate by forming interparticle bonds until they reach the micrometer size range. The linear portion of the plot is characteristic of a size-independent of growth rate. Departure from linearity at larger particles indicates aggregation. The typical size of primary agglomerates, at  $\sim 0.1$   $\mu\text{m}$ , agrees with the TEM observation,



Figure 13. Transmission electron micrograph of hydroxyapatite obtained in a MSMPR reactor.

which suggests an ordered agglomeration, because the resulting particles have polyhedral shapes characteristic of the equilibrium form of HAP. Another argument in favor of this particular mechanism is the short relaxation time (a few seconds) for the precipitation of HAP at 373 K, as recorded by the pH variation or precipitation yield measurements. A crystal with such high interfacial energy as HAP grows according to a surface controlled mechanism, i.e., parabolic dependence between the supersaturation and the rate of growth, usually with very small values of the rate constant of the process  $K_G$ . Thus, the formation of the submicronic particles observed, seems to obey a nucleation-ordered aggregation mechanism.

#### Surface energy and aggregation

Since the classical theory of Derjaguin-Landau-Verwey-Overbeek (DLVO), which considers a balance between repulsion forces is due to the overlap of the electric double layers of the particles and attractions in terms of London and van der Waals interactions (41), several models of particle formation by nucleation and aggregation have been proposed, generally based on this theory (42,43) or acid-base surface interactions (44) for non-directional aggregation, or by the influence of impurities and templates for directional aggregation (45,46).

The classical theory of nucleation relates the size of the critical nucleus to the supersaturation, interfacial energy of the system, and temperature through the well known relationship of the total free energy related to the formation of a nucleus of cubic shape and the characteristic size  $L$ :

$$\Delta G = 6L^2 \gamma - L^3 \Delta \mu / \Omega \quad \text{Eq.(4)}$$

where  $\gamma$  is the interfacial energy,  $\Delta \mu$  is the difference in the free energy between the solution and the crystal,  $\Delta \mu = \kappa T \ln(a/a_0) = kT \ln \beta_0$ , expressed in joules, where  $a$  is the activity of the solute in solution, and  $a_0$  is the activity in equilibrium or the activity of the crystal,  $\beta_0 = IAP/K_{SP}$ , where IAP is the initial ionic activity product and  $K_{SP}$  is the thermodynamic activity product, and is the volume of a molecule.

The relation between the size of the critical nucleus, the interfacial energy and the supersaturation is:

$$L^* = 4\gamma\Omega / \Delta \mu = 4\gamma\Omega / kT \ln \beta_0 \quad \text{Eq.(5)}$$

For the case of hydroxyapatite, the interfacial energy (44,47,48) varies from an estimate of  $\gamma = 160 \text{ mJ/m}^2$  to  $9 \text{ mJ/m}^2$ ,  $\Omega = 2.64 \times 10^{-22} \text{ cm}^3$  and  $^{53}K_{SP} = [Ca]_5^5 [OH][PO_4]^3 = 7.3 \times 10^{-61}$  (at 85 °C) where [ ] indicate activity.

The two terms to the right of Eq. [4] can be used to quantify the free energy balance associated with the formation of 1 mol of particles of size  $L$ . If we plot them for various values of  $\gamma(\text{HA})$  given in the literature (9 to 160  $\text{mJ/m}^2$ ), we obtain a diagram, (Fig. 14), showing the size of the critical nucleus, which yields different values of the supersaturation  $\beta_0$ . Taking a supersaturation of  $10^{20}$  for  $\gamma = 160 \text{ mJ/m}^2$  or a supersaturation of  $2 \times 10^{13}$  for  $\gamma = 96$ , it yields a critical nucleus of  $6.4 \times 10^{-10} \text{ m}$ , which is the size of an HA molecule. For a value of  $\beta_0 \approx 10^{10}$  the size of the critical nucleus varies from  $1.43 \times 10^{-9} \text{ m}$  for  $\gamma = 160 \text{ mJ/m}^2$  to a much lower values with decreasing  $\gamma$ .

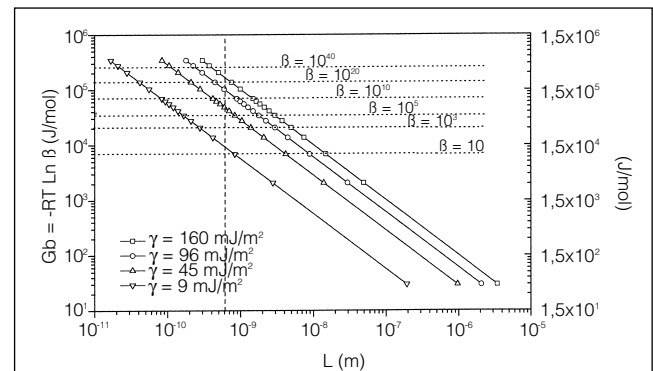


Figure 14. Plot of the bulk ( $G_b$ ) and surface ( $G_s$ ) free energy balance, as expressed in Eq.[4], associated with the nucleation of 1 mol of hydroxyapatite particles of size  $L$  and different interfacial energy, as reported in the literature. The vertical line indicates the characteristic size of one hydroxyapatite molecule.

Considering a residual supersaturation in continuous crystallization of  $\beta_R > 10^{18}$ , the nucleation of HA in this system appears to be non-classical. Essentially, there is no barrier for nucleation under the described experimental conditions, even at the steady state of the continuous precipitation process. This, together with the polycrystalline character of the particles, suggests that the mass precipitation process is essentially lead by nucleation; i.e., most of the solute crystallizes during the nucleation stag, while the

crystal growth plays a minor role in the balance. The ordered aggregation of elementary nanocrystals formed by nucleation would be, therefore, responsible for the particle formation. Some crystal growth, at a constant residual supersaturation, may cause the cementing of the aggregates (agglomeration).

The precipitation of 1 mol of supercritical nuclei at an initial instantaneous (ideal mixing of reactants) supersaturation  $\beta_0$ , results in a free energy gain of:

$$\Delta G^*(\text{mol}) = (V_M/L^3) 6 \gamma L^{*2} - (V_M/L^3) \Delta\mu / \Omega L^{*3} = 6V_M\gamma/L^* - V_M\Delta\mu / \Omega = 6/4 V_M\mu / \Omega - V_M\Delta\mu / \Omega = 1/2 N \Delta\mu \quad \text{Eq.(6)}$$

(N is the Avogadro number)

which comes from the enormous amounts of surface free energy created. These results come from strict application of nucleation formalisms: the release of bulk free energy produced by the phase change is, paradoxically, counterbalanced by the creation of an even higher excess of surface free energy.

The higher the initial supersaturation, the higher the gain of free energy released in the nucleation process due to the newly created surfaces. Considering that the system also holds an enormous amounts of free energy associated to the residual supersaturation, one should expect the relaxation of the free energy either by mass crystallization (crystal growth) or by a decrease in the total solid surface by an aggregation-agglomeration process, but NOT by nucleation (which will produce new excess surface free energy). An increase of 1 order of magnitude of the particle size, leads to a decrease of 1 order of magnitude of the excess surface energy  $G_s$  (Fig. 14). The greater the initial (or the residual) supersaturation, the greater the tendency for aggregation in order to release the excess free energy.

These results allow us to understand a bit better the complex processes related to the early stages of formation of particles from solution, where we observe a competition between crystal growth, by the addition of growth units to a newly formed stable nucleus, against the tendency of the nuclei to collide and aggregate to minimize the surface energy. Both processes are controlled by diffusion coefficients and collision probabilities. We can, thus, assume that in precipitating systems where the particles have high diffusion coefficients, the surface potential is responsible for the aggregation of particles resulting in the absence of nanoparticles, while in system with low diffusion coefficients such as gels, or with small density of particles such as gases, the formation of nanoparticles is possible.

## Templates-based mechanisms

### The case of iron oxides

In addition to the classical model and the aggregation models, other more complex mechanisms of formation of uniform particles can take place. This is the case of the for-

mation of ellipsoidal  $\alpha\text{-Fe}_2\text{O}_3$  particles (Fig. 15) by aging ferric nitrate solutions in nitric acid media at 100°C for 32 h (49). X-ray diffraction studies on this powder revealed that it was not pure hematite but it contained a certain amount (~10%) of goethite ( $\alpha\text{-FeOOH}$ ) for which it was suggested that the latter precipitates first and then recrystallizes to hematite (49). It has been later found (50) that in effect, goethite was present in the solid at the initial stages of precipitation and that the hematite/goethite ratio increased with aging time. Moreover, a continuous decrease of the Fe(III) concentration in solution took place during the whole aging period, which seems to indicate that goethite precipitates first and then hematite heterogeneously nucleates on goethite particles and grows by diffusion of species from solution. In agreement with this mechanism are the electron microscopy observations at the initial stages of precipitation and the electron diffraction studies carried out on single ellipsoidal particles (50). Thus, the pattern obtained for the sections located far away from the middle of the ellipsoids was consistent with hematite single crystals having the c axis parallel to the longest particle dimension, whereas the pattern obtained for the middle of the particle showed additional spots (Fig. 15), which suggest the presence of goethite in the particle core. Figure 16 shows a schematic representation of this mechanism, which is similar to the one proposed for the formation of double-ellipsoidal shaped  $\alpha\text{-Fe}_2\text{O}_3$  particles from  $\text{FeCl}_3$  solutions, but in this case, the initially precipitated phase was  $\beta\text{-FeOOH}$  (51).

Another interesting case of directional aggregation by heterogeneous nucleation on solid templates, which later disappear but induce the development of morphologies that reproduce those of the template, is the case of magnetite crystallized on  $\text{Fe}(\text{OH})_2$  hexagonal platelets yielding an aggregate preserving the hexagonal platelet-like morphology (26). It may also happen that the templates direct the initial morphology, as in the case of the formation of several morphologies of hematite,  $\alpha\text{-Fe}_2\text{O}_3$ , from a template of akaganeite,  $\beta\text{-FeOOH}$  (51).

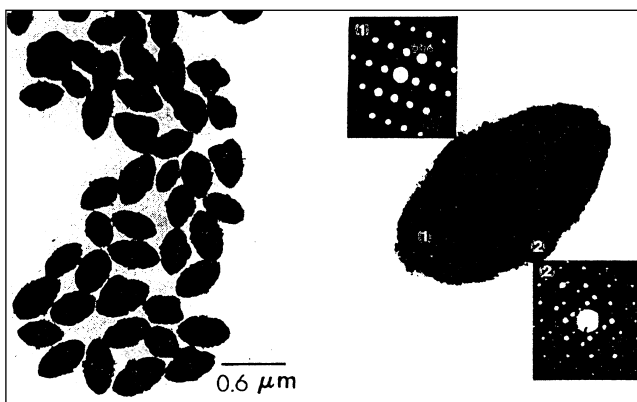


Figure 15. TEM micrographs of ellipsoidal  $\alpha\text{-Fe}_2\text{O}_3$  particles formed by heterogeneous nucleation on goethite cores (left), and electron diffraction patterns (right) obtained from two different regions on a single particle.

### The case of hydroxyapatite (HA) ( $\text{Ca}_5(\text{OH})(\text{PO}_4)_3$ )

Another excellent example of the influence of substrates on the particle formation is given by HA. The important observation in bones and teeth is the low crystallinity of the HA particles, evaluated by XRD methods, with diffraction domains smaller than the particles. This points to the existence of particles formed by aggregation of precursor crystals of a few nm in size. This low crystallinity is also observed in the early stages of HA precipitation (53), although some authors (54) indicate a progressive ordered agglomeration of the initial elementary particles to yield a structured particle which presents, consequently, higher crystallinity. Furedi (55) suggested that ACP (amorphous calcium phosphate) chain-like agglomeration of precursor particles acts as a template for the crystallization of OCP (octacalcium phosphate) and directs the formation of fiber-like crystals of this phase.

The results observed in the precipitation of HA from complex Ca-citrate solutions also shows peculiar mechanisms. HA was precipitated from Ca/citrate/phosphate homogeneous solutions using microwave and conventional heating techniques under refluxing conditions. The Ca-citrate complexes were prepared from soluble  $\text{Na}_3\text{cit}\cdot 2\text{H}_2\text{O}$  or  $\text{K}_3\text{cit}\cdot 2\text{H}_2\text{O}$  salts. On heating these solutions, the Ca-Cit complexes are decomposed resulting in solutions also supersaturated in  $\text{Na}_3\text{cit}$ , yielding a coprecipitate of this salt with HA particles in the nanometer size range of 30-60 nm. (Fig. 17).

The specific surface area measurements (BET method), XRD, FTIR and microscopy analyses show that in the case of precipitation from Ca/citrate/phosphate using sodium salts as reagents the particle formation mechanism involves the coprecipitation of sodium citrate, which acts as a template. The heterogeneous nucleation of nanosized HA can also be interpreted in terms of surface free energy excess minimization by the interaction of the supercritical nuclei with this template. The lower value of the total surface free energy, as compared to the continuous precipitation system, avoids the need for the formation of primary aggregates. Afterwards, these nuclei grow to their final nanometer size; the template-particle interaction prevents the formation of HA aggregates and thus allows the formation of primary nanosized particles. The formation of HA nanoparticles

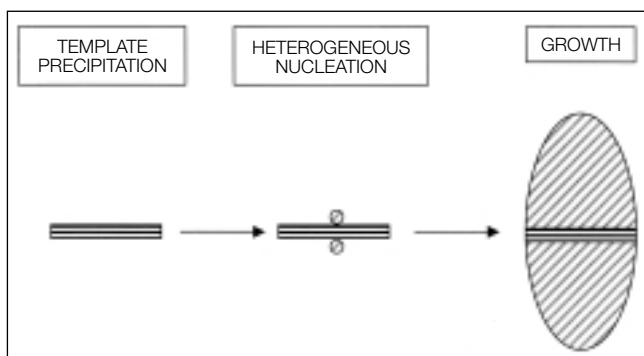


Figure 16. Schematic representation of the formation mechanism of the complex ellipsoidal  $\alpha\text{-Fe}_2\text{O}_3$  particles shown in Fig. 15.

in the presence of templates such as collagen was observed (56).

It is interesting to note that this coprecipitation mechanism offers a unique way to obtain nanosized solid phases in natural and artificial crystallization from solution, which would be otherwise impossible to obtain due to surface energy excess.

### Proposal for a heuristic mechanism for the production of monodispersed particles

The formation of solid particles from a homogeneous solution is a complex process requiring a number of sequential steps. The first step is nucleation, understanding by this the formation of the initial stable condensed phase. It can happen that the initially formed solid phase IS NOT the same phase as the final solid encountered (Ostwald stages rule). This is due to the creation of disequilibria (supersaturation) in the solution with respect to several possible precipitating phases. Usually, the more disordered phases, which are the more soluble, precipitate first due to their lower surface energy, and the system tends to equilibrium with respect to this phase. However, the system remains supersaturated with respect to the more insoluble phases which tend to precipitate, and by so doing, cause the solution to lose solute and become undersaturated with respect to the first precipitates which redissolve. Sometimes, as has been shown above,

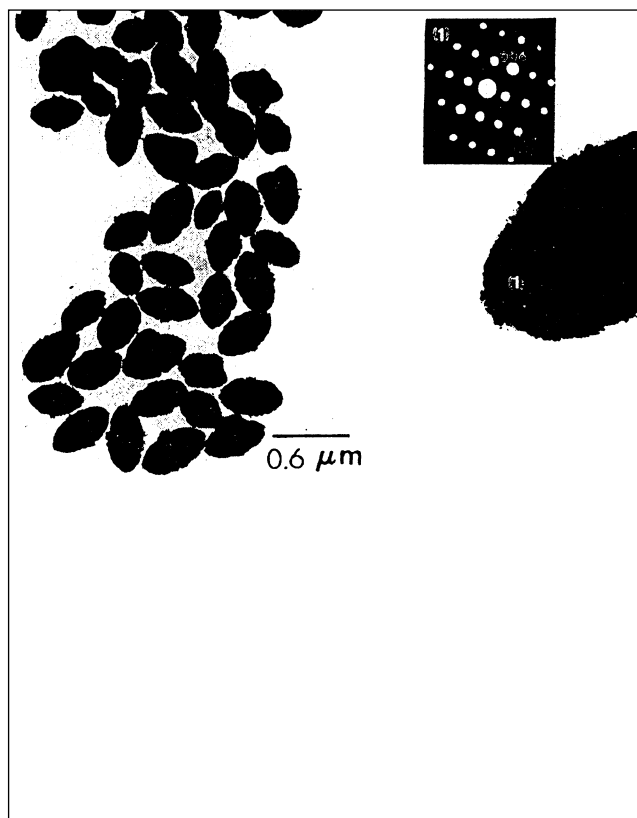


Figure 17. Transmission electron micrograph of hydroxyapatite obtained by microwaves activated batch reactor using Ca-citrate complex solutions formed from  $\text{Na}_3\text{cit}\cdot 2\text{H}_2\text{O}$  reactants.

the first precipitates act as templates for the heterogeneous nucleation of the final solid.

There are a number of examples in the literature showing the formation of monodispersed systems from a single burst of nucleation and from continuous nucleation manner. The LaMer approach to monodispersed particle production is simply a development of the classical theory of homogeneous nucleation. This approach to monodispersivity is similar to the procedure employed in industrial crystallization to obtain a narrow Crystal Size Distribution, i.e., making a Batch Crystallization using a high initial supersaturation and leaving the system to decrease the supersaturation by the solute incorporation in the newly formed crystals.

The formation of monodispersed particles (MDP) in a solution by aggregation of smaller particles implies a *controlled mechanisms of the process*. This *process control* requires some *sensors and actuators* in the forming solution, able to lead the system toward the production of uniform particles. The control mechanism should be linked to the interactions taking place during the particles processing (shaping): nucleation, growth, and aggregation.

As systems with *different compositions* yield monodispersed particle populations of different characteristic size and shape, the agent of control must be a solution component different from the particle components, i.e., *an impurity in a broad sense*. Most of the experiments describing MDP production indicate that the final particles are formed by their pure components with no change in crystal composition and structure; only the morphological properties change. We must, therefore, assume that if there is a controlling mechanism, this must be related to *interaction of impurities with the crystal surface*. This interaction must be reversible; otherwise, we will find the impurity incorporated in the crystal. The reproducibility of the particle morphology in a sequential precipitation, indicates that the actuators act in similar conditions and with similar chemical potentials in all sequences. Therefore, the control process must be connected to a reversible process of impurity-surface interactions that did not provoke incorporation of the impurity to the bulk particle, i.e. weak-medium surface adsorption. On the other hand, it is a known fact that all the solution components are able to adsorb on the solid surface more or less efficiently, i.e. with higher or lower residence times on the surface, including the particle components.

We can make an hypothesis on a formation process yielding MDP of well define morphology and shape, by stating that there are specific interactions of an agent –an impurity– that control the unit particle shape and the aggregation behavior of the system. This ruling impurity should have certain characteristic properties: It must adsorb efficiently, and by so doing it competes with the growth units for the surface sites, eventually blocking the particle growth after the burst of nucleation. On the other hand, it must act as an aggregation agent, most probably by disturbing the potential field around the particles and creating sites on the surface, –impurity adsorption sites– where favorable interactions between the particle carrying the impurity and other particles

take place in a manner similar to that described by Matijevic (57), assuming surface charge segregation, or as he puts it, «discreteness of charges on the particles surfaces, rather than the normally accepted smooth distribution». Finally, it must have a role in the interruption of the aggregation process in order to yield particles of a definitive size and shape, even if the process of precipitation continues. Moreover, this agent must be responsible for the final morphology of the particles.

All these controlling influences on the particle evolution must be linked to characteristic interactions related to variables associated to the evolution of the system, namely, the number of species in the solution and their concentration, specially the pH, or in the case of the particles, essentially the surface. From the analysis of the balance of surface energy in the precipitating process and the tremendous driving force for aggregation, we must be aware that when two tiny particles with a characteristic nanometrical size (i.e. with an enormous surface/volume relation), are put in contact, we are creating a highly reactive grain border where surface diffusion, annealing and even nucleation are favored in the crown formed at the intersection of the two particles. This sintering process, and the subsequent reduction of total surface area of the aggregate, can be responsible for the desorption of the impurity inducing aggregation, which returns to the solution and can be used for a new sequence of nucleation-adsorption-aggregation-desorption.

There is no simple explanation as to why particles attain a certain size and stop growing and/or aggregating. We can assume, however, on the basis of the previously described model, that the overall sintering process between the tiny particles reduces the *solid surface curvature*, which is linked to its reactivity/solubility (Herring's theorem, cited by R. Kern in (58)), and the surface energy reaches a characteristic minimum value and no more aggregation (which creates more surface) is favored.

## Acknowledgements

This work was financed by Project MAT-95-1010-C03-01 of the Spanish Plan of Research. The authors R.R.C. and J.G.M. belong to the Excellence Research Team GRQ93-8044 financed by the Autonomous Government of Catalonia.

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## About the authors

*The production of nanometric and micrometric solid particles uniform in size and shape is a fascinating area of research, which finds many applications of technological interest in diverse fields such as electronic, ceramics, pigments, catalysis, etc. Significant progresses have been made in recent years, particularly on the preparation of a large number of inorganic colloids by precipitation. However, an important question that needs to be satisfactorily explained in these colloidal systems is the precise determination of the mechanisms of particle formation.*

*The authors of this article belong to three of the Institutes of Materials Science of the CSIC, Barcelona, Madrid and Sevilla. The group of Barcelona have a large experience in mechanisms of crystal growth and thin films formation, new methods of solid synthesis, precipitation and industrial crystallization. The authors from Madrid and Sevilla have developed, along 20 years, an internationally recognized expertise in the preparation and characterization of particulate materials and the structural and magnetic properties of nanoparticulated materials for high density recording. All these groups currently participate in Projects financed by the Materials Program of the Spanish Plan of Research and the CEC Program BRITE-EURAM. The authors collaborated in a NATO Project with the University of Clarkson (USA), and they have published together several articles on the mechanisms of formation of uniform colloidal particles in solution, notably a theoretical paper in *Advanced Materials*, 7(2), 212-216, 1995.*

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