Chemical Control of Biomineralization

➢ *High level of regulation associated with biologically controlled mineralization depends on chemical control of precipitation and crystallization*

➢ *Principles of precipitation*

Outline

- ➢ *Solubility*

- ➢ *Solubility product*

- ➢ *Supersaturation*

- ➢ *Nucleation*

- ➢ *Oriented nucleation-epitaxy*

- ➢ *Crystal growth*

- ➢ *Crystal growth inhibition*

- ➢ *Crystal morphology*

- ➢ *Polymorphism*

- ➢ *Phase transformations*

Solubility

➢ *Definition: the solubility of an inorganic salt is the number of moles of the pure solid that will dissolve in 1 liter of solvent at a given temperature*

➢ *Dissolution occurs when the free energy required to disrupt the lattice bonding, ΔG_L, is offset by the free energy released in the formation of aqueous species, such as hydrated ions (ΔG_H), ion pairs (ΔG_{IP}) and complexes (ΔG_C)*

➢ *The free energy of solution DGS is given by*

$$\Delta G_S = \Delta G_L - (\Delta G_H + \Delta G_{IP} + \Delta G_C)$$

➢ *In general an ionic compound will be highly insoluble for cation and anion radii of similar size*

Solubility

➢ *Free energy is dependent on both enthalpic and entropic factors*

➢ *It is also influences by changes in the structure*

➢ *Several cations and anions can be incorporated into the lattice of HAP*

➢ *Fluoride, in particular, that's why it is used extensively in dentistry (prevention of tooth decay)*

Solubility of apatites vs. pH
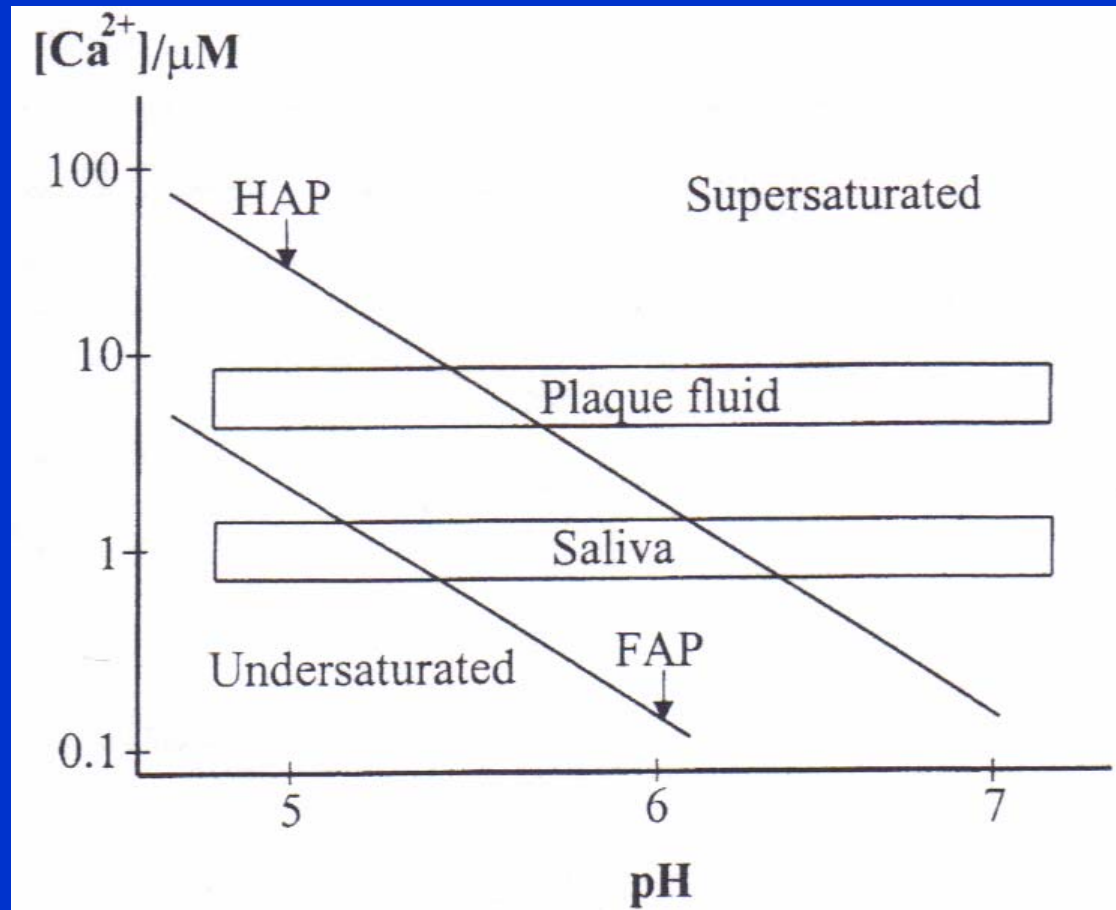
Solubility Product

➢ *The solubility of an inorganic salt can be related to an equilibrium constant, the solubility product K_{sp}, provided there is negligible complexation*

➢ M_nX_m *(solid)* $\leftrightarrow$ nM^+ *(aq)* + mX^- *(aq)*

➢ $K_{sp} = [M^+]^n[X^-]^m$

➢ *$[M^+]$ and $[X^-]$ are the effective concentrations (activities) of ions in solution in equilibrium with the solid phase*

➢ *The value of K_{sp} can be used to calculate the free energy of solution ΔG_S*

➢ $\Delta G_S = -RTlnK_{sp}$

Solubility Products of Biominerals

Mineral	Solubility product ($\log K_{sp}$)	
Calcium carbonate		
Monohydrite	−7.39	
Vaterite	−7.60	
Aragonite	−8.22	
Calcite	−8.42	
Calcium phosphate		
Brushite ($CaHPO_4 \cdot 2H_2O$)	−6.4	−3.2*
Octacalcium phosphate ($Ca_8H_2(PO_4)_6$)	−46.9	−6.7*
Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$)	−114.0	−7.1*
Fluoroapatite ($Ca_{10}(PO_4)_6F_2$)	−118.0	−7.4*
Amorphous silica		−2.7*
(Quartz)		−3.7*
Iron oxides		
Ferrihydrite	−37.0	
Goethite (α-FeOOH)	−44.0	
(Hematite, α-Fe_2O_3)	−42.5	
Group 2A sulfates		
Gypsum ($CaSO_4 \cdot 2H_2O$)	−5.03	
Barite ($BaSO_4$)	−9.96	
Celestite ($SrSO_4$)	−7.40	

*Values quoted as mol l^{-1}.

How Meaningful is the Solubility Product?

➢ *Difficult to apply when there is complexation*

➢ M_nX_m *(solid)* $\leftrightarrow$ *nM^+ (aq) + mX^- (aq)*

➢ *Not applicable for covalent solids (silica)*

➢ *Difficult to determine in biological fluids*

➢ *Not a "true" constant. It increases with diminishing crystal size.*

➢ *Ostwald ripening: small crystals dissolve, large crystals continue to grow*

Supersaturation

➢ *The relative supersaturation S_R is defined as*

$$S_R = AP/K_{sp}$$

➢ *The absolute supersaturation SA is defined as*

$$SA = (AP - K_{sp})/K_{sp}$$

➢ *As S_R increases the thermodynamic driving force for precipitation increases*

➢ *In inorganic systems supersaturation can be achieved in many ways: chemical reactions, temperature changes, variations in solution composition, solvent evaporation, etc.*
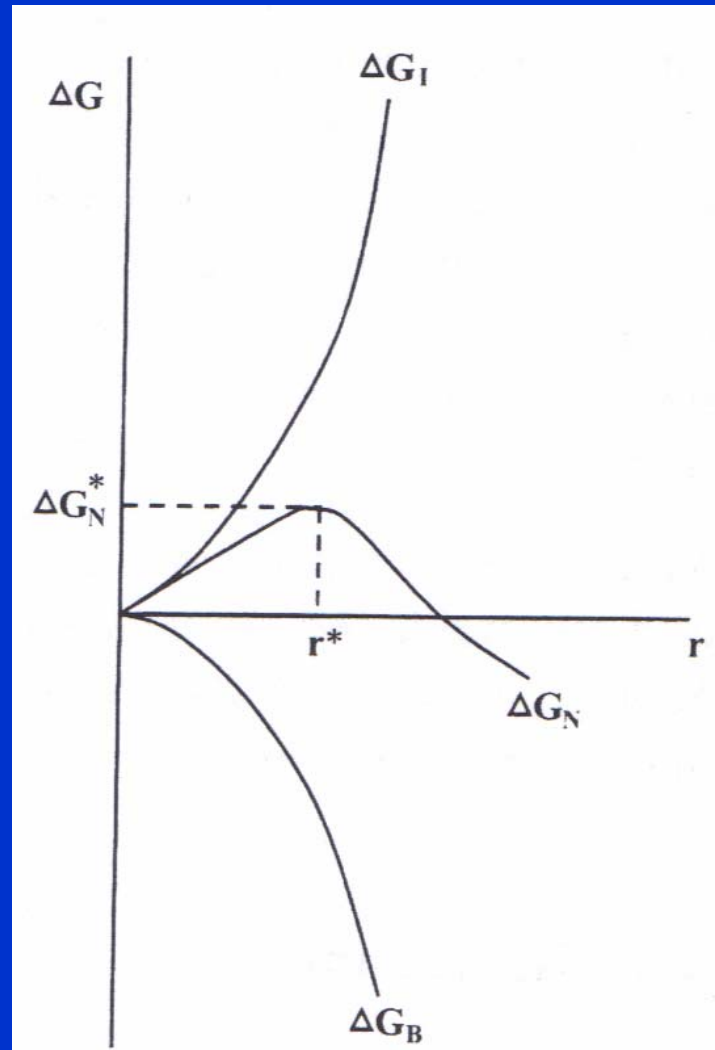
Nucleation

➢ *Kinetic constraints*

➢ *Homogenous nucleation*

➢ *Heterogenous nucleation*

➢ *In biomineralization heterogenous nucleation occurs*

nanostructured precursor — Ca^{++}, CO_3^- → calcite (1 μm)
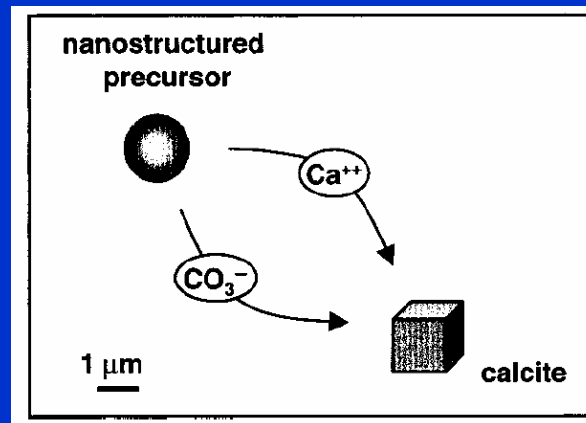
# Mathematical considerations of nucleation

➢ *The free energy of formation of a nucleus ΔG_N is the difference between the surface (interfacial) and bulk energies*

➢ $\Delta G_N = \Delta G_I - \Delta G_B$

➢ ΔG_I *is always positive and dependent on surface area*

➢ ΔG_B *is negative and a function of volume*

➢ *For the classical case of a spherical nucleus*

$\Delta G_I = 4\pi r^2 \sigma$ *(σ is the interfacial energy per unit surface area)*

➢ $\Delta G_B = 4\pi r^3 \Delta G_V / 3V_m$

Mathematical considerations of nucleation

Activation energy of homogenous nucleation
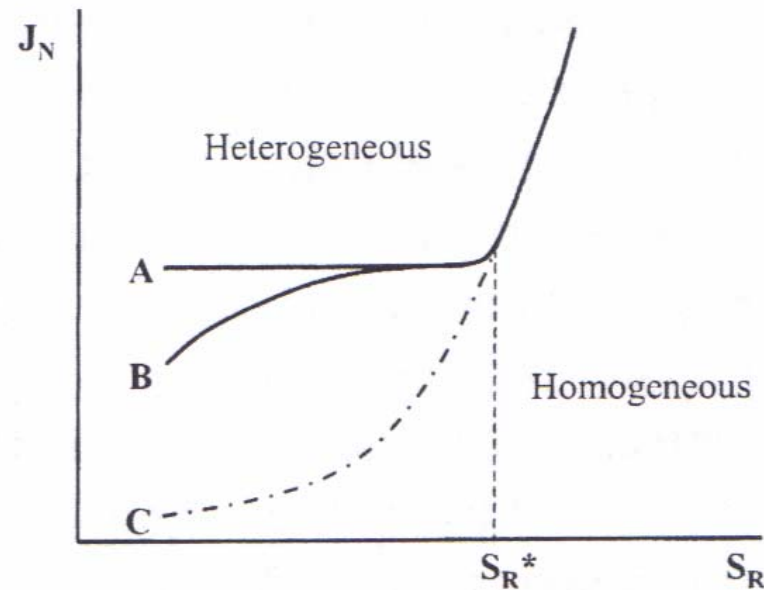
Nucleation rate
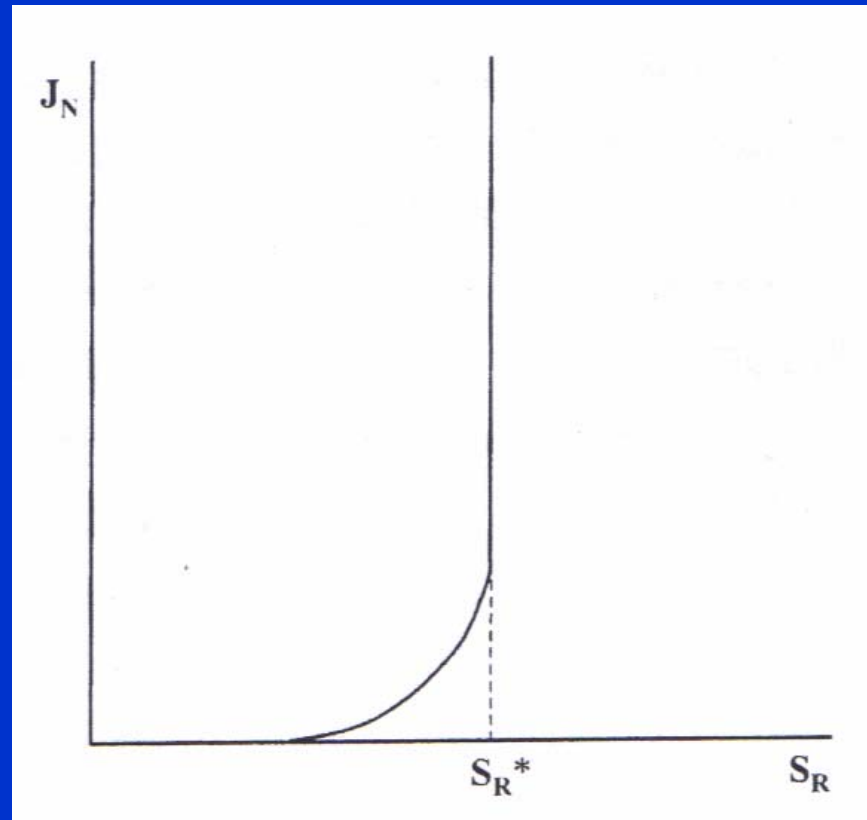
Measurable nucleation rates (defined as the number of nuclei formed in a unit volume per second) can be 1 million to 1 billion $m^{-3}s^{-1}$

Issues to consider

➢ *Increase in supersaturation decreases the activation energy for nucleation*

➢ *Biological systems need to fine-tune the supersaturation in order to achieve control over nucleation*

➢ *Relatively small changes in interfacial energy (σ^3) have a large effect on nucleation rates*

➢ *The critical nucleus size is reduces for lower values of σ*

➢ *This is why heterogenous nucleation is the norm for most cases (impurities)*

Control of nucleation rates

Rate of nucleation (J_N) as a function of relative supersaturation (S_R) in the presence of extraneous particles with (A) equal, and (B) variable nucleation efficiencies; and (C) without extraneous particles.

Epitaxy

➢ *Definition: the oriented overgrowth of inorganic crystals on insoluble substrates*

➢ *The substrate may consist of a mineral with different structure and chemical composition to that of the overgrowth*

➢ *The two phases are crystallographically oriented with respect to each other*

➢ *High degree of lattice matching*

Examples of epitaxy

Substrate	Overgrowth	Lattice misfit %
PbS	NaI	8
	KCl	5
	NaBr	−1
	NaCl	−6
	AgBr	−4
	AgCl	−7
CaCO$_3$	RbBr	7
	RbCl	3
	KBr	3
	NaI	1
	KCl	−2
	NaBr	−7
CaF$_2$	NaBr	8
	NaCl	3
	LiBr	0
	LiCl	−6
NaCl	NaBr	6
	NaCN	6
	AgBr	3
	AgCN	3
	AgCl	1
	KF	−5

Crystal Growth

The growth of an inorganic crystal from pure solution requires the continuous addition of ions to the surface and their subsequent incorporation into lattice sites

Crystal growth is well documented in many textbooks since the beginning of the 20th century

Recently, crystal growth has been revived due to a powerful technique called AFM, atomic force microscopy

Mechanisms of Crystal Growth

The rate of growth of an inorganic crystal from pure solution is given by

$$J_G = k(S_A)^x$$

k = the rate constant, S_A = the absolute supersaturation,

*x = depends on the mechanism of the rate-determining step*

Mechanisms of Crystal Growth

There are four main scenarios:

➤ *mass transport and diffusion-limited growth at very high values of supersaturation (x = 1)*

➤ *polynucleation of surface growth islands at high supersaturation (x > 2)*

➤ *Layer-by-layer growth at moderate supersaturations (x = 1)*

➤ *screw dislocation growth at low supersaturation (x = 2)*

Active sites in Crystal Growth

➢ *Crystal growth is a secondary nucleation process*

➢ *The surface of a growing crystal contains active sites of higher binding energy*

➢ *The main types of active sites are steps and kinks*
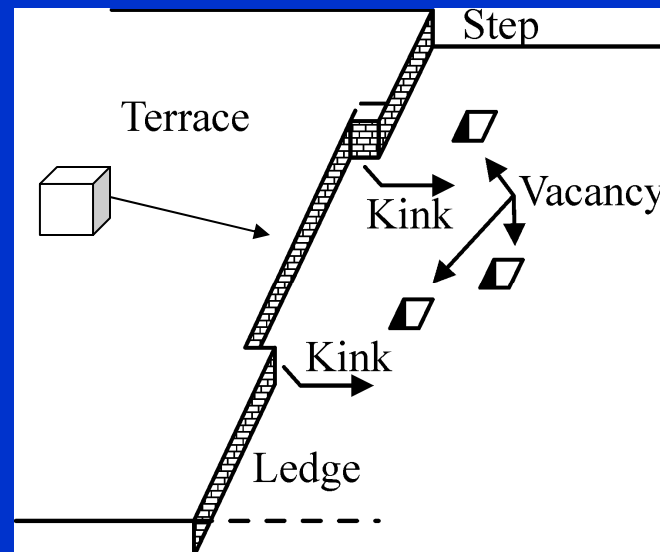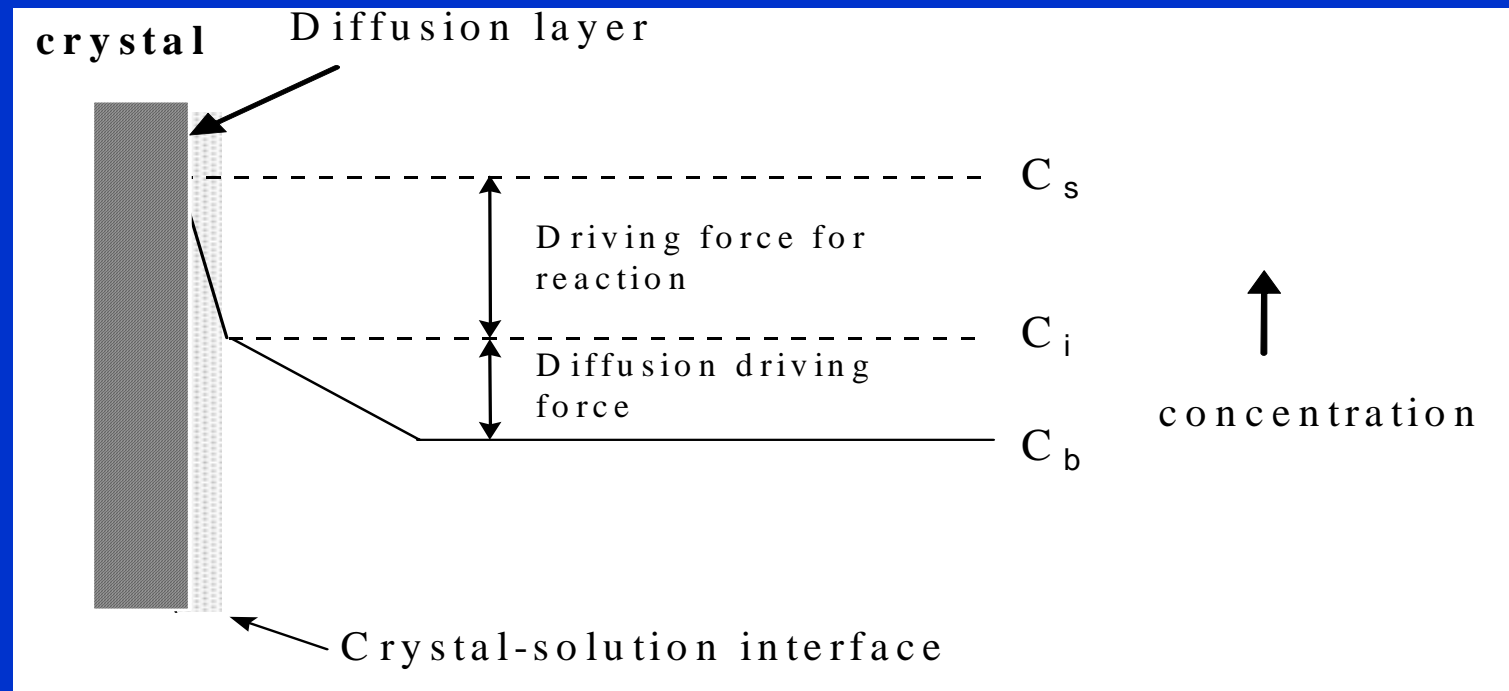
Mechanisms of Crystal Growth

➢ *Bulk diffusion of ions from solution to the crystal surface*

➢ *Surface adsorption and dehydration of ions on the crystal surface*

➢ *Two-dimensional diffusion across the surface to the steps*

➢ *One dimensional diffusion along the step to the kink site*

➢ *Incorporation into the kink site*
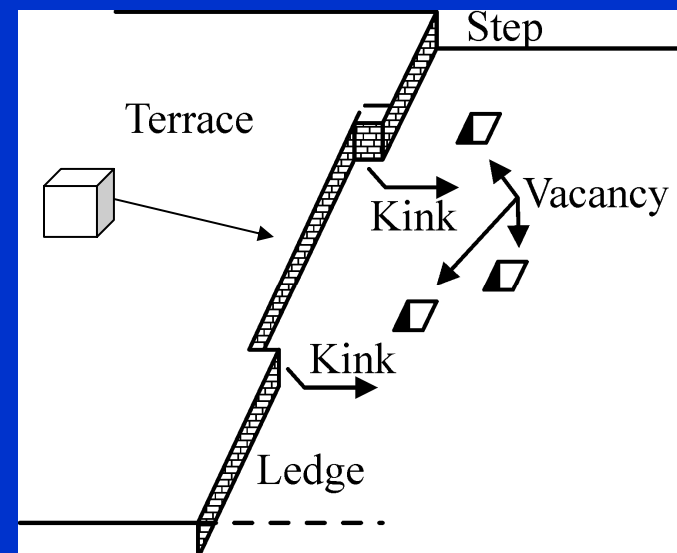
Diffusion-limited crystal growth

Screw-like crystal growth

A   B   C   D