Natural and synthetic biomineralization

**Last time:**
- enzymatic recognition of biomaterials
- Cytokine signaling from biomaterials

**Today:**
- introduction to biomineralization and biomimetic inorganic/organic composites
- Interfacial biomineralization

**Reading:**

**Supplementary Reading:**
- 

**ANNOUNCEMENTS:**
REMINDER: NO CLASS NEXT TUESDAY
Complex macro- and microstructures of biological inorganic materials

Central tenets of biomineralization:

--organic molecules regulate nucleation, growth, morphology, and assembly of inorganic materials

--often employ molecular recognition at organic-inorganic interfaces to control syntheses

Radiolarian: Microskeleton of amorphous silica

Coccolith: CaCO$_3$ microskeleton

A. hexagona: Microskeleton of amorphous silica
HYDROXYAPATITE

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Paradigms in biomineralization

Two mechanisms of templating complex natural crystals:

1. **Interfacial Inorganic Growth**
   - Nucleation at/within organized boundaries
   - Kinetically crystal growth

2. **Epitaxial Inorganic (Crystal) Growth**
   - Growth from template biomolecules
   - Equilibrium crystal growth directed by template
Interfacial inorganic deposition
interfacial inorganic deposition

Utilization of 2-phase systems for compartmentalized deposition

4 main classes:

- Vesicular mineralization
- Microemulsion
- Micelle
- Dendrimer
Vesicular biomineralization

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Vesicular biomineralization

**VESICLES PROVIDE CONTROL OF:**

1. **CONTROL PH:** Ion solubility varies with pH
2. **CONTROL ION FLUX:** Control reactants
   - Ionic strength affects chemical potential of inorganics
   - Na⁺, K⁺
   - Ion transporters
3. **NUCLEATION KINETICS**
   - E.g., alkaline phosphatase: produces HPO₄²⁻
   - Carbonic anhydrase: removes H₂CO₃...
4. **CRYSTAL STRUCTURE AND MORPHOLOGY**
   - Proton pumps
Vesicular biomineralization

\[ \text{SOLID} \quad M_{2+}X_{2-} \quad \Rightarrow \quad \text{IONS IN SOLUTION} \quad \nu_+M_{\nu+} + \nu_-X_{\nu-} \]

\[ K_{sp} = \text{SOLUBILITY} = \left[ [M^{2+}]^{\nu+} [X^{2-}]^{\nu-} \right] \]

\[ S = \text{SUPERSATURATION} = \left[ [M^{2+}]^{\nu+} [X^{2-}]^{\nu-} \right] / K_{sp} \]

\[ S > 1 \quad \text{FAVORS SOLID FORMATION} \]

\[ \downarrow \quad \text{VESICLE SURFACES ALLOW HETEROGENEOUS NUCLEATION AT LOW TOTAL ION CONCENTRATIONS} \]
Vesicular biomineralization

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Please see: Figure 1 and Figure 5.1 in Mann, S. Biomineralization: Principles and Concepts in Bioinorganic Materials Chemistry. New York, NY: Oxford University Press, 2001.
Mechanisms for control of biomineral shape

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Spatial control of chemical deposition:

- Lipid bilayer
- Growing mineral
- Sequentially activated ion transporters

Growth direction
Example biological mineralization: diatom and radiolarian microskeletons

Mineralization nucleated at exterior surface of vesicles


Example biological mineralization: diatom and radiolarian microskeletons

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Biological vesicular mineralization: human growth plate cartilage and tooth dentine

Hypertrophic chondrocytes/odontoblasts

Ion channels
Transport proteins
Acidic phospholipids

Ca$^{++}$
PO$_4^-$

CaHPO$_4$ nucleation
HA crystallization

MATRIX VESICLES
ECM

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Synthetic vesicular mineralization

Vesicular mineralization

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Natural and synthetic vesicular biomineralization

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Microemulsion biomineralization

Aq CaHCO₃

Organic (oil) phase

SDS

Gas-evolving microemulsion biomineralization

Microemulsion mineralization

Chemistry of CaCO₃ deposition in vesicles:

\[
Ca^{++} (aq) + 2HCO_3^- (aq) \rightarrow CaCO_3(s) + CO_2(aq) + H_2O
\]

At equilibrium:

\[
K_{eq} = \frac{[H_2O][CO_2(aq)][CaCO_3(s)]}{[Ca^{++}(aq)][HCO_3(aq)]^2} = \text{constant}\]

At given T, P

![Diagram of gas-evolving microemulsion biomineralization](image-url)
Mineralizing bicontinuous microemulsions

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Coupling growth with self-assembly: micelle-directed inorganic crystallization

Coupling growth with self-assembly: micelle-directed inorganic crystallization

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Please see: Figure 1 in Li, M., H. Schnableffer, and S. Mann.

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Please see: Figure 2 in Li, M., H. Schnableffer, and S. Mann.
Organic templating of inorganic materials

Epitaxy of Inorganics
Optimization of inorganic biomaterial properties—nature does it better

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Organic template control of inorganic nucleation

Nucleation of solid phase:

\[ \Delta G_{\text{nucl}} = \Delta G_{\text{surface}} - \Delta G_{\text{bulk}} \]

\[ = 4\pi r^2 \sigma - \frac{4}{3}\pi r^3 \frac{\Delta G_{\text{form}}}{V} \]

\(\sigma > 0\) surface energy of nucleating crystal

Modified by the presence of a nucleating surface

Fixed by chemistry of system

Free energy change to form solid from free ions

Molar volume

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Organic template control of inorganic nucleation

Nucleation of solid phase:

1. **Homogeneous Nucleation**
2. **Surface (Heterogeneous) Nucleation**
Organic templates can select crystal structures

\[ \Delta G_{\text{Nuc}}^{\text{B}} \]

- **Non-specific Surface Nucleation**
- **Structure-specific Selection of \( B \)**

1. \( A \) = No Surface
2. \( B \) = Templating Surface

**Lower energy barrier for \( A \) means \( 17 \) is kinetically favored**
What are the organic templates?

Templates used by nature:

- PROTEINS → FORM HIGHER-ORDER STRUCTURES
- POLYSACCHARIDES
- LIPIDS → LESS SELECTIVE: 2D FLUIDS

Template functional groups correlate with structure to be nucleated:

- CARBOXYLATE MOIETIES:
- Asp, Glu
- Ca$^{2+} \rightarrow$ CaCO$_3$, HA

- H-BONDING MOIETIES:
- Ser, Thr

β-sheets
α-helices
Provide periodic repeat motifs
How are free energy barriers modified by organic templates?

Lattice matching for epitaxial nucleation of inorganic:
Charge distribution effects on templated nucleation

Table removed due to copyright reasons. Please see: Table 1 in Mann, et al. 1993.
Charge distribution effects on templated nucleation

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Please see: Figure 4.20 in Mann, S.

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Please see: Figure 4.23 in Mann, S.
2 mechanisms of surface-mediated nucleation:
Controlled nucleation and growth vs. preferential nucleation and growth

• Organic templates can preferentially nucleate inorganics without ordering or aligning the crystals

• Templated crystal growth requires both recognition of individual molecules and a larger underlying lattice to drive ordered nucleation

• Obtaining periodicity in organic templates:
Further Reading