Bone Biomineralization and Regeneration

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Medical Mineralogy involves the study of the mechanisms of cells or biomolecules interactions with minerals and aqueous solutions in processes relevant to human health. Mineralogists can uniquely contribute by emphasizing the critical role of the crystal structure, composition, particle size, bulk and surface chemistry of the mineral or amorphous solid phase to the thermodynamics or kinetics of the relevant reactions. These ideas are illustrated with two examples involving bone.

Bone is a hierarchical, composite material of collagen molecules and fibrils in strict spatial registry with plate-shaped, nanocrystals of non-stoichiometric hydroxyapatite and non-collagenous proteins. The mechano-biochemical functions of bone depend critically on this architecture. Incredibly, the molecular-level mechanisms of bone biomineralization are still not understood, despite six decades of research since the two-dimensional structure of collagen was first determined. We used Molecular Dynamics (MD) simulations based on low resolution X-Ray structure to develop the first high-resolution three-dimensional collagen fibril structure up to the 100s of nm length-scale. Hamiltonian Replica Exchange MD results showed that calcium phosphate clusters nucleate in specific "hole" zones within the fibril, because charged amino acid side chains of the collagen molecules are oriented in towards the hole zones, thus, attracting Ca^{2+} and phosphate ions to those zones. Further, using HRTEM, we showed that even small molecules, like citrate and amino acids, can modulate crystal growth resulting in platey nanocrystals. Umbrella sampling potential of mean force simulations suggested small molecule adsorption in preferred crystallographic directions, thus modulating shape.

The goal of bone tissue engineering is to design bioactive scaffold materials loaded with soluble factors that induce osteogenic cell differentiation and promote bone regeneration. We have shown that soluble silica is a pro-osteoinductive factor to human mesenchymal stem cell (hMSCs). Hence, even without extraneous soluble factors, a scaffold that releases silica faster should be more osteoinductive than a slower-dissolving silicate. The hypothesis was confirmed by comparing osteoinductive potential of pseudowollastonite (β-$CaSiO_3$), which has a strained three-ring silicate structure, to its more stable, chain silicate polymorph, wollastonite (α-$CaSiO_3$). Thus, crystal structure can be used one predictive property of the osteogenic potential of silicate bioceramics.