

An investigation of calcium phosphate prenucleation clusters

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Understanding crystallization processes at a molecular level begins with understanding stable species in solution and how these species aggregate. Calcium phosphate nucleation and growth is particularly important due to its role in bone formation[1] and defining how the amorphous precursor to bone forms and crystallizes. While the existence of Posner's cluster ($\text{Ca}_9(\text{PO}_4)_6$) has been postulated since the 1970s as an aggregation unit for hydroxyapatite,[2] experimental results have differed on the nature of precursor species with some suggesting instead $\text{Ca}(\text{HPO}_4)_3^{4-}$ as the prenucleation cluster.[3] While the high charge of the suggested cluster makes aggregation seem unlikely, the possibility of entropic gain allowing for a thermodynamically favorable result makes further investigation necessary.

Here computer simulation has been used to probe the thermodynamics of the early stages of calcium phosphate association. We explored the binding mechanisms of various calcium hydrogen phosphate clusters (including CaHPO_4 , $\text{Ca}(\text{HPO}_4)_2^{2-}$, $\text{Ca}(\text{HPO}_4)_3^{4-}$ complexes) and whether their aggregates are thermodynamically feasible as well as the thermodynamics of the aggregation of Posner's cluster. Simulations were run using a force field parameterized with a specific thermodynamic focus, including targeting aqueous free energies of solvation for the phosphate and calcium ions, as well as the solubilities of phosphate mineral phases.[4]

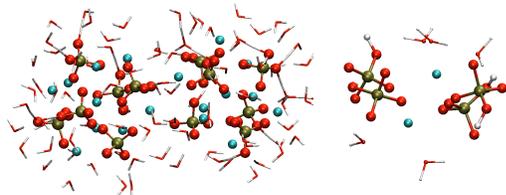


Figure 1. Left: The association of two Posners' clusters; Right: a $\text{Ca}_2(\text{HPO}_4)_4$ cluster. (Red: O, tan: P, Cyan: Ca, White: H).

- [1] Olszta et al (2007) *Mater. Sci. & Eng. R Rep.* **58**, 77-116.
[2] F. Betss and A.S. Posner (1974) *Mater. Res. Bull.* **9**, 353-350. [3] Habraken et al. (2013) *Nat. Commun.* **4**. [4] Demichellis et al. (2018) *J. Phys. Chem. B.* **122**, 1471-1483.