

## Simulating the effect of peptides on calcium carbonate nucleation

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The nucleation mechanism for calcium carbonate remains controversial. Recent experiments and simulations found no evidence for thermodynamically stable pre-nucleation clusters [1], concluding that classical nucleation theory could describe the nucleation of calcium carbonate. However, this can be a multistep, multi-phase process involving dense liquid and solid amorphous phases. Earlier work [2] also invokes this phase. Their experiments suggest that it is stabilised by the presence of polyaspartate; they observe a polymer-induced liquid phase (PILP) as advocated by Gower.

We simulated aqueous solutions with  $\text{Ca}^{2+}$ ,  $\text{HCO}_3^-$ ,  $\text{CO}_3^{2-}$  ions including arginine (positive), aspartate (negative) and glycine (neutral) at about pH 10. We considered both low (a few mM; close to experiment) and high (about 0.5M) concentrations.

At low concentration we saw cluster formation between  $\text{Ca}^{2+}$  ions, the amino acids and  $\text{HCO}_3^-$ ,  $\text{CO}_3^{2-}$  ions involving also 'spectator ions' like  $\text{Na}^+$ ,  $\text{Cl}^-$ . The solution exhibits classical behaviour with free ions, ion pairs and other small clusters whose size distribution decays exponentially. We do not find 'prenucleation clusters' in the sense usually defined. At high concentration the amino acids self-assemble into aggregates, facilitated by 'spectator' ions and usually  $\text{HCO}_3^-$ . Liquid-like clusters form from the remaining calcium carbonate. These are also seen at the surface of the amino acid aggregates.

We considered the effect of oligopeptides (hexamers of the above amino acids) at the higher concentrations. Here, we do observe some assembly of the hexamers facilitated by the calcium carbonate. The calcium carbonate here forms liquid-like networks connecting the hexamers rather than just collecting at interfaces. Thus, the oligopeptides seem to stabilise a dense liquid phase - a very similar behaviour is found for positive, negative and neutral organics. We discuss the implications of these results for the role of a dense liquid phase in the nucleation mechanism for calcium carbonate.

[1] P.J.M. Smeets, A.R. Finney *et al.* *P.N. A. S.* **114** (2017) E7882. Henzler *et al.*, *Sciences*, **4** (2018) eaa06283.

[2] M.J. Bewernitz, D. Gebauer, J. Long *et al.* *Farad. Disc.* **159** (2012) 291.