Molecular dynamics simulations of the interaction of glycosaminoglycan saccharides with hydroxyapatite surfaces: Implications for crystal growth

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The biomineral hydroxyapatatite (HAP) is commonly found in mammalian tissue. A substituted crystal structure of the mineral is the inorganic component of bone[1], and in humans it is also present in teeth, the Randall's plaques (possible centre of formation for kidneys stones) and other small calcifications. The formation of the appropriate structure is controlled by various cells via secretion of several biomolecules into the surrounding tissue. The biomolecules can influence the spontaneous biomineralization of the apatite structures, either by providing a template for crystal nucleation; by adsorbing onto crystal surfaces and thus inhibiting crystal growth; or by sequestering dissolved mineral ions.

Glycosaminoglycans (GAGs) are polysaccharide molecules that are abundant in mineralised tissues. A GAG molecule is an unbranched polymer chain of two different types of monosaccharide linked together in alternation[2]. It has been found that under in vitro conditions of limited calcium availability, GAGs, including chondroitin sulphate, and their proteoglycans inhibit the deposition of hydroxyapatite, because the adsorption of GAG molecules on the mineral surfaces is an obstacle to the mechanism of crystal growth[3].

In this work we use computational methods to investigate the interfacial interactions between GAGs and HAP. We present molecular dynamics (MD) simulations of chondroitin sulphate saccharides adsorbed onto a slab of HAP in the presence of interfacial water. Adsorption structures have been calculated for the thermodynamically preferred (0001) surface, and the (01$\bar{1}$0) surface, which is the dominant plane of apatite nanocrystals in a biological environment. We have simulated the adsorption of the monosaccharides GlcA and GalNAc 4-sulphate independently to isolate the essential HAP–saccharide interactions for each adsorbate.

[1] A. S. Posner, *Nature*, 1964, **204**, 1050–1052. [2] L. Kjellén and U. Lindahl, *Annu. Rev. Biochem.*, 1991, **60**, 443–475. [3] S. G. Rees, R. P. Shellis, and G. Embery, *Biochem. Biophys. Res. Commun.,* 2002, **292**, 727–733.