Impact of carboxylated molecules on cation hydration dynamics and implications for calcification

L.M. HAMM[1]*, A.F. WALLACE[2] AND P.M. DOVE[1]

Department of Geosciences, Virginia Tech, Blacksburg, VA 24061 USA (*correspondence: maehamm6@vt.edu)
[2]Earth Science Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA

Biomolecules rich in aspartic acid (Asp) are known to play a role in biomineral morphology and polymorph selection, and have been shown to greatly enhance the growth kinetics of calcite. The mechanism by which these compounds favor calcification may be related to their effects upon cation solvation; dehydration of the cation is considered the rate-limiting step for crystal growth and water exchange rates are thought to be important in mineral growth and dissolution processes. To understand the impact of carboxylated molecules on the solvation dynamics of cations, we investigated the influence of Asp on the water exchange rates of cations. The reactive flux method was employed to calculate water exchange rate constants for divalent cations relevant to calcification (Mg^{2+}, Ca^{2+}, Sr^{2+}). Residence times were also determined directly for Ca^{2+} and Sr^{2+}, ions which have relatively fast rates of water exchange. Exchange rates were then recalculated after introducing Asp into the system. All simulations were carried out with the LAMMPS software employing the TIP3P model of water, CHARMM22 force fields, and ion-water potential parameters from Aqvist.

Preliminary simulations reproduce the expected solvation trends based on cation radius. The energy barrier for water escape from the primary hydration shell is greatest for Mg^{2+} and smallest for Sr^{2+}, and water residence times within the first shell increase in the order: $Sr^{2+} < Ca^{2+} < Mg^{2+}$. In the presence of Asp, complexation of Sr^{2+} and Ca^{2+} with a carboxylate group results in a decreased total first shell coordination number and an increase in the frequency of water exchange events about the cation. When Sr^{2+} and Ca^{2+} are complexed with Asp, residence times for inner-sphere water molecules are reduced to less than half of those calculated for the free cations in solution. Continuing work is focused on determining the impact of Asp on the solution dynamics of Mg^{2+} and understanding how ion-Asp separation affects cation water exchange rates.

Solution scattering combined with crystallography and computation: Defining dynamic macromolecular structures

MICHAL HAMMEL*

Physical Biosciences Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA (*correspondence: mhammel@lbl.gov)

Crystallography supplies unparalleled detail on structural information critical for mechanistic analyses; however, it is restricted to describing low energy conformations of macromolecules within crystal lattices. Small angle X-ray and Neutron scattering (SAXS and SANS) offers complementary information about macromolecular folding, unfolding, aggregation, extended conformations, flexibly linked domains, shape, conformation, and assembly state in solution, albeit at the lower resolution range of about 50 to 10 Å resolution, but without the size limitations inherent in NMR and electron microscopy studies. Together these techniques can allow multi-scale modeling to create complete and accurate images of macromolecules for modeling allosteric mechanisms, supramolecular complexes, and dynamic molecular machines acting in diverse processes ranging from eukaryotic DNA replication, recombination and repair to microbial membrane secretion and assembly systems. SAXS and SANS provide the basis to examine molecular interactions in solution and to study macromolecular flexibility and conformational changes that have become increasing relevant for accurate understanding, simulation, and prediction of mechanisms in structural cell biology and nanotechnology [1, 2].

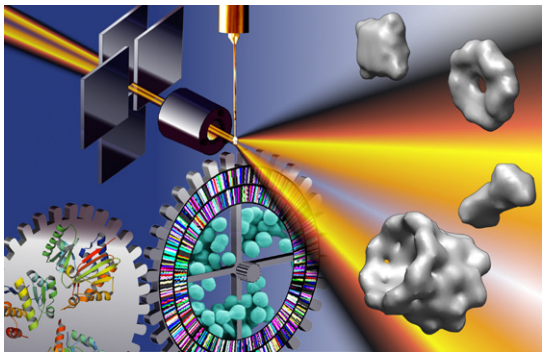

Figure 1: Small Angle X-ray Scattering and the structure.

[1] Hura, G. L., A. L. Menon, *et al*. (2009). *Nat Methods* **6**, 606-612. [2] Putnam, C. D., M. Hammel, *et al*. (2007). *Q Rev Biophys* **40**, 191-285.