Biomineralization and Biomineralization-Inspired Drug Design: Calcite - Peptide Interactions

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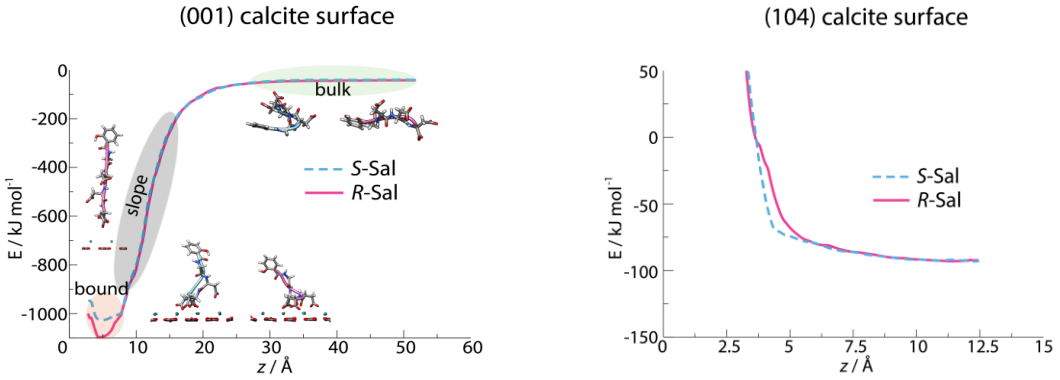
The field of interface chemistry has been heavily focused in recent years on the development of systems that could be used for the controlled introduction and release of active pharmaceutical compounds in the living organisms and tissues. Some of the most interesting systems in this respect, attracting interest from both the pharmaceutical and food industry, are the bioinorganic composites of calcite (calcium carbonate, $CaCO_3$) functionalized by small, biologically active molecules, with the aim of controlled drug delivery. [1] In this respect, we decided to investigate the interactions of calcite with two highly active biomolecules, which are experimentally found to strongly interact with the biomineral, [2] in an attempt to uncover the roles of flexibility and chirality in biomineralization and biomineralization-inspired drug design.



More precisely, using advanced simulation techniques we characterized the adsorption behavior of two epimeric peptides, namely *R*- and *S*-Sal (N-Sal-Gly-*S*-Asp-*R*-Asp-*S*-Asp and N-Sal-Gly-*S*-Asp-*S*-Asp-*S*-Asp respectively, where N-Sal denotes the N-terminal residue which is a salicylic acid derivative), on both the stabile (104) and growing (001) surfaces of calcite. This, on one hand, allowed us to analyze the conformational behavior of the adsorbed peptides in detail, while, on the other hand, permitted us to investigate the underlying thermodynamics of the process by calculating free energy profiles of adsorption. We thereby found that even small differences, such as the change in the chirality of only one constituent amino acid, can change the conformational behavior of the peptide to an extent significant enough to induce different binding patterns and interactions on mineral surfaces, leading to an overall different adsorption of active biomolecules/peptides.

[1] M. Fujiwara, K. Shiokawa, K. Morigaki, Y. Zhu, Y. Nakahara, *Chem. Eng. J.* **2008**, *137*, 14-22.
[2] M. Ukrainczyk, M. Gredičak, I. Jerić, D. Kralj, *J. Colloid Interface Sci.* **2012**, *365*, 296-307.