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# Multiscale Modelling of Milk Protein Interaction With Iron and Aluminum Surfaces

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In this work, the bionano interface structure is investigated by a methodology that accounts for the interaction between inorganic solid nanoparticles (NPs) and protein biological molecules at the interface [1].

The relationship between nanomaterial properties and the interaction with different materials is key to a deeper understanding and the design of new nanomaterials and nanoplatform systems. Here we are interested to study the interaction of cow milk protein with metals such as iron and aluminum used in milk processing. Milk proteins are essential for applications ranging from nutrition to bio and chemical technology. Moreover, a variety of natural and anthropogenic sources introduce aluminum and iron into the food chain. Therefore, there are a number of pathways for aluminum and iron into milk and dairy products [2].

Moreover, NPs entering biological liquids acquire a layer on the surface known as protein corona [3]. The composition and configuration of corona determine the biochemical reactivity and sensitivity of NPs. Therefore, it is essential to understand the competitive adsorption of proteins on metal surfaces to rank the proteins by the binding affinity. For this statistical models such as QSAR and machine learning are very efficient in comparison to investigating these interactions by measurements, which are very costly and time consuming.

In order to do that, we first start with all atomistic simulations for each amino acid side chain analogous (SCA) on a NP surface surrounded by water. NPs are modeled as surface slabs in atomistic level and nanosecond Metadynamics simulations were used to simulate the free energy associated with the interaction of cow milk proteins with water molecules and a metal iron and Aluminum surface. In the subsequent step, we apply the first and second level of coarse-grained United Atom (UA) model [1] to evaluate the adsorption energies of the proteins on the iron NP surface. The 3D structures of each protein obtained from AlphaFold will be compared with those predicted computationally by I-TASSER from amino acid sequences. We will then develop mathematical models to predict the binding energy of proteins based on these predictions and 2D and 3D protein descriptors, enabling the rapid characterization of proteins.

First results for 6 main milk proteins based on binding energy heatmaps and Boltzmann average energies from UA show that for both Al-110 and Fe-110, alpha s1 casein and alpha s2 casein are more strongly bound to the surface, while beta casein and beta lacto globulin are less strongly bound on Al-100 and Fe-110 respectively.
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