Multiscale Modelling of Biomolecules at Inorganic Surfaces

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Understanding of processes at hydrated surfaces of inorganic nanomaterials in biomolecular media is of crucial importance in many technological and biomedical applications, as well as in investigation of molecular mechanisms behind possible hazard effects of nanoparticles in living organisms. Experimentally it is very difficult to get information on details of the hydrated surface structure and biomolecular adsorption at nanosurfaces because of very small volume of the relevant region of space relative to the bulk. Physics-based computer modeling provides alternative route to characterize bio-nano interface. The challenge here lies in the range of scales that needs to be crossed from the detailed surface chemistry in atomistic representation to the relevant length scales covering typical nanoparticles and biomolecules (proteins and lipids). Here a systematic multiscale approach is presented that allows one to evaluate atomistic interactions at the bionano interface from the first principles simulations, and then proceed, without any empirical parameterization, to coarse-grain (CG) models enabling modeling of real-size nanoparticles with proteins and lipid membranes.

This approach is illustrated on modeling of biomolecular adsorption on TiO_2 nanoparticles. We start from ab-initio molecular dynamics (AIMD) simulations of TiO_2 surfaces in water from which information on detailed TiO_2 surface chemistry and hydroxylation pattern is obtained. Furthermore, AIMD simulations are used to parametrize atomistic force field for classical MD simulations, using DDCE6 partitioning of electron density and determination of partial atom charges and Lennard-Jones parameters from it. Next, *ab-initio* derived atomistic force field is used in classical molecular dynamics simulations of TiO_2 surfaces in water solution containing also lipid molecules. These simulations demonstrated that lipids bind to TiO_2 surface by their polar groups, and that strength of this binding depends on the lipid type and TiO_2 form (anatase vs rutile). Atomistic simulations were also used to determine interaction potentials for CG models by the Inverse Monte Carlo method, which provides for CG models the same structural properties as those observed in atomistic simulations. CG simulations of real size nanoparticles in presence of large amount of lipids showed deposition of lipids at the surface and formation of lipid bilayer attached to the nanoparticle surface. Implications of the obtained simulation results for toxicological in-vivo studies on inhalation of TiO_2 nanoparicles are also discussed.