Project B3: Modeling size dependent polysaccharide nanoparticle self-assembly

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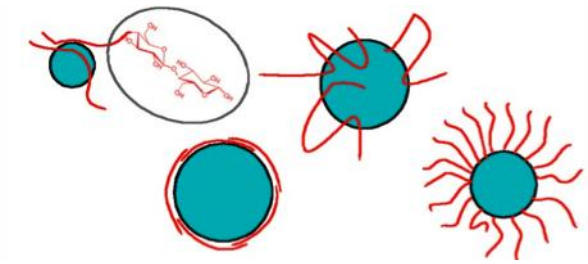
US partner: **Berkowitz (UNC)**

Outline. Polysaccharides are stable, non-toxic, biodegradable, and biocompatible macromolecules that offer a wealth of biochemical and biomechanical functionality. These merits make them promising materials to tune the surface properties of different nanoparticles and lipid vesicles. Polysaccharides either adsorb to the particles or are grafted on its surface. To achieve better control over surface nanostructure and functionality, a detailed understanding of the adsorption processes and the factors affecting properties of the saccharide shell is required. As one important factor, many biologically derived polysaccharides behave as polyelectrolytes and their conformation and charge density depend on pH and ionic strength of the system. Here we are interested in the questions of how properties such as the adsorbed quantity, conformation, charge density and mobility will be influenced by the presence of a surface, and how these characteristics depend on the nanoparticle size and shape. We will consider the frequently used, molecule types Chitosan, a weak polycation and Hyaluronan, a weak anion.

Research within the German group. A coarse-grained (CG) model for the polysaccharides will be developed based on atomistic Molecular Dynamics (MD) simulations of disaccharides and short oligosaccharide chains. The free energy maps for the glycosidic angles will be measured and used to sample likely conformations of large polysaccharide molecules using Monte Carlo (MC) sampling and CGMD. The effect of pH and ionic strengths can be approximated with protonation moves for titratable. Treating the particles initially as rigid spheres with charged or titratable sites at the surface, the effect of particle size and concentration on polysaccharide conformation and charge will be investigated. More specific interactions between non-bonded saccharide monomers and between saccharides and the particle can be added as necessary using the force matching method.



Cartoon of different conformations of the polysaccharide chains at the particle surface. These will depend on the system conditions, the interplay of particle curvature and adsorption strength and on the adsorption dynamics (kinetic trapping).

Longer-term perspective. In the continuation period, the systems' response to pH changes will be studied with CGMD simulations. The dynamics and the extent and reversibility of conformational changes in this switching process will be investigated for the different particle shell geometries and their conformation compared to those obtained from assembly at the final conditions. Effects of cross-linkers added to the polysaccharide shell on the switches may also be tested.

Complementary work in US partner group. The previously described studies will be complimented by all atom MD simulations of the interaction of Chitosan, Hyaluronan and Dextran oligo-saccharids with lipid bilayers, to gain a better understanding of the differences observed in coating vesicles with these molecules. The Berkowitz group has considerable experience with modeling and analyzing the interactions of lipid bilayers with other molecules.

Status of the project. The project will interact closely with project B2 (Gradzielski) studying polymer coated nano-particles and their properties. The topic is also related to project B1 (Weikl) through simulations planned in the US Changes in molecular conformation stimulated by external fields are studied in project A3 (Stark).