IMPRS on Multiscale Biosystems

Title: Simulation of the interaction of dendritic polymers with bone proteins and inflammation markers
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In collaboration with: Prof. Dr. Rainer Haag (FU)

Project description: On-going studies in the Haag group show that dendritic polymers functionalized with anionic groups like phosphate, phosphonate, biphosphonate or sulfate show anti-inflammatory activity and enhanced affinity towards bone. These polymers are hence promising candidates for targeted delivery of bioactive compounds to inflamed sites and bone. For example, the anti-inflammatory properties of dendritic polyglycerol sulfate arise from its inhibition of selectin proteins and its different affinity for hydroxyapatite and collagen - components of bone or cartilage - should allow for targeted drug delivery. The aim of this project is to investigate the molecular scale mechanisms of interaction of anionic dendrimers with selectin or collagen, answering questions such as: How do polyelectrolytes bind to selectin? Why do sulfate-based dendrimers in particular have such high binding affinity for selectin, and what is the role of salt in binding? What is the mechanism of selectin inhibition? How do the various polymers interact with collagen? Why do polysulfonates have the highest affinity for collagen? How does the stiffness of the polymeric scaffold and the density of surface functional groups affect binding to target molecules?

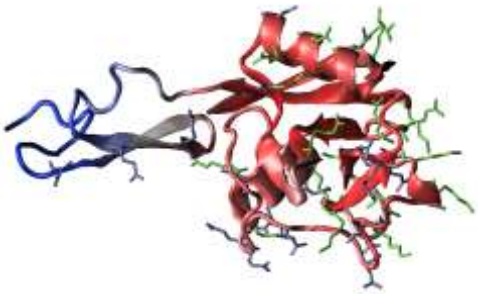

Figure 1: Structure of L-selectin.

The student will address these issues using a variety of particle-based simulation methods, with emphasis on classical molecular dynamics. Advanced techniques to enhance sampling of configuration space will be systematically used to calculate thermodynamic observables like binding free energies. Ab initio methods will be used to parameterize new compounds for classical simulations. The project will benefit from frequent discussions with the Haag (FU) and Fratzl (MPIKG) groups, currently investigating these issues using experiment. This project is mainly theoretical/computational, but the student will have the opportunity to perform experiments (e.g. dynamic light scattering, titration) on model systems, allowing him/her to acquire valuable extra skills and knowledge for his/her future career.

Required background: Strong knowledge of chemical physics, physical chemistry and physics. Prior experience with particle-based simulation techniques (atomistic or coarse-grained molecular dynamics, Monte Carlo, ab initio calculations) is an advantage.
Paper to read before the interview: Weinhart et al., *Synthesis of Dendritic Polyglycerol Anions and Their Efficiency Toward L-Selectin Inhibition*, Biomacromolecules 2011, 12, 2502.
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