IMPRS on Multiscale Biosystems

Title: **Thermodynamics of interactions of polyanionic carbohydrates with bacteriophage proteins.**

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In collaboration with: Biopolymer research groups of the MPI Department of Theory and Biosystems

Project description:

Carbohydrate-protein interactions are ubiquitous in nature and mediate the exchange of specific information [1]. The affinity of proteins towards sugars is tightly linked to the functional context of the respective interaction. It is therefore very important to study the driving forces for these recognition events and to understand in which way structural features of protein-carbohydrate complexes influence the thermodynamics and the mechanism of binding. Negatively charged polysaccharide components are ubiquitous on the cell surfaces of bacterial pathogens. Accordingly, they represent important recognition structures for proteins. Systematic structural thermodynamics studies have mainly focused on lectins that specifically recognize neutral, i.e. uncharged carbohydrate structures [2]. However, extracellular carbohydrate matrices existing as gels require the presence of negatively charged building blocks to bind water. Consequently, anionic carbohydrates are also present in capsules and biofilms that shield bacteria from the environment and from antibiotics.

Neuroinvasive *E. coli* strains K1 and K5 as well as *Neisseria meningitidis* serogoup B strains produce capsules composed of α-2,8-linked polysialic acid (polySia). They cause severe neonatal meningitis. The human immune system cannot respond to polySia encapsulated pathogens because polySia is also present on eukaryotic cell surfaces. In our lab we have recently engineered a set of polySia binding proteins. So far, no quantitative thermodynamic studies are available that relate protein binding site architecture to polySia affinity [3]. Aim of the project will be the analysis of polySia protein binding with isothermal titration calorimetry. Moreover, polySia binding rates are influenced by the inherent flexibility and depend on the length of polySia molecules. The candidate will also investigate these polySia binding dynamics with different fluorescence spectroscopy techniques and with surface plasmon resonance in combination with computer simulations of polySia. The thorough characterization of polySia protein complexes is an important prerequisite both for engineering of polySia binding proteins and understanding polySia binding thermodynamics.

References: [**1]** Gabius, H.J., et al., Trends Biochem Sci, 2011. 36(6): p. 298-313. **[2]** Dam, T.K. and C.F. Brewer, Chem Rev, 2002. 102(2): p. 387-429. **[3]** Schulz, E.C., et al., J Mol Biol, 2010. 397(1): p. 341-351.

Required background: The successful candidate has a strong biochemical background and motivation for quantitative biophysical experimental as well as theoretical work. Good communicative and networking skills for the interdisciplinary project are very much desired.

Paper to read before the interview: References 1 and 3.

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http://www.uni-potsdam.de/en/ibb/researchgroups/fullprofessors/physical-biochemistry/group-members/dr-stefanie-barbirz-glycobiochemistry.html