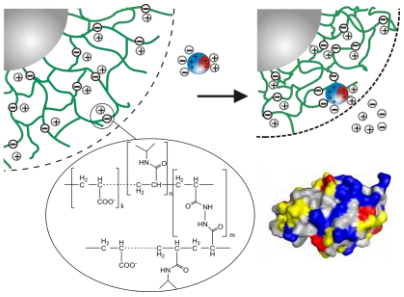
Project B4: Protein assembly on polymeric nanoparticles

Project leader: **Ballauff (HUB)**
Co-supervisor: **Gradzielski (TUB)**
US partner: **Zauscher (DU)**

Outline. The adsorption of proteins onto surfaces is a central problem in many areas of modern biotechnology and in the field of biomaterials. Proteins will adsorb from aqueous solution virtually to any surface and an understanding of the driving forces and the kinetics is of fundamental importance for drug delivery and applications of nanoparticles in medicine. Nanoparticles will be immediately covered by a dense layer of protein when injected into the blood stream. This "corona" then will determine the response of the body to these particles and a precise knowledge of the composition of the corona and its temporal evolution is necessary for e.g., nanotoxicology. Moreover, adsorption may often be accompanied by a slow denaturation and the immune system of the body "sees" a denatured protein and not the material of which the nanoparticle is composed. In addition to this, adsorbed proteins may slowly be released by adsorption of other proteins and the corona may thus change with time (Vroman effect). Dynamics of protein adsorption is therefore a central problem in this field.



Adsorption of proteins onto charged core-shell microgels. The charged patches on the surface interact with the network and lead to its shrinking.

Research within the German group. The doctoral researcher working on this project will perform experimental work on the adsorption of proteins to well-defined nanoparticles. Here we plan to use core-shell microgels that have been the subject of previous studies by us. These particles consist of a polystyrene core of ca. 100 nm diameter onto which a dense shell of crosslinked poly(N-isopropylacrylamide) (PNIPA) chains are grafted. The surface layer of crosslinked PNIPA presents a well-defined model surface that is strongly curved. The main aim of this project will be the detailed investigation of competitive adsorption of proteins by time-resolved experiments. Here blood proteins, such as HSA and fibrinogen, will be used. As in previous studies, isothermal titration calorimetry done at different temperatures will be used to explore the thermodynamics of the adsorption of single proteins in detail. Labeling proteins by fluorescent markers will then allow us to study the competitive adsorption of proteins. Time-resolved fluorescence spectroscopy will give additional information about the kinetics of protein adsorption. The dynamics of protein adsorption will be furthermore analyzed by time-resolved SAXS. This method will then lead to detailed information about the distribution of the proteins within the surface layer. All data achieved on these strongly curved particles can be compared to data obtained on planar surfaces. The theoretical understanding and modeling will be done in close collaboration with the group of J. Dzubiella. Here special attention will be paid to a quantitative modeling of the various forces leading to protein adsorption.

Longer-term perspective. The general goal of this project is a detailed understanding of the driving forces of protein adsorption to highly curved surfaces. This knowledge can then be used to modify given particles for a well-defined uptake into cells for e.g. drug delivery or imaging. In this respect this project is complementary to similar work done on polymerically modified nanoparticles in project B2 (Gradzielski).

Complementary work in US partner group. The Zauscher group has experience with atomic force microscopy (AFM) nanomechanical measurements. His group will apply these techniques to measure the adhesion strength of the adsorbed proteins to the NP surfaces, and provide details of the mechanical properties of the stimulus-responsive PNIPA corona.

Status of the project. The project will interact closely with project B2 (Gradzielski). Self-assembly of organic molecules at curved interfaces of nanoparticles are studied in project B5 (Schoen).