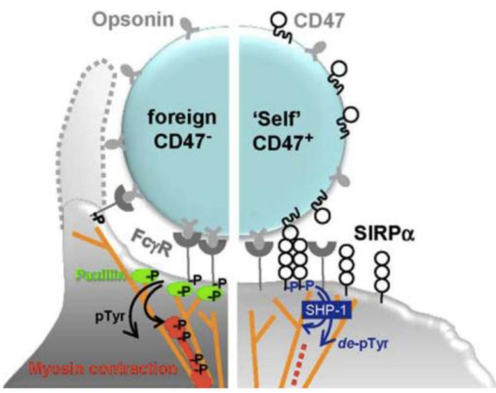
Project C4: Adhesion and engulfment by multi-component membranes

Project leader: **Lipowsky (MPIKG)**
Co-supervisor: **Weikl (MPIKG), Schoen (TUB)**
US partner: **Discher (UPenn)**

Outline. The objective of this theoretical project is to develop and study simplified model systems for the process of phagocytosis (see figure), in which “particles” and damaged cells are engulfed by cells of the immune system. This process starts with membrane adhesion followed by partial engulfment that involves the molecular recognition between receptors and ligands on the two surfaces. Depending on the receptor-ligand complex, the engulfment process is either abandonned at an incomplete stage (see right part of figure), or extended to complete engulfment of the phagocytotic particle (see left part of figure). The underlying molecular mechanisms that decide between these two different pathways are poorly understood, even though several receptors and ligands have been identified.



(Left) Complete engulfment of “foreign” particle and (Right) No engulfment of “self” particle. The two types of particles are distinguished by the ligand molecules anchored at their surfaces. [R. Tsai and D. Discher, J. Cell Biol. ***180****, 989 (2008)]*

The model system that will be addressed in this project consists of a vesicle that enwraps a “particle”, which may be rigid, soft, or even a fluid droplet. In contrast to previous theoretical studies, the membrane of the vesicle is taken to contain several components which are enriched or depleted via the adhesion process. This change in the membrane composition leads to a change in the affinity between the two surfaces. One objective of this project is to determine how the free energy barrier for engulfment is affected by this change in surface-surface affinity. Additional objectives are the effects of membrane tension and spontaneous curvature on this barrier.

Research within the German group. The doctoral researcher will start from the results of the current IRTG project on the phase behavior of adhering vesicles with multi-component membranes and consider the corresponding phase behavior for the adhesion to spherical particles. The engulfment by one-component or chemically uniform membranes has been previously studied both for rigid and for fluid droplets. These studies will now be extented to multi-component membranes using analytical theories for the membrane morphology as well as simulations of coarse-grained molecular models.

Longer-term perspective. At a later stage of this project, the effect of actin networks in contact with the enwrapping membrane will be described via localized forces and force patterns. These forces may act to enhance or to reduce the engulfment process arising from the surface-surface affinity. One objective of this subproject is to identify force patterns that are able, via small changes in the magnitude and sign of the applied forces, to switch between the two pathways that lead to no engulfment and complete engulfment.

Complementary work in US partner group. Discher continues his previous experimental studies on the engulfment of particles and red blood cells by macrophages, (see figure). The theoretical project proposed here is directly related to these ongoing experiments.

Status of the project. The project will interact closely with the projects C3 (Dimova) and C2 (Hildebrandt), in which multicomponent vesicles and membranes will be studied experimentally. The projects B1 (Weikl) and B2 (Gradzielski) will investigate membrane-nanoparticle interactions, which are also essential for the project described here.