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## Interactions from lipid membrane deformations

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# Summary

All life forms consist of basic building blocks known as biological cells. Each cell is surrounded by a lipid membrane that serves as a protective barrier. The lipid membrane also plays a decisive role in the function of the cell through the numerous proteins that are located at the periphery or embedded in the liquid membrane. The proper organization of these proteins is essential for the effective functioning of the cell membrane, as irregularities can lead to disease. Alongside well-known forces like electrostatic and hydrophobic interactions influencing protein organization, there exists a distinctive interaction arising from protein deformation on the membrane, irrespective of the proteins' chemical composition. Studying membrane deformation from proteins is particularly challenging, yet it holds great importance. This aspect adds a unique dimension to the intricate organization of proteins, influencing the overall functionality of the cell membrane. Despite efforts by physicists using analytical approaches, experimental tools, and computer simulations, there remain numerous unanswered questions surrounding the organization of biological membranes.

Since biological cells are very complex, it is almost impossible to identify a single force among the many interactions. Instead, we use simpler models to filter out the interactions we are interested in. In our study, we used giant unilamellar vesicles (GUVs) that mimic cell membranes and added colloidal particles that act like proteins.

In our research, we investigate the various interactions between colloidal particles and lipid membranes, emphasizing the importance of shape, and multi-body deformation-induced forces. We use a mixture of experiments, computer simulations and theoretical analyzes to understand the different aspects of this complex interaction.

In **Chapter 2**, we employed GUVs and colloidal dumbbell particles consisting of two interconnected spheres as a model system to study ligand-receptor mediated endocytosis. We showed that the neck connection between the two spheres has a significant impact by slowing down the wrapping of dumbbells by a GUV. We identified two distinct final states of wrapping: one lobe or both lobes of the dumbbell fully engulfed by the membrane. Furthermore, we uncovered that factors such as membrane tension and the initial position of the particle influence the wrapping pathway. Using molecular dynamics simulations, we were able to quantitatively assess the time frames of the key intermediate steps in this process. Importantly, we observed that wrapping time increases with the increase in tension, leading to valuable insights into microviscosity of the membrane. These results enhanced the

understanding of the effects of particle shape on endocytosis, which has potential implications in fields ranging from food science to drug delivery.

In **Chapter 3** we investigated the three-body interactions mediated by deformation. The deformation-mediated interaction is not simply pairwise additive, i.e. the interaction of three deforming membrane objects cannot be predicted simply by knowing the pairwise interactions. Using a model system consisting of sticky colloidal spheres and GUVs, we have found an attractive interaction between three membrane-deforming colloidal particles that lead to two distinct configurations. These configurations turned out to be a linear configuration and an equilateral triangular configuration for three particles with an equal interaction energy to the pair interaction. We have shown that the presence of a third particle does not enhance the deformation-mediated interaction, but slightly increases the distance between the particles. Our work highlights the complexity and non-additive behavior of membrane-mediated forces and helps to better understand the arrangement of proteins on a cell membrane.

In **Chapter 4** we have controlled the deformations on the membrane. So far, all other experimental studies have focused on particles that were attached to the membrane from the outside, thereby deforming it inwards. Here, we used an optical trap to pull a tube from a GUV that deforms the membrane outward in the opposite direction. We found a repulsion between the tube and a particle completely wrapped by the membrane. We additionally modified patchy particles to exhibit partial adherence to the membrane, discovering that the attraction force between these particles was four times stronger than that observed between fully-wrapped particles. This study highlights the ability of deformation interactions to cause both attraction and repulsion between particles, with the magnitude of these interactions depending on the degree of deformation they cause. By elucidating this phenomenon, our research makes a valuable contribution to the larger puzzle of membrane-mediated forces.

In **Chapter 5** we developed an innovative model system in which spherical colloids were positioned between heavy, deflated GUVs and a flat substrate. This approach greatly facilitated the experiments and allowed us to quantify the interactions between many symmetric spherical particles deforming a membrane. We found strong long range attractive forces between two particles positioned under the membrane. This long-range attraction was 30 times stronger than the interaction observed between two fully-wrapped particles in close proximity. When we inserted up to 36 particles under the GUV, we found that they quickly form the most compact organization, a hexagonal packing. However, the introduction of additional particles showed non-additive effects and led to a substantial reduction in attraction force. In addition, as the number of particles increases, the stable hexagonal order transitions to a fluid cluster, accompanied by an increase in the diffusion coefficient. This chapter underscores the pivotal influence of many membrane-deforming objects in closed spaces.

In **Chapter 6**, we explored the fascinating world of interactions mediated by anisotropic deformation. Employing an attachment-free approach as in chapter 5, we investigated the interactions between a diverse range of colloidal shapes, including ellipsoids, dumbbells, cubes, scalene triangles, tetrahedra, and bent rods. An attractive force was found between all these particles, leading to their self-

assembly into specific structures. The complementarity of shapes proved to be a key factor in the formation of specific arrangements, with particles aligning, touching flat sides or forming locally stable states to minimize the overall curvature of the membrane by forming clusters that are as compact as possible. This chapter provides valuable insights into the role of shape in the interactions between membrane-deforming objects.

In summary, this work has improved our understanding of the interplay between colloidal particles and lipid membranes. It has shed light on the influence of shape on membrane uptake. In addition, we have investigated the many-particle effect and shape deformation on membrane-mediated interaction. Our results could contribute to a better understanding of protein organization at the cell membrane and find practical application in the development of food or drugs to increase uptake efficiency.