Interplay of Curvature and Composition in Membranes

Thomas Weikl 01.04.1970
1996: Diploma, Physics
(Freie Universität Berlin)
Thesis: Interactions of rigid membrane inclusions
1999: PhD, Physics
(Max Planck Institute of Colloids and Interfaces, Potsdam)
Thesis: Adhesion of multicomponent membranes
2000-2002: Postdoc
(University of California, San Francisco)
Since 2002: Group Leader
(Max Planck Institute of Colloids and Interfaces, Potsdam)
2008: Habilitation, Physics
(University Potsdam)
Thesis: Transition states and loop-closure principles in protein folding

Biological membranes are the 'skin' of our cells and cell organelles. They consist of a large variety of different lipids and proteins, and are highly flexible and fluid, which allows drastic changes in membrane shape and curvature. The interplay of molecular composition and curvature of the membranes is crucial for their biological function. Our group investigates this interplay during the encapsulation of nanoparticles **[1]**, in the formation of membrane domains **[2]**, and upon membrane adhesion **[3]**.

Cooperative Wrapping of Nanoparticles

Recent advances in nanotechnology have led to an increasing interest in how nanoparticles interact with biological matter. While biomedically designed nanoparticles are promising carriers for drug delivery, the wide application of industrial nanoparticles has also led to concerns about their safety. To enter the cells or cell organelles of living organisms, nanoparticles have to cross biomembranes. The membranes deform and wrap around nanoparticles if the adhesive interaction between the nanoparticles and membranes is sufficiently strong to compensate for the cost of membrane bending. While the wrapping of single nanoparticles by membranes has been studied intensively in theory and simulations, relatively little is known about the organization and elastic, membrane-mediated interactions of multiple nanoparticles adsorbed on membranes. These interactions arise because the elastic deformations of membranes depend on the distance between the adsorbed particles.

Our group has recently found strongly attractive elastic interactions between spherical nanoparticles adsorbed on vesicles **[1]**. These attractive interactions lead to bound states of the particles with a morphology that depends on the ratio of the area and volume of the vesicles, which is typically characterized by the reduced volume $v \leq 1$. The maximal value $v = 1$ of the reduced volume corresponds to the area to volume ratio of a sphere. For large values of v, nanoparticles are only partially wrapped by the vesicle since the area to volume ratio does not allow full wrapping. For such values of v, we have found bound states in which two particles are equally wrapped by the vesicle (**Fig. 1a**). For smaller values of v, we have found strongly bound states in which two or more particles are cooperatively wrapped by a membrane tube that protrudes into the vesicle (**Fig. 1b and c**). This tubular confinement of several nanoparticles constitutes a novel route to encapsulate nanoparticles reversibly in vesicle membranes. In experiments, the amount of confined nanoparticles as well as their release may be controlled by changes in the osmotic conditions, which lead to changes in the reduced volume of the vesicles.

The wrapping and membrane-mediated interactions of the nanoparticles arise from the interplay of membrane bending and adhesion. The total energy is the sum of the bending energy of the vesicle and the overall adhesion energy of the particles. We have determined the minimum total energy of the vesicle and particles with simulated annealing Monte Carlo simulations of triangulated vesicles in contact with particles. In **Fig. 2**, the minimal total energy E of a vesicle with two adsorbed particles is displayed as a function of the particle distance r. At the reduced volume $v = 0.96$, the total energy E(r) exhibits local minima at the contact distance $r = 2R_p$ of the particles and at a distance r between $6R_p$ and $9R_p$, separated by an energy barrier. The local minimum of E at the contact distance $r = 2R_p$ corresponds to the bound state of the particles shown in **Fig. 1a** in which both particles are symmetrically wrapped by the vesicle membrane. At $v = 0.92$ and 0.94, we find additional branches of low-energy conformations with negative values of E at distances $r < 3\ R_p$ of the particles. In these low-energy conformations, the particles are jointly but asymmetrically wrapped by a membrane tube that invaginates into the vesicles (**Fig. 1b** and snapshot at bottom left of **Fig. 2**). In these conformations, the wrapping of the particles is asymmetric since the particle at the tip of the invagination is more strongly wrapped. Besides these low-energy conformations, we have found branches of higher-energy conformations with positive values of E in which the particles are symmetrically wrapped as in **Fig. 1a**. In addition, we have investigated the adhesion of membranes via adsorbed nanoparticles **[4]**.

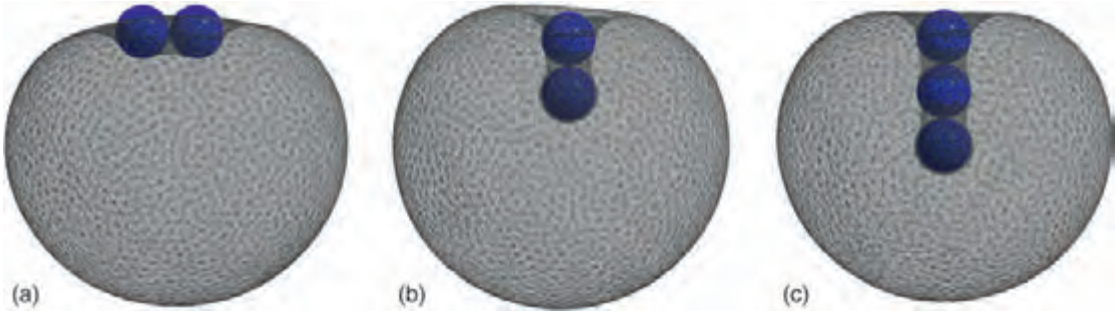

Fig. 1: (a) Bound state of two particles for the reduced volume $v = 0.96$ of the vesicle and the rescaled adhesion energy $u = U R_p^2/\kappa$ of the particle where U is the adhesion energy per area, R_p is the particle radius, and κ is the bending rigidity of the vesicle membrane. - (b) Strongly bound state of two particles for $v=0.92$ and $u=2.33$. - (c) Strongly bound state of three particles for $v = 0.88$ and $u = 2$. In (b) and (c), the particles are jointly wrapped by a membrane tube that protrudes into the vesicle.

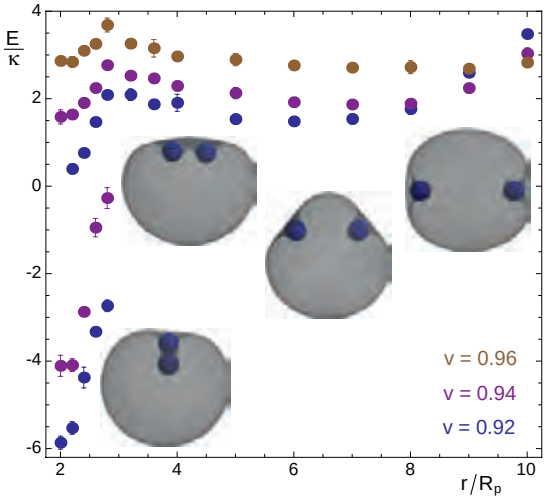

Fig. 2: Minimal total energy E of a vesicle with two adsorbed particles as a function of the particle distance r for the rescaled adhesion energy u=2.33 and the values v=0.92, 0.94, and 0.96 of the reduced volume. The minimal total energy E is given in units of the bending rigidity κ of the membrane. The particles with radius R_p are in contact at the distance r=2R_p. The four snapshots represent minimum energy conformations for the reduced volume v=0.92 at particle distances with r/R_p = 2, 3.2, 6 and 9.

Vesicles with Multiple Lipid Domains

Multicomponent lipid vesicles with coexisting liquid-ordered and liquid-disordered domains are widely used as model system for the lipid bilayers of cells. The liquid-ordered domains have a significantly higher bending rigidity than the liquid-disordered domains. Our group has investigated the coupling of curvature and composition of vesicles that contain such domains **[2]**. We have modeled these vesicles as triangulated surfaces, and have determined their equilibrium morphologies with Monte Carlo simulations. The total energy of the vesicles is the sum of the overall bending energy of the vesicle and the line energy of the domains. We have found that the interplay between the bending energies of the domains and the line energy of the domain boundaries can lead to multi-domain morphologies in which the flexible liquid-disordered domains are located in more strongly curved sections of the vesicles (**Fig. 3**).

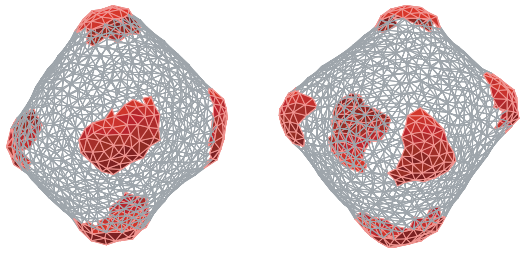

Fig. 3: Stable multi-domain morphologies of vesicles with coexisting liquid-ordered (grey) and liquid-disordered domains (red). In these morphologies, the more flexible liquid-disordered domains are located at more strongly curved 'edges' of the vesicle.

Protein Domains in Cell Adhesion Zones

Submicron scale domains of membrane-anchored receptor proteins play an important role in cell signaling. Central questions concern the stability of these microdomains, and the mechanisms leading to the domain formation. In immune-cell adhesion zones, microdomains of short receptor-ligand complexes form next to domains of significantly longer receptor-ligand complexes. The length mismatch between the receptor-ligand complexes leads to membrane deformations and has been suggested as a possible cause of the domain formation. The domain formation is a nucleation and growth process that depends on the line tension and free energy of the domains. Our group has derived general expressions for the line tension between domains of long and short receptor-ligand complexes and for the adhesion free energy of the domains with a combination of analytical calculations and Monte Carlo simulations **[3]**. We have found that the length mismatch of receptor-ligand complexes alone is sufficient to drive the domain formation, and have obtained submicron-scale minimum sizes for stable domains that are consistent with the domain sizes observed during immune-cell adhesion.

T. Weikl, A. H. Bahrami, J. Hu, H. Krobath, T. Stieger, G. Xu
thomas.weikl@mpikg.mpg.de.

References:

[1] Bahrami, A. H., Lipowsky, R., and Weikl, T. R.: Tubulation and aggregation of spherical nanoparticles adsorbed on vesicles. Phys. Rev. Lett. **109**, 188102 (2012).

[2] Hu, J., Weikl, T. R., and Lipowsky, R.: Vesicles with multiple membrane domains. Soft Matter **7**, 6092-6102 (2011).

[3] Krobath, H., Rozycki, B., Lipowsky, R., and Weikl, T. R.: Line tension and stability of domains in cell-adhesion zones mediated by long and short receptor-ligand complexes. PLoS ONE **6**, e23284 (2011).

[4] Stieger, T., Schoen, M., and Weikl, T. R.: Adhesion of surfaces mediated by adsorbed particles: Monte Carlo simulations and a general relationship between adsorption isotherms and effective adhesion energies. Soft Matter **8**, 11737 (2012).