Membrane Adhesion

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 cells. On the one hand, membranes separate the cell interior from the environment. On the other hand, they allow a vital exchange of matter. In addition, they are involved in central biological processes such as photosynthesis and recognition. The membranes are elastic and can attain a multitude of different shapes. The elastic properties depend on the different lipids and proteins that constitute the membranes.

Membrane Domains at Corrugated Substrates

Biological membranes contain a multitude of lipid molecules. Although the lipid molecules diffuse quickly through the fluid membranes, they are not homogeneously distributed. Instead, they tend to form domains that are either rich or poor in cholesterol. The cholesterol-rich domains are stiffer than the cholesterol-poor domains, which has direct implications on the membrane curvatures. The membrane curvatures, in turn, influence the domain formation. Curvature and domain formation thus depend on each other.

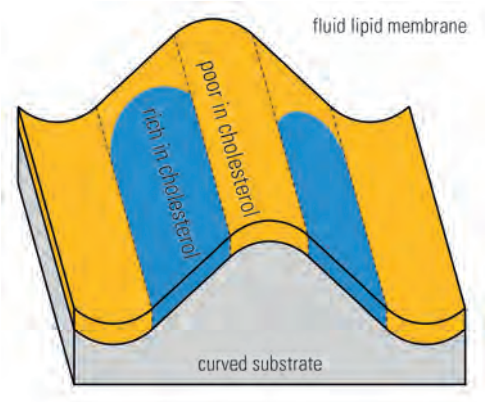

Fig. 1: Fluid lipid membrane on a corrugated, solid substrate. The membrane contains domains that are rich (blue) or poor (yellow) in cholesterol. The cholesterol-rich domains are stiffer than the cholesterol-poor domains and tend to avoid the curved parts of the membrane along the ridges and valleys of the substrate, provided the line tension between the domains does not exceed a certain threshold value.

The question now is: Can curvatures that are imposed on the membrane, e.g. by a corrugated substrate, cause stable domain patterns? In general, it is difficult to control the size of lipid domains since they readily coalesce and grow into larger and larger structures. However, if the membranes adhere to a substrate with a geometrically structured surface, the stiffer cholesterol-rich domains tend to avoid the curved parts of the membrane. The resulting domain patterns are stable as long as the curvature of the substrate surface exceeds a threshold value that depends on the line tension of the domains boundaries **[1]**. Below this threshold, a single cholesterol-rich domain forms, which covers many ridges and valleys of the substrate.

These theoretical arguments explain patterns that have already been observed in experiments. They might also help to understand why biological membranes exhibit only small domains rich in cholesterol, while in artificial, "biomimetic" membranes rather large domains are formed. In contrast to artificial membranes, biological membranes are attached to the cytoskeleton of the cell, i.e. to a network of polymers that actively curves the membranes. Besides other active cell processes, these curvatures could stabilize membrane patterns with small cholesterol-rich domains.

Interactions Mediated by Adhesive Particles

The adjustment of surface interactions is crucial for controlling the adhesiveness of biological cells and membranes. These interactions are often dominated by the composition of the membranes, but can also be affected by molecules or particles in the surrounding medium. The concentration of these particles is an additional control parameter for the membrane interactions, a parameter that is often easier to adjust than the membrane composition, and can be varied over a wider range than external parameters such as temperature.

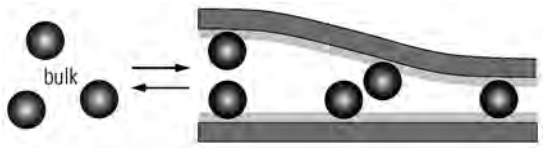

Fig. 2: Two membranes in contact with a solution of adhesive particles. A particle can bind the two membranes together if their separation is slightly larger than the particle diameter (particle on the right). At large separations, the particles can only bind to one of the membranes (particles on the left).

On the one hand, non-adhesive particles can induce attractive 'depletion' interactions between membranes or surfaces, because close contact of the surfaces reduces the excluded volume for the particles. On the other hand, adhesive particles can directly bind two membranes together if the membrane separation is equal to or slightly larger than the particle diameter, see **Fig. 2**. At larger separations, the particles can only bind to one of the membranes.

We find that the effective, particle-mediated adhesion energy of the membranes is given by

$$U_{ef} \approx \frac{k_B T}{d^2} \ln \frac{1 + q\phi e^{2U/k_B T}}{\left(1 + q\phi e^{U/k_B T}\right)^2} \qquad (1)$$

for small volume fractions Φ and large binding energies U of the adhesive particles **[2]**. Here, d is the particle diameter, T denotes the temperature, and q is a dimensionless parameter that depends on the range of the interaction between the particles and the membranes.

Interestingly, the effective adhesion energy (1) exhibits a maximum at an optimum volume fraction of the particles, see **Fig. 3**. At this volume fraction, the particle coverage of two planar parallel membranes turns out to be close to 50 % for large separations ('half coverage'), and 100 % ('full coverage') for short, binding separations. Bringing the membranes from large separations within binding separations thus does not 'require' desorption or adsorption of particles at the optimum volume fraction.

The effective adhesion energy (1) can be understood as a difference of two Langmuir adsorption free energies **[2]**. The adhesion energy can also be generalized to cases in which the adhesive particles or molecules specifically bind to receptors anchored in the membranes **[2]**. Examples are biotinylated lipids, which can be crosslinked by the protein streptavidin.

Diffusion of Receptor-Ligand Bonds

The adhesion of cells is mediated by membrane receptors that bind to complementary ligands in apposing cell membranes. It is generally assumed that the lateral diffusion of mobile receptor-ligand bonds in membrane-membrane adhesion zones is slower than the diffusion of unbound receptors and ligands. We have found that this slowing down is not only caused by the larger size of the bound receptor-ligand complexes, but also by thermal fluctuations of the membrane shape **[3]**. In our model, the fluctuations reduce the bond diffusion constant in planar membranes by a factor close to 2 in the biologically relevant regime of small bond concentrations. Active cell processes may enhance these membrane shape fluctuations **[4]**.

References:

[1] Rozycki, B., Weikl, T. R. and Lipowsky, R.: Stable patterns of membrane domains at corrugated substrates. Phys. Rev. Lett. **100**, 098103 (2008).

[2] Rozycki, B., Lipowsky, R. and Weikl, T. R.: Effective surface interactions mediated by adhesive particles. Europhys. Lett. **84**, 26004 (2008).

[3] Krobath, H., Schütz, G. J., Lipowsky, R. and Weikl, T. R.: Lateral diffusion of receptor-ligand bonds in membrane adhesion zones: Effect of thermal membrane roughness. Europhys. Lett. **78**, 38003 (2007).

[4] Rozycki, B., Weikl, T. R. and Lipowsky, R.: Stochastic resonance for adhesion of membranes with active stickers. Eur. Phys. J. E **22**, 97-106 (2007).

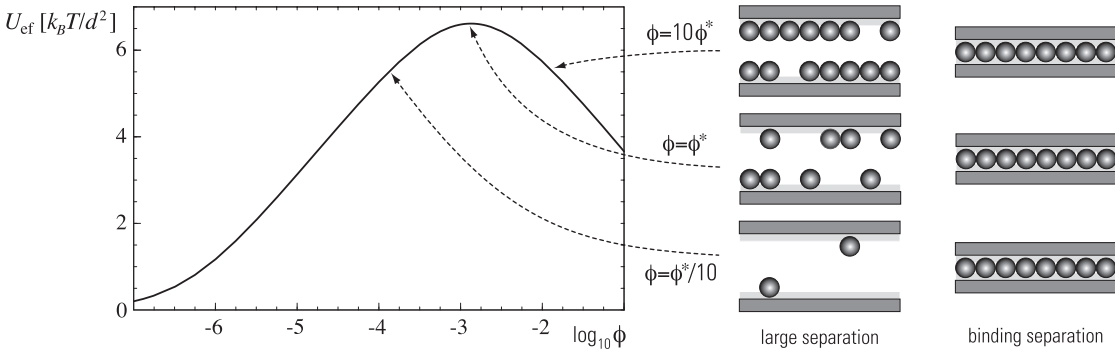

Fig. 3: Effective adhesion energy U_{ef} of the membranes, given in eq. (1), as a function of the particle volume fraction Φ for the binding energy $U = 8\,k_BT$ and $q = 0.25$. The effective adhesion energy is maximal at the optimal volume fraction $\Phi^* \approx \exp(-U/T)/q \approx 1.34\ 10^{-3}$. At the optimal volume fraction, the particle coverage of two planar parallel membranes is about 50 % for large separations, and almost 100 % for small separations at which the particles can bind to both membranes.

T. Weikl, J. Hu, H. Krobath, B. Rozycki
thomas.weikl@mpikg.mpg.de