Properties of Thermally Fluctuating Vesicles

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Properties of Thermally Fluctuating Vesicles

All forms of life are based on the principle of screening small regions from the chemical conditions of the surrounding. Lipid membranes are an excellent material for this purpose. Vesicles basically consist of a closed fluid membrane shell, which is impermeable for most larger molecules. On the other hand, lipid membranes can be penetrated by water molecules and due to their fluidity they can adapt to steric constraints imposed by the environment **[1]**. The research on vesicles provides much insight into the behavior of living cells. Many mechanical and chemical cell properties can be mimicked using lipid membranes and vesicles. An effect that depends on chemical and mechanical properties is the formation of solid domains in a fluid membrane of a vesicle **[2]**. We investigate the stability of different domain shapes by a comparison of their free energies **Fig. 1**.

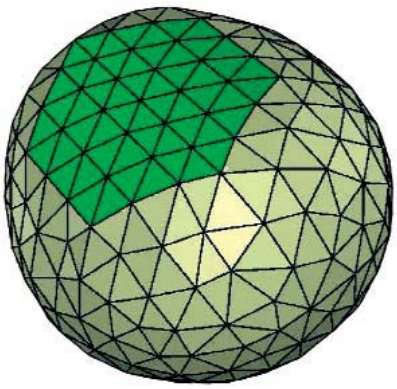

Fig. 1: Model of a vesicle with a solid domain.

Vesicles are not only important to mimic cell properties they can also be used as transport vehicles for the specific application of medically active agents. Not only do they protect their load in the inside from immune reactions of the body, there is also evidence that they can squeeze through small skin pores **[3]**. An investigation of this effect is discussed in the last paragraph.

At first, some more basic aspects are discussed, namely the spontaneous asphericity of free vesicles and a method to measure the binding free energy of vesicles adhering to a substrate.

Basic Properties of Vesicles

The deformation of lipid membranes results in a change of the bending energy. In the simplest case the membrane has no spontaneous curvature, which means, it is preferentially flat. The bending energy is proportional to the bending rigidity κ.

In the presence of larger molecules that cannot permeate through the membrane, an osmotic pressure acts on the vesicle. These molecules are therefore called "osmotically active". The pressure vanishes if the vesicle reaches a volume where the concentration of osmotically active molecules in- and outside the vesicle is equal. In this way, the volume of the vesicle can be controlled by the external molecular concentration.

Free Fluid Vesicles are not Exactly Spherical

We consider a vesicle with no spontaneous curvature in the absence of osmotically active molecules. For very low temperatures, the vesicle assumes the shape with the lowest configurational energy, which is a sphere. For finite temperatures it is often assumed that the vesicle performs small fluctuations around the preferred spherical shape. This is, however, not true. In Monte Carlo simulations we have calculated the free energy F(d) as a function of the order parameter d, which is a measure for the asphericity of the vesicle **[4]**. The parameter d is positive for prolate vesicle shapes, negative for oblate shapes, and zero for sphere-like vesicles. In **Fig. 2** a typical plot of F(d) is shown, which has two minima at about d=+0.1 and d=-0.1, which are the preferred degrees of asphericity. At d=0 there is a distinct maximum, which means that the vesicle is preferentially aspherical. A similar behavior still exists for a small osmotic excess pressure inside the vesicle, which generally stabilizes the sphere shape. For higher excess pressures, the maximum at d=0 vanishes.

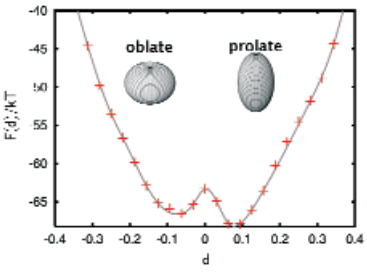

Fig. 2: Free energy F(d) of the asphericity d.

Vesicles Adhering to a Substrate

In living organisms as well as in biomimetic systems, cells or vesicles are often adhering to a substrate. Prominent examples are biosensors in which cells are in contact with metallic electrodes **[5]**. An important quantity is the adhesion strength W, i.e. the adhesion energy per adhering membrane area. It depends on the material properties of the membrane and the substrate and is often difficult to measure in the experiment.

With Monte Carlo simulations we studied systematically the adhesion behavior of a vesicle with a total area A and bending rigidity κ as a function of the temperature T, the adhesion strength W, and the range s of the adhesion potential (see **Fig. 3**).

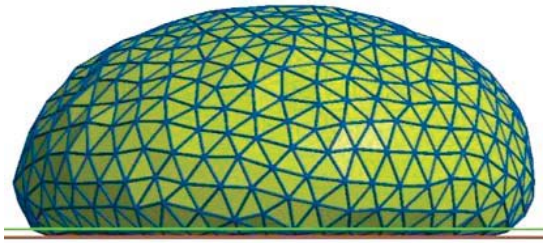

Fig. 3: Snapshot of an adhering vesicle.

We considered vesicles in the absence of osmotically active molecules **[6]** as well as vesicles with osmotically stabilized volumes V. In both cases it is found that the relative adhesion area A_{ad}/A is a linear function of T/κ if the temperature is not too large. An example is given in **Fig. 4**. With and without osmotically active molecules the dependence of A_{ad}/A on the parameters W, κ, T, s, and, eventually, V can be expressed in a simple formula. If s is approximately known and κ is not strongly temperature-dependent, the formulas can be used to determine W and κ by measuring the adhesion area for two different temperatures.

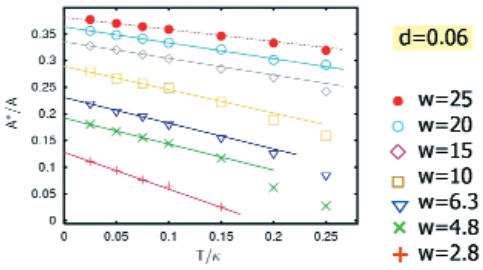

Fig. 4: Relative adhesion area A_{ad}/A as a function of T/k for various values of $w=WA/(2\pi\kappa)$.

Vesicle Transport through Small Pores

A pharmacological application of vesicles is the transport of medically active substances. One important aspect is the transport of vesicles through skin pores which allows carrying active agents into deeper skin regions. It is predicted that the vesicles are pushed through a skin pore by a transdermal concentration gradient of osmotically active molecules. With the help of computer simulations we have found that different molecular concentrations c_1 and c_2 on each side of a small pore is indeed able to drag a vesicle through it **(Fig. 5)**. In the simulations we calculate the free energy barrier $F(A_2)$ for the partial area A_2 having passed the pore. As shown in **Fig. 6** the barrier vanishes for a sufficiently large concentration c_1 and the vesicle is pushed through the pore. The time needed to pass the pore was estimated to be about 70 seconds.

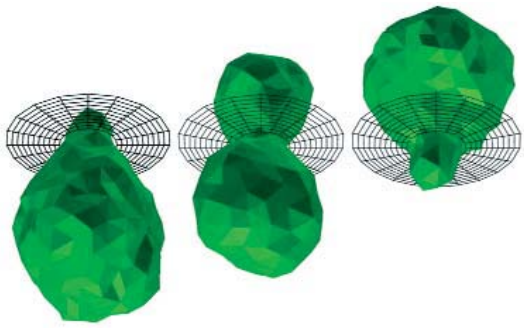

Fig. 5: Snapshots of a vesicle moving though a pore.

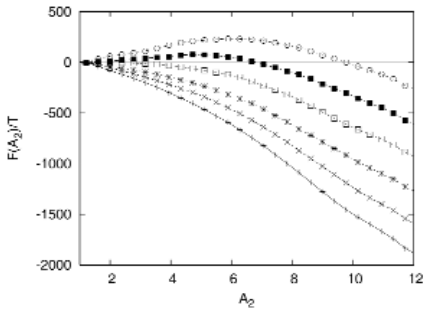

Fig. 6: Free energy barrier for a vesicle moving through a pore.

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