The behavior of liposomes near solid surfaces

Theses

Annamária Takáts-Nyeste

Supervisor: Prof. Imre Derényi

Department of Biological Physics, Eötvös Loránd University

Budapest, 2016.

Motivation

Phospholipid bilayers have a great significance both in medicine and biotechnology. Liposomes like to touch to solid surfaces if it is energetically favorable. These vesicles decompose spontaneously and spread along the surface forming a supported lipid bilayer (SLB). Despite the widespread usage of lipid bilayer and the available numerous experimental data related to the above process, the theoretical description of this phenomenon is very incomplete.

The theoretical description of SLB formation via liposome decomposition is important, on one hand, to define the condition needed for this process, on the other hand, to predict some behavior which is unobservable due to the spatio-temporal resolution of the currently used experimental methods.

My PhD thesis focuses on the theoretical background of vesicle rupture. With the advices of my supervisor I have built up a model based on overdamped dynamics to study the spreading of liposomes on solid support. We have also investigated the influence of the properties of the surface of the support.

Conclusions

1. We have built up a model to explain the rupture of liposomes

In our model, we have combined the previous observations: pores may open in the membrane of a surface adhered, spherical-cap-shaped vesicle. Via these pores, the vesicle loses some of its volume due to the Laplace pressure, which leads to both the reseal of the pore and the growth of the adhered area. If growth of the adhered area is faster than the reseal of the pore, the vesicle will spread on the surface forming a solid supported bilayer. Otherwise, after the closure of the pore, the process re-starts. The three dynamical variables are the volume of the vesicle, the radius of the adhered area, and the radius of the pore, which are described by three ordinary differential equations. The variables are coupled to each other by the surface tension, which depends on the instantaneous geometry of the liposome.

We applied two assumptions: i) the surface tension is homogeneous, which is invalid when very large vesicles (at least 1 mm in diameter) are used, but in most experimental situations this assumption is plausible; ii) the geometry of the liposomes is always described by a spherical cap, which is true until the final stages of vesicle rupture, however, when this assumption loses its validity, the rupture completes anyway.

We solved the model numerically, and we could conclude that

a) By varying the used parameters in a realistic range we have reproduced several previous experimental data such as:

- the vesicle spreads or not along the surface

depending on the strength of the adhesion between the surface and the membrane.
- the larger the vesicle, the higher the probability it ruptures.
- the time-scale of the rupture is in the same range as it has been experimentally measured.

b) Our work has revealed that rupture is very sensitive to the initial geometry of the vesicle which explains that some vesicle liposomes rupture instantly upon adhesion and others do not.

c) By using an osmotic shock the problem of the initial geometry can be solved but this cannot solve the problem of the non-rupturing spherical vesicles.

2. We have extended the above model with membrane-membrane adhesion

When it was energetically favorable, the adhesion between two adjacent membrane site was taken into account, which led to hat-shaped vesicles with a spherical cap crown and a double bilayer brim. It resulted in an additional ordinary differential equation (the radius of the crown). The numerical solution of this extended model revealed that

a) After pore formation we have detected the appearance of double bilayers in each case, but usually these have a very short lifetime.

b) By varying the used parameters we have produced long lasting double bilayers but the parameters are fine tuned.

c) Assuming that a little pore is always open nearby the contact line we have detected long lasting double bilayers in a wide range of parameters which is in great agreement with experimental data.

3. We have determined the change of the activation energy if the pore opens nearby the contact line

We defined the lowest activation energy, which is an unstable equilibrium. We took into account that the pore formation at the contact line led to the disappearance of the curvature at the adhesion edge, and the appearing free bilayer edge may fuse with the edge of a nearby bilayer patch. We could conclude that

a) Our calculations have revealed that the activation energy of pore opening decreases due to the disappearance of the curvature energy of the contact edge and the prompt adhesion of the membrane next to the nucleation point.

b) If the pore opens nearby a free bilayer edge the activation energy is zero. This is consistent with the experimental observation that bilayer formation significantly speeds up after the rupture of the first vesicle.

c) The effects on vesicle rupture: i) this “new” activation energy should be taken into account when the rate of pore formation is calculated, ii) the growth of the adhered area is not isotropic, however, it has relevance only at the final stage of the rupture.

4. We studied the behavior of liposomes when a nanopore is burnt into the surface

We assumed that the adhesion energy inside the nanopore is different from the adhesion energy on the support, the vesicle's surface and volume are constant, and the curvature energy was ignored. We defined the geometry belonging the energy minimum with analytic calculations (balance of forces), which led to the following conclusions

a) We have calculated the values of the adhesion energy when spanning occurs depending on the radii of the vesicle and the nanopore analytically.

b) We have shown that vesicles always span above the nanopore if the adhesion energy inside this is lower than the half of the adhesion energy outside the pore.

List of publications

Papers related to the theses:

Takáts-Nyeste, Annamária and Derényi, Imre: Rupture of lipid vesicles near solid surfaces. Physical Review E, Volume 90, Page 052710, 2014. DOI: 10.1103/PhysRevE.90.052710

Takáts-Nyeste, Annamária and Derényi, Imre: Development of Hat-Shaped Liposomes on Solid Supports. Langmuir, in press, 2014. DOI: 10.1021/la503774t

Submitted manuscripts and preprints related to the theses:

Takáts-Nyeste, Annamária and Derényi, Imre: Formation of nanopore-spanning lipid bilayers. To be submitted

Derényi, Imre and *Takáts-Nyeste, Annamária*: Pore formation along the contact line of surface-adhered liposomes. Submitted to Langmuir

Works unrelated to the theses:

Horváth, Gábor; Csapó, Adelinda; *Nyeste, Annamária*; Gerics, Balázs; Csorba, Gábor; and Kriska, György: Erroneous quadruped walking depictions in natural history museums. Current Biology, Volume 19, Issue 2, Pages R61-R62, 2009. DOI: 10.1016/j.cub.2008.12.011

Takáts-Nyeste, Annamária and Derényi, Imre: Vesicle rupture in the presence of charged surface and lipids. To be submitted