UMCS

UNIWERSYTET MARII CURIE-SKŁODOWSKIEJ W LUBLINIE
Wydział Chemii

Dr hab. Paweł Bryk, prof. uczelni

Dr hab. Paweł Bryk, prof. uczelni
Katedra Chemii Teoretycznej
Wydział Chemii
Uniwersytet Marii Curie-Skłodowskiej

Review of the doctoral thesis of Jeel Linesh Raval, M.Sc. entitled

"Shapes and shape transformations of vesicles induced by their adhesion to rigid bodies"

Biomembranes consisting of auto-assembled phospholipid bilayers constitute an important part of every living cell. In order to maintain cell's integrity such an envelope must be easy to bend but hard to stretch. While typically lipid membranes can stretch only within few percent of the relaxed area, they can easily bend on the nanometre scale and are susceptible to various deformations. Understanding the connection between the mechanical properties of the cells and vesicles and their shape is one of the longstanding important research areas.

The subject of the Thesis submitted by Jeel Linesh Raval also belongs to this category. The Author addresses the question of how surface adhesion of a vesicle influences its shape and mechanical stability. This problem may become relevant in situations "in vivo", for example a cell may adhere to the internal surface of a blood vessel, or "in vitro" by arranging a suitable experimental setup involving for example AFM.

In the Thesis the vesicle adhesion problem is being studied by means of a continuum mechanical approach due to Helfrich, and its extensions. Within this approach the vesicle is assumed to behave like an elastic sheet of effectively zero thickness embedded in 3D space. The bending energy stems from a mismatch between the local curvatures and the spontaneous curvature. It is assumed that the system does not undergo any topological changes. The adhesion gives rise to another contribution to the energy functional. In order to simplify numerical calculations the Author assumed that all vesicles are axisymmetric. The resulting final form of the functional was minimized subject to some constraints such as constant volume or constant surface area.

pl. Marii Curie-Skłodowskiej 5, 20-031 Lublin
tel: +48 81 5377758, fax: +48 81 5333348
e-mail: pawel.bryk@umcs.pl

NIP: 712-010-36-92
REGON: 000001353

The Thesis consists of 7 chapters, two appendices, and lists 119 references. It also contains 54 figures with some of them being neat 3D renderings of various vesicle shapes. The main scientific findings of the Thesis are presented in three chapters. In Chapter 4 the Author considered the single component vesicle systems where the adhesion radius (due to the rotational symmetry the part of a vesicle adhered to a surface has to be a disk) was treated as an additional minimization constraint. Chapter 5 contains the results of calculation for the single component vesicle systems but with the adhesion strength considered as a parameter. Finally, Chapter 6 describes the results of calculations for the multi-component vesicle systems. Those calculations assumed that the spontaneous curvature is concentration dependent, while the concentration profile was described by a hyperbolic tangent form.

The major findings of the Thesis include:

- Adhesion may promote formation of a bud attached to the main vesicle body via a small neck. These structures were also found for the adhering vesicles with zero spontaneous curvature. Interestingly, such structures were not detected for the free vesicles with this value of the spontaneous curvature. Small changes in the adhesion strength may promote or inhibit budding.
- For one-component membranes the oblate vesicle seems to be the preferred stable shape as the adhesion strength is increased. This finding holds for both zero and non-zero spontaneous curvature systems.
- Vesicles with the local curvature of the adhered membrane similar to that of the substrate will stick to the surface more easily. This mechanism may be used to separate vesicles based on their shape.
- For two-component systems adhesion can lead to either mixing or separation of the membrane components depending on the shape of a vesicle. While for the budded structures there is a tendency to support the mixed state upon an increase of the adhesion radius, the opposite can be found for the non-budded vesicles. In general the high curvature components tends to migrate towards the base of the vesicle.

- The fact that for some systems multiple stable solutions have been found, as well as that small changes in adhesion strength could lead to large changes in adhesion radius, suggests that adhesion may trigger transformation of vesicles between two different classes of shapes.

The scientific content of the Thesis has to be rated very highly. The above mentioned findings contribute to our better understanding of the adhesion of cells as well as their shape transformations. In addition the results of the Thesis have some potential for applications in biotechnology.

Some issues however were not completely clear to me and would need further clarification:

- on page 39. the Author stated that "It is interesting to note that the height of the vesicle increases when larger and larger part of the vesicle membrane is attached to the flat surface". Just by inspecting Figures 4.4, 4.5 and 4.6 I can actually infer the opposite, the height of the vesicle decreases with increasing the radius of the attached part of the vesicle.
- The varying adhesion strength is considered in Chapter 5. However the results are presented in terms of the reduced adhesion strength. This gives little information on how strong the adhesion is in typical experimental situations, for example when compared with adhesion of a droplet of water of similar size. Some "real world" comparisons would better depict the adhesion strength for example in Fig.5.1 where we observe a transition from the free state of a vesicle to the pinned state.
- In Chapter 6 the Author mentions strong segregation regime. In the theory of polymer mixtures or copolymers the strong segregation regime corresponds to a system where the polymers are stretched at the interface, hence the corresponding interfacial width is rather small and the interface is sharp. On the other hand in the weak segregation regime the polymers are less stretched and the interface is more diffuse. It is clear that within the Helfrich type of theory the polymer degrees of freedom are not explicitly taken into account but perhaps just by looking at the width of the interface vs. the dimensions of a phospholipid molecule; could it be that the lipid chains at the interface would indeed belong to the "polymer" strong segregation regime?

The editorial side of the submitted Thesis is practically faultless. Clear figures with beautiful renderings and superb English make the Thesis a pleasure to read.

In conclusion, The Author has formulated and solved an original and interesting scientific problem. The scientific content of the Thesis has already been published in two papers and the third is in preparation. In addition Jeel Linesh Raval is a co-author of another two publications. I conclude that the requirements of the article 187 of the Polish act about academic degrees from 20 July 2018 (Dz. U. 2018 poz. 1668 with later amendments) are fulfilled and that Jeel Linesh Raval should be allowed to the next stage of the doctorate degree procedure.

Paweł Bryk

Dr hab. Paweł Bryk, prof. uczelni

Lublin 25.05.2022