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Report on the Ph.D. Thesis of mgr. Jeel Linesh Raval, titled *Shapes and shape transformations of vesicles induced by their adhesion to rigid surfaces*

The goal of this report is to review the Ph.D. Thesis of Ms. Jeel Linesh Raval, titled *Shapes and shape transformations of vesicles induced by their adhesion to rigid surfaces*, prepared under supervision of prof. dr hab. Wojciech Góźdź from the Institute of Physical Chemistry, Polish Academy of Sciences, and Professor Aleš Iglič from the University of Lubljana, Ljubljana, Slovenia. The thesis was prepared within the International Ph.D. Studies of the Institute of Physical Chemistry of the Polish Academy of Sciences in Warsaw, Poland.

The thesis consists of 118 pages, 7 chapters and 2 appendices. It provides 119 citations. It contains also information about publications of Ms. Raval: she is the first author of two publications related to the thesis, and a coauthor of two other publications.

The purpose of the thesis is to analyze the influence of adhesion of vesicles on their shapes. The adhesion to flat rigid surfaces and axially symmetric shapes of vesicles are assumed. Motivation to consider such systems in explained in Section 1, where importance of adhesion and shapes of biological cells is outlined, and the concept of budding transformation of a vesicle shape is introduced. Sections 2 and 3 contain theoretical description of the model of vesicles. The Helfrich expressions for the elastic vesicle energy are given, both for free and adhered vesicles. These expressions are next generalized for two-component vesicles, with two different equilibrium curvatures that can displace along the membrane, leading to segregation or, on the contrary, to a uniform spreading of each curvature along the membrane.

The results are presented in Secs. 4-6. In Sections 4 and 5, vesicles of a single equilibrium curvature are considered. In Section 4, vesicle shapes are studied for a given size of their adhesion area to the flat rigid surface. In Section 5, vesicle shapes are determined for a given adhesion strength of their attachment to the flat rigid surface. In Section 6, multi-component vesicles with two different equilibrium curvatures are investigated for a given adhesion strength of their attachment to the flat rigid surface. Finally, conclusions are outlined in Section 7.

Different families of stable shapes of the adhered vesicles have been found and their stability ranges have been determined, for certain values of the reduced volume, v, and of the reduced spontaneous curvature, c_0. The results for free vesicles from Ref. [92] have been reproduced. A new class of adhered budded shapes, called the "oblate-bead", has been found.

Budding of adhered vesicles has been observed for certain ranges of the parameters, especially for a lower reduced volume. It was shown that a very small change in adhesion strength can either induce or suppress budding. For a fixed reduced adhesion strength, the increase in the reduced spontaneous curvature increases the stability range of adhered vesicles.

Two-component vesicles have been also considered, with two different equilibrium curvatures that are free to move along the membrane. Both mixing and lateral segregation of components have been observed for different shapes of the adhered vesicle. The shape in turn depends on the adhesion strength and the reduced volume. In general, non-budded shapes (in particular, oblate shapes) seem to promote segregation of the components. Some of the budded shapes can be associated with the mixing of the components when the radius of adhesion is increased (in particular, the so-called "pear-up" shapes, with a large difference in size between the smaller upper and the larger lower parts of vesicle, as shown in Figure 6.18). Interestingly, the rotation of such a shape (the so-called "pear-down" shape, with a large difference in size between the larger upper and the smaller lower parts of vesicle, as shown in Figure 6.20) leads to segregation of the components for all the considered adhesion radii.

The results of the thesis are presented in a systematic way. In general, they are carefully described, with the use of a clear and elegant graphical representation. My detailed remarks and questions are the following.

1) In the description of the theoretical method, it would be good to explain in details how the minimization of the energy is performed, how the local energy minima and the ranges of stable shapes are obtained, and also how the conclusions of stability and meta-stability are related to the local energy landscape.

2) Also, which curves in the energy plots (e.g. Figure 4.1-4.3) correspond to stable vesicles, and which describe the meta-stable ones?

3) What is the definition of E used in Figures 4.1-4.3 and later ones? Isn't it just F, defined in Sec. 3 by eq. (3.4.4)?

4) In the vertical labels of the plots in Figures 4.1-4.3 and later ones, it should be $E/8\pi\kappa$ rather than $E/8\pi k$.

5) Do vesicle shapes seen in nature and in experiments are close to axially symmetric? How useful are the results based on the assumption of the axial symmetry?

6) Vesicle shape is not periodic, as stated above Eq. (3.1.7).

7) On page 24, the notation used for 2x2 tensors g_{ij} is not good. Usually, the subscripts label different components of a tensor.

8) It seems that equation (2.4.1) refers to the lack of adhesion, but above it there is a sentence about the adhesion radius, could you explain it?

9) Why for $c_0 = 0$, i.e., for straight equilibrium, shapes of vesicles with the lowest energy are so far from straight, as visible in Figure 4.1?

10) Could you explain the physical meaning of the second term in Eq. (2.1.2)?

Concluding, my opinion about the Ph.D. Thesis of Ms. Raval is positive. The author studied theoretically in detail the dependence of vesicle shapes on the system parameters, finding new shapes and relating them to possible applications, such as segregation of the parts of the membrane with different equilibrium curvatures. Taking into account the content of this report, I conclude that the Ph.D. Thesis of Ms. Raval meets the requirements of the Polish law (art. 187 ustawy z dnia 20 lipca 2018 r. Prawo o szkolnictwie wyższym i nauce, Dz.U. z 2018 r., poz. 1668 ze zm.). Therefore, I recommend the thesis to be accepted, and I recommend to allow Ms. Raval to defend it.

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