Geometrical Constraint Equations and Geometrically Permissible Condition for Vesicles

YIN Ya-Jun(殷雅俊)*, YIN Jie(尹杰)

School of Aerospace, Department of Engineering Mechanics, Tsinghua University, Beijing 100084

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The application of a geometrical constraint equation for lipid bilayer vesicles is investigated. First, both the physical meaning and the mathematical formulation for the spontaneous curvature of vesicles are clarified. Second, the geometrically permissible conditions and phase diagrams for vesicles, from which the criteria for the formation, existence and disintegration of vesicles may be determined, are revealed.

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How to depict the topological structures[1] and to predict the shape transitions[2−4] in lipid bilayer vesicles is of special importance[5,6] in physics and cell biology. As far as the vesicle topology is concerned, one of the most important theoretical subjects is the equilibrium differential equation. In past years, the solutions to the differential equation have been intensively explored, whereas the constraints to this equation are seldom discussed. This initially motivated the authors to write this Letter.

The so-called geometrical constraint equation is directly deduced from the equilibrium differential equations of vesicles. For a vesicle with uniform rigidity, this differential equation (i.e. the Helfrich–Ou-Yang equation) is[2,3]

$$2k_c\nabla^2 H + f = 0, \tag{1}$$

where f is the same scalar function

$$f = \Delta p - 2\lambda H + k_c(2H - c_0)(2H^2 + c_0 H - 2K), \tag{2}$$

∇^2 is the Laplace–Beltrami operator; $\Delta p = p_{\rm out} - p_{\rm in}$ is the difference between the outer and inner pressures; $\lambda = \lambda_{\rm in} + \lambda_{\rm out}$ is the sum of the surface energy density on the inner and outer surfaces; k_c is the elastic modulus, and c_0 is the spontaneous curvature. In classical differential geometry, the Laplace–Beltrami operator ∇^2 satisfies the conservation integral[7]

$$\oint_A \nabla^2\varphi dA = 0, \tag{3}$$

where φ is as a function of C^∞ definable elsewhere on a closed surface. Hence f in Eq. (1) should obey

$$\oint_A f dA = 0. \tag{4}$$

Equation (4) is mainly a geometrical (instead of physical or mechanical) constraint to Eq. (1). Therefore, here we call this equation the geometrical constraint equation. It should be emphasized that Eq. (4) is universal valid for any closed vesicle with any topological structure, which makes the equation very important. Surprisingly, the application of Eq. (4) has never been reported in the literature. Thus it may be interesting to ask the following questions: What does the geometrical constraint equation mean? What problems can this equation solve? Is there any new knowledge involved in this equation?

The meanings of the geometrical constraint equation may be annotated as follows. (a) Generally, a vesicle may be mathematically considered as a closed surface embedded in three-dimensional flat space. Because this closed surface possesses complicated micro substructures, it may not be generated freely. A special condition such as Eq. (4) must be satisfied. (b) Mechanically, Eq. (4) may be the necessary condition for vesicles to keep equilibrium. (c) Mathematically, this equation is either the inevitable outcome of the integral characteristics of the differential operator ∇^2, or the precondition for the existence of Eq. (1) and its solutions. (d) Biologically, Eq. (4) may lead to the geometrically permissible criteria for the formation, existence and disintegration of a vesicle with certain topology.

To obtain more detailed information, uniform vesicles with constant Δp, λ, k_c and c_0 will be focused on in the following. In this case, Eq. (4) may be rewritten by combining with Eq. (2),

$$\Delta p = \frac{2\lambda + k_c c_0^2}{A}\oint_A H dA - \frac{4k_c}{A}\oint_A H(H^2 - K)dA - \frac{2k_c c_0}{A}\oint_A K dA, \tag{5}$$

In Eq. (5), all quantities, except for c_0, have clear physical or geometrical meanings. Hence, if Eq. (5) is considered as a algebraic equation for c_0, then the physical meaning of c_0 may become available. Previously, c_0 was usually regarded as an important physical quantity and explained roughly as a parameter reflecting the asymmetry of the bilayer and the environment. However, what are the detailed asymmetric factors? The answer may be obtained from Eq. (5). The first factor is the pressure difference Δp that shows the asymmetry in external loading acted on outer and inner surfaces. The second factor is the surface energy density λ that represents the asymmetry in surface tension on outer and inner surfaces. The third factor

* Email: yinyj@mail.tsinghua.edu.cn

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is the curvature rigidity k_c that reflects the asymmetry in the ability of resisting deformation. The fourth factor is the scale that discloses the asymmetry in the vesicle size. The fifth factor is the topological structure that records the asymmetry of the bent space occupied by the vesicle curved surface. In other words, Eq. (5) clearly and quantitatively discloses the influences of all the asymmetric factors on parameter c_0.

Among the above factors, the fourth and fifth ones may be further annotated as follows: Eq. (5) displays the close relations between the vesicle scale, topology and innate physical properties. At large scale, the innate physical properties of a material are usually independent of each other. However, vesicles can be formed in a nano scale. In this case, innate physical properties of a vesicle, such as λ, k_c and c_0, are strongly coupled with each other. The smaller the scale is, the stronger the coupling is. In addition, under a large scale, the topology of a material usually does not affect its innate physical properties. However, in a nano scale, a vesicle topological structure intensively affects the innate physical property c_0. Thus the smaller the scale is, the stronger the influence is.

As an algebraic equation with the order of two, Eq. (5) completely determines the value of c_0. Nevertheless, c_0 must be a real number for a practical vesicle. This strict requirement leads to the important concept termed the geometrically permissible conditions and phase diagram for vesicles. To reveal the detailed meanings of this concept, the simplest example, i.e., a spherical vesicle with radius R, is analysed. In this case, Eq. (5) becomes

$$c_0^2 + \frac{2}{R}c_0 + \frac{\Delta pR + 2\lambda}{k_c} = 0. \tag{6}$$

Thus c_0 can be solved to be

$$c_0 = \frac{1}{R}\Big[-1 \pm \sqrt{1 - \frac{(\Delta pR + 2\lambda)R^2}{k_c}}\Big]. \tag{7}$$

A real c_0 requires

$$1 - \frac{(\Delta pR + 2\lambda)R^2}{k_c} \geq 0. \tag{8}$$

This inequality is the geometrically permissible condition that defines a physical parameter space in which the geometrically permissible ranges for Δp, λ, k_c and R may be limited. The spherical vesicle may exist inside this space and may disappear outside. The boundary of the space is correspondent to critical states at which the criterion for the formation or disintegration of a spherical vesicle may be established:

$$\Big[1 - \frac{(\Delta pR + 2\lambda)R^2}{k_c}\Big]_{cr} = 0. \tag{9}$$

This criterion puts forward a useful method for measuring k_c:

$$k_c = [(\Delta pR + 2\lambda)R^2]_{cr}. \tag{10}$$

How to measure k_c by experiment has been a difficult problem before. Now this difficulty may be partially overcome as follows. At the moment when a spherical vesicle vanishes, the critical values of R_{cr} and $(\Delta p)_{cr}$ may be recorded, and λ is usually measurable. Consequently k_c may be easily computed from Eq. (10).

Under the properly selected coordinate system, the physical parameter space mentioned above will form the geometrically permissible phrase diagram for spherical vesicles. To plot this diagram audiovisually, the authors rewrite inequality (8) into the following dimensionless form: $\Delta\bar{p} + 2\bar{\lambda} \leq 1$, where $\Delta\bar{p} = \Delta pR^3/k_c$ is the dimensionless pressure difference and $\bar{\lambda} = \lambda R^2/k_c$ is the dimensionless surface energy density. Thus the geometrically permissible phase diagram for spherical vesicles may be drawn on the $\Delta\bar{p} - \bar{\lambda}$ plane (see the district beneath the line in Fig. 1).

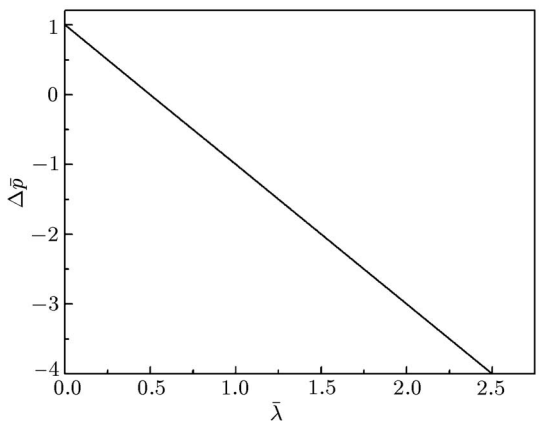

Fig. 1. The geometrically permissible phase diagram for spherical vesicles.

In summary, we have dealt with the geometrical constraint to the existence or formation of vesicles. As well as the existence, the stability of vesicles is another problem of special interest. Hence, an attractive idea may be stimulated: What will happen if the two aspects are combined and studied together? Because the problem of stability itself is very important, the above topic will be explored in succeeding papers.

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