Equilibrium Shape Equation and Geometrically Permissible Condition for Two-Component Lipid Bilayer Vesicles

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Abstract. Equilibrium shapes of vesicles composed of a mixture of partially miscible amphiphiles are investigated. To take into account the influences of the composition, a simple phenomenological coupling between the composition and the curvatures, including the mean curvature and the Gauss curvature of the membrane surface, is suggested. By minimizing the potential functional, the general shape equation is obtained and solved analytically for vesicles with simple shapes. Besides, the geometrical constraint equation and geometrically permissible condition for the two-component lipid vesicles are put forward. The influences of physical parameters on the geometrically permissible phase diagrams are predicted. The close relations between the predictions and existing experimental phenomena published recently are shown.

Key words: amphiphile, geometrically permissible condition, lipid bilayer, shape equation, vesicles

1. Introduction

Amphiphilic molecules in aqueous solutions often self-assemble into layer membranes. These membranes usually exhibit a wide variety of geometrical shapes. Over the past twenty years, many scholars have explored various shapes of real biomembranes such as the biconcave shape of erythrocytes by using elastic continuum models [1–4]. However, in these works, membranes are, almost without exception, treated as structureless and homogeneous layers [5]. In fact, practical biomembranes are usually composed of different types of molecules. These molecules may differ in their head groups, the length of their hydrocarbon chains, or the number of unsaturated bonds [6]. In such a multi-component system, compositions may be both laterally inhomogeneous within each monolayer and different across the two monolayers [6]. As a result, an inhomogeneous spontaneous curvature is created and a coupling between compositions and geometrical shapes is induced [6, 7].

To describe the multi-component systems, simple phenomenological models have been constructed and successfully used in explaining various phenomena, for

example, (a) revealing a large class of possible shapes [9]; (b) describing some unusual dynamical behaviors such as the flicker of red blood cells [10]; (c) describing the crenation of red blood cells [11]; (d) depicting the change of vesicle topologies such as budding, fission and fusion [12–15].

In this paper, the geometrical shapes of vesicles composed of two types of amphiphiles are studied. In the theoretical model, the coupling between composition and membrane curvature is included. In contrast to previous research [5–8] in which composition-mean-curvature coupling and composition-Gauss-curvature coupling are treated separately, the present model will involve two classes of couplings simultaneously. The paper is organized as follows. In Section 2, the general shape equation and geometrical constraint equation for two-component vesicles are derived. In Section 3, two simple analytical solutions of the shape equation are investigated, the influences of the physical parameters on the geometrically permissible phase diagrams are analyzed, and the relations between the predictions and existing experimental phenomena published recently are shown.

2. Shape Equation and Geometrical Constraint Equation

2.1. THE EQUILIBRIUM SHAPE EQUATION

The total potential functional (Π) for a two-component lipid vesicle is written as

$$\Pi = F_c + F_d + \Delta p \int dV + \lambda \oint dA \quad (1)$$

$$F_c = \frac{k_c}{2} \oint (2H - c_0)^2 dA + k_G \oint K dA \quad (2)$$

$$F_d = \alpha \oint (2H - c_0) \rho dA + \beta \oint K \rho dA + \frac{\gamma}{2} \oint \rho^2 dA \quad (3)$$

where F_c is the curvature elastic energy of the membrane [16, 17]. F_d is the energy reflecting the coupling between the composition, the mean curvature H and the Gauss curvature K ; c_0 is the spontaneous curvature; $\Delta p = p_{\text{out}} - p_{\text{in}}$ is the pressure difference between the outer and inner layers; $\lambda = \lambda_{\text{in}} + \lambda_{\text{out}}$ is the sum of the surface energy densities on the inner and outer surfaces; ρ is the local area fraction of the minor component lipid; k_c and k_G are elastic moduli; α and β are coupling constants [5–8]; γ is the molecular energy [6].

Suppose arbitrary and sufficiently small virtual displacement, $\psi = \psi(u^1, u^2)$, takes place along the normal direction of the membrane's surface. The equilibrium configuration of the biomembrane may be ascertained by minimizing the potential functional Π

$$\delta^{(1)}\Pi = \delta^{(1)}F_c + \delta^{(1)}F_d + \Delta p \delta^{(1)} \int dV + \lambda \delta^{(1)} \oint dA = 0. \quad (4)$$

The shape equation of the two-component lipid vesicle is (see the Appendix)

$$k_c \nabla^2 (2H - c_0) + \alpha \nabla^2 \rho + \beta \bar{\nabla}^2 \rho + f = 0 \quad (5)$$

where

$$\begin{aligned} f = & \Delta p - 2\lambda H + k_c(2H - c_0)(2H^2 + c_0H - 2K) + 2\alpha\rho(2H^2 - K) \\ & + \gamma\rho^2H + 2\beta\rho HK. \end{aligned} \quad (6)$$

Equation (5) is a nonlinear differential equation on a curved surface. For a two-component vesicle, its shape will be determined once the distribution $\rho = \rho(u^1, u^2)$ on the vesicle's surface is given.

Equation (5) shows that the local area fraction ρ of the minor component lipid strongly affects the shape of the vesicle. If $\rho = 0$, Eq. (5) will degenerate to the Ouyang-Helfrich equation for uniform lipid bilayer vesicles. Thus the Ouyang-Helfrich equation can be considered as a special case of Eq. (5).

2.2. THE GEOMETRICAL CONSTRAINT EQUATION

For any scalar function φ differentiable on a curved surface, the scalar differential operators ∇^2 and $\bar{\nabla}^2$ satisfy the conservation equations $\oint_A \nabla^2 \varphi dA = 0$ and $\oint_A \bar{\nabla}^2 \varphi dA = 0$ [18]. Thus the function f in Eq. (5) should observe

$$\oint_A f dA = 0. \quad (7)$$

This is the geometrical constraint equation for two-component lipid bilayer vesicles. The meaning of the geometrical constraint equation for single-component lipid bilayer vesicles has been systematically discussed in Ref. [19]. These discussions are also valid for two-component vesicles here. Mathematically, Eq. (7) is the necessary condition for the existence of the Eq. (5) and its solutions. Mechanically, it may be the necessary condition for a two-component vesicle to keep equilibrium. Physically, this is the necessary condition for the existence of a two-component vesicle with a certain topology. Equation (7) defines a “parameter space” and relates all the physical parameters such as Δp , λ , k_c , c_0 , ρ , α , β and γ . In other words, these parameters are dependent on each other in the parameter space. Vesicles may exist inside the space and disintegrate outside the space.

Equations (5) and (7) form the theoretical framework that is valid not only for two-component vesicles, but also for two-component liposomes. In short, any two-component vesicle or liposome should satisfy Equations (5) and (7) simultaneously.

3. Analytical Solution and Geometrically Permissible Condition

3.1. SPHERICAL VESICLES

The mean curvature and Gauss curvature for a sphere with radius R are [20]

$$H = -\frac{1}{R}, \quad K = \frac{1}{R^2}. \quad (8)$$

Substitute Eq. (8) into Eq. (7) and suppose that ρ is a constant. Then a quadratic equation is obtained

$$c_0^2 R^2 + 2c_0 R + \frac{2\alpha R}{k_c} \rho - \frac{\gamma R^2}{k_c} \rho^2 - \frac{2\beta}{k_c} \rho + \frac{\Delta p R^3}{k_c} + \frac{2\lambda R^2}{k_c} = 0. \quad (9)$$

Equation (9) is the geometrical constraint equation for spherical vesicles. If Eq. (9) is satisfied, the sphere is a solution for the shape equation. For convenience, a few dimensionless parameters are introduced

$$\frac{\alpha R}{k_c} = \bar{\alpha}, \quad \frac{\beta}{k_c} = \bar{\beta}, \quad \frac{\gamma R^2}{k_c} = \bar{\gamma}, \quad \frac{\Delta p R^3}{k_c} = \Delta \bar{p}, \quad \frac{\lambda R^2}{k_c} = \bar{\lambda}. \quad (10)$$

Then Eq. (9) becomes

$$c_0^2 R^2 + 2c_0 R + 2\bar{\alpha} \rho - \bar{\gamma} \rho^2 - 2\bar{\beta} \rho + \Delta \bar{p} + 2\bar{\lambda} = 0. \quad (11)$$

The solution of Eq. (11) can be expressed as

$$c_0 R = -1 \pm \sqrt{1 - 2\bar{\alpha} \rho + 2\bar{\beta} \rho + \bar{\gamma} \rho^2 - 2\bar{\lambda} - \Delta \bar{p}}. \quad (12)$$

To get real roots for $c_0 R$, the parameters must satisfy the relation

$$\Delta \bar{p} + 2\bar{\lambda} \leq 1 - 2\bar{\alpha} \rho + 2\bar{\beta} \rho + \bar{\gamma} \rho^2. \quad (13)$$

Inequality (13) is the geometrically permissible condition for spherical vesicles.

3.2. CIRCULAR CYLINDRICAL VESICLES

The mean curvature and Gauss curvature for a circular cylinder with radius R are [20]:

$$H = -\frac{1}{2R}, \quad K = 0. \quad (14)$$

Substitute Eq. (14) into Eq. (7) and suppose the local area fraction of the minor component lipid is a constant. One gets the geometrical constraint equation for a circular cylinder

$$c_0^2 R^2 + \frac{2\alpha R}{k_c} \rho - \frac{\gamma R^2}{k_c} \rho^2 + \frac{2\Delta p R^3}{k_c} + \frac{2\lambda R^2}{k_c} - 1 = 0 \quad (15)$$

If Eq. (15) is satisfied, the circular cylinder is a solution for the shape equation. Equation (15) may be changed into dimensionless form through Eq. (10) and solved as follows

$$c_0 R = \pm \sqrt{1 - 2\bar{\alpha}\rho + \bar{\gamma}\rho^2 - 2\Delta\bar{p} - 2\bar{\lambda}} \quad (16)$$

To obtain real roots for $c_0 R$, the parameters must satisfy

$$2\Delta\bar{p} + 2\bar{\lambda} \leq 1 - 2\bar{\alpha}\rho + \bar{\gamma}\rho^2 \quad (17)$$

Inequality (17) is the geometrically permissible condition for circular cylindrical vesicles.

3.3. GEOMETRICALLY PERMISSIBLE PHASE DIAGRAMS FOR TWO TYPES OF VESICLES

On the $\Delta\bar{p} \sim \bar{\lambda}$ plane, the regions described by inequalities (13) and (17) are called the “geometrically permissible phase diagrams” for spherical and circular cylindrical vesicles. Concretely, the spaces beneath the oblique lines are the “geometrically permissible phase spaces” (GPPS) for the two types of vesicles.

The influences of ρ and $\bar{\gamma}$ on the GPPS are shown in Figure 1. The larger the value of ρ or $\bar{\gamma}$ is, the larger the GPPS. This means that the minor component of lipids and the molecule energy may benefit the formation of vesicles and prevent the vesicles from disintegration. Both for spherical and in circular cylindrical vesicles, the GPPS is very sensitive to the change of ρ , but insensitive to the variation of $\bar{\gamma}$. In other words, the effect of ρ is very strong, while the influence of $\bar{\gamma}$ is very weak.

The influence of $\bar{\alpha}$ on the GPPS is opposite to those of ρ or $\bar{\gamma}$ (see Figures 2(a) and 2(b)): The increase of $\bar{\alpha}$ may narrow the GPPS. This implies that the positive coupling between the average curvature and the area fraction may hold back the formation of vesicles and accelerate vesicle disintegration.

In a circular cylindrical vesicle, the Gauss curvature is zero. Thus the effect of $\bar{\beta}$ on the GPPS disappears in circular cylindrical vesicles but exists in spherical ones. Similar to ρ , the increase of $\bar{\beta}$ will enlarge the GPPS for spherical vesicles (see Figure 2(c)). Thus the positive coupling between the Gauss curvature and the area fraction will strengthen the formation of vesicles and prevent the vesicles from disintegration.

Figure 1. Geometrically permissible phase diagrams for spherical and circular cylindrical vesicles about the influences of the area fraction ρ and $\bar{\gamma}$; (a) and (c) show phase diagrams for spherical vesicles, (b) and (d) show phase diagrams for cylindrical vesicles.

Figure 2. Geometrically permissible phase diagrams for spherical and circular cylindrical vesicles about the influences of $\bar{\alpha}$ and $\bar{\beta}$; (a) and (c) show phase diagrams for spherical vesicles, (b) shows a phase diagram for cylindrical vesicles.

As curvature couplings, the effects of $\bar{\alpha}$ and $\bar{\beta}$ are completely inverse in spherical vesicles. This is reasonable because in a spherical vesicle the average curvature is negative but the Gauss curvature is positive.

3.4. RELATIONS BETWEEN PREDICTIONS AND EXPERIMENTAL PHENOMENA

The numerical results above may be heuristic. The couplings between compositions and curvatures may either strengthen the formation or stimulate the disintegration of closed membranes such as vesicles or liposomes. Here a question may be asked: Once the geometrical permissible condition is violated, what will happen to a disintegrating closed membrane? There are two possibilities. One is complete disintegration, i.e. the two-component membrane will collapse and disappear. Another one is partial disintegration, i.e. the closed membrane will dissolve part of its surface and an open membrane with free edge may be generated. This judgment seems to coincide well with the recent experimental discovery of the opening-up of liposomal membranes by talin [21]. It is reported in Ref. [21] that the morphology of liposomes may be changed by interactions between liposomal membranes and talin. When talin is added to a liposome solution, liposomes open stable holes and are transformed into cap-shaped liposomes. The holes become larger with increasing talin concentration, and finally the cup-shaped liposomes are changed into open lipid bilayer vesicles. These interesting experiments are close related to the predicted results in Section 3.3 above. In a word, the present theory has the potentiality to predict various topologies of two-component membranes and may agree qualitatively with experimental phenomena.

4. Conclusions

The minor lipid intensely affects two-component vesicles in the following aspects: The equilibrium differential equation, the geometrical shapes and topological structures, the existence of vesicle, the geometrically permissible phase diagrams, and so on. In a word, the present paper lays a solid basis for quantitative investigations to the shapes and shape transitions of two-component vesicles. Besides, it will enable us to explore the stabilities of two-component vesicles in a forthcoming paper.

It should be noted that the present theory just coincides qualitatively with some experimental results. Quantitative experiments are still necessary to support the reliability and correctness of the theory.

Appendix

In Eq. (4), three terms [17] may be directly written as follows

$$\begin{aligned} \delta^{(1)} F_c = & k_c \oint \nabla^2 (2H - c_0) \psi dA \\ & + k_c \oint (2H - c_0)(2H^2 + c_0 H - 2K) \psi dA \end{aligned} \quad (\text{A.1})$$

$$\delta^{(1)} \oint dV = \oint \psi dA, \quad \delta^{(1)} \oint dA = - \oint 2H \psi dA \quad (\text{A.2})$$

where $\nabla^2 = \nabla \cdot \nabla$ is the Laplace-Beltrami operator and ∇ is the conventional gradient operator on curved surfaces. In Eq. (4), $\delta^{(1)} F_d$ and $\mu \delta^{(1)} \oint \rho dA$ are new variational terms and will be formulated below. From Eq. (2), it is easy to get

$$\begin{aligned} \delta^{(1)} F_d &= \alpha \delta^{(1)} \oint \rho (2H - c_0) dA + \beta \delta^{(1)} \oint K \rho dA + \frac{\gamma}{2} \delta^{(1)} \oint \rho^2 dA \\ &= \alpha \oint \delta^{(1)} (2H - c_0) (\rho dA) + \alpha \oint (2H - c_0) \delta^{(1)} (\rho dA) \\ &\quad + \beta \oint \delta^{(1)} K (\rho dA) + \beta \oint K \delta^{(1)} (\rho dA) + \frac{\gamma}{2} \oint \delta^{(1)} \rho (\rho dA) \\ &\quad + \frac{\gamma}{2} \oint \rho \delta^{(1)} (\rho dA). \end{aligned} \quad (\text{A.3})$$

The mass conservation law for two components will assure

$$\delta^{(1)} (\rho dA) = \delta^{(1)} \rho dA + \rho \delta^{(1)} dA = 0. \quad (\text{A.4})$$

The $\delta^{(1)} H$, $\delta^{(1)} K$, $\delta^{(1)} dA$ terms can be cited from Refs. [16, 17]

$$\begin{aligned} \delta^{(1)} H &= \frac{1}{2} \nabla^2 \psi + (2H^2 - K) \psi, \quad \delta^{(1)} K = \bar{\nabla}^2 \psi + 2HK \psi, \\ \delta^{(1)} dA &= -2H \psi dA. \end{aligned} \quad (\text{A.5})$$

Substitution of Equations (A.4) and (A.5) into Eq. (A.3) will lead to

$$\delta^{(1)} F_d = \oint [\alpha \nabla^2 \rho + \bar{\nabla}^2 \rho + 2\alpha \rho (2H^2 - K) + \rho^2 \gamma H + 2\beta K H \rho] \psi dA \quad (\text{A.6})$$

where $\bar{\nabla}^2 = \nabla \cdot \bar{\nabla}$ is a new operator [15, 20] and $\bar{\nabla}$ is a new gradient operator [15, 18, 22]. Substituting Equations (A.1), (A.2) and (A.6) into Eq. (4), Eq. (5) can be obtained.

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