Helfrich shape equation for axisymmetric vesicles as a first integral

Wei-Mou Zheng and Jixing Liu
Institute of Theoretical Physics, Academia Sinica, P.O. Box 2735, Beijing 100080, China
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A first integral of the general equation for axisymmetric shapes of lipid bilayer vesicles is obtained. The relation between the widely used Helfrich shape equation and the general shape equation is clarified and a modified version of the Helfrich shape equation that is equivalent to the general equation is proposed.

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I. INTRODUCTION

For almost two decades the study of the equilibrium shape of lipid bilayer vesicles in aqueous solution based on Helfrich spontaneous-curvature theory [1], and especially the application of Helfrich theory in explaining the usual shape of red blood cells obtained from normal individuals, has been an attractive topic. Among numerous works dedicated to this study the Helfrich shape equation describing axisymmetric vesicle played a special role. This equation has been widely used to seek both analytically and numerically [1–9] the axisymmetric vesicle shape in different conditions. Its successful application is demonstrated by the very good agreement between the theory and experimentally observed red-cell shapes [10] obtained by fitting only one parameter. However, it was noticed previously that the general shape equation derived by Ou-Yang and Helfrich [11,12] in axisymmetric case reduces to a third-order differential equation while the Helfrich shape equation is a second-order one, and that the equivalence of these two equations only holds for describing the spherelike shapes of vesicles [13]. But the systematic analysis on the relation between these two equations has never been made.

There are three shape equations for axisymmetric vesicles in use. They are the Helfrich shape equation, the equation first derived by Peterson [6] and later frequently used by Lipowsky and co-workers [14,15] and the axisymmetric version of the general shape equation. Very recently, Hu and Ou-Yang, based on the same bending energy of the spontaneous-curvature model, considered the difference among these equations from the viewpoint of a variational method [16]. They correctly pointed out that the shape equation adequate for describing an axisymmetric vesicle should be the one obtained by minimizing the effective free energy of the vesicle with respect to the variation of the infinitesimal normal displacement from the equilibrium surface of the vesicle. Among three shape equations, only the last one satisfies this requirement. According to their analysis, the second equation, which is of the same order as the correct third one, should be abandoned. As for the first equation, after comparing the exact solutions, they concluded that only the sphere solution given by the Helfrich shape equation is consistent with the solution of the general equation, while two other exact solutions (cylinder and ring) from both equations are incompatible.

This new development, naturally, raised questions such as the following: (i) Is there any general relation between the Helfrich shape equation and the general equation? If there is, what is it? (ii) How should one evaluate the previous results of vesicle shapes obtained from the Helfrich shape equation, especially those results obtained numerically such as the biconcave shape of red blood cells, or precisely stating, should they be completely abandoned or are they still correct in certain conditions?

The purpose of this paper is to answer these questions. The article is organized as follows. In Sec. II, by inspecting the structures of the equations, the first integral of the general equation is derived which reveals clearly the relation between the Helfrich shape equation and the general equation. Based on this relation the validity of the Helfrich shape equation is examined. In Sec. III some concluding remarks are made, and a modified form of the Helfrich shape equation is proposed.

II. THE FIRST INTEGRAL OF GENERAL SHAPE EQUATION

A lipid bilayer vesicle formed in aqueous solution is considered as a simple model for biological membranes or cells [17–19]; the equilibrium shape of the vesicles is determined by minimizing the Helfrich curvature free energy [1]

$$F=\tfrac{1}{2}k_c\oint(c_1+c_2-c_0)^2dA+\lambda\oint dA+p\int dV\ . \quad (1)$$

In this expression k_c, c_1, and c_2 are the elastic modulus and two principal curvatures of the vesicle surface; parameter c_0, being a measure of asymmetry with respect to the two sides of the vesicle membrane, is the spontaneous curvature; p and λ are two Lagrangian multipliers introduced by the constraints that the volume and the total area of the vesicle are constants—physically they can be explained as the pressure difference across the membrane and the tensile stress, respectively.

Considering a vesicle of an axisymmetrical shape, denoting by ρ the distance between the symmetric axis and a point on the contour of the vesicle surface, and taking the variation of the axisymmetric form of free energy (1) with respect to the principal curvature along the parallel of the latitude of the vesicle gives the Helfrich shape equation

$$\mathcal{H}\equiv\cos^2\psi\frac{d^2\psi}{d\rho^2}-\frac{\sin(2\psi)}{4}\left[\frac{d\psi}{d\rho}\right]^2+\frac{\cos^2\psi}{\rho}\frac{d\psi}{d\rho}-\frac{\sin(2\psi)}{2\rho^2}-\frac{p\rho}{2k_c\cos\psi}-\frac{\sin\psi}{2\cos\psi}\left[\frac{\sin\psi}{\rho}-c_0\right]^2-\frac{\lambda\sin\psi}{k_c\cos\psi}=0\ , \tag{2}$$

where ψ is the angle made by the surface normal and the symmetric axis of the vesicle. This equation has been widely used to obtain different axisymmetric shapes of the vesicle and fruitful results obtained as mentioned above.

Another shape equation later derived by Ou-Yang and Helfrich [11,12] can be applied to an arbitrary shape of vesicles. In the axisymmetric case it reduces to [16]

$$\cos^3\psi\frac{d^3\psi}{d\rho^3}-4\sin\psi\cos^2\psi\frac{d^2\psi}{d\rho^2}\frac{d\psi}{d\rho}+2\frac{\cos^3\psi}{\rho}\frac{d^2\psi}{d\rho^2}+\cos\psi(\sin^2\psi-\tfrac{1}{2}\cos^2\psi)\left[\frac{d\psi}{d\rho}\right]^3-\frac{7}{2}\frac{\sin\psi\cos^2\psi}{\rho}\left[\frac{d\psi}{d\rho}\right]^2-\left[\frac{c_0^2}{2}-\frac{2c_0\sin\psi}{\rho}-\frac{\sin^2\psi-2\cos^2\psi}{2\rho^2}+\frac{\lambda}{k_c}\right]\cos\psi\frac{d\psi}{d\rho}-\frac{p}{k_c}-\frac{\lambda\sin\psi}{k_c\rho}-\frac{c_0^2\sin\psi}{2\rho}+\frac{(1+\cos^2\psi)\sin\psi}{2\rho^3}=0\ . \tag{3}$$

Since the original equation is free of prior requirements on the shape of the vesicle, and in the derivation a variation is taken with respect directly to the surface, accordingly it is more general than the Helfrich shape equation. Therefore we call Eq. (3) the general equation describing the shape of axisymmetric vesicles. It is rather impressive that the exact ring solution, an axisymmetric shape with a nonzero genus, was predicted [20] from the equation and later successfully confirmed by experimental observations [21,22].

The relation between Eqs. (2) and (3) (or its original version) was discussed by different authors and the opinions are diverse, even contradictory. While Ou-Yang and Helfrich claimed that the relation is inclusive by stating that the general equation (in its original version) "can be obtained by generalizing and forming derivative" of Eq. (2) without showing the explicit procedure [12,23], one of the authors provided an explicit expression [Eq. (22) of Ref. [13]] showing that the relation is only partially inclusive. Until very recently, Hu and Ou-Yang strikingly challenged the correctness of Eq. (2) by claiming that Eq. (2) was derived by erroneous application of variation method [16], which implies that the relation should be exclusive.

To clarify this puzzling problem, by closely inspecting the structure of Eqs. (2) and (3), and guided by the expression (22) of Ref. [13], we notice that Eq. (3) can be exactly expressed as

$$\frac{1}{\rho}\frac{d}{d\rho}[\rho\mathcal{H}\cos\psi]=0\ , \tag{4}$$

which can be proved by direct differentiation (for details see the Appendix). This expression clearly reveals the connection between Eqs. (2) and (3), and indicates that any solution satisfying Eq. (2) should be also a solution of Eq. (3).

Integrating Eq. (4) yields the first integral of Eq. (3)

$$\rho\mathcal{H}\cos\psi=C \tag{5}$$

or

$$\mathcal{H}-\frac{C}{\rho\cos\psi}=0\ , \tag{6}$$

where C is an integration constant.

Since expression (5) is the first integral of the general equation (3), it equivalently determines the axisymmetric shape of vesicles as Eq. (3) does. Accordingly, Eq. (6) explicitly indicates the missing term in the Helfrich shape equation. One immediately conceives that the Helfrich equation recovers to Eq. (3) only when the integration constant C vanishes and that the general equation includes the Helfrich equation as a special case. For a spherelike axisymmetric shape, since near the point on the surface where the axis of symmetry passes we have that $\rho\propto\psi\sim o(1)$; from Eqs. (2) and (5) the constant C of integration must equal to zero whenever $d\psi/d\rho$ is finite at the pole $\rho=0$. Thus Eqs. (2) and (3) are completely equivalent for spherelike cases which, fortunately, are the only cases found in the literature when the Helfrich equation was used.

To illustrate the above statements we reexamine the three well-known exact solutions, i.e., sphere, cylinder, and ring solutions given by Eqs. (2) and (3).

A. Spherical solution

Substituting the expression of a sphere with radius r_0

$$\rho=r_0\sin\psi \tag{7}$$

into Eqs. (2) and (3), respectively, the same relation between p, λ, c_0, and r_0,

$$pr_0^3+2\lambda r_0^2+k_cc_0r_0(c_0r_0-2)=0\ , \tag{8}$$

is obtained [12,13,16]. Putting the same solution into Eq. (6) gives

$$C=0\ , \tag{9}$$

as it should be. The Helfrich shape equation coincides with the general equation.

B. Cylindrical solution

For the cylinder defined by

$$\rho=r_0\ ,\quad \psi=\frac{\pi}{2}\ , \tag{10}$$

the relation obtained from Eq. (3) is

$$pr_0^3+\lambda r_0^2+\frac{k_c}{2}(c_0^2r_0^2-1)=0\ . \tag{11}$$

Since Eq. (2) is singular for cylinder, the limiting procedure $\cos\psi\to 0$ has to be taken. When Eq. (10) is substituted in Eq. (2), from the requirement that both the leading terms of singularity and the next order terms must vanish we have

$$pr_0^3+2\lambda r_0^2+k_c(c_0r_0-1)^2=0 \tag{12}$$

and

$$\lambda r_0^2+k_c\left[\frac{c_0^2r_0^2}{2}-2c_0r_0+\frac{3}{2}\right]=0\ . \tag{13}$$

The expressions (11) and (12) have been regarded as contradictory to each other in Ref. [16] and hence as evidence that the Helfrich equation is incompatible with the general shape equation. However, by noticing the fact that subtraction of (13) from (12) recovers relation (11) and that substituting Eq. (10) into Eq. (5) gives

$$C=-\frac{1}{2k_cr_0}[pr_0^3+2\lambda r_0^2+k_c(c_0r_0-1)^2]\ . \tag{14}$$

It is verified that the cylindrical shapes given by the Helfrich shape equation do belong to the class of cylinder solutions of Eq. (3) with the additional constraint $C=0$. It is interesting and surprising enough to be aware that the cylinder determined with the Helfrich equation is nothing but the only stable equilibrium cylinder obtained from the general shape equation [12].

C. Ring solution

For a shape of ring scaled as

$$\rho=x+\sin\psi\quad (0\le\psi\le 2\pi)\ , \tag{15}$$

where $1/x$ is the ratio of its generating radii, Eq. (3) gives [16]

$$x=\sqrt{2}\ ,\quad \lambda=k_c\left[2c_0-\frac{c_0^2}{2}\right]\ ,\quad p=-2k_cc_0\ . \tag{16}$$

The same substitution in Eq. (2) gives

$$x=\sqrt{2}\ ,\quad \lambda=k_c\left[2c_0-\frac{c_0^2}{2}\right]\ ,\qquad p=-2k_cc_0\ ,\quad c_0=-\tfrac{1}{2}\ . \tag{17}$$

Noticing that substituting expression (15) into Eq. (6) yields

$$C=2c_0+1\ , \tag{18}$$

we see that the ring solution obtained from the Helfrich shape equation falls into the class of ring shapes given by the general equation. However, the ring shape given by Eq. (2) is subject to one more condition $c_0=-\frac{1}{2}$, which comes from requirement $C=0$.

III. CONCLUDING REMARKS

In Sec. II the first integral of the general equation describing the axisymmetric shapes of vesicles is derived. Based on it, the systematical discussion of the relation between the Helfrich shape equation and the general equation is carried out. The validity of the Helfrich equation is then clarified. To conclude we should like to emphasize the following.

(i) Up to now a rather rich variety of axisymmetric shapes of spherelike vesicles has been explored with the Helfrich shape equation by many authors. These results should be positively valued as on achievement in the study of lipid bilayer vesicle. For the spherelike shapes these solutions are completely the same as those of the general equation.

(ii) It is certain that the general equation describing the axisymmetric shape of vesicles will provide richer vesicle shapes than the Helfrich shape equation. However, because the general equation is a third-order ordinary differential equation and highly nonlinear, it is difficult to attack directly. The present first integral might reduce the difficulty. From the first integral the Helfrich shape equation can be generalized as

$$\cos^2\psi\frac{d^2\psi}{d\rho^2}-\frac{\sin(2\psi)}{4}\left[\frac{d\psi}{d\rho}\right]^2+\frac{\cos^2\psi}{\rho}\frac{d\psi}{d\rho}-\frac{\sin(2\psi)}{2\rho^2}-\frac{\tilde{p}\rho}{2k_c\cos\psi}-\frac{\sin\psi}{2\cos\psi}\left[\frac{\sin\psi}{\rho}-c_0\right]^2-\frac{\lambda\sin\psi}{k_c\cos\psi}=0\ , \tag{19}$$

where

$$\tilde{p}=p+\frac{2k_cC}{\rho^2}\ . \tag{20}$$

Equation (19) is identical to the Helfrich shape equation except for the replacement of the constant parameter p by a modified pressure difference $\tilde{p}$ depending on p, k_c, ρ, and C. Equation (19) is equivalent to the general shape equation (3) and it reduces to Helfrich shape equation when $C=0$. The existing numerical methods for Helfrich shape equation may then be directly employed with only minor modification.

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APPENDIX: PROOF OF EQUATION (4)

In this appendix we prove Eq. (4) by direct differentiating expression $\rho\mathcal{H}\cos\psi$ term by term:

$$\rho\mathcal{H}\cos\psi=\rho\cos^3\psi\frac{d^2\psi}{d\rho^2}-\rho\frac{\sin\psi\cos^2\psi}{2}\left[\frac{d\psi}{d\rho}\right]^2+\cos^3\psi\frac{d\psi}{d\rho}-\frac{\sin\psi\cos^2\psi}{\rho}-\frac{p\rho^2}{2k_c}-\frac{\lambda\rho\sin\psi}{k_c}-\frac{\rho\sin\psi}{2}\left[\frac{\sin\psi}{\rho}-c_0\right]^2 . \quad (A1)$$

Differentiating each term of Eq. (A1) and dividing it by ρ yields

$$\frac{1}{\rho}\frac{d}{d\rho}\left[\rho\cos^3\psi\frac{d^2\psi}{d\rho^2}\right]=\cos^3\psi\frac{d^3\psi}{d\rho^3}-3\cos^2\psi\sin\psi\frac{d^2\psi}{d\rho^2}\frac{d\psi}{d\rho}+\frac{\cos^3\psi}{\rho}\frac{d^2\psi}{d\rho^2} , \quad (A2)$$

$$-\frac{1}{\rho}\frac{d}{d\rho}\left[\frac{\rho\cos^2\psi\sin\psi}{2}\left[\frac{d\psi}{d\rho}\right]^2\right]=-\sin\psi\cos^2\psi\frac{d^2\psi}{d\rho^2}\frac{d\psi}{d\rho}+\frac{2\cos\psi-3\cos^3\psi}{2}\left[\frac{d\psi}{d\rho}\right]^3-\frac{\sin\psi\cos^2\psi}{2\rho}\left[\frac{d\psi}{d\rho}\right]^2 , \quad (A3)$$

$$\frac{1}{\rho}\frac{d}{d\rho}\left[\cos^3\psi\frac{d\psi}{d\rho}\right]=\frac{\cos^3\psi}{\rho}\frac{d^2\psi}{d\rho^2}-\frac{3\sin\psi\cos^2\psi}{\rho}\left[\frac{d\psi}{d\rho}\right]^2 , \quad (A4)$$

$$-\frac{1}{\rho}\frac{d}{d\rho}\left[\frac{\cos^2\psi\sin\psi}{\rho}\right]=\frac{2\cos\psi-3\cos^3\psi}{\rho^2}\frac{d\psi}{d\rho}+\frac{\sin\psi\cos^2\psi}{\rho^3} , \quad (A5)$$

$$-\frac{1}{\rho}\frac{d}{d\rho}\left[\frac{p\rho^2}{2k_c}\right]=-\frac{p}{k_c} , \quad (A6)$$

$$-\frac{1}{\rho}\frac{d}{d\rho}\left[\frac{\rho\lambda\sin\psi}{k_c}\right]=-\frac{\lambda\cos\psi}{k_c}\frac{d\psi}{d\rho}-\frac{\lambda\sin\psi}{k_c\rho} , \quad (A7)$$

$$-\frac{1}{\rho}\frac{d}{d\rho}\left[\frac{\rho\sin\psi}{2}\left[\frac{\sin\psi}{\rho}-c_0\right]^2\right]=-\left[\frac{c_0^2}{2}-\frac{2c_0\sin\psi}{\rho}+\frac{3\sin^2\psi}{2\rho^2}\right]\cos\psi\frac{d\psi}{d\rho}-\frac{c_0^2\sin\psi}{2\rho}+\frac{\sin^3\psi}{2\rho^3} . \quad (A8)$$

Summing up the seven expressions from (A2) to (A8) and grouping terms on the right-hand side carefully gives

$$\frac{1}{\rho}\frac{d}{d\rho}[\rho\mathcal{H}\cos\psi]=\cos^3\psi\frac{d^3\psi}{d\rho^3}-4\sin\psi\cos^2\psi\frac{d^2\psi}{d\rho^2}\frac{d\psi}{d\rho}+2\frac{\cos^3\psi}{\rho}\frac{d^2\psi}{d\rho^2}+\cos\psi(\sin^2\psi-\tfrac{1}{2}\cos^2\psi)\left[\frac{d\psi}{d\rho}\right]^3-\frac{7}{2}\frac{\sin\psi\cos^2\psi}{\rho}\left[\frac{d\psi}{d\rho}\right]^2-\left[\frac{c_0^2}{2}-\frac{2c_0\sin\psi}{\rho}-\frac{\sin^2\psi-2\cos^2\psi}{2\rho^2}+\frac{\lambda}{k_c}\right]\cos\psi\frac{d\psi}{d\rho}-\frac{p}{k_c}-\frac{\lambda\sin\psi}{k_c\rho}-\frac{c_0^2\sin\psi}{2\rho}+\frac{(1+\cos^2\psi)\sin\psi}{2\rho^3} . \quad (A9)$$

The right-hand side of this expression is exactly the left-hand side of Eq. (3), which directly leads to Eq. (4).

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