A THEORY FOR THE SHAPE OF THE RED BLOOD CELL

K. H. ADAMS

From the Department of Mechanical Engineering, Tulane University, New Orleans, Louisiana 70118

ABSTRACT A theory of mechanical stability is formulated based on the electrostatic energy density contained within a biological membrane. Stable cell shapes are taken to correspond to a minimum value for the total electrostatic energy. The theory is applied to the red blood cell, and it is shown that the normal biconcave shape indeed corresponds to the shape of minimum electrostatic energy. The results are compared with theories based on bending energy relations.

INTRODUCTION

The problem of the normal shape of the red blood cell has been one of considerable historical interest. A number of theories have been put forth, none of which appear to offer a unique answer to the problem. Canham (1970) has recently reviewed many of the theories and has proposed one based on a minimum bending energy condition to explain the biconcave shape. This theory predicts shapes that are close to observed shapes. However, the theoretical justification for a bending energy condition based on isotropic elastic plate theory is questionable. Fung and Tong (1968) conclude that bending effects are small in an analysis of the sphering of the red blood cell based on elastic membrane theory. Fung (1966) concludes that the normal biconcave shape of the red blood cell corresponds to the natural shape of the red cell membrane.

The problem of the shape of the red blood cell is reconsidered in this report in order to account for certain mechanical equilibrium and deformability aspects of the red cell membrane recently proposed by Adams (1972, 1973). A stability criterion for cell shape is formulated based on the total electrostatic energy contained within the cell membrane. The theory is applied to the problem of the normal shape of the red blood cell. In addition, the electrostatic energy theory is compared with the bending energy theory proposed by Canham (1970).

ELECTROSTATIC ENERGY

The electric field within a biological membrane of arbitrary curvature, resulting from uniform surface charge densities, has previously been given by Adams (1972) as

$$E(y) = \frac{\sigma_i}{\epsilon}\frac{[R_1 - (t/2)][R_2 - (t/2)]}{(R_1 + y)(R_2 + y)}, \qquad (1)$$

where σ_i is the uniform surface charge density of univalent anions on the inside surface of the membrane and ϵ is the membrane permittivity. The y axis extends along the outward normal direction to the membrane surface with the origin, for the case given by Eq. 1, taken to be on the middle surface of the membrane of thickness t and principal radii of curvature R_1 and R_2. Integration of Eq. 1 across the thickness of the membrane results in a membrane potential $| \Delta\Phi |$ given by

$$| \Delta\Phi | = \frac{\sigma_i}{\epsilon} \frac{[R_1 - (t/2)][R_2 - (t/2)]}{(R_1 - R_2)} \ln \left[\frac{[R_1 - (t/2)][R_2 + (t/2)]}{[R_1 + (t/2)][R_2 - (t/2)]} \right]. \quad (2)$$

Eq. 2. may be solved for σ_i and substituted into Eq. 1 to give the electric field as

$$E(y) = \frac{| \Delta\Phi |}{\ln \left[\frac{[R_1 - (t/2)][R_2 + (t/2)]}{[R_1 + (t/2)][R_2 - (t/2)]} \right]} \frac{(R_1 - R_2)}{(R_1 + y)(R_2 + y)}. \quad (3)$$

The electrostatic energy density in a dielectric of permittivity ϵ is given by Reitz and Milford (1960) as

$$w = \tfrac{1}{2}\epsilon E^2, \quad (4)$$

where w is the electrostatic energy per unit volume. The surface energy contained in the electrostatic field or electrostatic energy per unit area of membrane surface is obtained by integrating the energy density over the thickness or

$$W_a = \int_{-t/2}^{t/2} w \, dy = (\epsilon/2) \int_{-t/2}^{t/2} E^2 \, dy, \quad (5)$$

where ϵ is assumed to be uniform through the thickness of the membrane. Substitution of Eq. 3 into Eq. 5 and integration across the membrane thickness results in the following expression for the surface energy associated with the electrostatic field

$$W_a = \frac{\epsilon | \Delta\Phi |^2}{2 \left\{ \ln \left[\frac{[R_1 - (t/2)][R_2 + (t/2)]}{[R_1 + (t/2)][R_2 - (t/2)]} \right] \right\}^2} \left\{ \frac{(R_1 - R_2)(R_1 + R_2)t}{[R_1^2 - (t^2/4)][R_2^2 - (t^2/4)]} + \frac{2t}{[R_1^2 - (t^2/4)]} - \frac{2}{(R_1 - R_2)} \ln \frac{[R_1 - (t/2)][R_2 + (t/2)]}{[R_1 + (t/2)][R_2 - (t/2)]} \right\}. \quad (6)$$

Eq. 6 is an exact expression which may be approximated as

$$W_a \cong \frac{\epsilon | \Delta\Phi |^2}{2t} \left[1 + \frac{1}{12} \left(\frac{t}{R} \right)^2 \right], \quad (7)$$

where

$$1/R = (1/R_1) + (1/R_2)$$

is the sum of the principal curvatures or the first curvature of the surface (Weatherburn, 1955). Eq. 7 is obtained by expansion of Eq. 6 where all terms of order $(t/R)^3$ are considered small compared with unity or terms of order $(t/R)^2$ and are therefore eliminated.

A stability criterion for cell shape may now be stated in the following manner. Stable cell shapes result when the total electrostatic energy is at a minimum. The total electrostatic energy is obtained by integration of W_a over the entire cell surface area A_c, or

$$W_t = \int_{A_c} W_a \, dA_c; \tag{8}$$

By substitution of Eq. 7 into Eq. 8, we find

$$W_t = \frac{1}{2} \int_{A_c} \frac{\epsilon \mid \Delta\Phi \mid^2}{t} \left[1 + \frac{1}{12} \left(\frac{t}{R} \right)^2 \right] dA_c. \tag{9}$$

According to the stability criterion, a stable cell shape is reached when the functional given by Eq. 9 is at a minimum.

SHAPE OF THE RED BLOOD CELL

Before applying the stability criterion to the red blood cell, the following points must be considered. For a given cell shape, the energy functional given by Eq. 9 may be readily calculated. Moreover, we require that the given cell shape satisfy mechanical equilibrium conditions and that in comparing two different shapes, the two states must be admissible to each other in terms of the deformability of the cell membrane.

The questions of membrane equilibrium and deformability have been considered in detail elsewhere (Adams, 1972, 1973). The conclusions reached, which are important to the present analysis, are that the biconcave shape of the red blood cell is an equilibrium configuration with no hydrostatic pressure drop across the cell membrane and that the presumed fluid nature of the membrane allows for an infinite number of shapes of the same cell area and volume.

If the red blood cell area and volume are regarded as constant and independently specified, the stability problem reduces to one of determining the unique shape of the infinite set of admissible shapes that results in a minimum value for the energy functional given by Eq. 9. The problem may be stated mathematically in the following way.

Let z be the axis of symmetry for an axisymmetric cell and $z(x)$ be an analytic expression for the cell shape in meridional section (z-x plane). For biconcave or biconvex shapes, the cell area and volume are given by

$$A_c = 4\pi \int_0^{x_{max}} x \, [1 + (dz/dx)^2]^{1/2} \, dx, \tag{10}$$

and

$$V_c = 4\pi \int_0^{x_{max}} zx \, dx. \tag{11}$$

In addition, the energy functional given by Eq. 9 results in

$$W_t = \frac{\epsilon \mid \Delta\Phi \mid^2}{2t} \cdot \left\{ A_c + \frac{\pi t^2}{3} \int_0^{x_{max}} \frac{x}{[1 + (dz/dx)^2]^{1/2}} \left[\frac{d^2z/dx^2}{1 + (dz/dx)^2} + \frac{1}{x} \frac{dz}{dx} \right]^2 dx \right\}, \tag{12}$$

where ϵ, $\mid \Delta\Phi \mid$, and t are assumed to be constant. A stable cell shape corresponds to the function $z(x)$ which satisfies Eqs. 10 and 11 and which results in a minimum value for Eq. 12.

DISCUSSION

Although the problem of the shape of the red blood cell has been properly posed, an exact solution will not be attempted due to mathematical complexities. An approximate solution to the problem is, however, available due to Canham (1970). With reference to the shape of the red blood cell, Canham has shown that accurate cell shapes are predicted by modified ovals of Cassini if the cell area and volume are constrained to constant values and the functional F_1 is minimized where

$$F_1 = \int_{A_c} [(1/R_1)^2 + (1/R_2)^2] \, dA_c. \tag{13}$$

The values used by Canham for cell area and volume were directly determined on individual cells which corresponded to the normal range of cell sizes as determined by Canham and Burton (1968).

In the present theory, stable cell shapes are predicted when the energy functional given by Eq. 9 is minimized or for membranes of constant ϵ, $\mid \Delta\Phi \mid$, and t, when the functional F_2 is at a minimum where

$$F_2 = \int_{A_c} [(1/R_1) + (1/R_2)]^2 \, dA_c. \tag{14}$$

By comparison of Eqs. 13 and 14, Eq. 14 may be written as

$$F_2 = F_1 + 2 \int_{A_c} (dA_c/R_1R_2), \tag{15}$$

where $1/R_1R_2$ is the second curvature or gaussian curvature of the surface (Weatherburn, 1955). For both biconcave and biconvex shapes, the surface integral of the second curvature is equal to 4π. This is a result of a theorem due to Gauss (Weatherburn, 1955). Therefore, Eq. 15 may be written as

$$F_2 = F_1 + 8\pi. \tag{16}$$

We see from Eq. 16 that Canham's observation that the biconcave shape of the red blood cell corresponds to a minimum value of F_1 is therefore sufficient to also show that F_2, and therefore the total electrostatic energy, is minimized for the biconcave geometry.

Canham's justification for choosing the surface integral of the sum of the squares of the principal curvatures is based on a minimum bending energy principle which, strictly speaking, is only valid for isotropic, linearly elastic plates. The principle is largely unfounded as applied to biological membranes especially when the fluid nature of the red cell membrane is taken into account. Moreover, the electrostatic energy principle as presently formulated would appear to provide a much simpler explanation for Canham's interesting result on the shape of the red blood cell.

SUMMARY

A theory is formulated for the mechanical stability of biological membranes based on electrostatic energy. The theory is applied to the problem of the normal shape of the red blood cell. By comparison with an approximate analysis due to Canham (1970) for red cell shape, it is shown that the present theory, based on minimizing the total electrostatic energy, results in biconcave shapes.

The author is grateful to Professor S. C. Cowin for many helpful discussions.

Received for publication 11 January 1973.

REFERENCES

ADAMS, K. H. 1972. *Biophys. J.* 12:123.
ADAMS, K. H. 1973. *Biophys. J.* 13:209.
CANHAM, P. B. 1970. *J. Theor. Biol.* 26:61.
CANHAM, P. B., and A. C. BURTON. 1968. *Circ. Res.* 22:405.
FUNG, Y. C. 1966. *Fed. Proc.* 25:1761.
FUNG, Y. C., and P. TONG. 1968. *Biophys. J.* 8:175.
REITZ, J. R., and F. J. MILFORD. 1960. Foundations of Electromagnetic Theory. Addison-Wesley Publishing Co., Inc., Reading, Mass. 110.
WEATHERBURN, C. E. 1955. Differential Geometry of Three Dimensions. Cambridge University Press, New York 1:69, 117.