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J. A. Adam

Old Dominion University, jadam@odu.edu

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(A Note on)² the Shape of the Erythrocyte

J. ADAM
Department of Mathematics and Statistics
Old Dominion University
Norfolk, VA 23529, U.S.A.
adam@math.odu.edu

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Abstract—A note on the shape of the red blood cell is revisited, utilizing variational calculus to find an extremum for the surface area of such a cell, using the volume as a constraint. A fairly significant error in the value of the volume is corrected, and the note concludes with a discussion of measures of cell shape (such as the sphericity index) which are more appropriate than the dimensional surface area to volume ratio.

Keywords—Variational calculus, Red blood cell, Sphericity index.

1. INTRODUCTION

The reasons for the biconcave shape of the human red blood cell have been investigated by several authors during the last three decades, often from the standpoint of elasticity theory (e.g., [1,2], and references therein). In 1974, Lenard [3] used methods of variational calculus to derive an equation for the cross-sectional shape of an erythocyte. By assuming that the dominant reason for the characteristic shape is efficiency of oxygen transfer and transport, Lenard used analytic expressions for the erythocyte surface area and volume to find the optimal cross-sectional shape of the cell, it is claimed, by maximizing the surface area to volume ratio. In fact, this is not strictly what was accomplished, for the volume was assumed to be constant and used as a constraint in the resulting Euler-Lagrange equation (see Section 2 below).

In view of the fact that this is an interesting and self-contained problem, and that not all of the mathematical details were included in the paper (for obvious reasons), this seemed to be an appropriate problem assignment for a graduate class in variational calculus. As the details began to unfold, it became clear that a significant ($\approx 12\%$) error in the resulting erythrocyte volume occurs in [3], and that another measure of shape, the dimensionless sphericity index, is a more appropriate quantity than the dimensional surface area to volume ratio used in that paper.

2. THE EULER-LAGRANGE EQUATION

Following [3], we consider the volume $V$ and surface area $S$ of a body with rotational symmetry about the $y$-axis (see Figure 1) to be

\[ V = \frac{2}{3} \pi \sigma y \text{ and } S = \pi \sigma y \]

I would like to thank C. Harrington, M. Locke, and I. McKaig for checking the volume and surface area calculations.
Figure 1. Cross-sectional shape of the erythrocyte.

\[ V = 4\pi \int_0^b xy(x) \, dx, \] (1)

\[ S = 4\pi \int_0^b x \left[ 1 + (y'(x))^2 \right]^{1/2} \, dx. \] (2)

The shape of the cross section of the cell near its rounded edge was assumed to be circular, following an earlier study by Szirtes [4], with radius \( r = 1.2 \mu \) (microns) (see [5]). This approximation is, therefore,

\[ y = \left[ r^2 - (x - a)^2 \right]^{1/2}, \quad x_1 \leq x \leq b, \] (3)

where \( x_1 \) is to be determined. The volume (unknown at this stage) is taken to be constant, and is introduced as a constraint in the functional

\[ J(y) = 4\pi \int_0^b \left\{ x \left[ 1 + (y')^2 \right]^{1/2} + \lambda xy \right\} \, dx, \] (4)

where \( \lambda \) is a Lagrange multiplier, and the integrand in (4) is denoted by \( f(y, y'; x) \). \( J(y) \) is extremized by those of \( f \) which satisfy the Euler-Lagrange equation, used here in the form

\[ \frac{\partial f}{\partial y} - \frac{d}{dx} \left( \frac{\partial f}{\partial y'} \right) = 0. \] (5)

This corresponds in \( 0 \leq x \leq x_1 \) to solutions of the following second-order nonlinear ordinary differential equation:

\[ y'' + \frac{1}{x} \left[ y'^3 + y' \right] - \lambda \left[ 1 + y'^2 \right]^{3/2} = 0, \] (6)

subject to the "initial" conditions \( y(0) = 0.5, \ y'(0) = 0 \). As noted by Lenard, a sequence of substitutions reduces (6) to a linear first-order ordinary differential equation. Thus \( p = y' \), followed by \( p = \phi(1 - \phi^2)^{-1/2} \) reduces (6) to

\[ \phi = \lambda - \frac{\phi}{x}, \]

whence

\[ \phi = \frac{\lambda x}{2}. \]
Following these variables back to \( y \) yields the solution to (6), namely,

\[
y = \lambda^{-1} \left\{ \frac{4 + \lambda}{2} - 2 \sqrt{1 - \left( \frac{\lambda x}{2} \right)^2} \right\},
\]

valid for \( 0 \leq x \leq x_1 \). Continuity of \( y(x_1) \) and \( y'(x_1) \) involves some rather tedious algebraic manipulations resulting in the following quadratic equation in \( x_1 \):

\[
\{(2r - 1)^2 + 4a^2\} x_1^2 - \left\{ 8a^3 - 2a(2r - 1) \right\} x_1 + a^2 + 4a^4 - 4a^2 r^2 = 0,
\]

where \( r = 1.2 \) and \( a = 3 \). The roots are \( x_1 \approx 2.4689 \) or 3 (exactly) and the larger value is rejected for reasons of continuity (see below).

Corresponding to the smaller root,

\[
\lambda = \frac{2(a - x_1)}{rx_1} \approx 0.3585.
\]

We denote the solution (7) corresponding to these values by \( y_1(x) \) and the form (3) by \( y_2(x) \).

We also define \( B \) as \( 2\lambda^{-1} \) and \( A = B + 1/2 \) in what follows. The volume integral (1) is

\[
V = 4\pi \int_0^{x_1} x y_1 \, dx + 4\pi \int_{x_1}^b x y_2 \, dx
= 4\pi \left\{ \left( \frac{Ax_1^2}{2} + 4B \left[ 1 - \left( \frac{\lambda x_1}{2} \right)^2 \right]^{3/2} \right) - 1 \right\}
+ \frac{a}{2} \left[ u \sqrt{r^2 - u^2} + r^2 \arcsin \frac{u}{r} \right]_{x_1-a}^r
- \frac{1}{3} \left( r^2 - u^2 \right)^{3/2} \left[ r \right]_{x_1-a}^r,
\]

where \( u = \pi - a \).

Similarly,

\[
S = 4\pi \int_0^{x_1} x \left[ 1 + (y')^2 \right]^{1/2} \, dx + 4\pi \int_{x_1}^b x \left[ 1 + (y')^2 \right]^{1/2} \, dx
= 4\pi \left\{ \frac{2}{\lambda^2} \left[ 2 - (4 - \lambda^2 x_1^2)^{1/2} \right] \right\}
+ r \left\{ a \arcsin \frac{u}{r} - \sqrt{r^2 - u^2} \right\} _{x_1-a}^r.
\]

Evaluating (9) and (10) accurate to three decimal places, we find \( V = 101.054 \mu^3 \) and \( S = 148.413 \mu^2 \). The latter result is in agreement with the value stated by Lenard, but for the volume he gives \( V = 90.618 \mu^3 \), a relative difference in our value of \( \approx 11.5\% \). This in turn affects his estimate of the resulting surface area to volume ratio, a topic we discuss in the next section.

Interestingly enough, these results correspond to a minimum of the functional (4). If \( \epsilon \eta(x) \) is a measure of the variation from the optimal path, the second variation of \( J \) is (see [6])

\[
\frac{\partial^2 J}{\partial \epsilon^2} \bigg|_{\epsilon=0} = \int_0^b \left\{ \eta^2 \frac{\partial^2 f}{\partial y^2} + 2\eta \eta' \frac{\partial^2 f}{\partial y \partial y'} + (\eta')^2 \frac{\partial^2 f}{\partial y'^2} \right\} \, dx,
\]

where \( f \) is evaluated on the optimal path (\( \epsilon = 0 \)). For the functional (4), the right-hand side of (11) reduces to

\[
4\pi \int_0^b x (\eta')^2 \left\{ 1 + (y')^2 \right\}^{-3/2} \, dx > 0,
\]
so this extremum is a relative minimum, contrary to what was claimed in [3]. The value of the other root for $x_1$ in equation (8) forces $\lambda$ to be zero, since $x_1 = a = 3$, which in turn requires $y$ to be constant. The value $y(0) = 0.5$ is not commensurate with $\lim_{x \to 3^+} y = 1.2$, so this discontinuous solution is excluded.

3. THE SPHERICITY AND FLATNESS INDICES

In his paper, Lenard calculates the "surface area to volume" ratio for the erythrocyte based on his calculated surface area and volume; this is $1.6378 \mu^{-1}$. The corresponding corrected ratio is $1.4687 \mu^{-1}$. The problem with this ratio is of course that it is a dimensional quantity, and therefore is numerically dependent on the units of (length)$^{-1}$ in which it is expressed.

A more meaningful measure of the relationship between surface area $A$ and volume $V$ for an object is the sphericity index, SI, defined by

$$SI = \alpha V^{2/3} A^{-1} \approx 4.836 V^{2/3} A^{-1},$$

(12)

where $\alpha = 4\pi (4\pi/3)^{-2/3}$ is chosen such that the SI for a sphere is unity. It is easily shown that for a cube, $SI \approx 0.806$; for a right circular cylinder with equal height and radius, $SI = 2^{1/3} \approx 0.794$. The measured erythrocyte sphericity indices cited by Canham [1], range from $\approx 0.734$ to $\approx 0.816$ (see, Table I, in that paper). For the corrected results of Lenard, $SI \approx 0.707$ and $0.657$ for the uncorrected.

One reason for the importance of a dimensionless measure of shape such as the SI is that geometry influences diffusion times; typically for a characteristic linear dimension $L$ and diffusion coefficient $D$, the diffusion timescale $T \sim L^2 D^{-1}$. For the diffusion of oxygen in water, $D \approx 10^{-5}$ cm$^2$ sec$^{-1}$, so $T(1 \mu) \approx 10^{-3}$ sec, whereas $T(1 \text{ m}) \approx 10^8$ sec $\approx$ 30 years. Thus, as pointed out by Edelstein-Keshet [7], flat shapes or long branched filaments are well suited for organisms that rely exclusively on absorption of nutrients or oxygen directly from their environment, because they can increase in volume without changing shape, and hence, the distance through which diffusion must act. In general though, as an organism increases its size it must increase its "flatness" if diffusion is to remain a dominant mechanism of fluid transportation. If not, bulk flow mechanisms become important; these two mechanisms are contrasted in a thought-provoking article by LaBarbera and Vogel [8] to which the interested reader is referred. In that article, the authors define a "flatness index"

$$\gamma = A^3 V^{-2}. \quad (13)$$

Clearly,

$$\gamma = \left( \frac{\alpha}{SI} \right)^3, \quad (14)$$

so it is a simple matter to go from one measure of shape to the other. For the erythrocyte discussed in this note, $\gamma \approx 320.117$ (compare $\gamma = 36\pi \approx 113.097$ for a sphere).

A final comment is perhaps in order about the shape of the erythrocyte. Implicit both in the paper by Lenard and the present note is the fact that diffusion is of considerable importance in the function of the red blood cell. Indeed, to quote Burton [9]: "Since the respiratory gases may have to reach the hemoglobin by diffusion through the contents of the red cell, a shape which allows diffusion to the innermost parts in the shortest time is advantageous". However, he also adds that "The process of exchange to all of the red cell contents is ... not dependent on diffusion alone".

Thus, it is clear that other factors play a role in determining the shape of the erythrocyte, which can be considered to be in equilibrium under the various physical forces acting on the cell (see [1]). It is possible that hydrodynamical considerations are of significance also (Newtonian and non-Newtonian, depending on the relative size of the vessel in which the cell is moving) for efficiency of circulation (in the sense of energetics). Such factors are, of course, outside the scope of this note.
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