SOME NEW MODEL GEOMETRIES FOR SICKLED ERYTHROCYTES

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Abstract. Proposed model geometries are described for six types of flattened sickled erythrocytes. These new types occur with some frequency in blood smears of patients with sickle cell disease. The six types of cells are designated as five-pointed star, witch, hypocycloid, deltoid, astroid, and semi-circular. Formulae are provided for the volume and surface area of each type and a figure showing the profile of each is included. Measurements of actual sickled cells *in vitro* could be used to find values for the volume and surface area of each type of cell by using parameter values for the appropriate model geometry. These would give close approximations that could be useful in clinical therapies and laboratory investigations for sickle cell anemia. Surface area to volume ratios can also be found to a close approximation for each cell type.

1. Introduction. Many different shapes of sickled red cells have been observed over the years since the first clinically reported case of sickle cell anemia in 1910 [1]. There are many sources that show electron micrographs of such cells, among the most comprehensive are Bessis [2] and Diggs and Bibb [3]. Earlier certain types of sickled cells were described mathematically and their surface area and volume were formulated [4]. In this study we provide a formulary for six new types of sickled cells which have been observed by Hiroshi Asakura, M.D., in the laboratory at Childrens Hospital of Philadelphia [5].

We feel that if these cell types can be described mathematically then it might play a role in distinguishing between cell types when cell fields are scanned. The numbers present, in a cell field, of one type of cell or the other may play a part in diagnosis or in treatment regimens. There are computer programs that will scan a cell field and attempt to identify types of cells from their shapes. These can be improved in their efficiency if we can describe certain cells more accurately and thus use mathematical concepts to distinguish between cells of similar shape. These are important considerations for sickle cell anemia. We note here also the roles played by surface area and volume in Fick's Law – for concentration of a solute in a cell [6]. Thus, we can incorporate the power of mathematics with the characteristics of sickled cells and hopefully hasten diagnosis and treatment using software engineering as a vehicle.

2. Geometry. All of the cell types to be discussed herein are what we call flattened cells with a distinct outline or shape and of a uniform thickness. So as the sickled cell sits in a preparation it will possess a surface area and a volume and appear flat when viewed from above. There is no rotational symmetry to these six types of cells. In what follows we will assume all cells are flat and of thickness t_0.

3. Five-Pointed Star. This type of sickled cell will have the outline of a circle with five isosceles triangles spaced around its circumference. Each triangle has its base as a chord of the circle so the area will have to account for these five overlap spots. We will assume the radius of the circle is r, the bases of the triangles form the sides of an inscribed pentagon, and the altitude of the triangles is h (Figure 1). Thus, the plane area will be

$$A = \frac{5r^2}{2}\sin\frac{2\pi}{5} + 5rh\sin\frac{\pi}{5}. \tag{1}$$

Then, using this plane area for both the top and the bottom of the cell of thickness t_0 we have a formula for the surface area

$$SA = 5r^2\sin\frac{2\pi}{5} + 10rh\sin\frac{\pi}{5} + 10t_0\left[r^2\sin^2\frac{\pi}{5} + h^2\right]^{\frac{1}{2}}. \tag{2}$$

The volume will be simply the plane area multiplied by thickness

$$V = \frac{5r^2t_0}{2}\sin\frac{2\pi}{5} + 5rht_0\sin\frac{\pi}{5}. \tag{3}$$

One might observe this type of cell but with the appearance of equilateral rather than isosceles triangles. The surface area and volume can be rederived for this case easily.

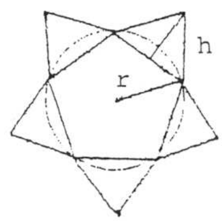

Figure 1: Five-pointed star

4. Witch of Agnesi. This cell type is based on the plane curve known as the Witch of Agnesi [7] given as the rational function

$$y = \frac{a^3}{x^2 + a^2}, \tag{4}$$

where parameter $a > 0$ (Figure 2). We will assume that this curve has length $2b$ as shown and that when the curve and its mirror image are put together at $\pm b$ that will represent this type of sickled cell. The plane area of this "made-up" pair of curves is given by

$$A = 4a^2 \tan^{-1}\left(\frac{b}{a}\right) - \frac{4a^3 b}{a^2 + b^2} \tag{5}$$

for parameters a and b. With thickness t_0 and plane area as above we obtain the total surface area as

$$SA = 8a^2 \tan^{-1}\left(\frac{b}{a}\right) - \frac{8a^3 b}{a^2 + b^2}$$

$$+ 4t_0 \int_0^b \frac{[(x^2 + a^2)^4 + 4a^6 x^2]^{\frac{1}{2}}\, dx}{(x^2 + a^2)^2}. \tag{6}$$

The integral in the third term will have to be integrated numerically. The volume of this cell will be provided by

$$V = 4a^2 t_0 \tan^{-1}\left(\frac{b}{a}\right) - \frac{4a^3 b t_0}{a^2+b^2}. \tag{7}$$

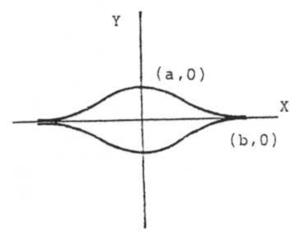

Figure 2: Witch of Agnesi

5. Hypocycloid. This plane curve is formed by rolling a small circle around the inside of a larger circle and our cell has five cusps [7]. We will have to describe the curve by using parametric equations

$$x(t) = \frac{4a}{5}\cos t + \frac{a}{5}\cos 4t$$

$$y(t) = \frac{4a}{5}\sin t - \frac{a}{5}\sin 4t, \quad -\pi \le t \le \pi, \tag{8}$$

where a is the distance from the origin to the cusp lying on the x-axis (Figure 3). The curve is symmetric about the x-axis. These parametric equations afford a nice way to derive formulas for surface area and volume. First, however, the plane area for a hypocycloid of five cusps is given by

$$A = 2\int_{-\pi}^{\pi} y(t)\, dx(t) = \frac{24}{25}a^2\pi. \tag{9}$$

This result immediately gives us formulas for surface area and volume for a five-cusped hypocycloid

$$SA = \frac{48}{25}a^2\pi + \frac{32}{5}at_0, \tag{10}$$

$$V = \frac{24}{25}\pi a^2 t_0. \tag{11}$$

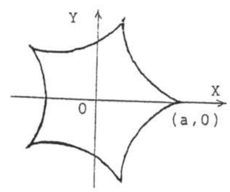

Figure 3: Hypocycloid

6. Deltoid. The fourth of our new cell types will also have to be given parametrically as

$$\begin{aligned} x(t) &= b(2\cos t + \cos 2t) \\ y(t) &= b(2\sin t - \sin 2t), \quad -\pi \le t \le \pi, \end{aligned} \tag{12}$$

where $3b$ is the distance on the x-axis from the center of the cell to the cusp. This cell (Figure 4) possesses an x-axis symmetry and has three cusps. Its plane area is given by

$$A = 2\pi b^2. \tag{13}$$

We can now provide formulas for surface area

$$SA = 4\pi b^2 + 16t_0 b \tag{14}$$

and volume

$$V = 2\pi t_0 b^2. \tag{15}$$

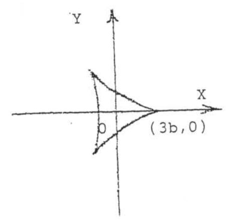

Figure 4: Deltoid

7. Astroid. Again we turn to parametric equations for our mathematical description

$$
\begin{aligned}
x(t) &= b\cos^3 t \\
y(t) &= b\sin^3 t, \quad 0 \le t \le 2\pi,
\end{aligned} \tag{16}
$$

which possesses symmetries with respect to the x-axis, y-axis, and origin; with parameter b as the distance from the cell's center to the cusp on the positive x-axis. There are four cusps all lying on the coordinate axes (Figure 5). The area enclosed by the astroid is given by

$$A = \frac{3}{8}\pi b^2. \tag{17}$$

We then arrive at a surface area

$$SA = \frac{3}{4}\pi b^2 + 6t_0 b \tag{18}$$

and volume

$$V = \frac{3}{8}\pi t_0 b^2 \tag{19}$$

for a cell of uniform thickness t_0.

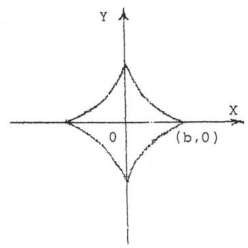

Figure 5: Astroid

8. Semi-Circular. We will describe this cell, last of our types, by using a rectangle "capped" by semi-circular ends. Then this assembly is bent into a semi-circular shape (Figure 6). The radii of the inner and outer arcs will be given by a and b, respectively. The cell will have a uniform width of $b - a$ and hence, the radius of the endcaps will be $(b - a)/2$. Its thickness will remain, as usual, t_0. The plane area of this cell will be

$$A = \frac{3}{4}(b-a)^2\pi + (b-a)[a(\pi+1) - b]. \tag{20}$$

The surface area will be given by

$$SA = \frac{3}{2}(b-a)^2\pi + 2(b-a)[a(\pi+1) - b]$$

$$+ 2(\pi b - b + a)t_0. \tag{21}$$

Our volume formula is then

$$V = \left(\frac{3}{4}(b-a)^2\pi + (b-a)[a(\pi+1) - b]\right)t_0. \tag{22}$$

Upon reflection, we think there is an easier way to derive formulas for plane area, surface area, and volume using properties of the semi-circular areas of which this cell is made up. We will not provide these here as they are rather obvious but it would be interesting to compare actual cell surface areas and volumes using the two sets of formulas to see what discrepancies, if any, exist. If a cell that is close to this type needs to be analyzed, this collection of formulas then serves as an approximation for that cell.

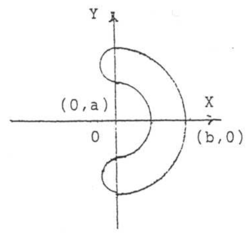

Figure 6: Semi-circular

9. Conclusions. The cell types above are reasonable geometric models for sickled cell of somewhat uncommon shape. Cells can assume these shapes, after blood withdrawal, due to hemoglobin condensation [3]. Efforts to reverse sickling by using electrical fields [8] or urea therapy [9] will be successful only when cell shape and its attendant surface area and volume are provided. Good geometrical models with their pertinent formulas are useful as tools allowing for rather precise measurements usable in some therapies to increase their efficiency.

All of the parameters used for these types of cells are readily measurable and we have been able to keep the number of parameters to a minimum for each cell described. These parameter values can be made available from *in vitro* preparations. Changes in surface area and/or volume from the normal cell to the sickled cell can be found using these geometrical models. The ratio of surface area-to-volume can be found once the requisite values are calculated. There are, no doubt, other shapes of cells one could investigate using these ideas but for the present these methods provide an avenue of approach.

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