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A MODEL OF CELL CLEAVAGE

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ABSTRACT A model is presented which describes, at least to a first approximation, the oserved changes in cell shape and the movement of surface markers associated with cleavage in some types of cells. The model postulates that the constraints governing cell cleavage are minimum surface area and constancy of cell volume. Equations are derived both for the case of symmetric as well as the case of asymmetric cleavage. It is pointed out that the generally symmetric character of cell cleavage is explicable if there is a positive correlation between internal cell pressure and the radii of curvature.

INTRODUCTION

Elegant experiments carried out by the Japanese cytologists, especially Hiramoto (1957), Dan (1958), and Ishizaka (1966) have made available quantitative data concerning the shape and movement of the cell membrane during cell cleavage. The data have been obtained by labeling dividing cells with carbon markers and then recording the successive positions taken up both by the membrane in general and the markers in particular. The data sustain Hiramoto's conclusion that, at least in the case of sea urchin eggs, cell cleavage occurs at constant volume. The corollary of this geometrical constraint is that if the cell is spheroidal before division, as is generally the case, then the surface area must increase by about 26% during cleavage. The movements of markers on the cell surface observed by the above investigators is consistent with such an increase in area. In the particular case of grasshopper spermatocytes, Ishizaka (1966) has demonstrated that these cells maintain a remarkable degree of symmetry and regularity of shape throughout cleavage. Furthermore, he has shown that the successive positions taken up by carbon markers can be calculated if it is assumed that the surface area increases monotonically, that the cellular profile may be represented by spherical zones, and that the volume remains constant.

In the following, it will be shown that the typical shape exhibited by dividing cells and the position of markers on the cell surface can be calculated from arguments of a general nature.

One possibly attractive approach to characterizing the shape of a cell during

Reprinted from the BIOPHYSICAL JOURNAL, 1967, Vol. 7, No. 6, pp. 659–673 *Printed in U.S.A.*

cleavage is to assign mechanical properties to the cell membrane and to impose some specified mechanism for constricting the cell while treating the cell contents as a fluid. Thus, for example, one might plausibly treat the membrane as a thin elastic sheet and assume that constriction is due to contractile fibers around the cleavage furrow. And, to some extent, such a model underlies the present approach. Nevertheless, it seems unlikely that the cell membrane is purely elastic, and rather more likely that it has mechanical properties possibly intermediate between, or an admixture of, those of an elastic material and a monolayer. Furthermore, an important constraint in the problem, namely that of constant volume, may be difficult to incorporate in a purely mechanical model. Accordingly, we eschew the strictly mechanical approach and adopt instead more general constraints which may be consistent with, but not confined to, a model of the elastic type alluded to above.

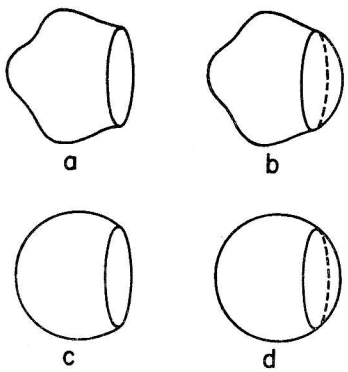

FIGURE 1 Illustration of the theorem that the closed surface of revolution which divides symmetrically at constant volume and minimum area consists of the union of two spheres. See text.

The procedure will be to derive the form of surface which is consistent with certain constraints and then to demonstrate that this surface is essentially isomorphous with that exhibited by at least some cells during cleavage. We first consider a closed surface of revolution and demand that the surface divide (i.e. pinch off) symmetrically in a plane perpendicular to the axis of revolution. This division is to take place subject to the constraints that (*a*) the volume remain constant and (*b*) the surface area be a minimum. It is readily shown, as in the following argument, that the surface satisfying these constraints is a segment of a sphere. Since cleavage has been assumed to be symmetrical, it is sufficient to consider, as in Fig. 1 *a*, one-half of a surface of revolution, of arbitrary profile. Now consider the spherical zone of Fig. 1 *c*, which is assumed to have not only the same volume as that of Fig. 1 *a*, but also to intersect the cleavage plane in a circle of the same radius (a construction which is always possible). That the spherical zone of Fig. 1 *c* has a lesser area than that of Fig. 1 *a* is demonstrated by adding to both figures a spherical "cap" which completes the sphere, as shown in Fig. 1 *b* and 1 *d*. Since, as is well known, a sphere has the least area for a given volume, it follows that the spherical segment of Fig. 1 *c* has a smaller area than the arbitrary profile of Fig. 1 *a*. Thus the surface of revolution

which is constrained to divide symmetrically at constant volume and minimum surface area consists of the union of two spheres. The next step is to derive the equations defining the surface formed by the union of two spheres.

DERIVATION OF EQUATIONS

(*a*) *Symmetrical Division*

More specifically, we wish to derive the equations which specify both the radius and the position of the center of the spherical segment at any given stage of division. The constant volume constraint is the basis of the derivation. The geometrical relations are illustrated in Fig. 2. The cleavage plane is represented by the ordinate axis, the axis of revolution by the abscissa. In the figure, the right-hand "daughter cell" has a radius r and a center displaced a distance c from the cleavage plane. The

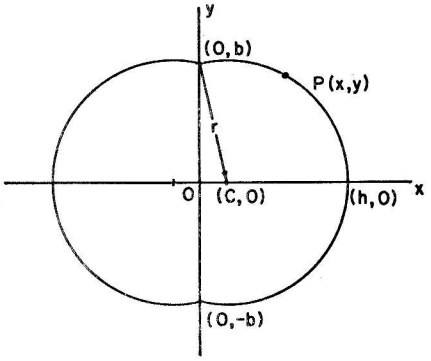

FIGURE 2 The geometrical relations and nomenclature used in describing the process of symmetrical cell cleavage.

maximum width of the daughter cell is given by the distance h betweeen the cleavage plane and the right-hand intercept on the abscissa. The radius, center, and width are related by the equation:

$$h = r + c \tag{1}$$

$$0 \leqslant c \leqslant r$$

But the volume V of a spherical segment of width h is given by:

$$V = (\pi/3)(3r - h)h^2 \tag{2}$$

We denote the initial radius of the mother cell by a. The volume of the daughter cell must at all times be half the volume of the mother cell, since, by assumption, division is symmetrical and at constant volume. Therefore, the relation:

$$V = (2/3)\pi a^3 \tag{3}$$

must obtain. At this point it is convenient to introduce the parametric relation:

$$u = c/r \tag{4}$$

$$0 \leqslant u \leqslant 1$$

Combining equations (1)-(4) so as to eliminate h and c we find:

$$r = a(1 + [3/2]u - [1/2]u^3)^{-1/3} \tag{5}$$

Equations (4) and (5) together describe the profile taken up by a cell which divides subject to the given constraints. As the parameter u varies between zero and one the daughter cell radius decreases by a factor of $\sqrt[3]{2}$ and the center is displaced from the cleavage plane a distance $\sqrt[3]{2}a$. The surface area (A_T) of a daughter cell, as well

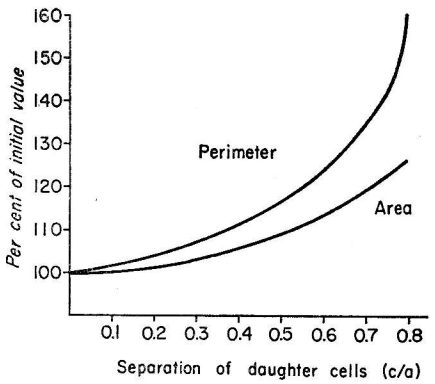

FIGURE 3 The surface area and perimeter of a daughter cell are plotted as a function of the separation between the center of the daughter cell and the cleavage plane.

as the perimeter (P_T), is readily shown to be given by:

$$A_T = 2\pi(u + 1)r^2 \tag{6}$$

$$P_T = 2r[\pi - \cos^{-1}(u)] \tag{7}$$

Note that by "perimeter" we mean that part of the circumference of one daughter cell passing through the cleavage plane at $(0, \pm b)$ and the point $(h, 0)$. The term "area" denotes the surface area of a solid of revolution geometrically equivalent to one daughter cell. The area and perimeter of a daughter cell, as defined above, are plotted in Fig. 3 as a function of the separation of a daughter cell from the cleavage plane (i.e., as a function c). The largest increase in these quantities occurs after separation is more than half completed.

The next step in the analysis is to derive an expression for the path followed by a marker put at any point $P(x, y)$ on the surface of the cell (see Fig. 2). It is clear from Fig. 2 that the profile of the dividing cell (under the given constraints) may be described by the equations for two interesecting circles having their centers dis-

placed equally on opposite sides of the cleavage plane. Accordingly, we have:

$$(x - c)^2 + y^2 = r^2 \qquad x \geqslant 0 \tag{8}$$

$$(x + c)^2 + y^2 = r^2 \qquad x \leqslant 0 \tag{9}$$

The movement of markers on the surface will, under the present assumptions, be due solely to increased area. A marker put on the original cell surface at a distance x_o from the cleavage plane may be associated with an annulus between the cleavage plane and the plane defined by $x = x_o$. This annulus, being a spherical zone of width x_o, has a surface are A_o given by:

$$A_o = 2\pi a x_o \tag{10}$$

Expressed as a fraction of the initial total area (A_i) of the daughter cell, the area of the annulus is:

$$A_o/A_i = 2\pi a x_o/2\pi a^2 = x_o/a \tag{11}$$

As division proceeds, the area will increase uniformly over the whole surface. Thus, if the marker moves from x_o to x it will then come to be associated with a spherical zone having an area A defined by:

$$A = 2\pi r x \tag{12}$$

But the total area A_T of the daughter cell at any stage of division is given by equation (6). As the change in area is uniform the fraction A/A_T must remain constant and equal to the fraction given by equation (11); i.e.,

$$\begin{aligned} A/A_T &= 2\pi r x/2\pi(u + 1)r^2 = x/(u + 1)r \\ &= x_o/a \\ \therefore\ x &= (u + 1)x_o r/a. \end{aligned} \tag{13}$$

The ordinate of the marker can be deduced from equation (8) or equation (9) for any given x coordinate. It is convenient to express x and y in terms of the parameter u, thus eliminating the explicit dependence upon r and c. This can be done by an appropriate combination of equations (5), (8), and (13). The results are:

$$x = (1 + [3/2]u - [1/2]u^3)^{-1/3}(u + 1)x_o \tag{14}$$

and

$$y = \frac{\sqrt{a^2 - [(u + 1)x_o - au]^2}}{[1 + (3/2)u - (1/2)u^3]^{1/3}} \tag{15}$$

Equations (14) and (15) together describe the path taken by a marker put on the surface of a cell at a distance x_o from the cleavage plane calculated on the assumption that the increase in area is uniform over the whole surface. One or two general features of the family of paths may be readily deduced from the equations. Since the coefficient of x_o in equation (14) is a monotonically increasing function of u for all positive values of u, it follows that the horizontal component of displacement increases monotonically. It is otherwise with the vertical component of displacement, the behavior of which depends upon x_o. This fact can be easily demonstrated by confining our attention to the net change in vertical displacement during cell division. Thus from equations (8) or (15) we have for the condition $c = u = o$ (i.e. no constriction) the relation:

$$y_o = \sqrt{a^2 - x_o^2} \tag{16}$$

At the end of the cleavage $u = 1$, and we have from equation (15) that:

$$y = 2^{2/3} \sqrt{(a - x_o)x_o} \tag{17}$$

Combining equations (16) and (17) gives:

$$y/y_o = 2^{2/3}\sqrt{x_o/(a + x_o)} \tag{18}$$

Accordingly we find:

$$y > y_o \quad \text{if} \quad x_o/a > 1/(2^{4/3} - 1) \doteqdot 0.658$$

whereas

$$y < y_o \quad \text{if} \quad x_o/a < 0.658$$

In summary, a marker on the surface of a cell dividing subject to the given constraints would move uniformly away from the cleavage plane and either toward the axis of revolution if the initial value of x_o/a were less than 0.658 and away from the axis if x_o/a were greater than 0.658. For a value of $x_o = 0.658$ the marker would experience no net vertical movement. Various aspects of the movements are illustrated in Fig. 4. It will be noted that the total displacement exhibits a minimum which occurs at a value of x_o/a of approximately 0.375.

It is of interest to apply the above equations to the case of cell cleavage in grasshopper spermatocytes. As remarked in the Introduction, it has been shown by Ishizaka (1966) that these cells undergo cleavage maintaining a high degree of symmetry. The cleavage and the movement of markers, as observed by Ishizaka (1966) are shown in Fig. 5. The open circles indicate the observed positions of the markers at successive times. The solid lines through the circles are the paths calculated from equations (14) and (15). Note that the only parameters required in the calculation, namely x_o and a, were obtained directly from the figure as published by Ishizaka.

(b) Asymmetric Division

It is of theoretical interest to derive equations for the case of asymmetrical cell cleavage, that is for the condition in which the cleavage plane is displaced from the equatorial plane. On reflection, it will be seen that some extra constraint must be imposed to achieve a complete formulation. In the absence of a knowledge of the

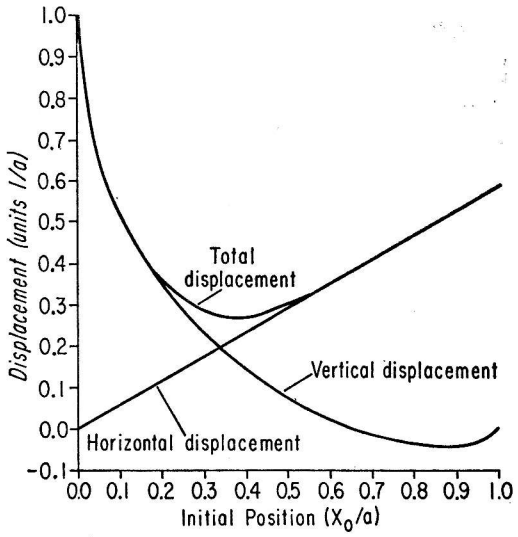

FIGURE 4 A graph illustrating the general character of the displacements experienced by particles put at various distances (i.e. x_0) from the cleavage plane (symmetrical cleavage). The displacement is either the distance or the projected distance between initial and final positions.

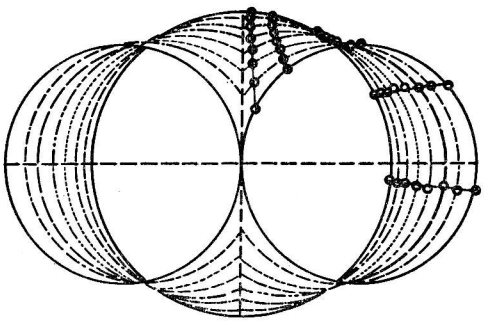

FIGURE 5 Adapted from a figure published by Ishizaka (1966) showing the profile and movement of markers (see open circles) exhibited by dividing grasshopper spermatocytes. The solid lines through the open circles represent trajectories calculated from equations (14) and (15). See text.

structure of membranes the imposed constraint will be necessarily of an arbitrary character. In the following we present for possible consideration three different constraints. Only the underlying assumptions and the final equations are given with but a brief indication of the derivation.

The geometrical relations for the asymmetric case are summarized in Fig. 6. The origin is taken at the intersection of the equatorial plane and the axis of revolution. The cleavage plane is displaced a distance d from the equatorial plane in the positive direction. The radii, r_1 and r_2, of the two daughter cells are now, in general, dif-

ferent, as are the distances c_1 and c_2 to the centers of the respective cells. Thus, there are four variables r_1, r_2, c_1, c_2, of which one is essentially independent. Accordingly, three equations are required to specify the motion. The four variables are related by a geometrical condition, as will be evident from Fig. 6. Thus two further conditions are required. One is furnished by the constant volume constraint. The final condition remains to be specified.

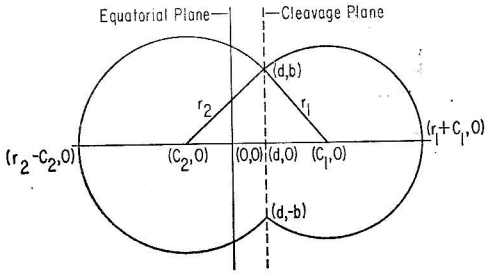

FIGURE 6 The geometrical relations and nomenclature used in describing the process of asymmetrical cell cleavage.

(i) *Uniform Interior Pressure.* In this derivation it is assumed that throughout cleavage the interior pressure is uniform, or equivalently, that no pressure gradient exists between the two daughter cells. In the absence of such a pressure gradient there should be no movement of fluid across the cleavage plane. Hence the volume of fluid on either side of the cleavage plane remains constant. We now derive the equations for asymmetric cleavage, proceeding on the assumption of uniform interior pressure. For simplicity in writing, the radius of the mother cell, denoted by a, has been set equal to unity. Accordingly, the parameters r_1, r_2, c_1, c_2, d, etc., are dimensionless in all of the following equations.

1. *Geometric relations.* It is evident from Fig. 6 that:

$$b = \sqrt{r_1^2 + (c_1 - d)^2} \tag{19}$$

$$b = \sqrt{r_2^2 + (-c_2 + d)^2} \tag{20}$$

Equations (19) and (20) provide a constraint of the form:

$$r_1^2 - r_2^2 = (c_1 - d)^2 - (-c_2 + d)^2 \tag{21}$$

2. *Constant volume condition.* With the nomenclature of Fig. 6, the volumes V_1 and V_2 of the two daughter cells are given by:

$$V_1 = (\pi/3)(3r_1 - h_1)h_1^2 \tag{22}$$

$$V_2 = (\pi/3)(3r_2 - h_2)h_2^2 \tag{23}$$

where

$$h_1 = r_1 + (c_1 - d)$$

$$h_2 = r_2 + (-c_2 + d)$$

As in the case of symmetrical cleavage, it is useful to introduce parametric relations of the form:

$$u_1 = (c_1 - d)/r_1 \tag{24}$$

$$u_2 = (-c_2 + d)/r_2 \tag{25}$$

where d is the displacement of the cleavage plane from the equatorial plane. The above parameters are defined within the following ranges:

$$0 \leqslant c_1 \leqslant r_1 + d \qquad -r_2 + d \leqslant c_2 \leqslant 0$$

$$-d \leqslant u_1 \leqslant 1 \qquad d \leqslant u_2 \leqslant 1$$

Note that c_2 is defined in such a way as to be always less than or equal to zero. The initial conditions are defined by putting c_1 and c_2 equal to zero. Combining equa-

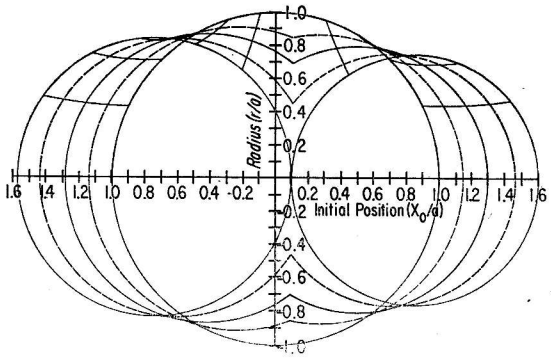

FIGURE 7 An illustration of the change in profile and the movement of surface markers for a hypothetical case in which $d = 0.1a$.

tions (21)–(25) and taking into account the initial conditions, we find:

$$(1 - u_1^2)r_1^2 = (1 - u_2^2)r_2^2 \tag{26}$$

$$(2 - u_1)(1 + u_1)^2 r_1^3 = (2 + d)(1 - d)^2 \tag{27}$$

$$(2 - u_2)(1 + u_2)^2 r_2^3 = (2 - d)(1 + d)^2 \tag{28}$$

The change in profile and the movement of markers (calculated on the same assumption as in the symmetrical case) on the surface is shown in Fig. 7 for a hypothetic asymmetry of 10% (i.e., $d = 0.1a$). This figure may be compared with symmetrical division as illustrated in Fig. 5.

Formulas for the area and perimeter as defined above are readily derived from Fig. 6. We find:

$$A_1 = 2\pi(1 + u_1)r_1^2 \tag{29}$$

$$A_2 = 2\pi(1 + u_2)r_2^2 \tag{30}$$

$$P_1 = 2r_1(\pi - \cos^{-1}[u_1]) \tag{31}$$

$$P_2 = 2r_2(\pi - \cos^{-1}[u_2]) \tag{32}$$

These expressions are plotted in Fig. 8 as a function of the parametric variable u_1, again for the case $d = 0.1a$. It is a curious fact that the area of the smaller (i.e.

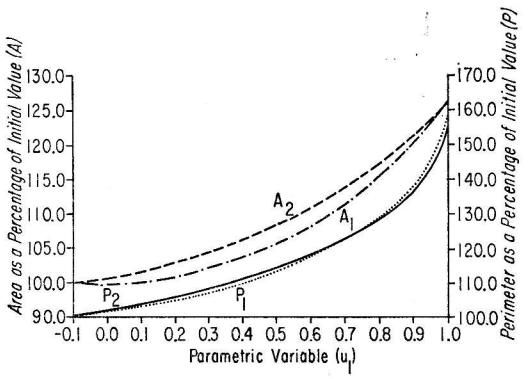

FIGURE 8 A plot of the area and perimeter for each daughter cell as a function of the parametric variable u_1 for the case of asymmetric cleavage ($d = 0.1a$).

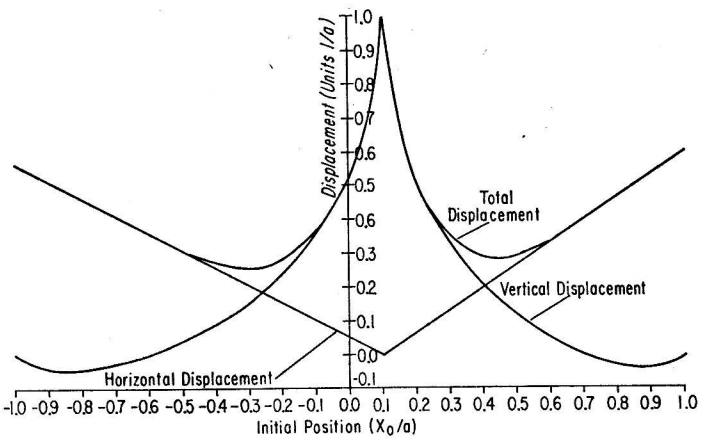

FIGURE 9 A graph illustrating the general character of the displacements undergone by particles put at various horizontal distances (i.e. x_0) from the equatorial plane. Asymmetric cleavage in which $d = 0.1a$.

right-hand) daughter cell actually decreases initially before entering a monotonically increasing phase. It can readily be shown that this decrease is characteristic of asymmetric cleavage under the given assumptions.

Various other aspects of the movements of markers for this type of asymmetric division are brought out in Fig. 9. As in the symmetric case the horizontal component of the displacement is uniformly away from the cleavage plane. The vertical compo-

nent of displacement and the total displacement exhibit minima which are in different locations as between the two daughter cells and as compared with the symmetric case.

The per cent increase in perimeter and area for the respective daughter cells, as given by equations (29)–(31) are plotted in Fig. 10 for various degrees of asymmetry up to 0.5. Note that the smaller daughter cell experiences the greatest increase in perimeter but the least increase in area.

(ii) *Uniform Film Pressure.* In this and the following alternative derivations of the equations for the case of asymmetric cleavage we make special assumptions about the nature of the membrane. In the present derivation we suppose that the membrane behaves as a two-dimensional gas, or as an idealized monolayer. In particular, we assume that the membrane is characterized by a uniform surface pressure which is inversely proportional to the surface area. As cleavage proceeds, the areas of each of the presumptive daughter cells will increase and the surface pressure will decrease. Since, by assumption, the surface pressure is uniform throughout the membrane, the changes in area will be such as to maintain the initial proportion between the areas of the daughter cells. That is, if the initial areas are given by A_{10}, A_{20}, and the areas at any subsequent time are given by A_1 and A_2, then

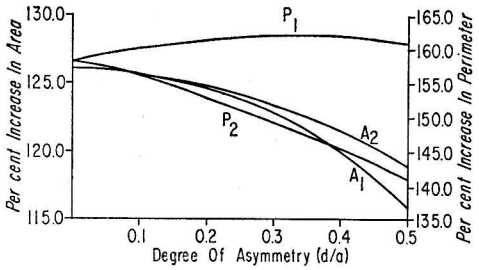

FIGURE 10 Per cent increase in surface area and perimeter (see text) as a function of asymmetry.

$$A_1/(A_1 + A_2) = A_{10}/(A_{10} + A_{20}) \tag{33}$$

Thus in the hypothetical case in which the surface pressure is halved, the areas of the two daughter cells would double, but the proportion between them would remain constant. Combining the equations for uniform surface pressure (or equivalently, constant proportionality of areas) with the equations given by the geometrical and constant volume constraints, we find:

$$u_2 = (1 - d)u_1/(1 + d) + 2d/(1 + d) \tag{34}$$

$$(1 - u_1^2)r_1^2 = (1 - u_2^2)r_2^2 \tag{35}$$

$$\{(2 - u_1)(1 + u_1)^2 + (2 - u_2)(1 + u_2)^2 \cdot [(1 + d)/(1 - d)]^{3/2}[(1 + u_1)/(1 + u_2)]^{3/2}\}r_1^3 = 4 \tag{36}$$

This derivation has the virtue that the equations can be solved directly. If we denote the initial and final volumes of the right-hand daughter cell by V_{1o} and V_{1f} respectively, then it is readily shown that:

$$V_{1o} = (\pi/3)(2 - d)(1 + d)^2 \tag{37}$$

$$V_{1f} = \{4/3\}\pi/\{1 + [(1 + d)/(1 - d)]^{3/2}\} \tag{38}$$

Furthermore, the volume of the right-hand daughter cell is a maximum when:

$$u_1 = (1 - d)/2 \tag{39}$$

Thus there is a movement of fluid from the larger to the smaller daughter cell initially [i.e., $u_1 < (1 - d)/2$] and a flow in the reverse direction subsequently. These changes in volume are small (of a few per cent only) for moderate degrees of asymmetry.

(iii) *Elastic Solution.* In this final derivation of the equations for asymmetric cleavage we treat the membrane as a linear elastic (Hookean) material. It is well to note at the outset that it is necessary to make a strictly ad hoc assumption as to what constitutes the unstretched or rest condition of the membrane. Merely for convenience we assume that the mother cell, prior to cleavage, represents the rest condition (contrary to our usual notions of the preparturition state!). Furthermore, we assume that the equilibrium condition is described by an equation of the form of Laplace's law. That is, if the tensions in the right and left daughter cell membranes are denoted by T_1 and T_2 respectively, then equilibrium is assumed to be defined by the relation:

$$T_1/r_1 = T_2/r_2 \tag{40}$$

The assumption that the membrane is linearly elastic implies that the tension in the membrane is a linear function of the thickness of the membrane, of the elongation of membrane, and of the Young's modulus "Ey." The elongations e_1 and e_2 of the right and left daughter cells respectively are given by:

$$\begin{aligned} e_1 &= [2/\cos^{-1}(d)]\,[r_1 \cos^{-1}(u_1) - \cos^{-1}(d)] && u_1 \leqslant 0 \\ &= [2/\cos^{-1}(d)]\{r_1[\pi - \cos^{-1}(u_1)] - \cos^{-1}(d)\} && u_1 \geqslant 0 \end{aligned} \tag{41}$$

$$e_2 = [2/\pi - \cos^{-1}(d)]\{r_2[\pi - \cos^{-1}(u_2)] - \pi + \cos^{-1}(d)\} \tag{42}$$

If the initial thickness of the membrane is denoted by w_o, then we have:

$$w_1 = w_o(1 - d)/([1 + u_1]r_1^2) \tag{43}$$

$$w_2 = w_o(1 + d)/([1 + u_2]r_2^2) \tag{44}$$

where w_1 and w_2 are the thicknesses of the right and left daughter cells respectively.

Thus the three equations specifying cleavage under the above assumptions are:

$$r_1^2(1 - u_1^2) = r_2^2(1 - u_2^2) \tag{45}$$

$$(1 - d)e_1/([1 + u_1]r_1^3) = (1 + d)e_2/([1 + u_2]r_2^3) \tag{46}$$

$$[(2 - u_1)(1 + u_1)^2 r_1^3 + (2 - u_2)(1 + u_2)^2 r_2^3] = 4 \tag{47}$$

where e_1 and e_2 are given by equations (41) and (42) respectively. It should be noted that there is again a movement of fluid across the cleavage plane according to this solution. This is not necessarily as surprising as it may first appear. If an elastic material, such as a balloon, is inflated, it will be found (experimentally and theoretically) that the pressure first rises and then falls. The effect may be attributed to the fact that the membrane gets thinner as it is inflated. The present case is analogous to the case of two such balloons connected together. In order to be consistent with equation (40) it is admittedly necessary to suppose that cleavage takes place infinitely slowly, so that equilibrium is preserved.

A possibly curious feature of the above three different derivations for asymmetric cleavage is that, numerically at least, and for small asymmetries, they are all very similar.

DISCUSSION

There is good agreement between the observed and calculated paths followed by markers placed on the cell surface during cell cleavage, at least for the case of symmetrically dividing grasshopper spermatocytes (see Fig. 5). It is true that these cells exhibit during cleavage an unusual degree of regularity; nevertheless, it seems reasonable to suppose that the model is a useful first approximation to the description of cleavage in many other types of cells. But whereas the model may apply to many animal cells, among others, it clearly does not, and is not intended to apply to plant cells, etc.

Alternatively, one can argue that in those cells which do not exhibit the form described by the present model, other constraints, possibly in addition to those cited above, may be operative. This viewpoint emphasizes the utility of obtaining further quantitative data relative to cell cleavage.

The case of asymmetric cleavage has been discussed above because it is of theoretical interest. As a practical matter it is clear that the majority of cells which have been studied so far do divide substantially symmetrically. At present visual estimates of this symmetry have a precision perhaps no better than 5%. Quantitative data on this point would be very useful. Nevertheless, the widespread occurrence of essentially symmetrical cleavage suggests that some common mechanism may be operative. Our study of asymmetric cleavage suggests the following process. Let us assume that the furrow region initially lies on a great circle of the mother cell (i.e., in an equatorial plane) so that cleavage begins symmetrically. Further let us assume that

a pressure exists within the cell which is positively correlated with the radius. Denote the pressure in the two presumptive daughter cells by P_1 and P_2. Initially we have, by assumption, that:

$$r_1 = r_2$$

and, therefore,

$$P_1 = P_2 .$$

Now disturb the system so that r_1 decreases relative to r_2. Thus we have:

$$r_1 < r_2$$

and, therefore,

$$P_1 < P_2 .$$

The pressure gradient is in such a direction as to tend to restore the initial condition of equality of the radii. Thus symmetric division would be expected to be stable under the given assumptions. On the other hand, if it is assumed that the cell membrane as a whole exhibits the property of constant tension independent of radius then it is readily shown that symmetrical cleavage would be inherently unstable and should be the exception rather than the rule. (An analogy is furnished by two soap bubbles connected by a tube.) Thus a plausible theoretical model of symmetric cleavage is obtained if there is initial symmetry in the location of the furrow and if there is an internal hydrostatic pressure which is a positive monotonic function of the radius.

Although one would like to interpret the model in terms of the mechanical properties of the cell membrane, this is clearly premature. For example, the movement of the surface markers is consistent with a uniform increase in surface area, at least in the case of grasshopper spermatocytes. But a uniform increase in area could arise either by uniform stretching, by a uniform insertion of new material, or by unfolding of a uniformly pleated membrane. Although uniform stretching may appear more likely, it is clear that more experimental evidence will be required before a convincing mechanical interpretation will be possible.

In summary, the profile and the movement of the cell membrane during cleavage are consistent with a model of cleavage predicated upon the constraints of constant volume and minimum area. This has been demonstrated in the case of symmetrically dividing grasshopper spermatocytes, but may reasonably be supposed to apply as first approximation in many other types of dividing cells. Finally, it may be noted that the general approach to the dynamics of cell shape, as outlined above, may prove useful in other problems of a similar character.

This work was dedicated to Professor A. C. Burton on the occasion of his retirement as President of the Biophysical Society.

This work was supported in part by NSF grant GB-5833.

Received for publication 15 May 1967.

REFERENCES

DAN, K. 1958. *J. Exptl. Biol.* **35**:400.
HIRAMOTO, Y. 1957. *J. Exptl. Biol.* **35**:407.
ISHIZAKA, S. 1966. *J. Exptl. Biol.* **44**:225.