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LETTERS TO THE EDITOR

A MODEL FOR CELL DIVISION*

The authors presented a study which deals with a very important topic, namely, the analysis of cell division via a mathematical model. Since the subject paper, and any further study based on this paper, will probably shed some new light on the understanding of the mechanics of cell division, it is believed to be proper to make detailed comments on its shortcomings. The purpose is, by drawing attention to these shortcomings, to contribute to the development of a more acceptable mathematical model of cell division.

The model investigated by the authors is a nonlinear elastic spherical membrane containing an incompressible fluid. Using the definition of bulk modulus B, one can determine the pressure change ΔP in the fluid caused by the volume change ΔV from the following equation:

$$\Delta P = B(\Delta V/V_0),$$

in which V_0 is the initial volume. In their analysis, the authors use the constant volume condition. In the numerical calculations, they point out that the constancy of volume checked to within 1.5%. In other words, if it is not meant otherwise, this statement implies that $\Delta V/V_0 = 1.5\%$ for the worst case. As an average, let us use $\Delta V/V_0 = 1.0\%$ in our calculations. Assuming that the fluid inside the membrane resembles water, take $B = 2.0 \times 10^{10}$ dyn/cm^2. Accordingly,

$$\Delta P = (2.0 \times 10^{10})(1/100) = 2.0 \times 10^8 \text{ dyn/cm}^2.$$

This is *ca* 10^6 times greater than any reported data on intracellular pressure. The volume change reported by the authors is caused by the approximations involved in the numerical technique, so the pressure change obtained above is not, naturally, taken into account. On the other hand, it is also plausible to suggest that there will not be such large pressure changes even if there is some volume change, since it appears that fluid may flow in or out through the cell membrane which is very highly permeable to, for instance, water. Moreover, the cell membrane is typically rather loose and wrinkled, so it would be reasonable to assume that some volume changes can be accommodated without any large pressure changes. As a result, it is not absolutely necessary for the cell to have constant volume during division.

The authors examined the deformation pattern of an initially spherical membrane for prescribed displacement at the equator. They do not present the intracellular pressure change during this deformation. Their constraint condition on the constancy of the enclosed volume implies that there is *no* change in the pressure during division. Experimental findings of Hiramoto (1968, referred to by the authors) indicate a significant intracellular pressure change. Figure 3 of Hiramoto (1968) clearly shows that "... at the beginning of cleavage, the pressure increases again and it reaches a peak during cleavage followed by a decrease during the second half of cleavage. The pressure increases by about tenfold during the first half of cleavage and decreases by a similar degree during the second half." The authors include the pressure term P_n in their equations (3.1); however, its variation (if there is any) during division is not presented. Our own numerical results from a related study are shown in Fig. 1 (Söylemez, 1978). The spherical membrane is made of Mooney material and the enclosed volume is not constrained to remain constant. The details of this investigation will be published separately. In Fig. 1 the nondimensional intracellular pressure (P_n/C_1) and the nondimensional constricting force (F_f/C_1h^2) are given as functions of the stage of cleavage. The notation used here is the same as that used by the authors. Since the authors do not present the intracellular pressure vs stage of cleavage curve, there is no way of comparing our results with theirs. Our results do *not* agree with the experimental findings of Hiramoto (1968) for given C_1 and h. Recognizing the fact that membranes made of the Mooney material and the so-called STZC material show a similar *kind* of behavior, we are tempted to suggest that intracellular pressure *vs* stage of cleavage curve for the STZC material follows the same trend as that given in Fig. 1; i.e. no decrease in pressure during the second half of cleavage.

The authors present the constricting force vs stage of cleavage curve, Fig. 8 of the subject paper. Our results and theirs are in total disagreement as far as the shape is concerned. The constricting force does not tend to zero as cleavage is completed for the Mooney material as opposed to the STZC material. A reconsideration of the equations given in the subject paper is in order.

Equation (4.2) of the authors' paper is reproduced below.

$$F_f = (T_1^* \cos\theta^* + P_n\hat{\eta})2\hat{\rho}. \tag{4.2}$$

All the quantities in this equation are positive. Assuming that $\hat{\eta}$ is short, let us neglect the contribution of the second term in parenthesis. Then,

$$F_f \cong 2\hat{\rho}T_1^* \cos\theta^*. \tag{a}$$

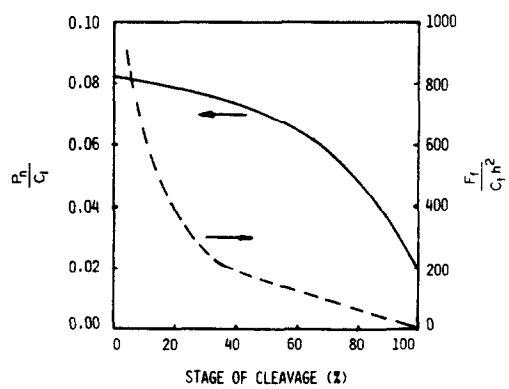

Fig. 1.

* By P. Pujara and T. J. Lardner, *Journal of Biomechanics* 12, 293–299, 1979.

Referring to Fig. 7 of the authors' paper, we see that θ^* is close to 0° and definitely *not* equal to 90°. Therefore,

$$F_f \cong kT_1^*\hat{\rho}, \tag{b}$$

where k is a positive constant near 1.0. The only way that F_f goes to zero as cleavage is completed is that $T_1^*\hat{\rho}$ goes to zero. The first of equation (3.7) of the authors' paper is reproduced below.

$$T_1 = \frac{C}{2}\frac{\lambda_1}{\lambda_2}[\Gamma(\lambda_1^2 - 1) + \lambda_2^2(\lambda_1^2\lambda_2^2 - 1)]. \tag{3.7}$$

At the equatorial plane of the dividing cell, this equation takes the following form:

$$T_1^* = \frac{C}{2}\frac{\hat{\lambda}_1}{\hat{\lambda}_2}[\Gamma(\hat{\lambda}_1^2 - 1) + \hat{\lambda}_2^2(\hat{\lambda}_1^2\hat{\lambda}_2^2 - 1)]. \tag{c}$$

Recalling the definition of $\hat{\lambda}_2$ which is

$$\hat{\lambda}_2 = \frac{\hat{\rho}}{r_0}, \tag{d}$$

equation (c) can be put into the following form:

$$T_1^*\hat{\rho} = \frac{C}{2}r_0\hat{\lambda}_1[\Gamma(\hat{\lambda}_1^2 - 1) + \hat{\lambda}_2^2(\hat{\lambda}_1^2\hat{\lambda}_2^2 - 1)]. \tag{e}$$

Totally completed cleavage corresponds to $\hat{\lambda}_2 = 0$ in which case equation (e) becomes

$$(T_1^*\hat{\rho})_{\hat{\rho}=0} = \frac{C\Gamma}{2}r_0\hat{\lambda}_1(\hat{\lambda}_1^2 - 1). \tag{f}$$

It can be seen from Fig. 5 of the authors' paper that $\hat{\lambda}_1$ increases rapidly as cleavage continues. It is always greater than one. An extrapolation of the authors' results given in their Fig. 5 yields $\hat{\lambda}_1 \cong 2.5$ at the completion of cleavage. An extrapolation of Hiramoto's experimental results given also in Fig. 5 yields $\hat{\lambda} \cong 4.0$ at the same stage. Using the authors' results together with their data, we obtain $F_f \cong 150 \times 10^{-4}$ dyn for the constrictive force at the completion of cleavage, rather than zero as given by the authors.

If the calculations presented above are correct, the authors' curve given in their Fig. 8 is wrong. The correction turns their curve into one similar to our curve given in Fig. 1. In this case, neither the Mooney material nor the STZC material is appropriate for a description of the cell membrane. The curves given in Fig. 1 of this Discussion can be made similar to the experimental curves if and only if it is assumed that the material constant C_1 (or C) does not remain constant during cleavage which, in turn, implies a different material type. In our own calculations, we have made this assumption and the deformed configuration of the membrane, the pressure and the constrictive force are all in satisfactory agreement with the experimental findings even for the Mooney material. The results will be published soon.

REFERENCES

Hiramoto, Y. (1968) The mechanics and mechanism of cleavage in the sea urchin egg. *Symp. Soc. expt. Biol.* **22**, 311–327.

Söylemez, H. (1978) Division of a nonlinear spherical membrane. Unpublished MS Thesis, Department of Civil Engineering, Middle East Technical University, Ankara, Turkey (Directed by N. Akkas).

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REPLY TO THE LETTER BY PROF. AKKAS ON "A MODEL FOR CELL DIVISION"*

We wish to thank Prof. Akkas for commenting in detail on certain aspects of our model for cell division. We agree with him that improvements in the mathematical description of cell division are needed. Our "passive" model attempted to provide a mathematical description which gave reasonable agreement between the directly observed variables such as displacements during cytokinesis and would give reasonable estimates for indirect variables such as stretch ratios. The constricting force variation with stage of division in particular, is an indirect result, with the exception of the direct force measurement by Rappaport (1967), which is open to discussion.

Our method of analysis was to integrate the equilibrium equations satisfying the boundary conditions and constant volume condition. As we note in the paper after equation (3.5), "...for a prescribed $\hat{\lambda}_2$, the values of λ_0 and P_n are determined by integrating equations (3.1) iteratively until the volume condition, equation (3.5), is satisfied." As the membrane stretches over the deformed shape, the internal pressure will increase. It is *not* correct to say that the pressure did not change in our analysis. We did not give the values of the pressure variation with stage in our paper in the interests of brevity but the results are presented below for a STZC material with $\Gamma = 0.25$:

Stage, %	(pr_0/C)
100	0
90	0.070
70	0.346
50	0.786
30	1.51
15	2.26

While Prof. Akkas notes from Hiramoto (1968) that the internal pressures are significant during division and while our model does in fact show an increase of pressure in agreement with Hiramoto's observation (with $pr_0/C = 1$, we find p is approx. 400 dyn/cm^2), we are of the opinion that this monotonic increase of pressure with stage of division is a defect in the model arising from an inappropriate constitutive relation for the membrane for small values of the equatorial radius. For the STZC material and for the Mooney material, the stress resultant $T_1 \to \infty$ as $\lambda_2 \to 0$. As a consequence, the model has the shortcoming that it is inappropriate near the equator at the later stages of cell division.

The calculation of the constriction force was carried out in the manner noted in the paper up to the 15% stage of division and the curve of the force was then extrapolated to zero. We were guided in this extrapolation to zero by the intuitive observation that at the end of division, the force in the membrane should drop to zero and by the results obtained by others as shown in Fig. 8. Again the applicability of the model to the later stages of division is inappropriate as noted above; the model gives values of the constriction force as noted by Prof. Akkas which are not realistic at the end of division. The selection of values at the membrane location shown in Fig. 7

* By P. Pujara and T. J. Lardner (1979) *Journal of Biomechanics* **12**, 293–299.