CYTOMECHANICS

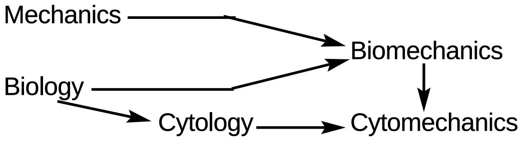
NURI AKKAS*

SUMMARY: The definition of cytomechanics is given. The importance of mechanics in understanding various cell activities is stressed. The necessary essentials on cell structure and of cell division are discussed. It is pointed out that cytokinesis in animal cells may be viewed as biomechanical instability problem.

Key Words: Cytology, biomechanics, cytomechanics, cytokinesis, instability, cell membrane.

INTRODUCTION

Mechanics is the science which studies the deformation and/or motion of bodies under the action of forces. This classical connotation will be used in the present work as opposed to statistical or quantum mechanics. The science which deals with organisms is called *biology*. It is the science of life in all its aspects. The study of form, function and living habits of all living things is the subject of biology. Thus, it turns out that the field of biology is almost indescribably large. *Cytology*, which is one of the numberous subdivisions of biology, is the study of cell structure and cell activities. An examination of the papers by cytologists reveals that words like force, deformation, motion, failure, etc. are occasionally used in explaining the observations. On the other hand, concepts like force, deformation, motion and failure are the basic ingredients of mechanics. Indeed, wherever there is motion (or deformation) there is mechanics. It is not surprising at all, therefore, to come to the conclusion that mechanics may play an important, but thus far neglected, role in a better understanding of various cell activities. The author proposed some years ago (Akkas, 1979) that the application of the principles of mechanics in cytology deserves to be called *cytomechanics* in its own right. This is a very natural extension of the field of *biomechanics* which is the application of the laws of mechanics to a biological system. The interrelationship among these fields can best be described through the following diagram (Akkas, 1979):



*From Ankara University, Faculty of Science.

The author has been promoting this idea and its applications since its introduction (Akkas, 1980 a, 1980b, 1981, 1987a, 1987b; Akkas and Engin, 1980, 1981). In addition, there appear to be two international conferences organized thus far which emphasize the mechanical aspects of cytology (Akkas, 1978c; Bereiter-Hahn, Anderson and Reif, 1987). In passing, it is interesting to note that the foundations of cell biology were formed in the 17th century and one of the most important advances of that period came from Robert Hooke (1635-1703). In 1665, Hooke published a collection of essays under the title *Micrographia*. In one of the essays, cork is described as a honeycomb of "cells". Thus, Hooke turns out to be the first to use the word "cell". On the other hand, Hooke is one of the famous men in mechanics. His most important contribution in mechanics is known as Hooke's law which states the relation between stres and strain. Therefore, it can be said that the origins of cytomechanics go bact to the 17th century, if not any earlier.

A mechanician's view of the animal cell as a biological unit and of the biomechanics of cytokinesis as an example of various cell activities has already been presented (Akkas, 1987b). The purpose of this work is to clarify some points and introduce new conjectures to lead to further discussion. Thus, it is recommended that the reader refer to Akkas (1987 b) for further details.

A basic concept in mechanics is modelling. It must be accepted that real problems, especially the biological ones, can not be simplified imposing only convenient restrictions. On the other hand, a solution to the problem must be obtained. Simplification of a problem is the common approach followed by mechanicians. The resulting mathematical or experimental models are, at the beginning, easy to handle. Working with simple models gives the mechanician and insight to the problem. Then, he can decide which aspects should be modified to obtain the next generation of the model. Each simplification, when decided to be an oversimplification, is discarded from the model and, thus, the new model becomes a bit more realistic. The mechanical models of cytokinesis will be discussed below.

THE CELL AND CYTOKINESIS

A cell is a discrete mass of cytoplasm enveloped in a selective and retentive membrane which is interchangeably called the cytoplasmic membrane or plasmalemma. According to the fluid mosaic model of Singer and Nicolson (1972), the plasma membrane is composed of lipids glycolipids, proteins, and glycoproteins. The matrix of the fluid lipid bilayer has a thickness of about 7.5 nm. Recall that cells range in size from the smallest bacteria only a few tenths of a micron in diameter (a pneumoccoccus is about 0.2 u in diameter), to certain marine algae and to the yolks of bird eggs, with dimensions of centimeters (the yolk of ostrich egg is about 7.5 cm in diameter). In the theory of membranes in mechanics, the radius - to - thickness ratio, R/t, is an important concept. If we take 7.5 nm as the thickness of the membrane, then the R/t ratio for cells ranges from 14 to 5 million. The smallest is for the pneumoccoccus and the largest for the ostrich egg yolk. Except for those near the lower limit, the values for R/t are within the limitations of the thin shell and membrane theories.

Is the 7.5 nm thick cytoplasmic membrane the "membrane" which should be used in possible applications of the membrane theory to various cell activities? The author's answer to this question is negative. The lipid bilayer is a continuum in two dimensions, but it has a molecular character in the third dimension. As reviewed kin Evans and Skalak (1980), it is difficult to increase the surface area of the lipid bilayer. Area increases of a few per cent result in rupture. On the other hand, large extensions are readily achieved at constant area. It is known that the cell surface area in cleaving cells increases by about 26%. If an increase of a few per cent in the surface area of the lipid bilayer results in rupture, the bilayer should rupture long before cleavage is completed. It is known that this is not the case. A cell has microvilli and ruffles which unfold during cleavage (Figure 1). Therefore, it is possible that the lipid bilayer proper is not even subjected to any actual area increase at all. Then, what is to carry the so-called in-plane forces which act in the plane

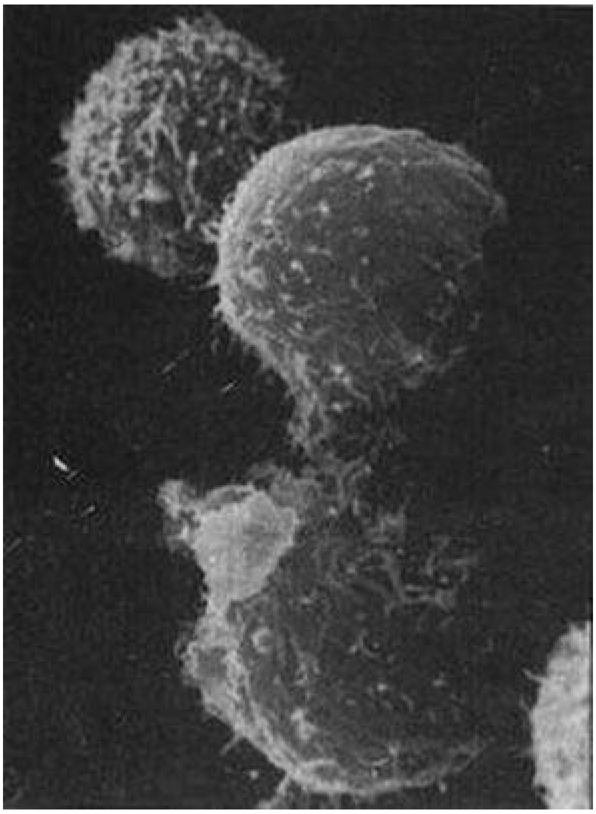


Figure 1: A cell undergoing cytokinesis. From Akkas (1987 c).

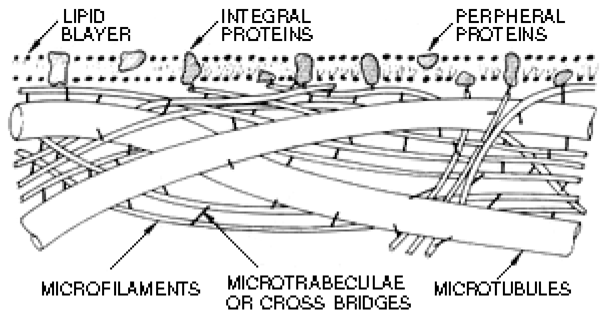


Figure 2: Schematic drawing of plasma membrane and membrane - associateated cytoskeletal components. Not drawn to scale.

of the cell "membrane". In other words, what is the "membrane" that we are talking about in applying the membrane theory of shells to the deformation analysis of cell surface. This brings us to the presentation of the concept of "cortex".

The "membrane" thickness mentioned in Hiramoto (1970) is in the order of a few microns. Obviously, this is not the thickness of the lipid bilayer alone but that of the so-called cortex (or cortical layer) which includes both the lipid bilayer and the submembraneous region containing the cytoskeletal components (Figure 2). The cortex thickness is not well defined because there is no definite inner boundary. Values ranging between 1u and 3u have been used by various investigators. Even the largest thickness puts the R/r ratio of commonly studied cell (such as the sea urchin egg) in the thin shell domain. Therefore, in the deformation analysis of average cells, the membrane theory of shells is applicable even when the cortex is used as the membrane. The cell surface stiffness characteristics which have been measured by various experimental techniques can be provided by the cortical layer. More information about this layer from a mechanical point of view can be found in Akkas (1987b).

Cytokinesis is the division of the cytoplasm and the plasma membrane. Prior to division, animal cells attain a roughly spherical configuration. Cytokinesis appears to be the relatively simple event of the division into two of the spherical membrance enveloping the cytoplasm. According to the currently accepted mechanism, the process begins with the formation of a furrow in an equatorial plane. The division furrow has a dense ring of parallel microfilaments, oriented properly, to provide the structural basis of constriction (Figure 3). It is the muscle -like contraction of the furrow ring that cause cleavage. The microfilaments of the ring are anchored to the plasma membrane. The concept of constricting ring has been used by Pujare and Lardner (1979) and Akkas (1980b) in their biomechanical model of cytokinesis. In these models the ring is a complete, circular one. The possible links between the ring and the underlying cortex are not considered. It appears that this complete ring model has its

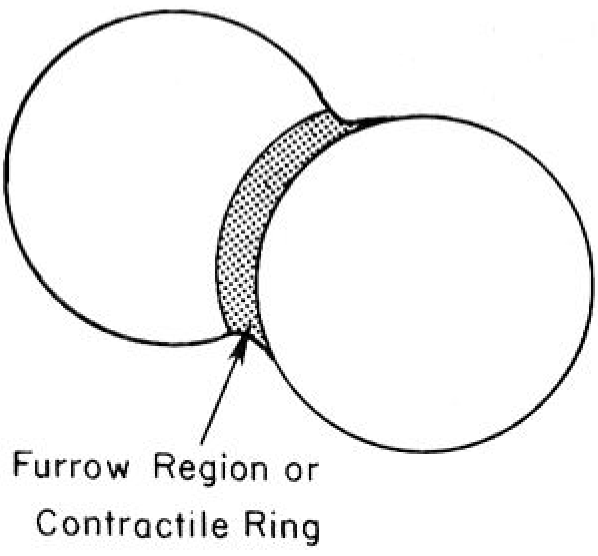


Figure 3: Furrow band.

unexplained points. It is known that, for constriction to start, the furrow does not have to be a complete ring. Microfilamentous band in the furrow region in the form of an incomplete ring can cause dimple-shaped partial constriction. The two untouching ends of the furrow ring must, therefore, be getting some support from, very likely, the cortex. This is feasible, because, as stated previously, the microfilaments of the furrow band may be linked to the cortex. The microfilaments of the furrow band are able to slide along each other. For a complete furow ring, this property of the microfilaments is sufficient to constrict the equatorial plane. For an incomplete band which is in the form of an arc of a circle, the microfilamentous band will not be in mechanical equilibrium unless it is supported by, say, the cortex. In accordance with this mechanical argument, it may be reasonable to state that the furrow band is linked to the cytoskeletal elements of the cortical layer and, thus, the constriction of the furrow ring is affected by the cortical layer also, in addition to the sliding ability of the microfilaments. We believe that observations and experiments on this point would be rewarding.

Figure 4 shows the variation of the constricting force in the furrow ring with stage of cleavage.

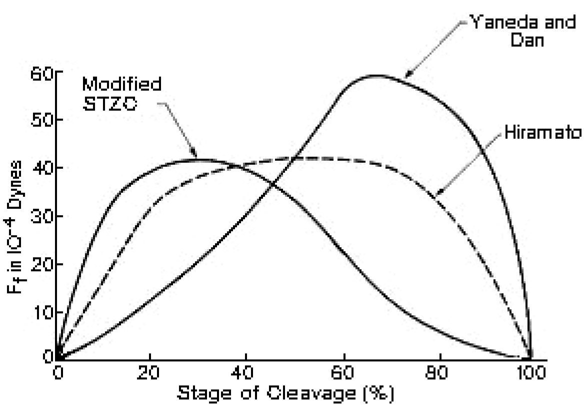


Figure 4: Variation of the constricting force with stage of cleavage. From Lardner (1987).

The figure is from Lardner (1987) and details can be found there. For our purposes it suffices to stress the fact that the ring force is zero at the beginning of cleavage, it goes through a maximum and it becomes zero again at the end of cleavage. From a mechanical point of view, this is an important observation because it leads to the concept of biomechanical instability. The curves similar to those in Figure 4 are called the force-displacement curves. The point corresponding to the maximum value of the force is called the limit point. Before reaching the limit point, one has to increase the force for larger displacements. But, when the limit point is reached and passed the displacement will increase although the force decreases. The limit point is the point of instability. The system (in this case, the cleaving cell) loses its stability when the ring force reaches the limit point. Once the limit point is passed the displacements of the system are expected to occur relatively fast. On the other hand, if the deformation process is displacement-controlled, then the last statement may not be valid anymore. In passing, it should be noted that the ring force is a function of the cell membrane stiffness and others. The stiffer the membrane, the harder should be the cleavage.

SUMMARY AND CONCLUSIONS

Mechaniciance have not yet entered the field of cytology at a noticeable level. We believe that cytology is full of problems which can be tackled by mechanicians and we also believe that this field deserves to be celled "cytomechanics" in its own right. In this work, some basic essentials of cell structure and of cytokinesis have been presented. Mechanical aspects have been stressed. Mechanical way of thinking led to the following conclusions: The constriction of the furrow band may be controlled by the cortical layer in addition to the microfilaments of the band. Cleavage may be considered as a biomechanical instability problem.

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