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Hydration–dehydration of cell cytoskeleton proteins and the problem of aging

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Abstract: **The role of water in cell cytoskeleton proteins and the change in its volume under the influence of temperature are considered. The mechanism of cell pulsation is proposed, the leading factor of which is hydration-dehydration of its cytoskeleton proteins.**

Keywords: **cell, proteins, cytoskeleton, hydration, dehydration, temperature, aging**

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Contents

1. INTRODUCTION

The article is dedicated to the memory of O.Ya. Samoilov, who opened for me the world of water - the world of very small and probably the most active molecules. His book "The structure of aqueous solutions of electrolytes and hydration of ions" [1] with its molecular-kinetic approach to the phenomenon of hydration of ions in solutions has been leading me in my research for many years.

This paper proposes a discussion of the role of water molecules in cell pulsations and in human aging.

1.1. In the experiments of Academician A.A. Ukhtomsky (physiologist, author of the doctrine of the dominant) on human muscle cells, in particular, it was shown that a muscle cell in heated water at 42°C reduces the volume [2].

A.A. Ukhtomsky in his works does not explain the result of this amazing experience. What should the student of O. Ya. Samoilov? Surely he should think about whether these small and ubiquitous molecules - water molecules - play an important role here. In **Fig. 1** shows the structure of an alpha helix protein. Thermal motion loosens the configuration, and the hydrogen bonds (shown by the dotted line in the figure) between the H and O atoms (the atoms are on different but adjacent turns) stabilize it. Heat movement affects these bonds, they weaken and even break in some cases. It is used by water molecules to be embedded between the turns of the protein. Water molecules, penetrating into the space between the turns, stabilize the spiral and at the same time lengthen it. It is in this that the high reactivity of water molecules, their "ubiquity" is manifested.

The alpha helix is used here as a visual model. The cell cytoskeleton is built from globular proteins. This is primarily actin. Note that actin

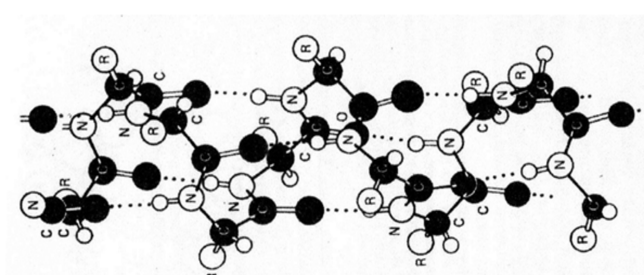

Fig. 1. *The structure of the a-helix* [3, p. 67].

is not only a motor protein, but also a structural one. It has now been established that actin is a structural protein of any eukaryotic cell. All that has been said about the introduction of water molecules into the inter-turn space of the alpha-helix remains valid for actin, since the actin globule is an alpha-helix coiled into a ball. The presence of water molecules between the turns of the protein was experimentally discovered in [4].

Let's return to the experience of A.A. Ukhtomsky. Let's propose a version: in the interturn space of cytoskeleton proteins there are water molecules. By doing this, they increase the volume of the cell. As the temperature rises, it becomes more and more difficult for them to stay there, and at 42°C water molecules leave the inter-turn space of the cytoskeleton proteins. This care reduces the volume of the cell. Conclusion: hydration of proteins of the cytoskeleton increases the volume of the cell, and their dehydration reduces the volume of the cell.

But what happens when the cell expands? Obviously, a suction force arises, which helps the cell to receive the substances necessary for its life through the membrane channels. And the compression of the cell through the channels displaces harmful metabolic products from it.

1.2. The experience of V.N. Zholkevich [5,6]: roots were placed under the glass (different, but more often corn). After some time, the walls of the glass began to fog up and then droplets of exudate appeared on the cut of the roots. About this experience V.N. Zholkevich mentioned, in particular, when making a report at the Presidium of the USSR Academy of Sciences. The report was published [5].

The version (mine, no others): the remnants of the cut cells lost water, which evaporated from them and with which the walls of the glass were fogged up. This water loss caused dehydration of cytoskeleton proteins, cell debris shrank, squeezing out droplets of exudate.

Conclusion: the inter-turn space of the cytoskeleton at normal temperature can accommodate a certain number of water molecules, which is determined by the cell genotype. This maximum amount of inter-turn water does not depend on the water content in the cell, but only up to a certain limit. If the water content in the cell falls below this limit, then there is a connection between the water content in the cell and the hydration of the cytoskeleton. Namely, less water in the cell means less water molecules in the inter-turn space of the cytoskeleton. Consequently, the hydration of the cytoskeleton is weaker, and, it should be noted, the cell volume decreases.

In the behavior of water molecules as in the experiment of A.A. Ukhtomsky, and in the experiment of V.N. Zholkevich has something in common. In the experiment of A.A. Ukhtomsky water molecules leave when the temperature rise reaches a certain limit - 42°C. And in the experience of V.N. Zholkevich, the limit in the content of water by the cell must be reached, after which a relationship is established between the total amount of water in the cell and the amount of water in the inter-turn space of the cytoskeleton.

1.3. Cell pulsations have been found experimentally in many works. Pulsations of the volume of parenchymal plant cells and the diameter of stems were experimentally found in the works of V.N. Zholkevich [5,6]. The pulsations of the endothelial cells of the blood capillaries were shown by electron microscopic studies of White [7]. S. Kuffler and J. Nicholls [8] described in detail the rhythmic changes in the membrane potential of the nerve cell. This work played an important role in understanding the mechanism of cell pulsation.

In the work of S. Kuffler and J. Nicholls [8] on the study of the membrane potential of a nerve cell, it was found that a positive charge outside the cell is created by sodium ions. There are practically no sodium ions inside the cell, but there are potassium ions, and proteins create a negative charge in the cell.

The membrane potential (**Fig. 2**) changes continuously: from -70 mV it increases to -50 mV, and then returns to its original state. This is followed by a new cycle, and so on, until an action potential arises. Fig. 2 it can be seen that the depolarization curve (1-3) is steeper than the repolarization curve (3-4).

The version of S. Kuffler and J. Nicholls: under the action of a charge gradient and a concentration

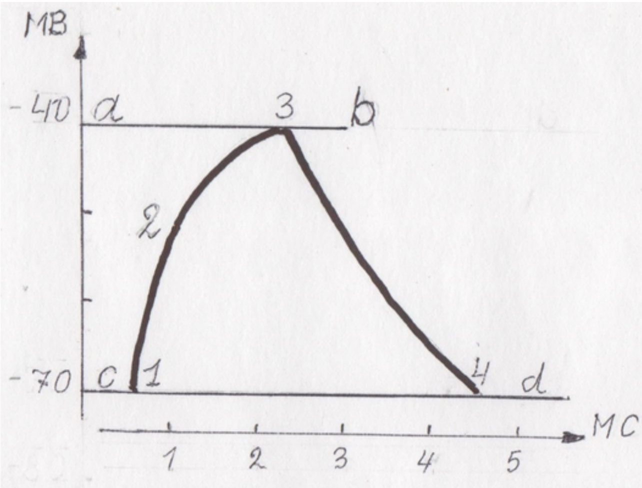

Fig. 2. *Changes in the membrane potential of the neuron body during its pulsation. cd - resting potential, ab - activation potential (threshold).*

gradient, sodium ions enter the cell. At a certain concentration of sodium ions, the enzyme sodium ATP-ase is activated. ATP hydrolysis begins with the release of heat and an increase in temperature. The rise in temperature removes sodium ions from the cell. After that, a new cycle begins.

2. MICRODYNAMICS OF HYDRATION-DEHYDRATION OF CELL CYTOSKELETON PROTEINS UNDER THE ACTION OF TEMPERATURE

The version by S. Kuffler and J. Nicholls requires important additions. Here they are: ATP molecules, as you know, do not float, but are attached to the cytoskeleton. It is here that the local temperature reaches 42°C and, according to the experience of A.A. Ukhtomsky proteins of the cytoskeleton are dehydrated. The cell, by contracting, removes sodium ions from the cell, moreover, we emphasize this, acting against the charge and concentration gradients. It is important that at the same time water molecules and harmful metabolic products leave through the membrane channels.

What happens next? The temperature in the cell decreases and dehydration is replaced by hydration - a spontaneous process of the introduction of water molecules into the inter-turn space of cytoskeletal proteins. The cell volume increases. An absorption force arises, which, together with a charge gradient (and after depolarization, a minus remains in the cell, and a plus outside the cell) and a concentration gradient of sodium ions (plus these cations are mainly created outside the cell) brings sodium ions into the cell. At the same time, water molecules and other substances necessary for the cell also enter the cell. Now it becomes clear the fact (see Fig. 2) that the depolarization curve is much steeper than the repolarization curve. Sodium ions enter the cell (depolarization) under the action of all three forces, and exit (repolarization) under the action of only the compression force, and the charge and concentration gradients prevent this.

Conclusion: with these additions, the version of Kuffler and Nicholls becomes a description of the mechanism of cell pulsation, in which, along with hydrolysis of ATP, hydration and dehydration of the cytoskeleton, and therefore water molecules, play a decisive role.

But back to O.Ya. Samoilov. It is no coincidence that potassium ions are in the cell. These large singly charged cations with "negative" hydration make water molecules even more active, even more reactive. And, therefore, in their presence, the hydration of the cytoskeleton increases and the amplitude of the pulsations increases.

Let us emphasize: pulsations are vital for the cell. With their help, the cell receives the necessary substances and is freed from metabolic products. In addition, it is a mechanism for converting thermal energy into mechanical energy. The transformation of thermal energy into mechanical energy is widely used in the body [9].

3. CONCLUSION

Now we can move on to the question of why a person is getting old.

The amount of water in humans decreases with age. If a 20-year-old has 75% water, then a 70-year-old has only 65% [10]. Moreover, the decrease is due to cellular water: between 20 and 70 years, the ratio of cellular to extracellular water decreases from 1.1 to 0.8 [10].

Let us propose a mechanism for the loss of water by a cell. Its essence is that water enters the cell at a lower temperature than it leaves it. An increase in temperature as a result of ATP hydrolysis weakens the bonds between water molecules. The water molecule is now easier to move and leave. Thus, with each pulsation, less water enters the cell than it exits. And this is cell dehydration. And it goes inevitably.

Discussing the experience of V.N. Zholkevich, we found out that with a sufficient content of water molecules in the cell, there is no connection between the decrease in water in the cell and the filling of the inter-turn space of the cytoskeleton with water molecules. For a person, this corresponds to youth and maturity. But the inevitable dehydration of cells leads to a limit, after which the amplitude of the pulsations begins to decrease. With further dehydration, the cell goes over this limit. This is where aging begins when dehydration of cells decreases the amplitude of their pulsations. Cells begin to receive less and more of the necessary substances and are cleared more and more poorly. First of all, these are excitable cells, and this applies to both cells that are dividing and those that do not. After 50 years, the brain loses 5% of its weight every 10 years [11,12]. Muscle loss is not less. By the age of 70, a person loses up to 12 kg of muscle [9]. There are many tens of theories and hypotheses of aging [11,13,14]. And in each case, apparently, after working, one can see that old age is the result of dehydration of excitable cells: brain cells, glands and muscles.

Oleg Yakovlevich Samoilov dreamed of a time when water in the body would not be considered simply as an environment in which life, cellular processes unfold. He was convinced that water molecules play a decisive role in these processes. Oleg Yakovlevich was a genius. If he hadn't died so early, he would have done more and better than we, his students. And many thanks to Margarita Nikolaevna Rodnikova for her work, for the existence of this seminar.

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