Changes in protein hydration means a transition mechanism of heat energy into mechanical one

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Abstract. Of particular importance is hydration of protein molecules that depends on the temperature and concentration of water molecules in any biological cell. The changes in hydration are based on the pulsation of cells as well as the other essential cellular processes, also accounting for actions of cross-striated and non-striated muscles. Alongside with that, the changes in hydration can be explained by a transition of heat energy into action.
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Introduction

The hydrated protein forms an entire unit consisting of protein molecules and water molecules. The entire unit possesses properties not exhibited by its component parts [1]. As an essential property of the hydrated protein molecule being an entire unit appears to be a capability of changing its length by changes in the hydration degree. The protein hydration is determined by the lobes of protein spiral turns between there are located water molecules. The larger that lobe is, the longer the protein molecule would be. This also relates to globular proteins of cytoskeleton, such as G-actin, since any globule appears to a spiral as well, only just convolved in a glomus (glomerus). By enhancement of globule's hydration there enlarges its volume. The protein hydration is accompanied by heat buildup (enthalpy change $\Delta H < 0$) and reduction of particles' amount, and consequently with reduction of entropy $\Delta S < 0$.

$$\Delta G = \Delta H - T \cdot \Delta S \quad (1)$$

This process goes on spontaneously having a negative value of Gibbs potential $\Delta G < 0$. You can see from (1) that at a certain temperature ($T_к$) the change in Gibbs potential will be equal to zero. It goes to show a balance of hydration and dehydration processes for the given protein molecule. At the temperatures below $T_к$ there spontaneously takes place hydration. At the temperatures above $T_к$ there spontaneously takes place hydration. Regarding the $T_к$-value can judged on the basis of experimental results performed by A.A. Ukhtomskiy [2]. He used to place myofibrils into preheated water and at 44^0C those myofibrils contracted. It is believed that $T_к$ ranges within 42^0-43^0C. The usage of reaction heat in a cell is possible owing to a unique water property, namely its anomalously high heat capacity [3].

The major part

The pulsation of cells appears to be a result of coincidence of two cycles: a heat cycle and a pressure cycle. Both cycles are built up on the principle of a balancing feedback. The hydration increases the temperature, and by enlarging a cell volume and by diminishing a particles' amount herein, will decrease the pressure in a cell. According to the Le Chatelier principle, in a cell there starts to take place a process decreasing an impact of hydration. Such a process appears to be the dehydration. The dehydration is accompanied by heat absorption. It reduces the temperature and shortens the protein molecules of cytoskeleton diminishing therewith a cell volume, and enlarging an amount of particles herein. There rises the pressure in a cell. All those things create the conditions for a transition from dehydration to hydration. The alternation of hydration and dehydration should have resulted in a long-term self-sustained wave process, i.e. the cellular pulsations. However, a part of hydration heat would dissipate. For that reason, a cell should have an independent source of heat. As a general rule such a source appears to be the hydrolysis of adenosine triphosphate (ATF). Accessing the heat of ATF-hydrolysis provides for cellular pulsation being a never-ending self-sustained wave process.

Such pulsations are manifested both in vegetative as well as animal cells. For instance, in V.N. Zholkevich's experiment with "aerating roots" some unbound dried roots were placed into closely tight empty test tubes. Simultaneously with water evaporation from the root (an internal wall of the test tube «became misted») there would appear exudate droplets at the root's slice: the evaporation diminished water concentration in the root's cells, and that reduced inter-turn hydration. As a result, the cells would contract and squeeze the exudate. Experimentally there was determined a self-sustained wave nature of water transport in plants. There was also shown a rhythmical volumetric change of cells, and it was also proved that motions of aqueous solutions in plant's living cells consist of two

successive phases. The first phase is water entrance into a cell (a relaxation phase). The second phase is water ejection in the direction of xylem vessels (a contraction phase) [4].

The pulsation property is exhibited not only by plant cells. For instance, it was discovered that to self-sustained wave processes also belongs activity of asynchronous muscles of insects. Such self-sustained oscillations could be induced while regulating loads upon muscles or stimulating them by electrical current. The capability of those muscles to function in their own rhythm upon non-availability of nervous impulses was proved in the experiments with pattern muscular filaments. In solutions with ATF and Ca^{2+}-ions such myofibrils would proceed to rhythmical fluctuations which could run on for hours together [5]. The fruit's heart would pulsate while its conductive is not shaped yet.

A direct experiment highlighting inter-turn hydration was described in a study on the examination of rhodopsin protein. There was applied an approach making use of roentgen radiation which forms hydroxyl radicals out of water molecules, modifying amino acids being close to each other and containing protein. By means of mass spectrometry there were determined chemical modifications and there were made molecular charts showing the whereabouts of water molecules within rhodopsin as it was activated by light as well as the location of water molecules in rhodopsin as there was not any light activation. Those charts showed that in response to light activation the water molecules would change their location in protein, and the protein itself would change its shape [6].

Let us give consideration to an essential component of homeostasis: relationship between the contents of sodium and potassium ions in a cell. Alongside with that it will serve as an illustration of the mechanism pattern of cellular pulsations. A cell contains potassium ions, and sodium ions are located outside it. During the first phase of pulsation – cell's volume enlargement – there occurs pressure reduction in a cell. The occurred pressure gradient would direct sodium ions into the cell. Apart from that pressure gradient, the sodium ions are affected by a negative charge in the cell and a concentration gradient of sodium ions between the cell and extracellular surroundings. The sodium ions would rush into the cell alongside with water molecules, oxygen and nutritional substances. The oxygen and nutritional substances would be adopted by the cell; however the sodium ions being imposed onto the cell would affect homeostasis. There is a need of the second pulsation phase: cell's contraction. For that purpose there would not be enough just to have hydration heat. There would help an ATF-hydrolysis, for the actuation of which there would be needed sodium ions in particular. Upon achieving a certain concentration of sodium ions in the cell, there would be activated an ATF-phase herein, and that one would start an ATF-hydrolysis. A localized temperature increase would weaken the hydration of cytoskeleton's protein molecules. The cytoskeleton's dehydration would contract the cell; the sodium ions alongside with water molecules' abundance and metabolism products would be withdrawn from the cell. The withdrawal of sodium ions from the cell would stop the ATF-hydrolysis. The homeostasis would be restored, and the cell would commence a sequent pulsation. It is believed that a similar mechanism is of paramount importance in the movement of a nervous impulse. The rhythmical emission and absorption of the heat in a nerve was determined experimentally; therewith the amount of discharged heat was by 20% more than the absorbed one [7]. It is consistent with the suggested pulsation pattern. Please note that within the framework of the pattern under consideration there is resolved an issue on the transition of heat energy into mechanical one in a cell. The hydration heat and ATF-hydrolysis heat would altogether lead to molecules' dehydration of cytoskeleton. The cytoskeleton molecules would shorten, and the cell would contract. The cell's volume reduction as a result of the contraction means manifestation of mechanical forces.

A pattern of Huxley's sliding fibers [8] is based upon the checked experimental data. The electronic microscopy showed that both the length of a myosin structure (thick filaments) as well as the actin fibers (thin filaments) will not change by sarcomere's contraction [9, 10]. The data of an X-ray structural analysis prove to the effect that a nature of subunits to be formed by filaments, by contraction remains unchanged as well [9]. But for all that you would have to get back to the function of cross-striated muscles since there still remains unsettled a crucial issue, namely – what is heat energy of the ATF-hydrolysis is spent for and how do occur the forces contracting the sarcomere?

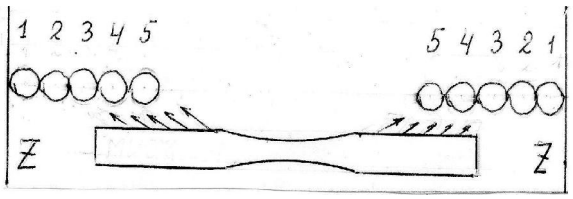

Fig. 1 sShematically illustrates the sarcomere's location prior to the arrival of Ca^{2+} ions.

Fig. 1 schematically illustrates the sarcomere's location prior to the arrival of Ca^{2+} ions.

F-actin is fixed within the sarcomere's walls (Line Z). Its globules are enumerated. There aren't any "bridges" between actin and myosin.

The action potential being an avalanche of sodium ions would spread over the system of T-tubes neutralizing and apparently also positively charging "cisterns" of sarcoplasmic reticulum out of which the Ca^{2+}-ions would go into cytosol [9,10]. Such an upheaval of potassium ions' concentration in the cytosol would at long last cause sarcomere's contraction. The Ca^{2+} ions primarily having an effect on tropomyosin would lift a blockade from actinomyosin formation (therefore the concentration of $Ca2^{+}$-ions should not be less than the concentration of C_1: See Fig. 2 and Fig. 3), and then reacting with troponin would give an opportunity to myosin's «heads» of displaying their ATF-phase activity, namely opening the way to ATF-hydrolysis (for that process the concentration of Ca^{2+}-ions should not be less than C_2: see Fig. 2). It is widely agreed [9, 10] that just ATF-hydrolysis heat would move actin's filaments lengthwise myosin. In this research work we just show in what a way the heat of ATF-hydrolysis would move those filaments.

Let us apply to the sliding theory an idea of globule-actin size enlargement, and consequently the length changes of the entire actin filament during bond formation between myosin and actin, since the myosin "heads" penetrating into actin's globules would increase their volume. A fundamentally different result would be obtained by the ATF-hydrolysis: it dehydrates the globules and reduces their volume. It should be noted that each actin's globule has got an ATF-molecule [9]. The ATF-hydrolysis heat would not only break the actin-myosin bonds, but also as it was pointed out, would dehydrate the globule. As a result, the bond breaking and dehydration would lead to the reduction of globule-actin volume (G-actin), and consequently would contract the length of the entire actin filament (F-actin). The Ca^{+2}-ions would move from the sarcomere's wall to its center (at the Z line there are located "cisterns", out of which there would come potassium ions [10]). The bigger distance from Z line and the closer it is to the sarcomere's center, the smaller concentration of those ions would be.

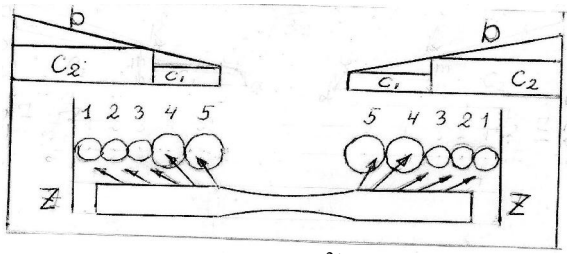

Fig. 2 The concentration of Ca^{2+}-ions in cytosol

Let us presume that at certain moments of time there emerged situations illustrated at Fig. 2 and Fig. 3. At these pictures the concentration of Ca^{2+}-ions is transferred by "b"-Line. At Fig. 2 the concentration of Ca^{2+}-ions in cytosol is higher than the C_1,-concentration which is necessary for the formation of actomyosin (the globules 4 and 5 are bounded with myosin), and it is also higher than the C_2,-concentration, after reaching of which there commences the ATF-hydrolysis (See Position of "b"-Line at Fig. 2). As a result of the ATF-hydrolysis the previously formed "bridges" are destroyed (in the globules 1, 2, 3), and those globules themselves are dehydrated. There would be created a situation when closer to the sarcomere's center there exist actin-myosin bonds (the globules 4 and 5 are bounded with myosin), since the ATF-hydrolysis at that section of the actin filament is blocked (the C_2-concentration is higher than the Ca^{2+}-concentration being transferred by "b"-Line). As it was mentioned, the formation of actin-myosin bonds would increase the size of associated globules, and that would move the adjacent still unbounded actin's globules further to the sarcomere's center, where they are found by the following «heads» of myosin (this is not shown at Fig. 2). This is a mechanism of «sliding» of the F-actin's end being far away from the Z-Line to the sarcomere's center. The second location would occur closer to the Z-line: the concentration of Ca^{2+}-ions is higher than C_2 and under the impact of potassium–ATF-phase activity of myosin's «heads» there goes on the ATF-hydrolysis. Its heat would break the previously formed actin-myosin bonds. The hydrolysis heat while breaking the bonds and dehydrating the globules would decrease the volume of globule-actin (the globules 1, 2, 3). Yet since the globules 4 and 5 of F-actin are bounded with myosin, and actin in its turn – with the sarcomere's wall (with the Z-line), then any reduction of globule-actin sizes 1, 2, 3 would shift the sarcomere's wall (the Z-line) to its center, and consequently would contract the sarcomere. It should be pointed out that hereby the ATF-hydrolysis heat would convert into mechanical operation of the sarcomere's contraction. Any enlargement of globule-actin sizes of the actin filament being at the far away end from the Z-line would be compensated by the decrease of globule sizes at its near end. For that reason, any "sliding" of actin filaments would not change their length.

Now, the sarcomere would have to return to its initial position.

The potassium pump would discharge the potassium ions into "cisterns". This is shown by lowering of "b"-line. At the far away end from the Z-line of actin filaments, the concentration of potassium ions in cytosol is lower than C_1 (See Position of "b"-

line at Fig. 3) and there will not occur any formation of actin-myosin bonds.

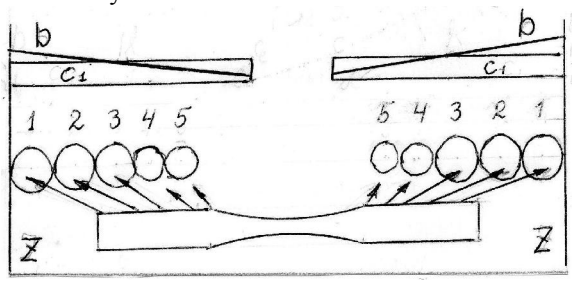

Fig. 3 The potassium pump would discharge the potassium ions into "cisterns"

Hereby the globule sizes of G-actin would decrease and would reach their initial value (the globules 4, 5 at Fig. 3). That process would move towards the Z-line as far as the potassium ions are removed from cytosol into the cisterns. At the sections of actin filaments being closer to the Z-line, where the concentration of potassium ions is higher than C_1, there would go on a recovery process of the bonds between actin and myosin previously destroyed by the ATF-hydrolysis heat (in the globules 1, 2, 3 at Fig. 3). Moreover, there would go on a spontaneous recovery of the hydration of those globules accompanied by the enlargement of globule actin sizes. Due to the fact that actin and myosin are not bounded yet, then the recovery of bonds would lead to the direction of sarcomere's wall (Z-line) to its initial position. After discharge of Ca^{2+}-ions into the «cisterns» the sarcomere and actin filaments would occupy their initial position. Such a pattern of "sliding" does not come into contradiction with the experimental results of Huxley [8], and it explains in what way the ATF-hydrolysis heat while weakening the actin hydration and decreasing the sizes of its globules, would be converted into mechanical energy of the sarcomere's contraction.

On the activity of non-striated muscles there depends functioning of the most important internal bodies. As distinguished from the skeletal muscles here there is not any need of a high rate of contractions, but their reliability and controllability. The cells of non-striated muscles are spindle-shaped, mononuclear and bonded with collagen. They position themselves parallel to each other and they form unbound muscular layers. Those cells contain actin and myosin filaments, however as distinguished from the skeletal muscles they are positioned not in a strictly orderly way, but diffusely. Instead of thick and thin fibrils they contain a large number of unbound actin filaments being positioned lengthwise the cell, and the myosin filaments are of minor thickness and smaller sizes than in the skeletal muscles being numerically insignificant [9, 11].

The controllability of contractions of non-striated muscles layers appears to be one of the major issues of organism's physiology. They are monitored by a set of miscellaneous signals, inclusive of impulses from the vegetative system as well as hormones. The reactions of cells in response to the activity of agonists of membranous receptive bodies have got as a rule 2 phases: a phase of quick contraction and a phase in the course of which there will be maintained a contracted condition (tonic contraction). The first phase is a short-term one and it would be caused by concentration increase of potassium ions in cytosol. However, the potassium ions would have an effect here not via a troponin-tropomyosin complex. As a condition for the formation of myosin-actin bonds there appears to be phosphorylation of one out of two myosin light chains (MLC) forming a part of each globule ("head") of myosin's molecules. The phosphorylation is catalyzed by an enzyme, i.e. by a myosin light chain kinase (MLCK). However, any kinase would become active only through its bonds with a Ca^{2+}-calmodulin complex. Consequently, any formation of myosin-actin bonds in non-striated (smooth) muscles during the first short phase of contraction would be under the control of Ca^{2+}-ions concentration, just as in the skeletal muscles [12].

The necessity for a long-run contraction would cause the second, i.e. tonic phase of non-striated (smooth) muscles contraction. Being weakened by the hydrolysis, the hydration of myosin globules («heads») would stop spontaneously if as it was mentioned already, the temperature would not exceed 42^0–43^0C. That would increase the globules volume and would reduce their contraction. There is a need for further phosphorylation of myosin light chains, and the formation of new myosin-actin bonds. There is a need for hydrolysis, the heat of which would anew dehydrate the myosin «heads» maintaining or even intensifying their contraction. The control actions over processes of a tonic phase are considered in details in the research study [12]. It is shown there that myosin phosphorylation under the conditions of concentration reduction of Ca^{2+}-ions is performed by enzymes, the activity of which does not depend on the potassium ions and is controlled by external signals via membranous receptive bodies. Those receptive bodies would activate protein kinases, the activity of which is directed to a level increase of myosin phosphorylation.

Summary statement

The major objective of the present research study was to focus attention of research scientists on the role of water molecules in cellular processes. In particular, on the changes in protein hydration as a

leading mechanism in cells' pulsations, in muscles' contraction and in advancement of nervous impulses. In this research study there has been advanced an idea to the effect that a mechanism of transition of the ATF-hydrolysis heat into its activity is implemented via the heat impact onto hydration, and consequently onto the size of protein molecules forming a cell cytoskeleton as well as on the size of myosin and actin globules during the activity of muscles. It can be assumed that the mechanisms being similar to those ones of cell's pulsation are of paramount importance during the motions of nervous impulses. The more in-depth study of a role of water molecules in cells, the comprehension of cells' pulsation mechanisms based on the changes in hydration, the activity of muscles, both cross-striated and non-striated (smooth) ones as well as the motions of nervous impulses will broaden the possibilities of practical medicine.

Conclusions

1. The suggested mechanism of heat transition into mechanical activity will facilitate our comprehension of cellular processes.

2. There should be paid more attention to the research studies, inclusive of experimental ones, to the role of water molecules in cells, in particular to the hydration of large cellular molecules, especially to the protein molecules and DNA-molecules.

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