EVOLUTIONARY ASPECTS OF THE GEL APPEARANCE AND ITS FUNCTIONS IN THE CELL CYTOPLASM

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Abstract. **A well-known phenomenon - the gel presence in the cytoplasm of animal cells in the light of evolution is considered. We also define the role of gel in evolution of the cell metabolism. We show how the gel emergence in the cytoplasm hade provided cells with intensification of their energy metabolism which is a general line of evolutionary development of the cellular world. We also show how cells use the gel structures to solve a number of vital tasks. Such tasks include the increasing in mechanical stability of cells, the formation of the transport structures from gel to transfer the active substances in the cytoplasm, the gel participation in cell dehydration regimes.**

Keywords: **cytoplasm, sol, gel, structured water, energy metabolism, cytoskeleton, gel channels, dehydration mechanisms**

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Contents

1. INTRODUCTION

The internal environment of a living cell - the protoplasm is the subject of intensive researches of modern cytophysiology. Still a century and a half ago Thomas H. Huxley, "Charles Darwin's bulldog" called protoplasm as the physical basis of life [1]. American cytologist Lewis V. Heilbrunn [2] argued that "if we are able to decipher the mysteries of life and mechanisms of vital activity, it is only through the study of protoplasm." The extra-nuclear part of the protoplasm is cytoplasm, its part without cell organelles and metabolites is cytosol. Cytoplasm and cytosol has not been studied sufficiently [3, 4]. The cytosol is a colloidal solution of proteins, enzymes, carbohydrates, lipids, low-molecular compounds (with a molecular weight of less than 300 Da and a linear dimension of not more than 1 nm [5]), inorganic salts in aqueous medium (with a pH between 5.0 and 7.4 [6]). Cytosol can be considered as a compartment bounded by the cytoplasmic membrane and contacted with the outer surface of all the intracellular organelles [7]. The distribution of ions between the cytosol and the surrounding environment is not symmetrical (K^+_{in}/K^+_{ex} = 139/4 mM, Na^+_{in}/ Na^+_{ex} = 12/145 mM, etc. [3]). The mechanism maintaining the cellular ion concentration gradient is also poorly understood [8].

The cytosol is mainly composed of water (approximately 70%) and proteins. The amount of proteins is high, close to 200 mg/ml, occupying about 30% of the cytosol volume [9-11]. At a high concentration of macromolecules in cytosol the water molecules can be bound to macromolecules [12, 13]. In this case two states of a colloidal solution are possible: an inviscid sol, or a viscous, gel-like gel.

Sol (from the Latin «solutio» – solution) is a highly dispersed colloidal solution with a liquid dispersion medium. The dispersed phase of organic substances and ions not bound in a spatial structure is distributed in the volume of this medium. The phase transition of sol to gel can occur during the coagulation and aggregation of the dispersed sol particles.

Gel (from the Latin «gelo» – solidifying) is a structured system of a three-dimensional macromolecular mesh (frame) filled with a low molecular solvent (water in the cell).

The mechanisms of the phase transitions «sol-gel» and «gel-sol» were considered in detail in the works of G. Ling [12] and J. Pollack [13]. It is necessary to have the large compounds with a threadlike periodic structure of the units that have an affinity for water and a sufficiently high concentration (non-globular proteins) to form a gel in an aqueous medium [12]. The gel formation is also possible in the solutions of globular proteins. However in this case their concentrations are required to be orders of magnitude higher than in the case of non-globular proteins. The change in cytosol parameters (for example, pH of an aqueous medium, temperature, penetration of biologically active agents, etc.) can cause the transformation of globular protein into non-globular protein with the gel structures formation. Under certain conditions this transformation can be reversible (**Fig. 1**).

In some cases the colloidal solution of the cell proteins is in the state of the constant first-order phase transitions «sol-gel» and «gel-sol» [14]. These transitions are nonlinear oscillations

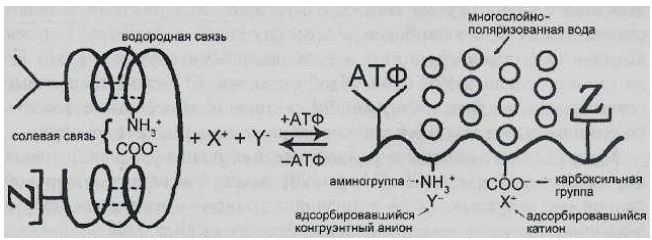

Fig. 1. *Scheme of phase transitions sol-gel* [12].

with a constantly changing varying period. The range of periodicity or rhythms of these phase transitions ranges from 10^{-10} seconds to several seconds, minutes, hours, days and more.

Despite the intensive researches in this field [15-19] the evolutionary aspect in them remains, for the time being, without due attention. This aspect is the main subject of research in this work.

2. EVOLUTIONARY ASPECTS OF GEL APPEARANCE IN THE CELL CYTOPLASM

The first stable isolated sources of free energy on Earth were the hydrocarbon aerosol nanodroplets with an open metabolism. At the final stage of abiogenesis these aerosol nanodroplets passed from the anoxic near-surface atmosphere into the aqueous medium of the primary hydrosphere of the cooling planet. The lipids and archaic enzymes from the nanodroplet surface were formed into lipid vesicles. The lipid vesicles included an aqueous solution of the carbon-containing compounds, archaic enzymes, viruses and nucleotides with the mechanisms of the anaerobic metabolism inherited from hydrocarbon droplets [20, 21]. Anaerobic assimilation of glucose from the surrounding aqueous medium proved to be a sufficient energy basis for the metabolic activity of the vesicles up to mitosis. A physical factor which is the leading factor in the changes of the vesicles metabolic regimes (activity and mitosis) was revealed in works [22-24]. It is the acidity changes in internal environment of the vesicles. This factor determines the order of the metabolic regimes changes. The maximum possible power of the metabolic processes groups that competed for the macroergic molecules in

vesicles was achieved by breeding in time of the action of these groups. Natural acidification of the internal environment during the utilization of the energy-intensive substrates contributed to proteins synthesis. The subsequent alkalization of the internal environment promoted the macroergic molecules synthesis. The cyclicity of the change in the acidity value began to determine the cyclicity of metabolic processes in the vesicles. This cyclicity made possible the existence of two states of the vesicles internal medium. These states are sol and gel. Also, the cyclicity made possible the dynamically phase transitions both the entire cytoplasm and its individual parts.

Appearance of the first protozoan cells-anaerobes, chromosomal and non-nuclear prokaryotes became the natural end of such development [24, 25]. Formation of photosynthesis based metabolism in some vesicles and subsequently cells ensured the gradual accumulation of oxygen in atmosphere. When the oxygen partial pressure in atmosphere reached 2 mm Hg, the archaic prokaryotes with complex metabolism including photosynthesis and utilization of the energy-intensive substrates by anaerobic and aerobic means had supplanted almost all other vesicles and had given rise to formation and development of the eukaryotic cells [24].

The colloid structures of the eukaryotes and prokaryotes compartments were involved in the cell metabolism kinetics through the phase transitions «sol-gel». The generation of energy over a wide range of the spectrum of electromagnetic and acoustic oscillations is observed in such transitions [26-28]. The oscillations had an extremely weak intensity and were registered against the background of thermal noise [29, 30]. Gel of some cell compartments can absorb the energy of the signals generated when sol of the adjacent cell compartments passes to gel. In this case gel of some compartments is converted to sol. The superweak interactions that determine these processes are now the subject of intensive researches [31]. The first and second order phase transitions are determined by the degree of rhythms synchronization of the «sol-gel» transitions between the adjacent cell compartments and by the matching rhythms of different periods.

The gel appearance in the cell cytosol was an important factor in optimization of the metabolic processes in cellular structures in the course of evolutionary transformations.

3. GEL AS A MEANS OF INTENSIFICATION OF THE CELLS ENERGETIC METABOLISM

Electric field growth in cytomembrane in the course of evolutionary transformations had become one of the important factors that provided a steady increase in the concentration of the biologically active substances in the cell cytoplasm and consequently the intensification of their energy metabolism [32]. The same, no less important factor which nature used for the same purpose was the gel.

We consider the energy metabolism as the leading type of the cell metabolism. Also we consider the steady intensification of the energy metabolism as the general line of the evolutionary development of the cellular world from the very beginning of its inception. Consider the role of the changes in the protein-ion-water complex in cytosol in this evolutionary process. There were no conditions for gel formation in the cytoplasm of the lipid vesicles and the first cells due to the underdeveloped energy metabolism at the initial stages of the pro-cellular structures nucleation. The significant energy consumption is required for the organization of the aqueous colloidal solutions that can be converted to gel when the necessary protein concentration is achieved. Note that solutions of the globular proteins are converted to gel at the incomparably higher concentrations than the nonglobular (filamentous) proteins. In the early stages of the cellular world development the globular proteins were the main catalysts of the metabolic processes in cytoplasm. Due

to denaturation under the peptidases action the structure of some globular proteins became ribbon structure which is characteristic of the modern nonglobular proteins. It is possible that such compounds became the primary basis for the formation of a peptide cytoskeleton network near the cytoplasm. This significantly increased the cells survival when they were affected by shear currents in the surrounding aquatic environment. The amount of these denatured ribbon proteins increased as the metabolism intensified and the rate of the peptidase activity increased. As a result, the prerequisites were formed for the formation of the volume structures from gel directly in cytosol and for the appearance of the separate compartments from gel. The ribbon proteins having an affinity for gel are included in these compartments. The globular proteins having hydrophilic and hydrophobic regions on their surface do not possess such an affinity for gel. This is because their form does not allow structure the water molecules at the level of the individual amino acids to the same extent as the ribbon proteins.

The gel structures growth in cytosol leads to a decrease of the free water proportion in it at a constant cell volume. The concentration of the globular proteins that are involved in energy metabolism accordingly increases. In turn the intensity of the energy metabolism significantly increases.

Thus the gel appearance in the cytosol was one of the means for intensifying of the energy metabolism in cells. This accelerated all the evolutionary processes.

4. THE ROLE OF GEL IN CYTOSKELETON EVOLUTION

The cytoskeleton in our opinion is the evolutionarily earliest gel structure in cells. The prerequisites for its appearance in cytosol of the first cells were the following factors. Firstly it was the activity of peptidases that disrupt the globular structure of proteins. Secondly it was the ability of enzymes to interact with the lipids of the inner membrane layer up to the incorporation of proteins into their structures. The evolutionary chain in this case can be constructed as follows. The proteins and their complexes that were embedded in membrane lipids formed the basis for the cytoskeleton formation. Parts of the proteins that protruded from lipids to the cytosol under the denaturing effect of peptidases gave rise to the formation of the cytoskeleton. This relates both to the basis of the cytoskeleton – its threadlike protein structures, and the protein bridges that distal them from the membrane lipids. The types of forces acting between the threadlike proteins in cytosol are Coulomb forces, van der Waals forces and other. These types of forces determined the interactions of such compounds and the ordering of their mutual arrangement near the membrane. The non-globular denatured proteins effectively structured the water molecules at the amino acid level. Therefore these proteins provided the conditions for gel formation by retaining of the several layers of bound water around the protein filaments. The protein stores grew in cells as evolutionary development which was characterized by a steady intensification of energy metabolism. This also applies to non-globular proteins. Their critical concentration corresponding to a transition to gel was realized first of all in the areas near membrane. Therefore the archaic cytoskeleton was formed just near the membrane over its entire area. The cytoskeleton was distanced from membrane and did not interfere with the cells transmembrane exchange with the surrounding aqueous medium, either by substrates of the cellular metabolism or by the water molecules. The appearance of the cytoskeleton significantly increased the cells survival. The cytoskeleton provided the cells with greater resistance to the damaging effects of shear currents in the surrounding aquatic environment.

We emphasize that the cytoskeleton, like any cellular structure, maintains the constancy of its composition and shape in the duct continuously

destroying and creating again its constituent elements. The rates of replacement of these elements can be very different in different areas of the cell. The uncompensated rates of growth and destruction of the skeletal network can be observed at the cell level when its metabolism regimes change. So in the phase of cell division during mitosis the cytoskeleton is completely destroyed and restored in each of the two individuals after the completion of mitotic activity. The growth rate of the cytoskeleton network is also dominated during the cell growth. Regional dominance of one of these rates can be compensated by the opposite dominance in another region of the cytoskeleton.

5. GEL TRANSPORT STRUCTURES IN CYTOPLASM

A characteristic feature of the eukaryotic cell cytoplasm is the constant movement of the cytoplasm inside the cell (cyclosis). This process is accompanied by the movement of substances and organelles. Transport of substances in the cytoplasm is realized through the endoplasmic reticulum. The endoplasmic reticulum is a system of the long branching tubules that penetrate the cytoplasm. The continuous cavities, through which the substances travel to different compartments of the cell, ensure the delivery of substances to the places of their most effective use in different metabolic processes. The participation of the cytoskeleton in such transport is presented in the work [33]. The substances are transported through their interactions with motor proteins and carrier proteins. The action of another most evolutionarily early of transport mechanism of the substances and even individual cellular structures was suggested in the previous chapter.

The special channels formed by the gel structures carry out such transport efficiently, with minimal losses [12, 13, 15]. The channel in the helium mass obtained in the experiment of T. Khirai [16] is schematically shown in **Fig. 2** (the picture is taken from the book of J. Pollack [15]). The channel is surrounded by a layer of structured water. The sol with large particles

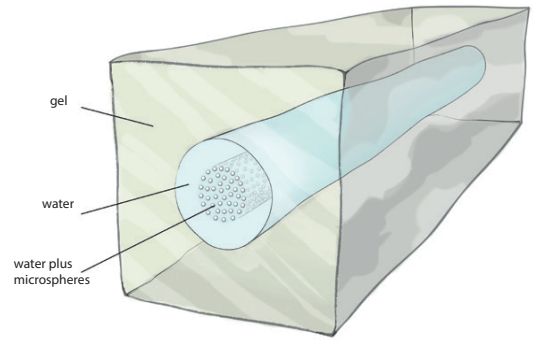

Fig. 2. *The helium channel in the cell cytoplasm (scheme)* [15].

and microspheres containing metabolites moves within the channel. Such channels provide the effective transfer of the biologically active substances in cells by water flows from the sites of their synthesis to the cytoplasm regions where the substances perform their functions most efficiently. However the directed transport of substances within cell cannot be explained only by simple diffusion and Brownian motion of large particles and microspheres. To form flows in the channel from gel it is sufficient to create a difference in the hydrostatic pressure at its inlet and outlet in an aqueous medium. Such channels can work only if their end structures are located near the cytomebrane in places where there is a local imbalance of water flows from the cell to the outside and, conversely, from the outside into the cell. This imbalance in water flows can be associated with an increase in the synthesis of substances in the regions near the membrane. This imbalance causes a local increase in the osmolarity of the aquatic environment. This can disrupt the balance of water flows through the membrane with dominance of the water flows entering the cell.

On the other hand a balance shift of the water flows can be caused by a change in the electric field strength in lipids of the membrane in its separate regions (Charakhchyan effect [32]). The flux entering the cell will predominate when the electric field is weakened. As an example, it happens when the large organic molecules are associated with a membrane. The reverse situation can occur in other membrane regions which are free of the molecules associates. The

electric field in lipids of such membrane regions is much higher than in the membrane regions with the associated coarse molecules. In this case the water flow from the cell outwards will predominate. As a consequence there was an opportunity to implement the conditions when water is «pumped» into the cytoplasm in some membrane regions and water is «pumped out» of the cytoplasm in other membrane regions that sometimes are very far from the first. It is this phenomenon that allows the use of gel structures to form the transport channels for water flows [15, 33].

6. GEL AS A MEANS OF THE CYTOPLASMIC DEHYDRATION

Special channels formed gel structure, work The mechanisms of the cytoplasmic dehydration arose on the basis of the above-mentioned effects. Emergence of the spore formation regime which was based on this effect provided the unicellular organisms survival during the periods of drought. Multicellular plants use this effect in the formation of the seeds and embryos. The effect of dehydration and filling of the skin cells with gel takes place both in the formation of a silver layer of human skin in normal state and in development of the pathologies such as psoriasis and eczema.

7. CONCLUSION

A possible variant of the division of the first pro-cellular formations cytosol (the lipid vesicles in the primary hydrosphere of the planet) into two phases (sol and gel) is considered in the work. This division was a decisive factor in the optimization of all metabolic processes in the nascent cellular structures. We showed the formation of the evolutionary transformations mechanisms with the participation of the sol-gel structures which provided the cells with following the general line of the evolutionary development of the living systems – the steady intensification of their energy metabolism. The principles and useful consequences of the operation of such mechanisms were identified. The role of gel in the formation and functioning of the cytoskeleton, as well as in the formation of the optimal structures for the metabolites transport was shown. The possibilities of the gel structures using for temporary stop of the cell metabolism under conditions unfavorable for their vital activity were indicated.

The analysis carried out covers a huge period of time. This period includes the time from the first gel structures appearance in the pro-cellular formations and up to the moment of the evolutionary development and the formation of a eukaryotes world. This analysis is schematic to a certain extent. It has more the staging character. But this does not diminish its significance. The main result of the work is the identification of the main function of the evolutionarily early gel structure. This function is the optimization and intensification of the energy cell metabolism.

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