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TO COMPUTER MODEL FOR SOME BIOLOGICAL HYPOTHESIS

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Abstract. In the present article the photoisomerization process of retinal molecule of rhodopsin is studied. For this aim the method of computer modeling for study the mechanism of photoisomerization process and the nature of forces causing the process of isomerization has been used. he primary act in this process is the isomerization of 11-cis-retinal to all-trans form, which has the same chemical structure as the cis-form, but a different physical structure - a straight, not bent molecule. After absorption of light energy rhodopsin begins to disintegrate. Since the orientation of the reactive sites of trans-retinal no longer fits in with the orientation of the protein reactive sites of opsin, this form of retinal begins to separate from opsin. Finally, the Schiff base is hydrolysed and trans-retinal is released into the cytoplasmic environment.

Keywords and phrases: Photoreceptors, retinal forms.

AMS subject classification: 97M50, 97M70.

Introduction. The human eye contains two types of light-sensitive cells (photoreceptors): highly sensitive rods are responsible for night vision, and less sensitive cones are responsible for color vision. Rhodopsin - a light-sensitive pigment (chromoprotein). The rods of the eye retina of marine invertebrates, fishes, almost all terrestrial vertebrates and man contain the rhodopsin (approximately 40%). Rhodopsin - the main visual pigment responsible for the color of the retina and the perception of electromagnetic radiation in "visible range", underlying in vision process.

Rhodopsin consists of two components. The part that absorbs visible light is called a chromophore - retinal (aldehyde of retinol (vitamin A)), and the protein of the visual pigments, which are bound to retinal, called opsin. The 11-cis-retinal forms the Schiff base linkage with a lysine residue of the seventh helix of opsin (Lys-296 in the case of bovine rhodopsin), and the Schiff base is protonated, which is stabilized by a negatively charged carboxylate (Glu-113 in the case of bovine rhodopsin). The β-ionone ring of the retinal is coupled whith hydrophobic region of opsin through hydrophobic interactions. Thus, the retinal chromophore is fixed in the retinal binding pocket of rhodopsin by three kinds of chemical bonds: covalent bond, hydrogen bond and hydrophobic interaction [1].

The mammalian rhodopsin structure is similar to bacteriorhodopsin - the membrane proteins of Archaea. Like animal visual pigments, these contain a retinal chromophore (although it is all-trans, rather than 11-cis form) and have seven transmembrane alpha helices. The halophilic archaea has the ability to carry out extremely non-chlorophyll type of photosynthesis. Bacteriorhodopsin carries proton transfer across the plasma membrane.

Opsin does not absorb visible light, but when it is bonded with 11-cis-retinal to form rhodopsin, the new molecule has a very broad absorption band in the visible

region of the spectrum. The peak of the absorption is around 500 nm, which matches the output of the sun closely. When a photon of light falls onto rhodopsin, the molecule absorbs the energy and the cis-double-bond between C-11 and C-12 in the retinal is temporarily converted into a single bond [2].

Note how the shape of the molecule changes as a result of this isomerization. The molecule changes from an overall bent structure to one that is more or less linear. All of this is the result of trigonal planar bonding (120^o bond angles) about the double bonds.

The double bond then reforms and locks the molecule back into position in a trans configuration of the all-trans-retinal. This isomerization occurs in a few picoseconds or less. Energy from light is crucial for this isomerization process: absorption of a photon leads to breaking the double bond and consequent isomerization about half the time (in the dark is almost never happens).

After absorption of light energy rhodopsin begins to disintegrate. Since the orientation of the reactive sites of all-trans-retinal no longer fits in with the orientation of the protein reactive sites of opsin, this form of retinal begins to separate from opsin. Finally, the Schiff base is hydrolysed and all-trans-retinal is released into the cytoplasmic environment. Changes in the spectral characteristics of the rhodopsin, following the absorption of a photon are explained by the conformational rearrangements induced by retinal isomerization. In vertebrates photolysis ends with separation chromophore from the protein (opsin) and output of retinal [3].

Computer method. A computer simulation, a computer model or a computational model, is a computer program, run on a single computer, or a network of computers, that attempts to simulate an abstract model of a particular system. Computer simulations have become a useful part of mathematical modeling of many natural systems in physics (computational physics), astrophysics, chemistry and biology, human systems in economics, psychology, social science, and engineering. Simulation of a system is represented as the running of the system's model. It can be used to explore and gain new insights into new technology, and to estimate the performance of systems too complex for analytical solutions.

Computer simulation is an effective method for the study of complex systems. Computer models easier and more convenient to study because of their ability to carry out so-called computational experiments, in those cases when the real experiments are difficult because of financial or physical barriers, or may give unpredictable results. Logic and formalization of computer models allows to identify the main factors that determine the properties of the original object being studied (or a class of objects), in particular, to investigate the response of a simulated physical system to change its parameters and initial conditions. Computer modeling concludes to conduct a series of computational experiments on the computer, the purpose of which is analysis, interpretation and comparison of results with the actual behavior of the object under study and, if necessary, a subsequent improvement of the model, etc.

To date, the methods of quantum chemistry and molecular dynamics are widely used in numerical modeling of electron and atomic structures of complex systems of molecular, crystalline and transitional (nano) size. This is due to the technological

development of appropriate mathematical software. Now the world has a rather lot of modern computing systems that implement the methods of quantum chemistry and molecular dynamics, however, for a wide range of users more accessible use of these methods is provided by the well-known quantum-chemical and molecular dynamic program HyperChem. It includes all the components of structure, thermodynamics, spectra, and kinetics [4].

Semi-empirical methods solve the Schredinger equation for atoms and molecules with the use of certain approximations and simplifications.

$$i\hbar\frac{\partial\Psi}{\partial t} = \widehat{H}\Psi.$$

All the methods of this group are characterized by the following: the calculation is only for the valence electrons; values of the integrals of certain interactions are neglected; the standard non-optimized basis functions of the electronic orbitals and uses some of the parameters obtained in the experiment are using.

Discussion. The method of computer modeling has been used for study the mechanism of photoisomerization process of retinal and the nature of forces causing the process of isomerization. For this aim HyperChem program was used [5].

As is known, the absorption of a photon by rhodopsin leads to a number of its photochemical transformations - photolysis. The primary act in this process is the isomerization of 11-cis-retinal to all-trans form, which has the same chemical structure as the cis-form, but a different physical structure - a straight, not bent molecule

This photochemical reaction is best understood in terms of molecular orbitals, orbital energy, and electron excitation. The absorption of a photon leads to the weakening of bonds in the retinal molecule. In cis-retinal, absorption of a photon promotes a p electron in the pi bond to a higher-energy orbital. This excitation "breaks" the pi component of the double bond between C11 and C12 and is temporarily converted into a single bond. This means the molecule can now rotate around this single bond, which it does by swiveling through 180^o.

The double bond then reforms and locks the molecule back into position in a trans configuration. Thus the light isomerizes the molecule from cis to trans, and as it did so, it changed the shape of the retinal from curved to straight. Essentially, the energy in a photon has been converted into atomic motion.

It can be concluded that under the light action in retinal potential barrier around the torsional vibrations of the bond C11 - C12 is reduced, so the repulsive force and the rotative moment between the atoms of the methyl groups C5 and C13 under the exposed light may cause rotation of the caudal fragment atoms of retinal molecule around C11 - C12 bond, which causes the molecule to straighten the bend with rotation that corresponds the isomerization of retinal chromophore (Fig.1) [6,7].

Because, in the cis-retinal, the hydrogens are on the same side of the double bond; in the trans-retinal, the hydrogens are on opposite sides of the double bond. In fact, all of the double bonds are in the trans-configuration in this isomer: the hydrogens, or hydrogen and -CH3, are always on opposite sides of the double bonds (hence, the name "all-trans-retinal").

Whereas the 11-cis-retinal fitted into the opsin binding site perfectly, all-trans-retinal is the wrong shape. The Schiff base linkage becomes unstable, and the molecule undergoes a series of shape changes to try and better fit the binding site, before eventually breaking free of the opsin altogether.

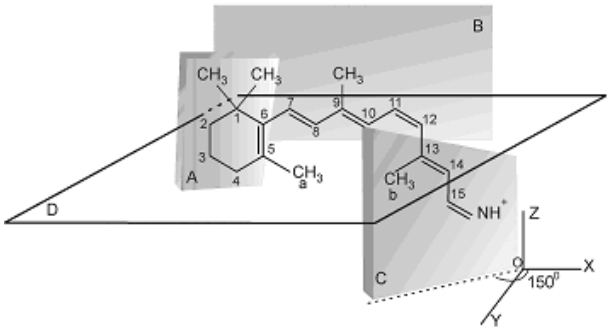

Fig. 1. The spatial configuration of 11-cis-retinl

The experiment showed that the absorption of a photon leads the electron density distribution along to the retinal molecule including Schiff base and opposite β-ionone ring (Fig.2). The β-ionone ring of the retinal at light action acquires a magnetic dipole moment under the action of which in the imidazole ring of histidine of the environment (opsin) located in the active center of rhodopsin the magnetic moment is induced. The mutual repulsion between them contributes to the dissipation of rhodopsin to trans-retinal and opsin. As a result of this interaction leads to the ejection of retinal out. We can assume that this leads to the release of a conjugated with rhodopsin ion channel channel in the cell membrane. The photolytic decomposition of rhodopsin causes the excitation of the visual nerve due to changes in ion transport in the photoreceptor.

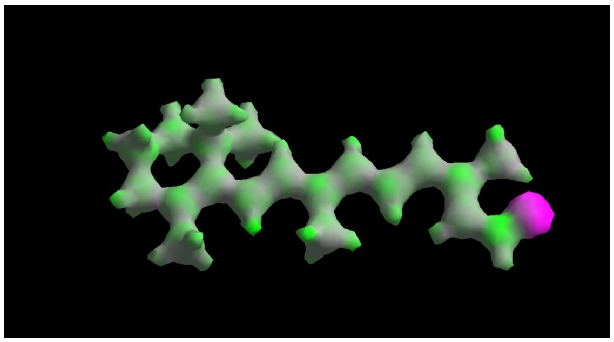

Fig. 2. Charge distribution in all-trans-retinal

"Strained" conformation of isomerized chromophore transforms its energy into further conformational changes of rhodopsin. These rapid movements of the retinal are transferred to the protein and from there into the lipid membrane and nerve cells to which it is attached. This generates nerve impulses which travel along the optic nerve to the brain, and we perceive them as visual signals - vision. The free all-trans-retinal is then converted back into the cis form by a series of enzyme-catalysed reactions, whereupon is reattaches to another opsin ready for the next photon to begin the process again.

Further research of rhodopsin has not only fundamental importance; it can be used for treating or preventing biochemical disorders of vision. Rhodopsin participates in vision process and in the transformation of light quantum of nerve impulses. The study of their structure and, most importantly, the mechanism of interaction with ligands, may open new possibilities for the design of new drugs efficient and secure. Computer technology and other methods will be of great use to determine the mechanism of the photoisomerization process of retinal in the field of nanotechnology.

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