Biophysical Reviews (2023) 15:1425–1861
https://doi.org/10.1007/s12551-023-01150-w

ABSTRACT

The 7th Congress of Biophysicists of Russia - conference proceedings

Abstracts

Published online: 11 October 2023

S1. Molecular biophysics. Structure and dynamics of biopolymers and biomacromolecular systems

S1.1. Molecular dynamics of α-helical poly-l-glutamic acid in water solution

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α-Helix is a basic element of secondary structure from which the globular proteins are built. Since true native protein exists in water solution the structural behavior of protein is determined essentially by their dynamic properties. However, the problem is rather complicated because a majority of protein structures has been obtained in the crystal state. Here we have studied the dynamic properties of poly-L-glutamic acid model in a helical conformation in water solution. It includes 16 Glu residues placed in 4.5 turns of right-handed α-helix structure built with the data of Pauling & Corey (1951). In acidic water solution at pH about 3.5 poly-L-glutamic acid undergoes the helical conformation. Thus, our model has non-ionized side carbonyl Glu groups, as COOH, and ionized terminal groups, as NH3+ and COO-. An analysis of all the atomic groups makes no special sense. So, we have concentrated solely on dynamic study of peptide skeleton from Cα-atoms. Computational system included helical fragment, water solution molecules, and ions of sodium and chlorine. There were introduced 11 Na and 9 Cl ions which supply zero total charge of the sysytem. Numerical simulations were performed on the hybrid supercomputing system K-60 at the Keldysh Institute of Applied Mathematics, Russian Academy of Sciences. The initial part of trajectories, from 0 to 500 psec, corresponds to the refinement and relaxation of the model. A dynamic trajectory of α-helical poly-L-glutamic acid has been calculated from 0.0 to 25.0 nsec. We have inspected fluctuations of the Cα-chain at each integer numbers of time, in nanoseconds. That has been done by calculating the absolute shift values of Cα-atom positions at the next 1.0 nanosec intervals. The model has displayed several fluctuation modes along the dynamic trajectory. The most interesting modes show the distinctive shifts of Cα-atoms. These modes include two adjacent in the turns clusters of Cα-atoms which are placed approximately at one side of the helix. The observed modes are intrinsically dynamic feature of a single fragment of α-helix structure. And they suggest playing a key role in dynamics of protein molecules.

S1.2. Multiscale modelling of DNA repair by photoenzymes

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Photolyase photoenzymes, binding to damaged DNA sites, repair the main DNA photoproducts formed under the action of UV radiation. The functioning of photolyases is based on the reaction of photoinduced intermolecular electron transfer. Especially interesting from the point of view of the chemical mechanism is (6-4) photolyase, which repairs the most cytotoxic (6-4) pyrimidine-pyrimidone photoproducts of DNA. Despite the extensive study of the (6-4) photolyase mechanism using the high-end experimental and computational methods, the chemical details of the repair reaction have not been definitively established. Multiscale modeling, combining classical molecular dynamics and quantum chemical calculations of photoexcited states and reaction coordinate, is able to resolve some of the contradictions existing today in understanding the (6-4) photolyase mechanism.
The present study considers the main stages of the (6-4) photoprodroduct repair by (6-4) photolyase including photoinduced electron transfer leading to the formation of a photoprodroduct radical, breaking and formation of covalent bonds in the photoprodroduct radical and back electron transfer. Using density functional theory calculations, optimized geometries were obtained for modeling the repair reaction involving various forms of the critically important amino acid residue His365, whose role in the repair has been extensively discussed in the literature. In the case of neutral His365, the photoproduct radical rearranges by the OH-group transfer, for which the enzyme reduces the reaction energy barrier. In the presence of protonated His365, electron transfer coupled to proton transfer takes place leading to the formation of a protonated (neutral) photoproduct radical. In order for the repair reaction to proceed along this path, it is necessary to adjust electron affinity of the photoproduct. Estimates of the effect of the macromolecular environment on electronic energies were carried by computing excited electronic states for structures comprising the repair rection coordinate using the multiconfiguration quantum chemical method XMCQDPT2-CASSCF. Within the framework of these calculations, the electronic coupling matrix elements were also evaluated. The influence of the macromolecular environment on electron transfer energies was evaluated using classical molecular dynamics. To assess the electron transfer reaction rate, the results of the quantum chemical and molecular dynamics calculations were combined. The estimated electron-transfer rates indicated that the rapid recombination of the radical pair takes place in the presence of neutral His365. The presence of protonated His365, acting as a proton donor for the photoproduct radical, may substantially slow down back electron transfer. Thus, the

Changes caused by severe hypoxia in all mitochondrial subpopulations of both LR and HR animals were comparable to the effects of previous hypoxic regimens. Organelle shape, matrix density, crista packing and inter-crista space did not significantly change. Nevertheless, the total number of both SSM and PNM increased compared to the control in the LR group, and did not change in HR rats.
Thus, the translocation and rearrangement of mitochondria under the sarcolemmal and nuclear membranes, observed at some exposures, can be considered as an adaptive, compensatory adaptive, reaction of the cell's mitochondrial apparatus to changes in the physiological state of the organism as a whole. Emergence of micro-mitochondria, which are considered to be precursors of small mitochondria, is also attributed to adaptation processes. Adaptation processes occurred in both animal phenotypes, but were more pronounced in LR animals. This is consistent with our earlier obtained data that hypoxic training leads to a significantly greater increase of lifetime in extreme hypoxia (3% O2) in LR than HR animals. Taking into account all the data obtained, a 12-day exposure to a 30–60 min hypoxia of moderate severity can be recommended for the treatment of patients in an altitude chamber, since optimal conditions for the adaptation of animals to hypoxia develop within this period.
The work was supported by a Russian Science Foundation grant No. 23-25-00441.

S2.210. Why opening-closing of two adjacent coupled gramicidin A channels in the lipid membrane synchronous?

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The pentadecapeptide gramicidin A (gA) is known to form an ion channel via head-to-head transmembrane association of two monomers. Earlier, dimers of synthetic gA analogues, with monomers either covalently linked [1,2] or connected via the binding of their biotin tags to the same avidin or streptavidin molecule [3] were studied. The conductance of these channels was found to be approximately twice the conductance of a single channel. The dual channels were long-lived, with the lifetime (minutes) being approximately one or two orders of magnitude longer than the lifetime of the original channel (several seconds, depending on the conditions), which was explained by the cooperative influence of neighboring, i.e., adjacent channels, on the elastic deformation of the lipid bilayer [1-4].
However, another property, namely, the synchronous switching on and off of doublechannels formed as a result of the interaction of two single gramicidin channels, was not fully understood. The current through the membrane was measured with a time resolution of about 1 ms. With such accuracy it can be said that double-conductance channels are formed simultaneously without a visible intermediate step. More precisely, such steps were sometimes observed [1-3], however, in 40% of events, the acts of opening-closing of double channels were simultaneous. Here, we used the ideas of the theory of excitons to hypothesize on a possible reason for such synchronization. We assume that the synchronization of the two channels is due to the existence of common vibrational modes associated with conformational mobility in these two closely spaced channels. To make it more clear, we are talking about the analogy with two harmonic oscillators with a strong coupling between them. We consider a model in which two conducting channels can interact with a conformational mode, which creates coupling between them and thus promotes their mixing. If we assume that the coupling constant depends on a slowly changing conformational coordinate, then we can explain (1) the synchronous switching on of the two channels; (2) the long-lived nature of the double-conductance state; (3) the formation of short-lived states with single conductance before the opening of the double channel; and (4) closing of the double channel via the same short-lived single states.
It can be proposed that the phenomenon of synchronous channel opening could take place not only with gA analogues, but also with some other channel-forming peptides, such as alamethicin and syringomycin, which are known for their ability to form channels of minimal conductance along with large (high-conductance) channels [5,6]. It is generally accepted that the conductance of the large channels is higher because of the involvement of an increased number of peptide monomers in the formation of the channel wall [5], thereby suggesting an increase in the internal pore dimensions. However, evaluation of the channel dimensions from water-soluble polymer exclusion revealed almost the same pore size for small and large channels of both alamethicin [7] and syringomycin [6]. These data could be explained by simultaneous opening of a number of single channels forming a cluster, similar to gA dual channels. It can be assumed that strong coupling of alamethicin single channels of minimal conductance with neighbouring ones leads to formation of collective open states, which may have different conductances depending on the number of single channels involved in the cluster.
1. R.L. Goforth et al., J. Gen. Physiol. 121 (2003) 477-493.
2. L. Al Momani et al., Biochem. Biophys. Res. Commun. 328 (2005) 342-347.
3. T.I. Rokitskaya et al., J. Gen. Physiol. 121 (2003) 463–476.
4. M.B. Partenskii, et al., J. Phys. Chem. 118 (2003) 10306-10311.
5. R. Latorre & O. Alvarez, Physiol. Rev. 61 (1981) 77-150.
6. Y.A. Kaulin, et al., Biophys. J. 74 (1998) 2918-2925.
7. S.M. Bezrukov & I. Vodyanoy, Biophys. J. 64 (1993) 16-25.

S2.211. α1-Adrenergic Receptors play a role in the electrical activity of the rats' heart

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Adrenoceptors have played a crucial role in the history of pharmacology. They were essential parts of the work that led to the Nobel Prize in Physiology or Medicine in 1988 and 1994 and the Nobel Prize in Chemistry in 2012. These prizes highlighted the roles adrenoceptors have played in our understanding of how GPCRs work and in the evolution of rational drug discovery. The almost ubiquitous expression of adrenoceptors and their pleiotropic responses has led to successful drugs for a myriad of diseases. In our research, we aimed to study the effect of the α1-adrenergic receptor agonist methoxamine (10-7 M) on the myocardial electrical activity of adult rats.
The study was carried out on adult rats (n=7), using the microelectrode technique. A preparation of atrial myocardium with preserved sinus node and spontaneous activity was prepared. Methoxamine was immersed in a particular solution "Tyrode". The results were processed using the Elph 3.0 program. The samples were tested for normal distribution. Statistical processing was carried out using paired Student's t-test. We examined the effects of the α1-adrenergic receptor agonist methoxamine at a concentration of 10-7M.
Methoxamine at a concentration of 10-7M decreases the area under the curve of the peak, and also the action potential duration at the level of 20% (APD 20%), 50% (APD 50%) and 90% (APD 90%) of repolarization ($p < 0.05$), while there was no changing in the duration of depolarization phase. Also, the values of the amplitude of the action potential, membrane potential and overshoot did not change. Methoxamine at a concentration of 10-7 M in adult rats caused an increase in the frequency of action potential.
Thus, it was found that stimulation of α1-adrenergic receptors affects the electrical activity of the heart of adult rats, by changing the duration of repolarization. This paper has been supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030).