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

Chirgadze Yu.N.[1], Likhachev I.V.[2], Balabaev N.K.[2], Brazhnikov E.V.[1]*
[1]*Institute of Protein Research of RAS, Pushchino, Russia;*
[2]*Institute of Mathematical Problems of Biology, Branch of Keldysh Institute of Applied Mathematics, Russian Academy of Sciences, Pushchino, Russia ;*
* tefg@vega.protres.ru

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

Domratcheva T.[1]*
[1]*MV Lomonosov Moscow State University;*
* t.domratcheva@lcc.chem.msu.ru

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

S9.624. Evaluation of locomotor activity induced by transcutaneous electrical spinal cord stimulation in patients with spinal cord injury

Militskova A.D.[1]*, Mukhametova E.R.[1], Yakovleva E.I.[1], Andrianov V.V.[1], Lavrov I.A.[1]
[1]*Kazan Federal University, Institute of fundumental medicine and biology, laboratory of Neuromodulation;*
* mamashotmilktea@gmail.com

The high prevalence of CNS pathologies caused by injuries and diseases of the spinal cord requires the development of new approaches of motor function rehabilitation. The method of the spinal cord electrical stimulation is one of the most promising in experimental and clinical practice, which makes available study the functions of various body systems. One of the recent years breakthrough is the identification of certain spinal cord areas, which electrical stimulation activates involuntary and voluntary movement in the lower extremities. There are two main methods of spinal cord stimulation to control locomotion – invasive stimulation using electrodes located on the dorsal surface of the brain (epidural stimulation) and non-invasive, when the electrodes are placed on the surface of the skin (transcutaneous electrical spinal cord stimulation (tSCS). Evaluation of the effectiveness of the electrical stimulation technique for inducing step-like movements with varying degrees of spinal cord injury arises interest.

The aim of this study was to evaluate the effects of transcutaneous electrical spinal cord stimulation on changes in motor activity parameters in patients with spinal cord injury (SCI).

The study involved 15 subjects (3 women and 12 men) with SCI at the level of C4-C5 and Th3-L2 vertebrae, with injury assessed on the AIS scale (American Spinal Cord Injury Association Impairment Scale), as A, B and C. Assessment of locomotor activity in subjects with SCI was carried out in the body weight unloading system (Redcord, Norway) in the supine position. tSCS was performed using two gel electrodes (24 mm) at the level of Th11-Th12 and Th12-L1 vertebrae. The stimulation frequency was 35 Hz, the stimulus intensity varied in the range from 20 to 115 mA. To register range of leg movements, a Vicon motion capture system (Nexus, UK) was used. Range of movements in the joints was calculated from the position of light-reflecting sensors located on the anatomical landmarks of the trunk and lower extremities along the axes of movement in the hip, knee, and ankle joints. The assessment of locomotor activity was carried out when the subjects attempted to perform stepping-like movements both without stimulation and during tSCS.

The assessment of locomotor activity caused by tSCS showed that the range of motion in the joints depends on the degree and level of spinal cord injury. Thus, in the case of incomplete SCI, locomotor activity in the lower extremities was initiated much more easily. In the group of subjects with SCI at the level of C4-5 vertebrae, there was a significant increase in angular movements in the hip, knee and ankle joints ($p \leq 0.05$). In the group of subjects with SCI at the level of Th3-Th9 vertebrae, a significant increase of range of movements was observed in the knee and ankle joints ($p \leq 0.05$). Similar stimulation in the group of subjects with SCI at the level of Th10-L2 vertebrae led to a significant increase in the values of range of movements only in the ankle joint ($p \leq 0.05$).

Thus, the observed effects of tSCS allows to increase the effectiveness of rehabilitation and opens up good prospects for the use of non-invasive transcutaneous stimulation in routine clinical practice for various groups of patients with spinal pathology.

This work was supported by the Strategic Academic Leadership Program of the Kazan Federal University (PRIORITET-2030).

S9.625. Evaluation of the effect of temperature receptors on the activity of meningeal afferent nerve fibers of the rat trigeminal nerve

Ananev A.[1], Fedorina A.[1], Telina E.[2], Gafurov O.[1]*
[1]*Kazan (Volga region) Federal University, Kazan, Russia;*
[2]*Kazan State Medical University, Kazan, Russia;*
* osgafurov@kpfu.ru

Maintaining body temperature is a vital process in homoiotherms. The fact that an increase in body temperature often leads to headache, led to discovery that thermoreceptors take part in migraine. It is believed that the trigger mechanism for migraine pain is the activation of trigeminal nerve fibers. It is known that channels from the TREK and TRP superfamilies serve as thermosensors in thermosensitive neurons, and different representatives of these channels are activated in different temperature ranges. Among TRP channels TRPV1 type is the most significant for migraine, and is activated at temperatures above 42°C; TRPV3, TRPV4, TRPM8, and TRPA1 types cannot be excluded from the possibility of their cooperative interaction and are activated at above 32°C, 27-34°C, 8-25°C, and below 16°C, respectively.

In this work, we investigated the effect of temperature changes on the electrical activity of the rat trigeminal nerve.

The experiments were carried out using a rat half-skull preparation. Action potentials (AP) were recorded from the trigeminal nerve isolated from the meningeal membrane and placed in a bath that was perfused with Krebs solution. Recordings were done using an extracellular electrode. During the experiment different conditions were applied for 10 minute as follows: control at a temperature of 22-23°C; increasing the temperature of the solution to 27°C; increasing the temperature of the solution to 37°C; lowering the temperature to 27°C, and adding capsaicin (1 μM).

Recorded APs were identified and grouped using cluster analysis that makes it possible to assess the contribution of individual nerve fibers to the overall electrical activity of the trigeminal nerve.

The average number of APs per 5 minutes in the control was 612±219 (mean ± sem; n=5). In 5 minutes after increasing the temperature of the solution from 22 to 27°C the amount of APs significantly increased up to 1616±347 (t-test; $p<0.01$). Within 5 minutes after the temperature was raised to 37°C the amount of APs increased from 1066±270 to 1421±314 ($p<0.05$). Subsequent application of capsaicin at a concentration of 1 μM slightly decreased frequency of AP from 1362±222 to 1271±281 ($p=0.86$).

A series of experiments with an increase in temperature from 22 to 37°C within first 5 minutes showed a significant increase in the amount of APs from 447±214 in control to 1764±717 (Wilcoxon T-test; $p<0.01$; n=9). Further use of capsaicin, after lowering the temperature down to 27°C, showed a non-significant increase in the amount of APs over a 5-minute interval from 931±388 to 959±358 ($p=0.75$).

Cluster analysis of APs recorded in the trigeminal nerve showed that the occurrence of APs in each cluster was different. Cluster analysis was carried out for a series of experiments with sequential increase in temperature to 27°C, and 37°C, followed by application of capsaicin. This regiment of several treatments was specifically designed in order to see how nerve fibers were able to "respond" to various conditions that lead to a change in electrical activity. A cluster was considered to being able to respond if the number of APs in this cluster doubled when the temperature increased to 27°C, 37°C, or after capsaicin was applied. As a result of the analysis, it was shown that 22% of the clusters did not respond to any of the actions; 16% of the clusters responded to an increase in temperature to 27°C; only 5% responded to temperature increase to 37°C;