The use of the ANIS method for the analysis of the primary structures of proteins makes it possible to identify hierarchically organized elements of the information structure (ELIS) in them. ELIS are characterized by their position in the primary structure of proteins and rank - level in the hierarchical structure. The application of the ANIS method to a set of proteins with a known spatial structure made it possible to obtain fragments of PDB files corresponding to ELIS of all possible ranks and classify them according to topological stability. The identification of the patterns described above, which describe the organization of natural polypeptide chains, makes it possible to move from the modification of native proteins to their design.

### S1.85. Puckering states of iononic rings of carotenoids

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The properties of the protein-pigment complex are determined by the pigment included in its composition and the way it is coordinated in the active center. In case of carotenoproteins, the configuration of the pigment binding site depends on the conformational dynamics of the carotenoid in their composition. One of the ways of changing the conformation for a carotenoid is the transition of its iononic ring between different variants of a non–planar structure – puckering states. In our study, the conformational dynamics of five different carotenoids was investigated within the framework of molecular modeling methods.
The iononic rings of astaxanthin (AST), beta-carotene (BCT), canthaxanthin (CAN), lutein (LUT) and zeaxanthin (ZEA) were selected as the objects of the study. The energies of puckering states were calculated within the molecular dynamics method using the GROMACS package. The duration of the simulation was 1 microsecond for each carotenoid. As a result, the energy profiles of puckering states (puckering maps) were characterized for the studied series of carotenoids. It has been shown that energy barrier for transition between two local minima for iononoic rings containing two sp2 hybrid carbon atoms (BCT, LUT, ZEA) is twice lower than for iononic rings of AST and CAN containing three sp2 hybrid carbon atoms. For AST, the removal of energy degeneracy for two puckering states due to the formation of an intramolecular hydrogen bond is shown. For each puckering state, within the framework of computational quantum chemistry methods using the ORCA package, profiles of the potential energy of rotation around C6 – C7 and C6' – C7' bonds were constructed. A significant modification of the corresponding profiles depending on the puckering state of the lateral cyclic group is shown. The research was funded by the Russian Science Foundation, grant number 22-74-00012 (https://rscf.ru/project/22-74-00012/).

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### S1.86. Quantum chemical modeling of intermolecular interaction of hyaluronic acid with amino acids from the composition of targeted delivery nanocontainers and target substances

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Recently, theranostics, a direction associated with the targeted delivery of a therapeutic and diagnostic agent to affected cells, has become increasingly widespread in medicine. One of the target substances is not only cells, but also mucin – protein tissue from the mucosa. One of the means of drug delivery are polymer capsules and nanogels based on protein structures. To study the complex formation during the delivery of a medicinal substance based on protein capsules, the analysis of the degree of hydrogen binding of hyaluronic acid as a delivered drug with amino acids from the composition of protein capsules and from the composition of amino acids included in the target substance was carried out. These amino acids can be included both in the composition of protein capsules and in the composition of the target substance. Lysine-proline and lysine-serine complexes were considered as the object of the study. It is well known that nitrogen-containing amino acids, in particular, lysine, serine and proline, play an important role in the formation of intermolecular interaction of protein structures with each other and with various substances, therefore, the assessment of the degree of complexation and the strength of hydrogen binding can be applied both to the assessment of the degree of interaction of the molecular layers of the capsule and to the assessment of the degree of stability of the attachment of the capsule. to the target.
Modeling of intermolecular interaction was carried out by methods of density functional theory with B3LYP functional and 6-31G(d) basis using Gaussian software package, preliminary optimization of molecules was carried out in Avogadro and GaussView software complexes. At the first stage, the calculation and analysis of the lysine-proline molecular complex was carried out. The calculated IR spectrum of the complex has a peak at a frequency of 3501 cm-1, which corresponds to the oscillation of the –OH group. This peak was chosen for the study of complex formation during the addition of a hyaluronic acid molecule. At the next stage, a hyaluronic acid molecule was attached to the molecular complex, and the resulting structure and IR spectrum of the resulting molecular complex were calculated and analyzed. In the calculated IR spectrum of the complex, the peak corresponding to the oscillation of the –OH group shifted to a frequency of 3396 cm-1, and the peak also became more pronounced, which indicates an increase in hydrogen bonds. The lysine-serine molecular complex was also investigated. The calculation and analysis of the structure and IR spectrum of the complex was carried out. The calculated IR spectrum revealed a peak at a frequency of 3586 cm-1, corresponding to the oscillation of the –OH group. This peak was selected for the analysis of the molecular complex after the addition of the hyaluronic acid molecule.
At the next stage, a hyaluronic acid molecule was attached to the lysine-serine complex, after which the resulting molecular complex was calculated and analyzed. On the calculated IR spectrum of the lysine-serine-hyaluronic acid molecular complex, the peak corresponding to the –OH group oscillation shifted to a frequency of 3325 cm-1, and also became more pronounced, which indicates an increase in hydrogen binding in the resulting complex.
Based on the analysis of the molecular complexes of amino acids that make up the protein delivery container and the target substance, as well as molecular complexes obtained by attaching a hyaluronic acid molecule to amino acid pairs, it can be concluded that in the case of the formation of a complex with a hyaluronic acid molecule, the strength of hydrogen binding increases, which may be useful in further research in the field of theranostics. In addition, when analyzing complexes consisting of one amino acid and a hyaluronic acid molecule, the hydrogen bonds formed in molecular complexes were weaker than in triple complexes.

### S1.87. Rat cardiomyocytes electrical activity during α2-adrenoreceptors stimulation after If currents blockade

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The α2-adrenoreceptors (α2-AR) in mammalian heart perform the functions of regulatory effects modulation. Activation of α2-AR inhibits the synthesis of cyclic adenosine monophosphate (cAMP) by adenylate cyclase. If currents of the myocardium cells are modulated by the level of cAMP, sympathetic and parasympathetic departments of the autonomic nervous system. Modulation of the If currents activity via cAMP is essential in the increase or decrease of heart rate by the departments of the autonomic nervous system. It has been shown that activation of adrenergic receptors activates If and thereby increases the chronotropic function of the heart through β-adrenoreceptor dependent increase in the level of cAMP. Since HCN channels and α2-AR are present in cardiomyocytes, it is possible that If currents are an effector of adrenergic regulation of the heart through this type of receptor as well. The aim of this study is to investigate the effect of α2-adrenoreceptor stimulation after If preliminary blockade on the electrical activity of rat cardiomyocytes.

The object of the study was 6 weeks old white rats, at the stage of the beginning of pubertal period of development. The preparation of the right atrium was prepared, keeping the sinoatrial node, then placed in the tray with the endocardial layer up and fixed. Thyrode's physiological solution was passed through the tub. Action potential registration was performed using the standard method of intracellular action potential registration. Microelectrodes filled with 3M KCl solution and 30 MOm resistance were fixed in the holder and immersed in the drug. The pharmacological drug used was ZD7288, a blocker of currents activated by hyperpolarization, in concentrations of 10-9 M and clonidine hydrochloride, an alpha2-adrenoreceptor agonist, in concentrations of 10-9 M. Such parameters of action potential as duration of action potential at 20%, 50%, and 90% repolarization, amplitude of action potential, and cycle length were studied.

Perfusion of clonidine hydrochloride at a concentration of 10-9 M against ZD7288 (10-9 M) increased action potential duration at the 20% level in 6-week-old rats from $6.34 \pm 2.86$ to $8.2 \pm 3.14$ ms ($p \leq 0.05$). The baseline value of action potential duration at the 50% level was $14 \pm 4.25$ ms. At 7 minutes after administration of the If blocker, there was an increase in this parameter to $19.85 \pm 3.57$ ms ($p \leq 0.05$). After administration of clonidine hydrochloride after If blockade, there was a significant increase in action potential duration of 50% to $22.13 \pm 4.6$ ms ($p \leq 0.05$). Clonidine hydrochloride after ZD7288 promoted a 90% increase in action potential duration from $30.45 \pm 6.54$ to $32.78 \pm 4.16$ ms ($p \leq 0.05$) by the 7th minute of experiment, to $32.54 \pm 4.66$ ms ($p \leq 0.05$) by the 15th minute of observation. Total cycle length increased from $115.1 \pm 8.56$ to $128.51 \pm 8.19$ ms ($p \leq 0.01$), and the frequency of action potential generation decreased from $326.8 \pm 43.22$ to $319.16 \pm 54.33$ units/min ($p \leq 0.05$) by the 7th minute of experiment.

Thus, stimulation of alpha2-adrenoreceptors after preliminary blockade of hyperpolarization activated currents caused an increase in atrial myocardial action potential duration due to prolongation of the repolarization phase of atrial myocytes of 6-week-old rats.

### S1.88. Rearrangement of the conformational structure of biomacromolecules on the surface of an oblate metallic nanospheroid in an alternating electric field

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At present, the use of spheroidal gold nanoparticles with biomacrochains adsorbed on their surface to create nanoprobes with adjustable plasmonic characteristics in biophysical and biomedical research, as well as in sensors based on the giant Raman scattering effect, is of great interest. In this case, the conformational structure of adsorbed macromolecules can be rearranged under the influence of either a static electric field [1–2] or electromagnetic radiation [3–4]. If an oblate metal spheroid is placed in an external uniform electric field that is directed along its axis of rotation, then charges will be induced on its surface, the distribution of which will differ significantly from the case of a polarized spherical metal nanoparticle: on the surface of an oblate spheroid when displaced from its center along the axis of rotation the surface charge density changes sharply, reaching values close to the maximum at a small distance from the neutral equator.

Using molecular dynamics simulation, conformational changes in polyampholytic polypeptides with different distances between oppositely charged units in the macrochain adsorbed on the surface of an oblate gold nanospheroid with a periodic change in time of its polarity along the axis of rotation were studied. At a low temperature and the lowest considered peak value of the dipole moment of an oblate nanospheroid in the absence and presence of sodium and chlorine ions, the conformational structure of the polypeptide changed from the initial enveloping nanoparticle to a conformation in the form of a narrow ring around the nanospheroid near the equator. At higher values of the peak value of the dipole moment of the nanospheroid, the macromolecular ring around the nanoparticle narrowed and swelled, and with a further increase in the amplitude of the polarizing alternating electric field, the desorption of the polypeptide occurred. The resulting conformational structures of polyampholytic polypeptides obtained from modeling with ions turned out to be similar to the conformations of the same polypeptides obtained from modeling without ions. At the same time, changes were observed on the distribution curves of the linear and radial atomic densities of polypeptides, associated with the partial neutralization of the charged subpolar regions of the nanospheroid by ions.

When modeling at high temperature, periodic changes in the conformational structure of adsorbed polyampholytic polypeptides on the surface of an oblate gold nanospheroid were observed at the frequency of an external polarizing alternating field. At times when the dipole moment of the nanospheroid was equal to zero, the conformational structure of the polypeptide was close to the starting conformation, completely enveloping the nanospheroid. And at times when the values of the dipole moment of the nanospheroid were maximum in absolute value, most of the charged units of the polypeptide were adsorbed on oppositely charged subpolar regions of the polarized nanospheroid. At the same time, most of the adsorbed charged amino acid residues were located on the edge of a vast subpolar region near the equator. The ejection of macrochain loops along the direction of the dipole moment vector of an oblate nanospheroid was also observed.

Within the framework of the quasi-stationary field approximation, an analytical model was constructed for the formation of the conformational structure of polyampholyte chain links interacting with the surface of an oblate nanospheroid polarized in an external alternating electric field. At sufficiently high frequencies of changes in the external field (but not violating the conditions of its quasi-stationarity), it is necessary to take into account the temporal dispersion of the permittivity of the metal of the nanoparticle. In the region of low frequencies, much lower than the plasma frequency of the metal, the formula obtained under conditions of a constant external field becomes valid for the field potential of a polarized nanospheroid. In the final expression of the model for the distributed density of polyampholyte chain links, the values responsible for the entropy effects of conformation formation and the effects of remote interaction of dipoles of polyampholyte links with an extended external field and the polarization field of the spheroid are singled out as separate factors. The calculation of the entropy factor is made in an approximate way by approximating the surface of the spheroid by fragments of the sphere. In this case, the correct account was taken of the curvature of the adsorbing surface over most of the compressed spheroid.