We propose a noninvasive label-free approach to investigate alterations in mitochondrial cytochromes under inflammation in cell lines using Raman spectroscopy. This approach can be used to study inflammation and other age-related diseases in model systems. Authors acknowledge financial support from RFBR (grant mol_a 18-34-00503\18).

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Studies of the sensory domain of histidine kinase QseC

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The gastrointestinal tract is one of the most complex heterogeneous environments in mammals, where most of microbial flora is located in the large intestine [1]. This microbial flora is necessary for a mammal to correctly assimilate nutrients [2]. Among bacteria, there may be pathogens, whose interaction with host can be a cause of various diseases. Due to the high density and diversity of bacteria in the gastrointestinal tract, they can interact with each other and with the host through various signaling systems [3].
One of such systems is a quorum-sensitive signaling system that includes two proteins: QseC and QseB. In this two-component system, QseC is a bacterial adrenergic receptor that activates virulence gene transcription through QseB. QseC is able to interact with adrenalin and noradrenalin and also with bacterial autoinducer 3 (AI-3) [4]. Elucidating the role of this two-component system in bacterial virulence and characterization of its signaling mechanism can contribute to development of new antibiotics.
Here, we studied the sensory domain of QseC. Four different genetic constructs have been prepared: two containing only the QseC sensor domain and two containing a fusion of QseC sensor domain and a fluorescent LOV domain. We determined the stabilizing buffer components and showed that membrane-proximal charged α-helix fragments are important for protein stability. We also showed that fluorescent chimeric constructs can be used to track protein expression and purification as well as its interaction with ligands.

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Closer look at unbinding transition of phosphatidylcholine membranes induced by calcium ions

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Calcium ions occupy a special place in biological processes, regulating the most important physiological and biochemical processes in an organism [1]. The presence of calcium ions with low concentration in the solution causes a transition of multilamellar vesicles (MLVs) of phosphatidylcholine membranes from the "bound" to "unbound" state—unbinding transition—and the spontaneous formation of unilamellar vesicles (ULVs) [2]. The complex analysis of unbinding transition of 1,2-dimyristoyl-sn-glycero-3-phosphatidylcholine (DMPC) multilamellar vesicles (MLVs) was done for calcium ion concentration range of 0–1.0 mM by small-angle neutron scattering (SANS), densitometry, dynamic light scattering (DLS), and atomic force microscopy (AFM).
The critical Ca^{2+} ion concentrations for DMPC (10 mg/ml) in $CaCl_2 \cdot 2H_2O/D_2O$ solvent were determined from the SANS data as 0.33(3) мМ in $P_{\beta'}$ and 0.37(2) мМ in L_α phases during heating; 0.56(3) мМ in $L_{\beta'}$ and L_α phases during cooling. However, a local decrease in the volume of DMPC molecules occurs before the unbinding transition: 1035 Å^3 at $C_{Ca^{2+}} = 0.25$ mM ($L_{\beta'}$, 10 °C) and 1120 Å^3 at $C_{Ca^{2+}} = 0.2$ mM (L_α, 55 °C). Spontaneous formation of ULVs from MLVs was observed by SANS at $C_{Ca^{2+}} = 0.3$ mM in both phases with the bilayer thickness of 4.12(3) nm and 3.64(4) nm in $P_{\beta'}$ and L_α phases, respectively. These values are in good agreement with bilayer thicknesses of the MLVs of DMPC in D_2O, obtained by passing a solution through a polycarbonate membrane with pores of 100 nm. The decrease in the area of the DMPC molecule in the formed system confirms the fact that the binding of the Ca^{2+} ions to oxygen from PO_4^- moieties of the lipid headgroup leads to reorientation of the P^- –N^+ dipole into the region of the intermembrane space.
In addition, not all MLVs are converted to ULVs, which was observed using DLS and AFM methods. Thus, size distribution of DMPC MLVs (1 mg/ml) by intensity has a bimodal form at $C_{Ca^{2+}} \geq 0.4$ mM ($L_{\beta'}$) and at $C_{Ca^{2+}} \geq 0.6$ mM (L_α). Peak positions were calculated as 66.5 nm (STD = 8 nm) and 553.0 nm (STD = 181 nm) at 20 °C; 80.9 nm (STD = 17 nm) and 497.2 nm (STD = 198 nm) at 55 °C.

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Membrane mimetic materials in protocell design and modeling

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Both structural and functional protocell models require compartmentalization of the reaction medium provided by membraneous or membrane-mimetic structures, which are necessary for reaction-diffusion processes, and hence, morphogenesis of the protocell ultrastructure. Formation of the complex membranous structures differing from the minimal surfaces requires a non-equilibrium state of the multiphase microheterogeneous system. Since the diffusion transport during morphogenesis within the cellular membrane-bounded microreactors is mostly a physical phenomenon and is not genetically controlled, it is possible to perform biomembrane and biomorphogenesis modeling using different membrane-mimetic systems, regardless of their chemical nature. The Turing model of morphogenesis describes the interactions between an abstract activator and inhibitor, rather than of specific biomacromolecules. The only requirement here is the possibility of the physical (in particular, rheological) modeling in the framework

of the similarity theory and the dynamical analogy principles. Formation of the biomorphic structures in membrane-mimetic systems (including protocells) can be controlled and determined by the similarity of the processes resulting from the physical and chemical membrane activity independent from its chemical composition. According to the basic physical and chemical principles, such membrane-mimetic systems can demonstrate a number of emergent complex properties, characteristic for biomembranes, such as charge and ion separation, selective transmembrane ion transport, maintenance of the concentration gradients and ion concentration oscillations, electrochemical potential generation (including photoinduced membrane potentials in the presence of photocatalytic centers), gas transport and assimilation, redox reactions involving adsorbed substrates and immobilized catalysts, osmotic properties, biomimetic analog of endocytosis based on the surface phenomena binary division of the membranous structures after achieving a critical specific surface area, and membrane coalescence. Considering the fundamental difference of the chemical compounds abundant at the early Earth from the current chemical composition of the living organisms, almost any type of the Fendler membrane mimetic materials can be suitable for protocell modeling, provided that an appropriate energy-rich external factor produces non-equilibrium conditions necessary for initiation of the morphogenetic processes and activation of the cascade chemical reactions across the membrane boundaries. The above principle combines structural and functional approaches to the protocell modeling and significantly extends the range of substances suitable for protocell design.

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Some features of HSP70 expression and content in peripheral blood of patients with obliterating arteriosclerosis

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It is known that chronic inflammation is associated with age-related diseases like atherosclerosis and neurodegenerative diseases. It was shown that HSP70 plays an essential role in the process of chronic inflammation. Mechanisms of HSP70 involvement in the development of diseases remain controversial, although in atherosclerosis, HSP70 were thought to act as autoantigens and trigger both cell- and antibody-mediated immune responses. A considerable increase of extracellular pool of HSP70 and level of antibody to the protein in serum of peripheral blood obtained from patients with arteriosclerosis was also shown. In this work, we investigated alterations of HSP70 serum content and expression in peripheral immune cells of patients with obliterating arteriosclerosis.

The obtained results testify to significant differences between healthy donors and patients in a number of parameters connected with HSP70. In particular, our data demonstrated an increased content of inducible HSP70 in lymphocytes isolated from peripheral blood of the patients as compared with healthy donors. Our preliminary results indicated also the presence of considerable level of surface HSP70 on lymphocytes obtained from a number of patients in contrast to healthy donor lymphocytes having no surface HSP70. Additionally, our data confirm the results of other authors concerning an increased serum level of extracellular HSP70 and antibody to the protein in the blood of the patients. An essential addition to the literature data is connected with those demonstrated in our study—a significant positive correlation of the measured parameters mentioned above with the level of vessel calcification that reflects the development of arteriosclerosis.

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Interference of a D-enantiomeric peptide with hetero-association of amyloid-β oligomers and prion protein

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder that affects millions of people worldwide. One hallmark of the disease is the aggregation of amyloid-β (Aβ) into soluble oligomers and insoluble fibrils. Several studies indicate that oligomers rather than fibrils are the most toxic species in disease propagation. Aβ oligomers bind with high affinity to membrane-associated prion protein (PrP), leading to toxic signalling across the cell membrane, which makes this interaction an attractive therapeutic target. Here, we studied the Aβ-PrP interaction in detail. Our data show that full-length, soluble human (hu) PrP(23-230), as well as huPrP(23-144) lacking the globular C terminal domain, bind to Aβ oligomers to form large complexes beyond the megadalton size range. Following purification by sucrose density gradient ultracentrifugation, the Aβ and huPrP contents in these hetero-assemblies were quantified by RP-HPLC. The Aβ/PrP molar ratio in the assemblies showed some variation in a narrow range depending on the molar ratio of the initial mixture. Specifically, the molar ratio in the assemblies of about 4 Aβ to 1 huPrP in presence of an excess of huPrP(23-230) or huPrP(23-144) suggests that four Aβ units are required to form one huPrP binding site. The Aβ binding all D-enantiomeric peptide RD2D3 competed with huPrP for Aβ oligomers in a concentration-dependent manner. Our results highlight the importance of Aβ oligomer-specific multivalent interactions and demonstrate that compounds can be identified which compete with PrP for these interactions.

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Investigation of the influence type of solvents (H_2O and D_2O) on the formation of oligomers in lysozyme solution by small-angle X-ray scattering

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The effect of protonated (H_2O) and deuterated (D_2O) water on the structure of the crystallization solution of lysozyme was studied. The structure of the solutions was investigated by small-angle X-ray and neutron scattering methods. At the initial stage of crystallization of lysozyme under crystallization conditions of tetragonal symmetry system crystal growth, it is shown that when the H_2O solvent is replaced by D_2O, dimers and octamers are formed corresponding to the structure of the future crystal in the same way as it happens in the case of the H_2O solvent.

Tetramer, hexamer, and higher-order oligomers were not detected under any conditions, while in the pure protein solution, in which