Precipitant ions influence on lysozyme mono- and oligomers stability
investigated by molecular dynamics simulation

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In recent papers [1-3] it was found that protein oligomers form during crystallization, playing the role of precursor clusters of the future crystal. The authors of this study proposed to use the molecular dynamics (MD) method to assess the stability of oligomers and to study the behavior of atoms and bonds in their structure. This approach implies modeling the MD of oligomers extracted from the crystal lattice of a protein and analyzing the mobility of atoms. Using the proposed method, the type of octamer formed in the pre-crystallization solution of lysozyme has already been identified [4].

In this paper, the approach developed in [4] was applied to examine the stability of the lysozyme monomer, octamer and two types of dimer (A and B) formed in solution under conditions of crystallization of tetragonal syngony. In order to investigate the influence of NaCl precipitant ions bound to the protein in the crystal, various combinations of sodium and chloride ions associated with lysozyme molecule were probed: 1) with Na and Cl ions, 2) only with Na ions, and 3) without any ions. Using the GROMACS program, 100-ns molecular dynamics trajectories of the oligomers and monomers in the presence and absence of precipitant in water were calculated at different temperatures from 278 to 318 K.

To evaluate the stability of oligomers, RMSF (Root Mean Square Fluctuations) graphs were plotted at every simulated temperature.

As a result, flexibilities of octamer and dimer A have regularly increased with the temperature growth only in the case of considering precipitant ions embedded in the crystal structure. The RMSF values of dimer B are approximately the same at temperatures from 283 to 313 K and become higher at 318 K for all simulations whether they were performed with bound precipitant ions or not. For monomers, the presence or absence of precipitant ions associated with the protein, as well as the presence or absence of such ions in solution, does
not significantly affect the lysozyme atoms mobility in the molecule.

Thus, the importance of Na and Cl ions associated with the lysozyme is shown as only results of simulating oligomer models containing precipitant ions are consistent with the ones obtained by small-angle x-ray scattering experiments on crystallization lysozyme solutions [1-3, 5].

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