Study of the behaviour of lysozyme oligomers in solutions by the molecular dynamics method at different temperatures

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Using the molecular dynamics simulation method, the stability of lysozyme octamer and two types of dimer (A and B) formed in solution under conditions of crystallization of tetragonal syngony was studied. 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 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.

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 [1-2].

[1] Kovalchuk, M. V., Blagov, A.E., Dyakova, Y.A., Gruzinov, A.Y., Marchenkova, M.A., Peters, G.S., Pisarevsky, Y. V., Timofeev, V.I., Volkov, V. V. (2016). *Crystal Growth & Design* **16 (4)**, 1792.

[2] Boikova, A. S., Dyakova, Y. A., Ilina, K. B., Konarev, P. V., Kryukova, A. E., Kuklin, A. I., Marchenkova, M. A., Nabatov, B. V., Blagov, A. E., Pisarevsky, Y. V. & Kovalchuk, M. V. (2017). *Acta Cryst.* **D73**, pp. 591-599

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