1P092

Theoretical Studies on Effects of Protein--protein Interactions on Azurin Complex Stability by Coarse-grained Model

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[Introduction]

The formation of protein--protein complexes are essential in many biological functions. These complexes can be homocomplexes and heterocomplexes. In such a complex system, protein--protein interactions will certainly play an important role on the dynamics and stability of protein complex. There are several experimental methodologies and computational methods to investigate the protein—protein interactions. All-atom molecular dynamics simulation has been commonly used to observe the dynamics of protein complexes in microscopic level. Nevertheless, the all-atom simulation needs high cost and long time range.

In this study, we develop a coarse-grained model that allows the simulation of larger systems at longer time scales. The off-lattice Gō model is implemented to represent the intramolecular interactions [1,2]. Meanwhile, we consider the 6-12 Lennard-Jones potential to represent the intermolecular interactions. We chose this potential because of its simplicity [3]. We also limit our focus on the homocomplexes of *Pseudomonas Aeruginosa* azurin complex, a small cupredoxin (128 amino acids) that can bind to many intracellular molecules.

In order to study the effects of protein--protein interactions to the stability of azurin complex, we observe the static and dynamical properties such as the displacement, surface area, and conformational changes. In addition, crowding effect will also be considered in our study.

[Method]

We simulated two to four apo-azurin taken from the X-ray crystal structure of wild type azurin (PDB ID: 4AZU) [4]. In our coarse-grained model, each amino acid is treated as a single bead located at the C_α position. The potential energy for the entire system includes Gō model (as the intramolecular interactions) and Lennard-Jones potential (as the intermolecular interactions). The beads are coupled to Langevin thermostat to mimic the effects of surrounding solvent and control a constant temperature at 300 K. We work with the friction constant, $\gamma = 0.5$ (τ^{-1}) where τ, a time unit, is of order 3 ps.

For the analyses, we monitored some physical properties calculated from the simulated trajectories such as root mean square displacement, surface area, and conformational changes.

[Results]

We monitored the RMSD of each chain to obtain information about how much the given conformation differs from the native structure. From the 300 ns simulation time, the averages of RMSD are 1.79 Å and 1.74 Å for chain A and B, respectively. We also monitored the total surface area to investigate the binding possibility between two azurin as shown in Fig. 1. At the first 50 ns the total surface area decreases, and then it becomes stable during the rest of simulation time. We can also confirm the binding possibility by looking at the conformational changes of azurin at Fig. 1. The more detailed observations show that the minimum distance between two chains becomes larger, while the average distance on the buried area is getting closer. Besides, the number of contacts between these two chains also increases. More detailed explanation and different cases will be shown in poster session.

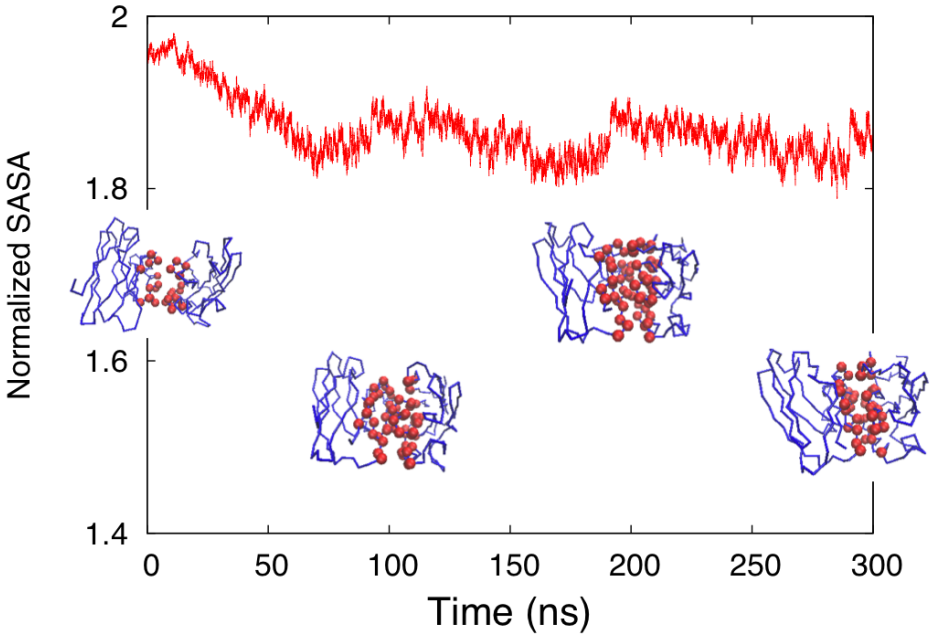

Fig 1. Time series of normalized total surface area is calculated at the residue level. The structures of azurin for every 100 ns are also shown, where the red spheres represent the contacted monomers in the binding site.

Keyword : Protein complex, Azurin, Protein--protein interactions, Coarse-grained model, Lennard-Jones potential

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