How to overcome the misfolding problem in computational protein engineering and design?

이선구*, Govindan Raghunatha, Sriram Sokalingam, Bharat Madan
부산대학교
(sungulee@pusan.ac.kr*)

Physics and chemistry based computational approaches allow us to evaluate the intra/inter molecular interactions in a protein. A number of industrially important proteins have been engineered and designed based on the approaches. They are currently a powerful tool in protein engineering and design, and they may become more efficient as the development of physics, chemistry and computer science. Despite the hopeful aspects of the computational approaches, there is a significant problem in the use of computational approaches for the efficient protein engineering and design. The current computational methods evaluate the energies and dynamics of the atomic interactions in a protein generally based on the final structure of a target protein. Therefore, although the designed mutations can be really effective at a level of final structure, there are many cases that the designed final structure cannot be obtained because the mutations designed based on final structure can dramatically affect the protein folding process and induce the misfolding of target protein. This kind of problem could be solved if we can predict the effect of designed mutation on the protein folding, but this is currently almost impossible and it is not sure this can be possible in the future due to the limitation of current physics and chemistry. Here, these limitations and the approaches to overcome such problems will be discussed. Specifically, the co-incorporation of stabilizing mutations with the computationally designed mutations will be introduced as an approach to overcome the misfolding problem in computational protein engineering and design.