52f Molecular Dynamics Simulations of Surfactant-Assisted Protein Folding in Vitro

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Protein refolding in vitro, an important step in the downstream processing of many genetically engineered proteins, is often thwarted by aggregation and misfolding of denatured proteins. A viable approach to assist protein folding thus enhance the recovery of active proteins is to add surfactants into a diluted protein solution. While the basic concept has been well established by experiments, a theoretical understanding is still missing on the interplay among surfactant-assisted protein folding, misfolding and aggregation. Industrial applications continue relying on empirical observations and lengthy trial-and-error experiments. As the first step towards rectifying this situation, we have investigated surfactant-assisted protein folding by using off-lattice molecular dynamic simulations based on minimalist models. We found that at appropriate surfactant concentrations, weakly hydrophobic surfactants facilitate protein refolding by creating new folding pathways but a strong hydrophobicity blocks the refolding due to the formation of over-intensive protein-surfactant complex. Surfactants assembled at the protein surface effectively prevent protein aggregation and more importantly compress the denatured proteins at high temperature. In other words, the addition of surfactants facilitates the collapse of denatured proteins and makes the native proteins more robust to the extremely denatured environment. Qualitatively the simulation results are found in good agreement with experimental observations reported elsewhere.