Effect of Surfactants on Surface-Induced Denaturation of Proteins: An Insight from Molecular Dynamics

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Effect of Surfactants on Surface-Induced Denaturation of Proteins: An Insight from Molecular Dynamics

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Proteins are marginally stable, and when they bind to interfaces the resulting conformational changes can lead to loss of biological activity. In order to stabilize proteins in experiments where surface-induced denaturation is an issue, surfactants are commonly used. [1] However, the mechanism by which they prevent surface- induced denaturation of proteins is not completely understood.

In the present work, the folding of the GB1 hairpin (shown in Fig. 1a) at the air-water, silica-water and ice-water surfaces is investigated, in the presence and absence of the surfactant Tween 80. Atomistic molecular dynamics (MD) simulations, coupled with the enhanced sampling method known as parallel bias metadynamics (PBMetaD) [2], are used for this investigation.

Our simulations reveal that GB1 is destabilized at the air-water and ice-water interfaces, but stabilized at the silica surface. Tween 80 stabilizes the protein at the air-water and ice-water surfaces (Fig. 1b), but slightly destabilizes the protein at the silica interface. The surfactant molecules bind to the air and silica surface, while they cluster around the protein in the case of ice. An orientation-dependent mechanism of the surfactants is also active, in which the protein is stabilized when the hydrophilic heads of the surfactant are oriented towards the protein, and destabilized when the hydrophobic tails point towards the peptide. The latter orientation stabilizes partially unfolded states of the protein, characterized by a larger non-polar surface area. The tails-toward-the-protein configuration is favored in a hydrophilic environment, explaining the mild destabilization observed at the silica-water interface. By contrast, the ice-water surface promotes the heads-toward-the-protein arrangement, that stabilizes the protein native structure. Finally, in the case of the air-water interface, the coating of the interface by the surfactant molecules, and the resulting inhibition of protein adsorption, accounts for the observed stabilization of the protein native structure. [3]

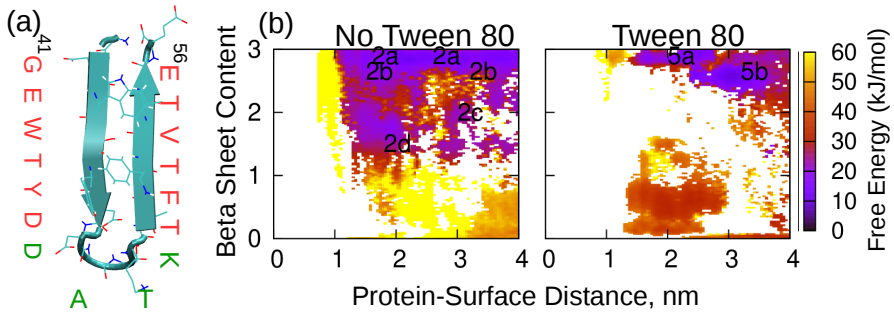

Fig. 1 *a) Cartoon structure of the GB1 hairpin. b) Free energy surface at the ice-water interface, in absence (left) or presence (right) of Tween 80.*

Overall, our simulations suggest that the amphiphilic nature of the surfactant, and its relative affinity for the protein and the surface eventually determines the effect on the protein structure.

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3. A. Arsiccio, J. McCarty, R. Pisano, J.-E. Shea, Effect of surfactants on surface-induced denaturation of proteins: Evidence of an orientation-dependent mechanism, J. Phys. Chem. B 122 (2018) 11390-11399.