Abstract

Elastin, composed of cross-linked tropoelastin monomers, is an essential extracellular matrix protein found in all the connective tissues providing elasticity and resilience to organs. It provides reversible deformation and the ability to expand without any fracture. It exhibits numerous age-related changes, including slow degradation and formation of amyloid-like structures in the human body.

In this thesis, we take a step towards unraveling the biophysical aspects of elastin in the presence of glucose, electric field, and its application in the field of drug delivery. First, we investigated glucose-induced conformational and structural changes in elastin. The results show that the diffusion decreases by 40% in the presence of glucose and a shift in the inverse transition temperature (ITT) towards lower temperature with a higher glucose concentration. Elastin forms fibril with aging, whereas the exposure of the electric field masks the phenomena of fibrillation. The decrement of the size of elastin depends on the strength of the exposed field as well as aging. Next, we estimate the transition path region (TPR) to understand the mechanism of folding/unfolding of protein over 1-D free energy landscape through numerical simulation. The results show that the TPR captures the anharmonicity in the transition state and varies linearly with the curvature of the transition state.

Hereafter, we explored the application of elastin as cargo for the curcumin nanomedicine for breast cancer therapy on two different cell lines. Since elastin is biocompatible for the human body and does not cause an immune response in the body, it degrades into non-toxic amino acids. The elastin-curcumin complex enforces ~80% cell death at a concentration of 100 μg/mL after 48 h of ncubation. Finally, to enhance the anti-cancer effect of curcumin, we have used graphene derivatives as a carrier for curcumin and applied on the same breast cancer cell lines, which show ~95% cell death at a concentration of 100 μg/mL after 48 h of incubation. The spectroscopic studies show curcumin adsorb on the surface of graphene derivatives through the π-π interaction between the phenolic group of curcumin and aromatic residues of graphene derivatives.

Keywords:

Elastin, ITT, Aggregation, TPR, Curcumin, Graphene derivatives, Breast cancer therapy