**MOLECULAR DYNAMICS SIMULATIONS AND FREE ENERGY CALCULATIONS OF PROTEINS**

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**ABSTRACT**

Nature provides peptides and proteins as a major source of inspiration for the engineering of responsive, protein-based nanomaterials for medical and biotechnology applications. Despite the scientific progress, how a protein dictates its functional three-dimensional structure and its physicochemical properties still remains an unsolved puzzle. A comprehensive understanding of them would provide us with the knowledge to develop novel bio-inspired materials with desired functionalities. The most abundant structure motifs of proteins that are found in nature are the α-helical coiled coil motif, which represents a convenient and used model for the analysis of protein folding studies and the analysis of motif-specific sequence-structure relationships. Several mathematical and computational techniques are employed to study proteins in aqueous solutions. Here we present a detailed study of biomolecular systems via Molecular Dynamics (MD) simulations, which provide direct insights in atomic detail. Our work concerns the detailed exploration of how a protein mutation can cause major changes in its physical properties, like its structural stability [1,2]. Two proteins have been studied: the dimeric RNA-binding ColE1 Repressor of Primer (wtRop) protein that is a paradigm of a highly regular 4-α-helical bundle, and its loopless mutation (RM6). An extensive investigation of the thermal stability of their native state in an aqueous solution is performed at three different temperatures. Key structural and conformational properties are calculated, such as α-helix dimensional properties, Ramachandran plot, and pair correlation functions, which reveal RM6 as more thermostable than wtRop protein.

In addition, we focused on the the protein folding problem by reversing the amino acid sequence of the well-characterized Rop protein in order to investigate the sequence-structure relationships. All-atom MD simulations of the reversed Rop (rRop) protein were performed using a series ofdifferent initial configurations in order to discover its native state, in collaboration with corresponding experimental findings. Simulation results indicate a perturbation of the helical structure compared to the wtRop protein [3].

Moreover, we calculated the free energy landscape of both wtRop and rRop proteins, using Metadynamics calculations, exploring various collective variables, such as the distance between the center of mass of the two monomers and the coordination number [3].

**KEYWORDS:** Biomolecules, Molecular Simulations, Protein Folding, α-helices, Metadynamics

**REFERENCES**

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