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Bringing biomolecules to life: The power of Molecular Dynamics

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Abstract: The tumor suppressor protein p53, crucial for cancer prevention, is negatively regulated by the ubiquitin ligase MDM2, which binds to p53's N-terminal transactivation domain, inhibiting its transcriptional activity and promoting its degradation. This feedback loop keeps p53 levels low in normal cells, but disrupting the p53-MDM2 interaction is a promising therapeutic strategy. To explore the binding and unbinding pathways of p53 in complex with MDM2, we conducted Molecular Dynamics (MD) simulations of the p53-MDM2 complex (PDB ID: 1YCR). Our study investigated the potential of mean force (PMF) using different force fields to analyze the free energy landscape of dissociation, while also examining p53's structural stability and dynamic behavior at varying distances from MDM2. These insights enhance our understanding of the molecular mechanisms governing p53 regulation and could aid in the design of novel cancer therapies.

Biography: Dhulakshi Karuna Hewage is a PhD student in Physics at the Southern Illinois University of Carbondale. She completed her undergraduate studies majoring in Physics at the University of Jaffna, Sri Lanka and her Master's degree in physics at Southern Illinois University, Carbondale. Her research work is on computational biophysics; it focuses on molecular simulations to explore biomolecular interactions and is working under the supervision of Prof. P. Sivakumar.