College of Natural Sciences & Mathematics
UNIVERSITY OF DENVER

Physics & Astronomy Colloquium

February 12, 4:00pm, Olin 105

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Exploring the Energy Landscapes of Intrinsically Disordered Proteins

The energy landscape theory provides a powerful framework for understanding how molecular systems explore their vast conformational spaces. While structured proteins typically fold into a well-defined native state, intrinsically disordered proteins (IDPs) defy this paradigm, lacking a single stable conformation. Instead, they exist as dynamic ensembles, fluctuating between multiple metastable states. This structural flexibility is essential for many biological functions but also plays a significant role in disease mechanisms. Understanding the energy landscapes of IDPs is crucial for uncovering how their conformational dynamics influence cellular processes and pathological conditions. In this seminar, by bridging statistical physics with molecular biophysics, we aim to provide a perspective on the role of energy landscapes in understanding protein function and disease. We introduce the Energy Landscape Visualization Method (ELViM), a reaction coordinate-free approach designed to explore the complex energy surfaces of IDPs. ELViM provides an intuitive two-dimensional representation of the conformational landscape, revealing key stability regions and transition pathways. As a case study, we examine Prostate-associated gene 4 (PAGE4), an IDP involved in prostate cancer progression. PAGE4 undergoes phosphorylation-dependent conformational shifts, altering its interaction network and influencing disease mechanisms. Using ELViM, we map PAGE4's energy landscape, illustrating how phosphorylation modulates its stability basins and functional transitions.