Dynamically driven correlations in elastic net models reveal sequence of events and causality in proteins

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April 20, 2024

Abstract

Protein dynamics orchestrate allosteric regulation, but elucidating the sequence of events and causal relationships within these intricate processes remains challenging. We introduce the Dynamically Perturbed Gaussian Network Model (DP-GNM), a novel approach that uncovers the directionality of information flow within proteins. DP-GNM leverages time-dependent correlations to achieve two goals: identifying driver and driven residues and revealing communities of residues exhibiting synchronized dynamics. Applied to wild type and mutated structures of Cyclophilin A, DP-GNM unveils a hierarchical network of information flow, where key residues initiate conformational changes that propagate through the protein in a directed manner. This directional causality illuminates the intricate relationship between protein dynamics and allosteric regulation, providing valuable insights into protein function and potential avenues for drug design. Furthermore, DP-GNM's potential to elucidate dynamics under periodic perturbations like the circadian rhythm suggests its broad applicability in understanding complex biological processes governed by environmental cycles.

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