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Dynamics of protein conformations

MARIA STEPANOVA, National Institute for Nanotechnology NRC

A novel theoretical methodology is introduced to identify dynamic structural domains and analyze local flexibility in proteins. The methodology employs a multiscale approach combining identification of essential collective coordinates based on the covariance analysis of molecular dynamics trajectories, construction of the Mori projection operator with these essential coordinates, and analysis of the corresponding generalized Langevin equations [M.Stepanova, Phys.Rev.E 76(2007)051918]. Because the approach employs a rigorous theory, the outcomes are physically transparent: the dynamic domains are associated with regions of relative rigidity in the protein, whereas off-domain regions are relatively soft. This also allows scoring the flexibility in the macromolecule with atomic-level resolution [N.Blinov, M.Berjanskii, D.S.Wishart, and M.Stepanova, Biochemistry, 48(2009)1488]. The applications include the domain coarse-graining and characterization of conformational stability in protein G and prion proteins. The results are compared with published NMR experiments. Potential applications for structural biology, bioinformatics, and drug design are discussed.