

Optimization, Validation, and Application of Coarse-Grained Models of Residue Interaction

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Fluctuations of proteins near their native conformations play important roles in function. Simple coarse-grained models, such as the Gaussian Network Model, have been shown to capture some of the features of equilibrium protein dynamics. We extend this model to include more than one interaction parameter between residues, using B-factors from 98 ultra-high resolution X-ray crystal structures to optimize the interaction parameters. By separating residue interactions into covalent and noncovalent we improve the average correlation between the model and the B-factors from 0.64 to 0.75. Further classification of the noncovalent interactions yields no improvement. We also use several coarse-grained models to predict the direction of dominant motions in proteins. The high-resolution structures provide a measure of the directionality of motion in the form of anisotropic B-factors. We perform a systematic comparison of several existing coarse-grained models of protein dynamics, and assess their fidelity to both isotropic and anisotropic temperature factors. We demonstrate the application of coarse-grained mode analysis to allosteric interaction in protein assemblies.