proportional to the protein's volume, the solvent accessible surface area, the integrated (over the surface area) mean curvature and the integrated (over the surface area) Gaussian curvature. The coefficients proportional to these geometrical measures are geometry independent thermodynamic coefficients, which characterize the interaction between the solvent and the protein. Since the thermodynamic coefficients are independent of the geometry, they can be calculated in a simple test geometry.

The separation of the solvation free energy into four geometrical measures and corresponding geometry-independent thermodynamic coefficients has important consequences: (1) It allows for fast and accurate calculation of the solvation free energy of a protein in a given geometrical configuration, which is important when comparing different structures of a protein. (2) It allows for fast and accurate calculation of the force on the protein in a given configuration mediated by the solvent, which is important in a simulation of the folding process of the protein.

2000-Plat

Dissociation and Unfolding of Insulin Dimers
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Insulin monomers bind one another through the folding of an interchain $\beta$ sheet. How does binding mediate protein folding? The energetics and rate of this fast folding process are difficult to translate into the mechanistic details that underlie classical paradigms such as conformational selection and fold-on-contact. We study the conformational dynamics at the dimer interface upon binding and dissociation using two-dimensional infrared spectroscopy (2D IR). 2D IR reveals coupling among $\alpha$ helix and $\beta$ sheet vibrations for secondary structural sensitivity with picosecond time resolution that can resolve all relevant structural changes. Cross-peak features provide monomer and dimer 2D IR signatures that yield the binding constant and its solvent and temperature dependence. These spectra are interpreted in detail using molecular dynamics simulations of insulin dimers, disordered and compact monomers to quantify the disordered monomer ensemble. Transient dissociation and unfolding are rapidly initiated using a nanosecond temperature-jump. Conformational changes occurring on the fastest resolvable nanosecond timescales are observed for the disordering of the interchain $\beta$ sheet insulin dimers.

2001-Plat

Evidence For Metastable States Of Lysozyme Revealed By High Pressure FTIR Spectroscopy
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Metastable protein conformations play an important role in the folding process because such partially disordered states can be gates for the misfolding pathway, leading sometimes to pathological structures, like fibrous aggregates. High pressure is a very useful tool in the study of metastable states, since application of the pressure is fully reversible, contrary to chemical agents. FTIR spectroscopy allows us to follow simultaneously three secondary structure, the packing (tertiary structure) and the aggregation of the protein using the amide I, amide II and the 1616 cm$^{-1}$ bands respectively. We performed a systematic study on the temperature-pressure phase diagram of lysozyme and found a two-step unfolding of the 1616 cm$^{-1}$ bands respectively. We performed a systematic study on the temperature-pressure phase diagram of lysozyme and found a two-step unfolding of the 1616 cm$^{-1}$ bands respectively. We performed a systematic study on the temperature-pressure phase diagram of lysozyme and found a two-step unfolding of the 1616 cm$^{-1}$ bands respectively. We performed a systematic study on the temperature-pressure phase diagram of lysozyme and found a two-step unfolding of the 1616 cm$^{-1}$ bands respectively. We performed a systematic study on the temperature-pressure phase diagram of lysozyme and found a two-step unfolding of the 1616 cm$^{-1}$ bands respectively.

2004-Plat

Measurement of Single Molecule Folding/unfolding Trajectories
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We have measured folding/unfolding trajectories of single protein G (B1 domain) molecules, a simple two-state folder, by simultaneously measuring the fluorescence intensity, lifetime, and spectrum at various concentrations of denaturant. Protein molecules were labeled by a fluorescence resonance energy transfer (FRET) pair, Alexa Fluor 488 and Alexa Fluor 594 and were immobilized on a glass surface coated with polyethylene glycol via streptavidin-biotin linkage. The vast majority of molecules (~ 85%) exhibits simple two-state trajectories, with either high or low values of the FRET efficiency, corresponding to the folded and unfolded states, respectively, with unresolved jumps between them. About 10% of the trajectories show transitions in the unfolded state that can be attributed to a ~20 nm spectral shift of the donor, as revealed by measurements of their emission spectra. The mean FRET efficiency of immobilized molecules matches the value measured in free diffusion experiments. There is a distribution of these values beyond the width expected from shot noise, which can, however, be quantitatively accounted for by the distribution of acceptor lifetimes. In spite of these complications from photophysics, rate coefficients obtained from the exponential distribution of residence times in either the folded or unfolded state yield relaxation times that agree within a factor of 3 with those measured on the dye-labeled protein by stopped flow kinetics. In addition, no correlation is observed between the donor and acceptor intensity in the unfolded state from microseconds to seconds suggesting that structural averaging between unfolded conformations occurs on the nanosecond timescale, as expected from previous measurements by B. Schuler and coworkers (PNA:1,4,2055,2007). All these results indicate that we have successfully

2002-Plat

Single Molecule FRET On Alpha Synuclein Membrane-bound Conformational States
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Alpha-Synuclein ($\alpha$S) is the primary component of the Lewy body plaques that are characteristic of Parkinson's disease (PD). Large insoluble $\alpha$S aggregates compose Lewy bodies, but smaller soluble $\alpha$S oligomers are implicated as the cytotoxic species in PD. Though $\alpha$S is natively unstructured in solution, it forms a N-terminal alpha helix upon binding to lipid membranes. Extensive evidence also shows that $\alpha$S gains structure upon forming oligomeric species. In order to learn more about the transition of monomeric $\alpha$S to toxic oligomeric species and to identify critical conformational states along this pathway, we use single molecule Förster resonance energy transfer (smFRET) and fluorescence correlation spectroscopy (FCS) to characterize the monomeric conformational states of $\alpha$S. Our evidence shows that $\alpha$S populations at least two distinct, monomeric conformational states, as a function of curvature, on lipid membranes or lipid mimetics. This finding demonstrates that $\alpha$S forms distinct conformations based on the curvature. Whether it binds synaptic vesicles or other cellular membranes. Perhaps one of these conformations is more susceptible to conversion to toxic species, and so this finding may enhance our understanding of how toxic oligomers are formed in PD.