

A Modified Ising Model for the Thermodynamic Properties of Local and Global Protein Folding–Unfolding Observed by Circular Dichroism and Small-Angle X-ray Scattering

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Based on the mean-field approximation, we have applied a modified Ising model to describe general protein unfolding behavior at thermodynamic equilibrium with the free energy contributed by the subgroup units (amino acids or peptide bonds) of the protein. With the thermodynamic properties of the protein, this model can associate the stepwise change of an unfolding fraction ratio profile with the local and global conformation unfolding. Taking cytochrome c (cyt c) as a model protein, we have observed, using small-angle X-ray scattering and circular dichroism (CD), the global and local structure changes for the protein in three kinds of denaturant environments: acid, urea and guanidine hydrochloride. The small-angle X-ray scattering and CD results are mapped to the unfolding fractions as a function of the pH value or denaturant concentration, from which we have extracted local and global unfolding free energies of cyt c in different denaturant environments using a modified Ising model. Based on the characteristics of the thermodynamic properties deduced from the local and global protein folding–unfolding, we discuss the thermodynamic stabilities of the protein in the three denaturant environments, and the possible correlation between the global conformation change of the protein and the local unfolding activities of the S—Fe bond in the Met80-heme and the α -helices.

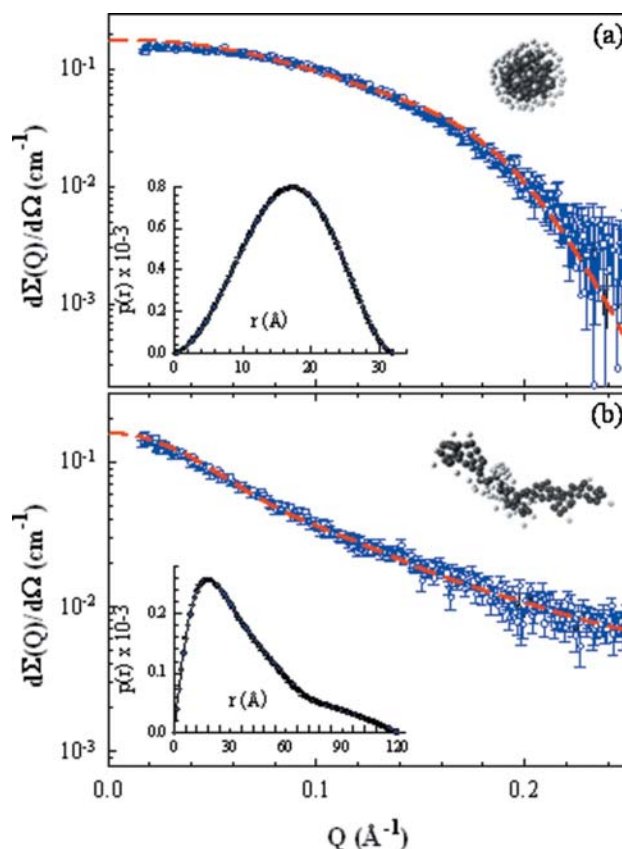


Figure 1 Dummy residue simulations (dashed curves) for the SAXS data of the folded (a) and the unfolded (b) cyt c in 2.75 M GuHCl. Also shown are the corresponding protein envelopes (dark beads) surrounded by a water layer (light beads). The inserts show the $p(r)$ functions Fourier transformed from the respective SAXS data.