

Analysis of the Uncertainty in Protein Stability Data

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Students in my laboratory seek to understand how the crowded environment in living cells affects the properties of globular proteins, the robots of the cell. Perhaps the most fundamental property of a protein is its stability, which can be defined rigorously using equilibrium thermodynamics. Specifically, stability is defined as $\Delta G_{den}^{o'}$, the difference in standard-state free energy between the folded, native state and the disordered, denatured state. The temperature dependence of $\Delta G_{den}^{o'}$ can be used to obtain the two additional fundamental parameters, the enthalpy ($\Delta H_{den}^{o'}$) and heat capacity (ΔC_p) of denaturation by applying the Gibbs-Helmholtz equation:

$$\Delta G_{D,T}^{o'} = \Delta H_{D,T_g}^{o'} \left(1 - \frac{T}{T_g} \right) + \Delta C_p \left[(T - T_g) - T \ln \left(\frac{T}{T_g} \right) \right],$$

where T_g is the midpoint of the transition. We have measured $\Delta G_{den}^{o'}$ values at various temperatures, and we know the sample standard deviations of the $\Delta G_{den}^{o'}$ values from repeating the experiment. We seek a program that takes our $\Delta G_{den}^{o'}$ values and generates hundreds of data sets based on the standard deviations, fits these datasets to the above equation and returns values of $\Delta H_{den}^{o'}$ ΔC_p with their uncertainties. A well written program with an easy to use graphical interface would not only help my lab, but would be used by many other groups around the world.