Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics

Electronic Supplementary Information

for

The protein folding transition-state ensemble from a Gō-like Model

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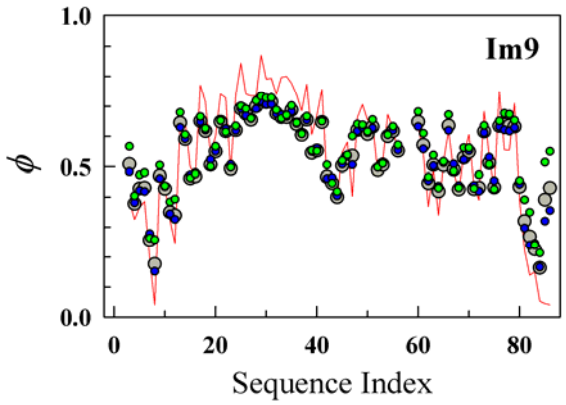

Fig. S1 Modeling Mutational Effects. ϕ-values for Im9 as a function of the sequence index when reducing the LJ-like interaction energy to 25% (blue), 50% (gray) and 75% (green) of their original values in the perturbation analysis (ϕ_i^P). The red curve plots the corresponding numbers for the wild-type protein estimated as the fraction of native contacts in the transition state ensemble (ϕ_i^Q; shown as a continuous line for the sake of clarity).

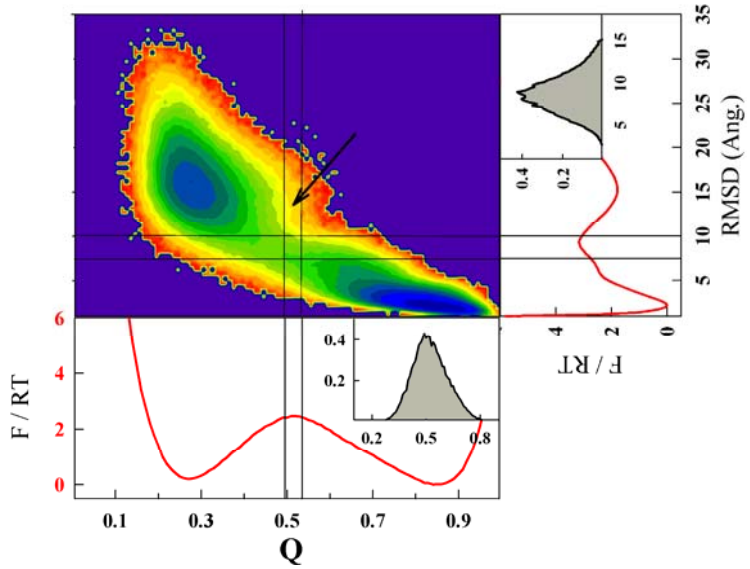

Fig. S2 Identifying the Transition State Ensemble. A two dimensional plot of the negative logarithm of the probability density at midpoint conditions for Im9 as a function of two coordinates *Q* (abscissa) and *RMSD* (ordinate) with the color code going from dark blue (highly populated) to dark red (less populated). The corresponding one-dimensional projections are shown at the bottom and to the right, respectively. The insets define the Bayesian probability to be in the transition path which is in turn employed to choose the swaths (horizontal and vertical lines) for transition state identification corresponding to a small rectangular area in the 2D projection. The arrow points to high *RMSD* values that are incorrectly identified as transition states based on just *Q* as a reaction coordinate.

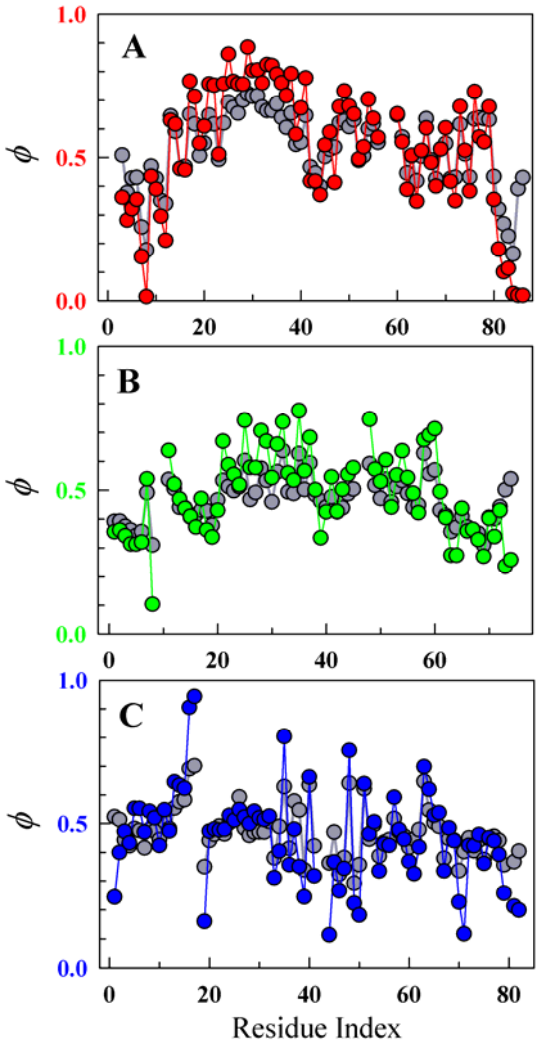

Fig. S3 Agreement between the methodologies in calculating ϕ-values as the fraction of contacts in the transition state ensemble (ϕ_i^Q) of each wild-type protein (Im9 –red; Ubq – green; SH3 – blue) and from the free-energy perturbation analysis (ϕ_i^P; filled gray circles). The correlation coefficients are 0.94, 0.87 and 0.87, respectively.

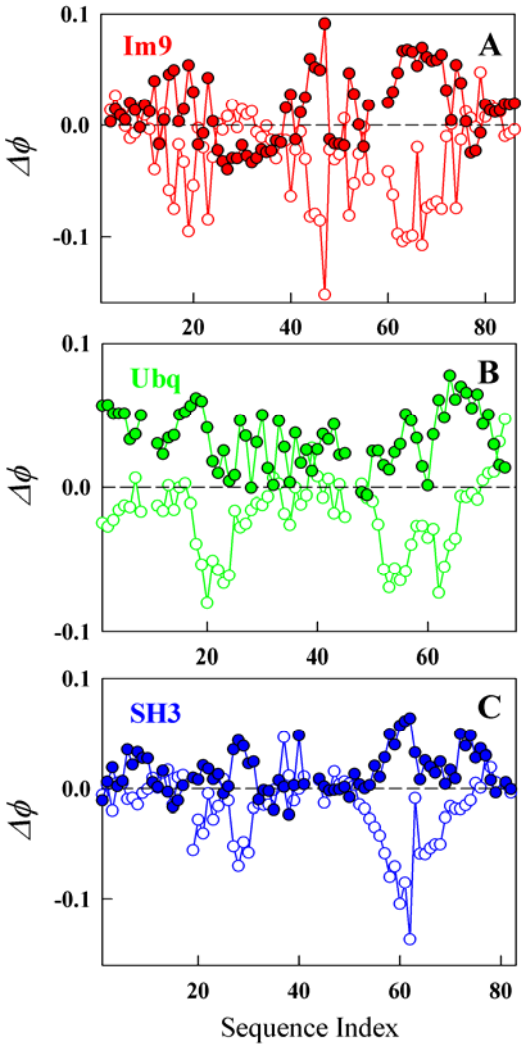

Fig. S4 Hammond Behavior in ϕ-values. Changes in ϕ-values in accordance with the Hammond behavior at stabilizing (open circles) and destabilizing (filled circles) conditions with respect to the midpoint for the three proteins.

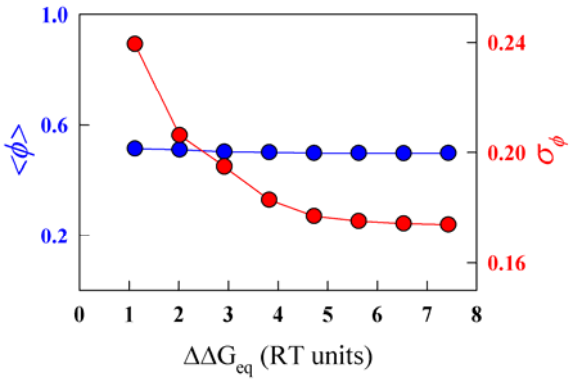

Fig. S5 Running mean (blue) and standard deviation (red) of the ϕ-values as a function of the degree of destabilization in the Gō-model calculations. The mean remains constant while the standard deviation decreases at large destabilizations.

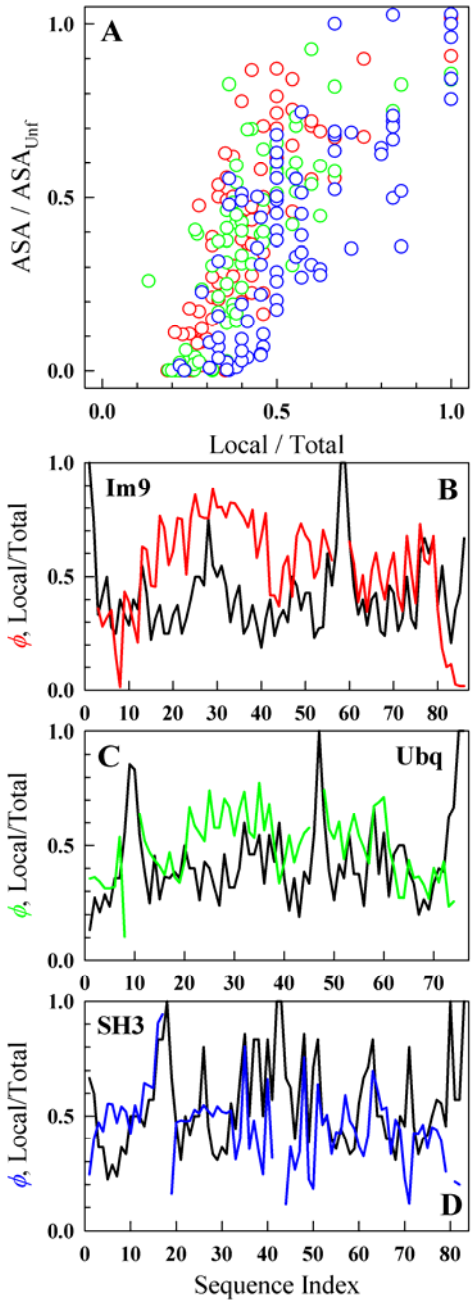

Fig. S6 A) The local/total ratio (see Methods) serves as a proxy for relative accessible surface areas of residues (with respect to a Gly-X-Gly peptide) in the native structure. The correlation coefficients are 0.81, 0.79 and 0.79, respectively, for Im9, Ubq, and SH3 (regression line not shown for clarity). B-D) Comparison of the simulated ϕ-values and the local/total ratio calculated from the native structure. It is clear that higher the degree of solvent exposure the higher the local/total ratio. This in turn produces small destabilizations upon mutation as only few interacting residues are affected thus resulting in larger ϕ-values. Also see Figure 5 in the main text. Note that the simple structural calculation reproduces the trends in simulated ϕ-values quite nicely.