Thermodynamic coupling of protonation and conformational equilibria in proteins: theory and simulation

Supporting Material

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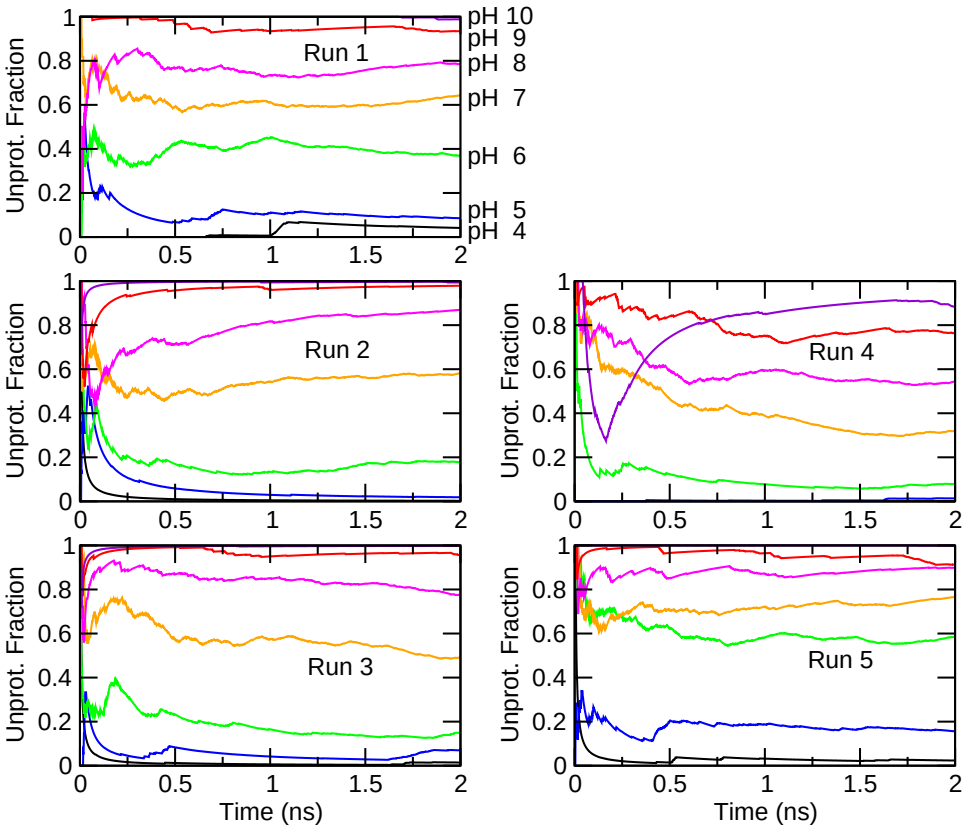

Figure S1: Cumulative unprotonated fraction for N100K of Δ+PHS SNase in the last 2 ns of the simulation runs 1–5.

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Error estimates for the calculated pK_{a} values

To estimate the uncertainty of the calculated pK_{a} values (fitting parameters k), we applied the well-known Monte Carlo "bootstrap" method (1). The method comprises three steps: (1) generate a large number (we used 1000) of independent bootstrap samples $S^*(i), i = 1...N$, where S represents the unprotonated fraction; (2) calculate the quantity of interest, e.g., the fitting parameter $k^*(i)$ for N bootstrap samples; and (3) calculate the standard deviation of the $k^*(i)$ values. For step (2) we assume that the probability of selecting a particular S value in each set S_i^* is given by a Gaussian distribution centered at $S^{\mathrm{final}}(\mathrm{pH})$ (Figure S2) and a sample standard deviation calculated from the cumulative S over the portion of the trajectory of interest (i.e. last 1.5 ns of the simulation).

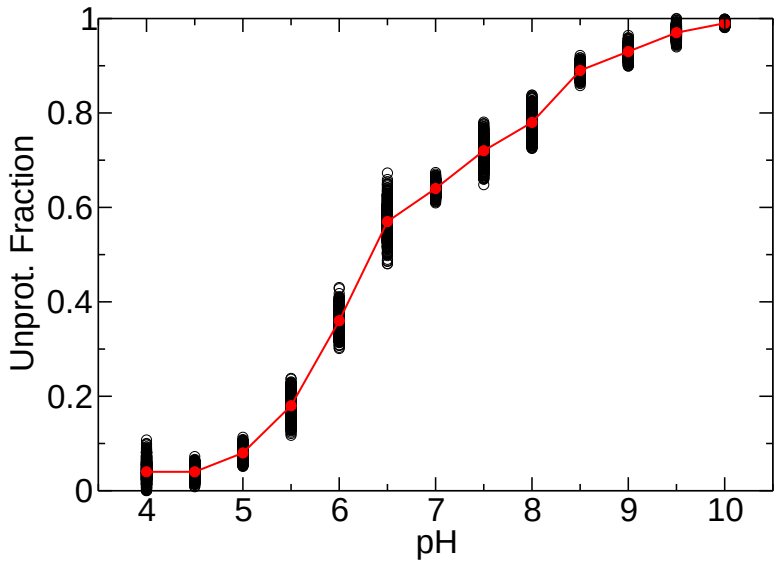

Figure S2: Error analysis of the calculated pK_{a} value for simulation run 1. The original data of unprotonated fraction are shown in filled red circles and connected by line. The 1000 independent bootstrap samples under each pH condition are displayed as open black circles. Deviations under various pH conditions reflect the maximum estimated errors.

References

1. Efron, B., and R. Tibshirani, 1986. Bootstrap methods for standard errors, confidence intervals, and other measures of statistical accuracy. *Stat. Sci.* 1:54–75.