Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supplementary Information for

How determinant is N-terminal to C-terminal coupling for protein folding?

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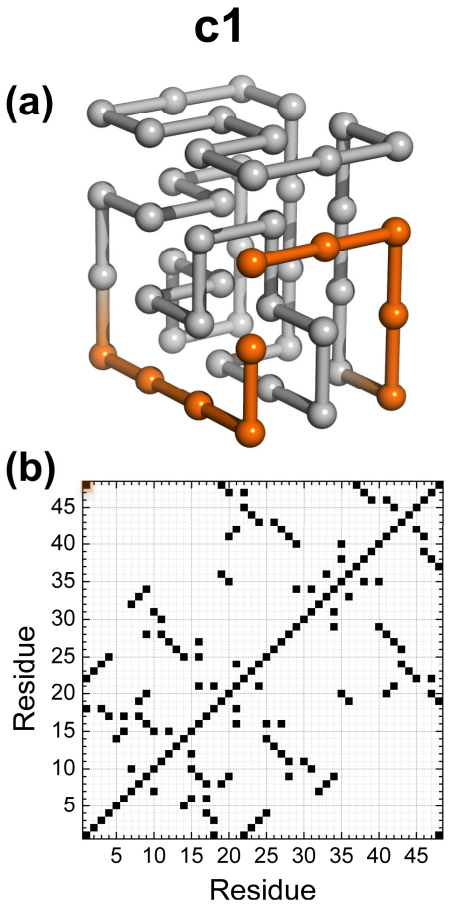
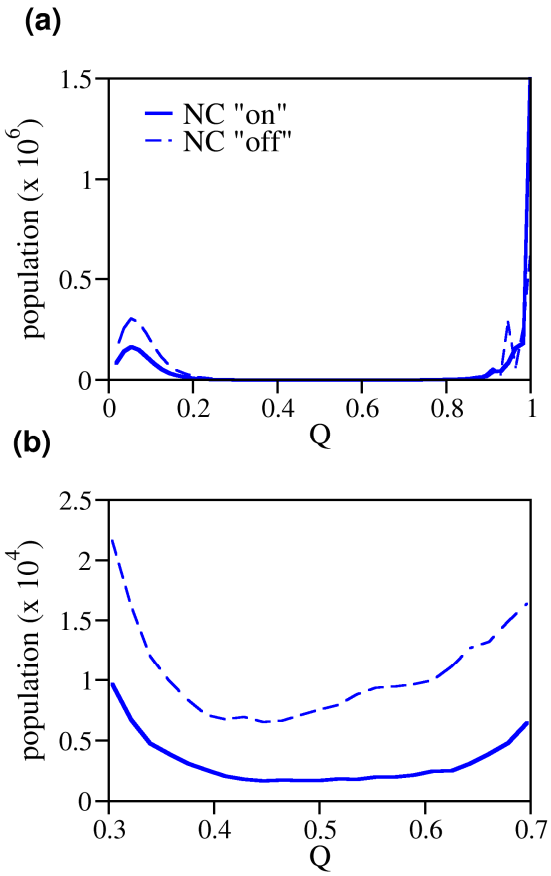
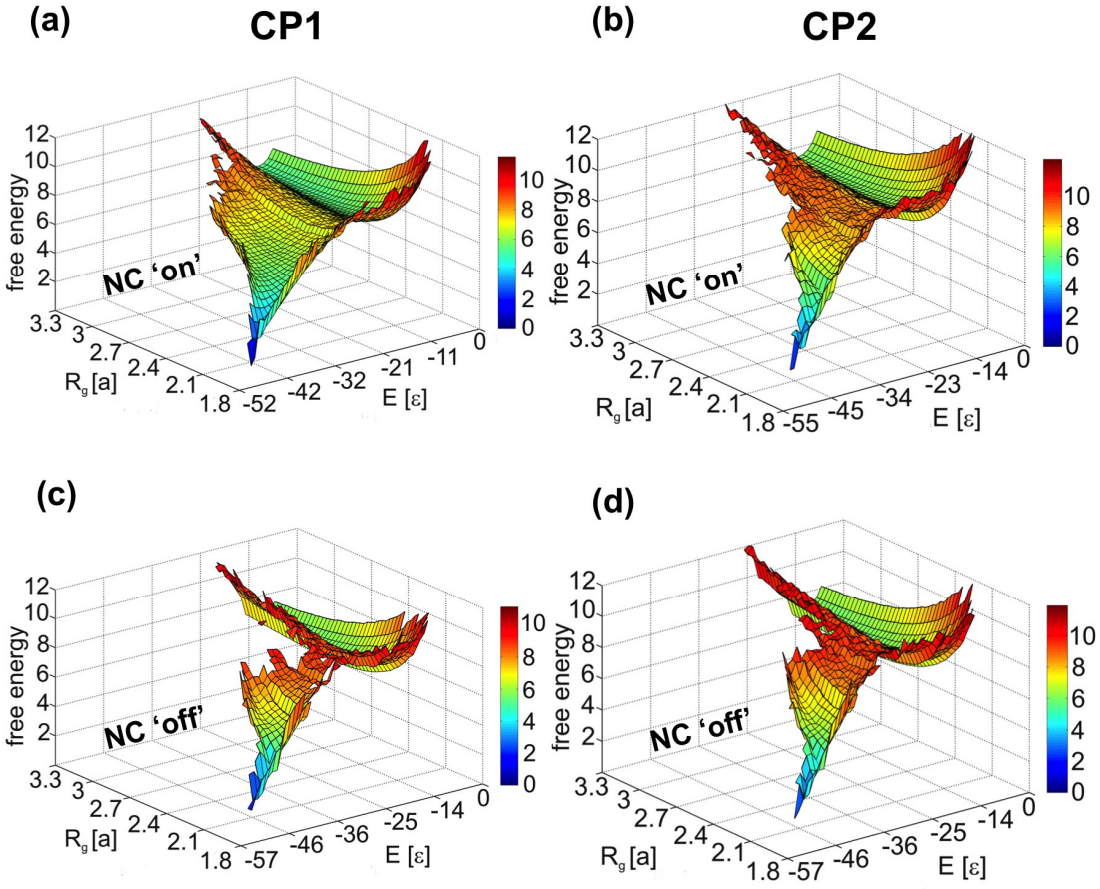


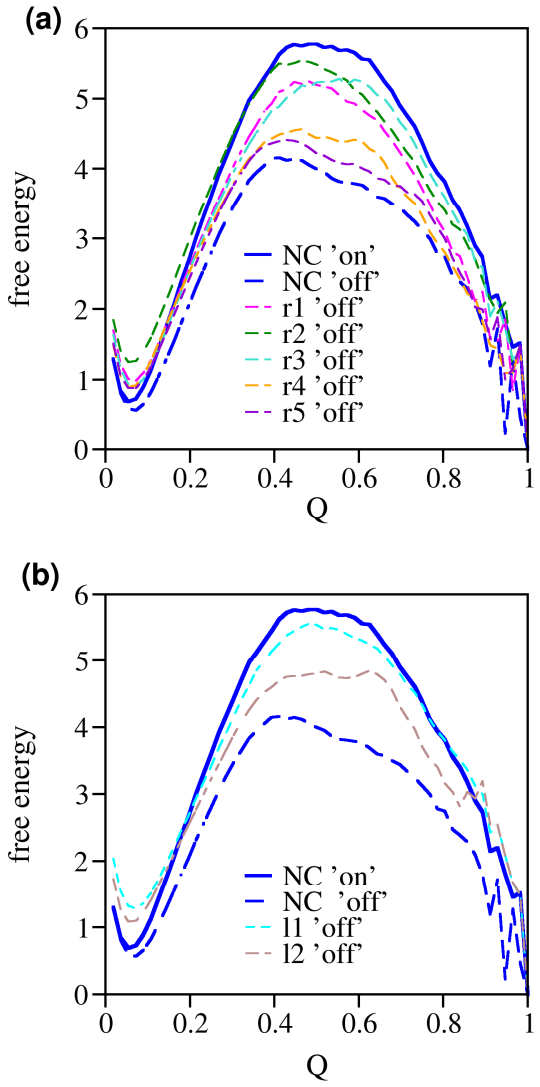
SI Figure 1. Lattice control model system. Three dimensional native structure (a) and native contact map (b) of the control model system c1 used in this study. In the native structure the chain termini is highlighted. Control system c1 is a circular permutant of CP0, CP1 and CP2 with low contact order. In its contact map there is only one interaction between the termini residues, which is also highlighted.



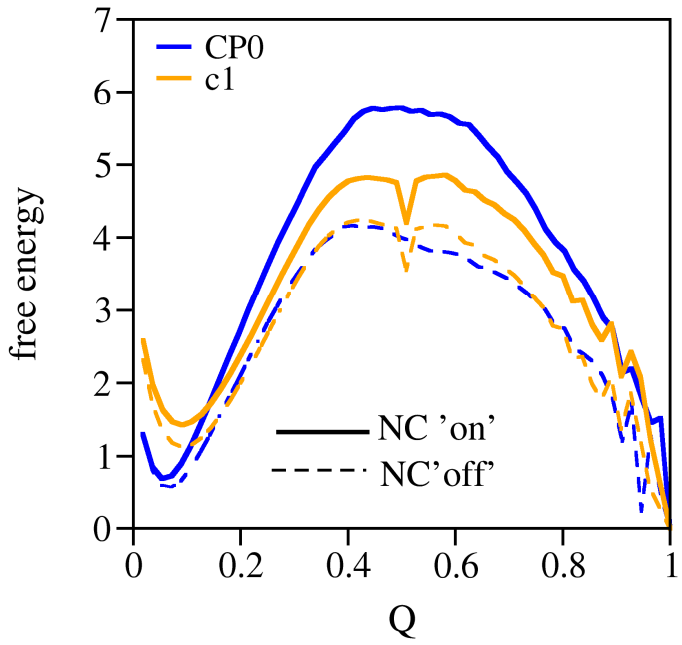
SI Figure 2. Effect of termini interactions on the thermodynamic cooperativity of the folding transition on lattice. (a) Histogram of conformations with fraction of native contacts Q sampled at T_m for model system CP0 revealing a bi-modal distribution (underlying a two-state transition) where the peak of the denatured ensemble is centred at Q=0.1 and that of the native ensemble corresponds to Q=1. Panel (b) shows a magnification of the region $0.3 \leq Q \leq 0.7$ to highlight the fact that conformations intermediate between native and denatured are substantially more sampled when the termini interactions are "switched-off".



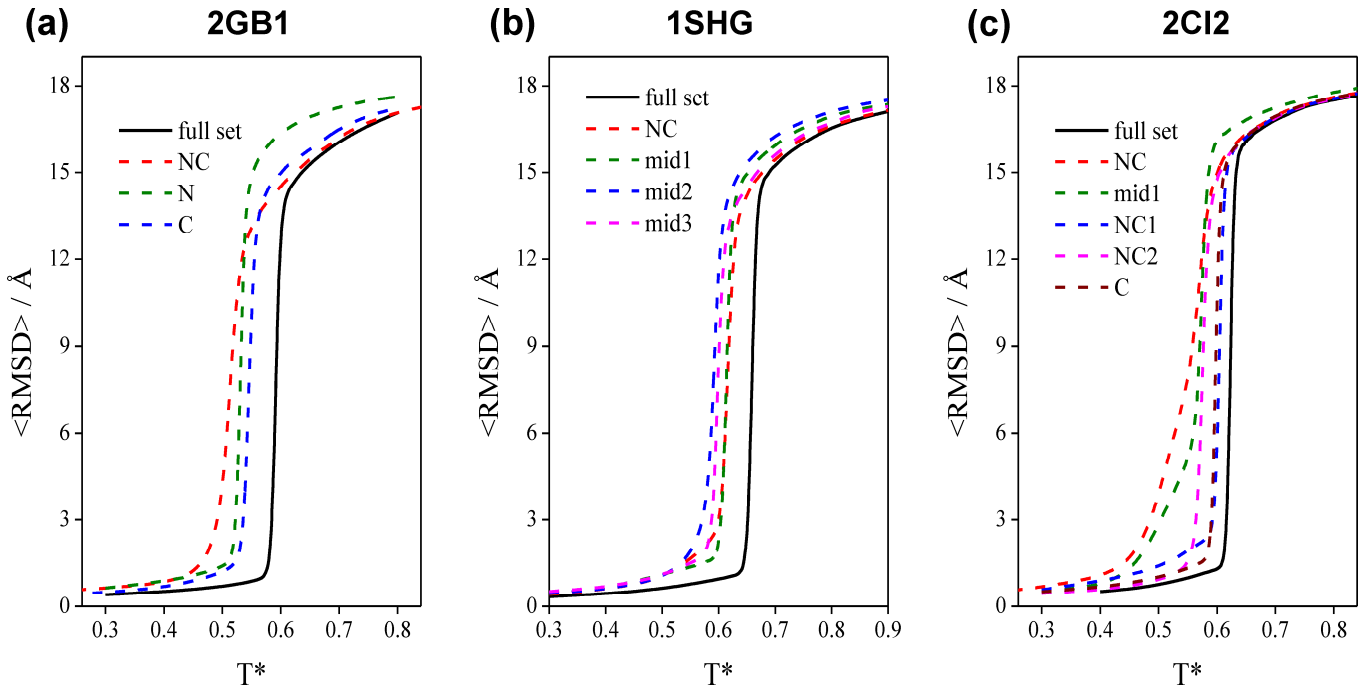
SI Figure 3. Effect of termini interactions on the thermodynamics of the folding transition on lattice. Free energy surface (i.e. free energy projected on the radius of gyration, R_g, and on energy, E) for model systems CP1 and CP2 when the termini interactions are 'switched-on' (a, b) and 'switched-off' (c, d).



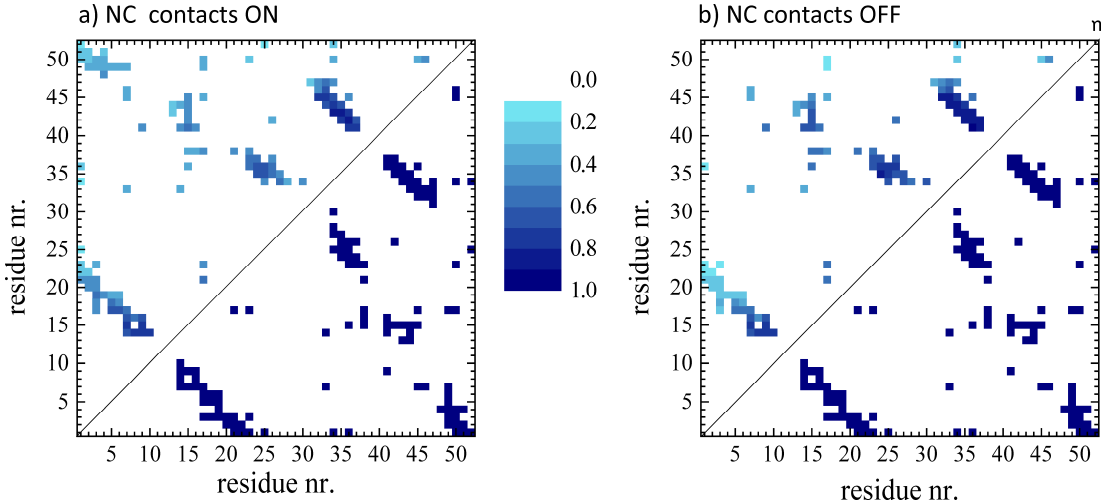
SI Figure 4. Control experiments on lattice. The effect of "switching-off" random native interactions on the folding transition of model system CP0 is compared with that of "switching-off" the NC interactions. (a) Five sets of four randomly selected native interactions were tested (r1-r5). Panel (b) reports the effect on the folding transition of "switching-off" four native interactions that are localized in the same region of the native structure of CP0. In this case, two sets of native interactions (l1, l2) were considered.



SI Figure 5. More control experiments on lattice. The effect of "switching-off" four NC interactions on the folding transition of model system CP0 is compared with that of "switching-off" one NC interaction in control system c1, a circular permutant of CP0 with low CO.



SI Figure 6. Insight into the off-lattice folding transition from the analysis of RMSD. RMSD as a function of temperature for the different off-lattice systems. The reported values represent the mean C_α RMSD (measured with reference to the native structure) evaluated over the ensemble of conformations sampled at each temperature in the replica-exchange simulations.



SI Figure 7. Transition state structure in the off-lattice model for 1SHG. Probability maps showing the likelihood of formation of each native contact in the transition state ensemble when the NC interactions are 'switched-on' (a) and 'switched-off' (b).

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SI Movie. Monte Carlo trajectory of 2CI2. Simulation snapshots from the folding trajectory of 2CI2 when the 27 NC interactions between the chain termini are "switched-off" at temperature T* = 0.52, which is slightly below T_m for this system.