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

Supplementary information file for

Hydrophobic confinement modulates thermal stability and assists knotting in the folding of tangled proteins

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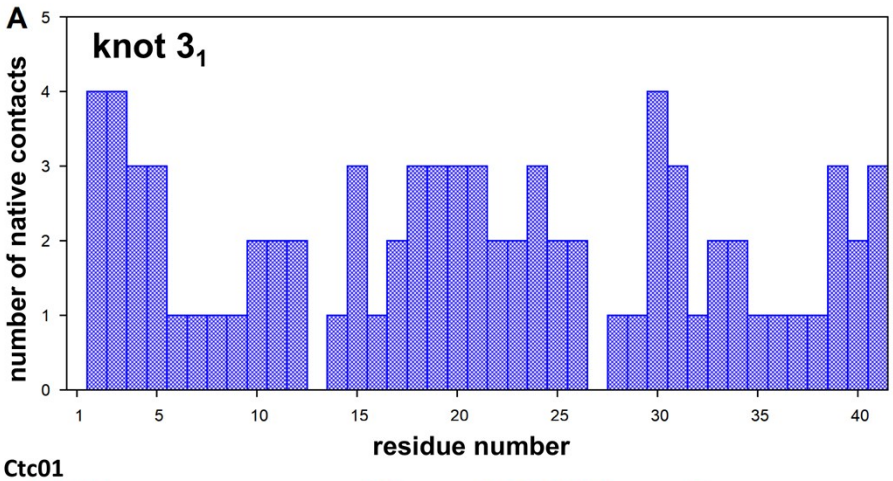
This file includes:
Supplementary Figures SI:1-SI:7



Ctc01
1-2-3-4-5-6-7-8-9-10-11-12-13-14-15-16-17-18-19-20-21-22-23-24-25-26-27-28-29
-30-31-32-33-34-35-36-37-38-39-40-41

Ctc14
1-2-3-4-5-6-7-8-9-10-11-12-13-14-15-16-17-18-19-20-21-22-23-24-25-26-27-28-29
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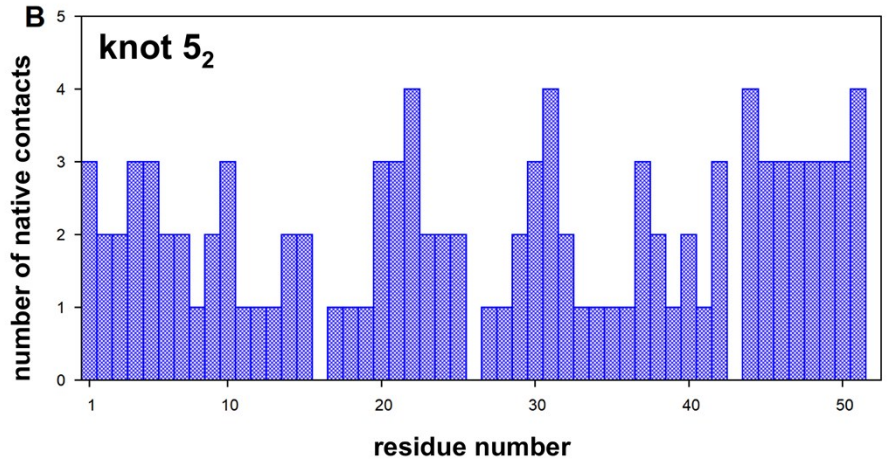
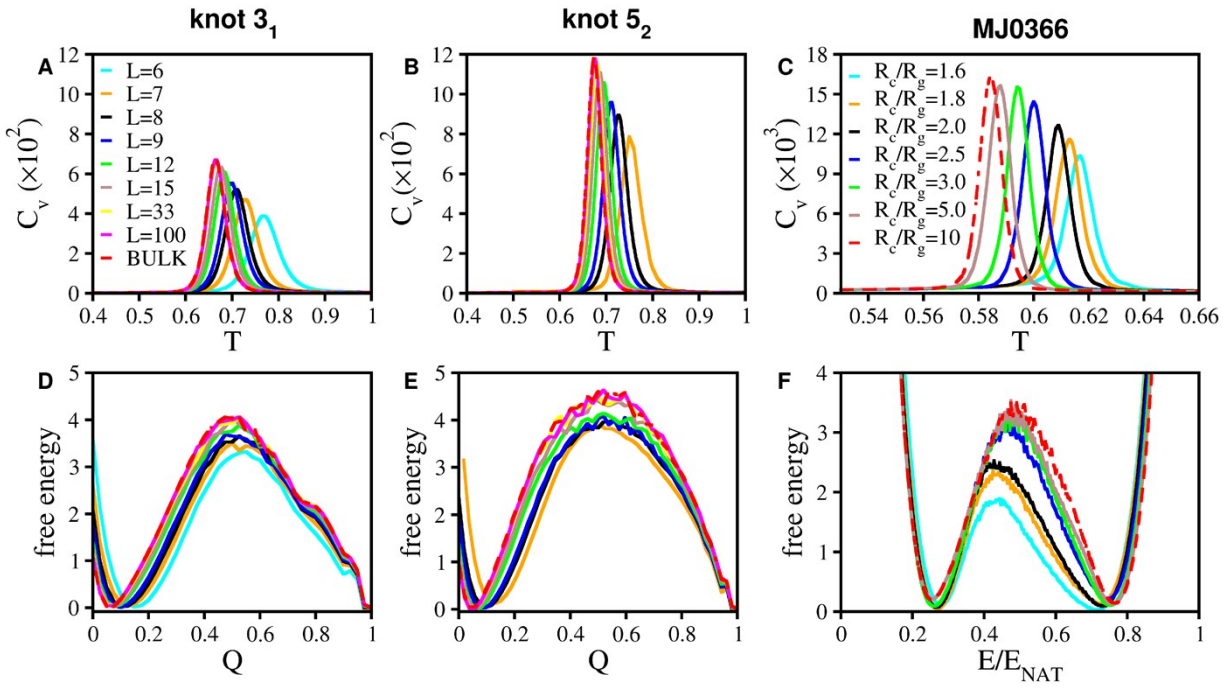


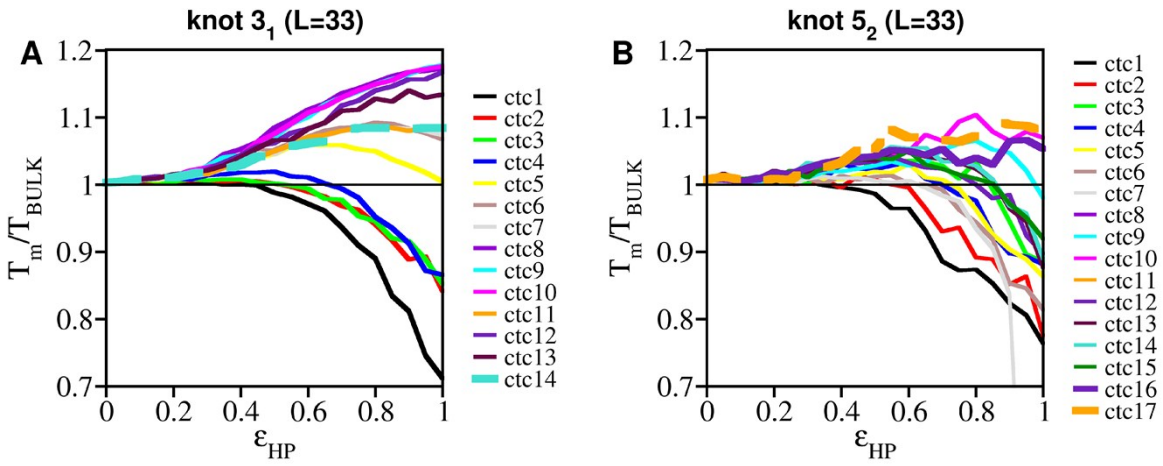
Ctc01
1-2-3-4-5-6-7-8-9-10-11-12-13-14-15-16-17-18-19-20-21-22-23-24-25-26-27-28-29
-30-31-32-33-34-35-36-37-38-39-40-41-42-43-44-45-46-47-48-49-50-51

Ctc17
1-2-3-4-5-6-7-8-9-10-11-12-13-14-15-16-17-18-19-20-21-22-23-24-25-26-27-28-29
-30-31-32-33-34-35-36-37-38-39-40-41-42-43-44-45-46-47-48-49-50-51

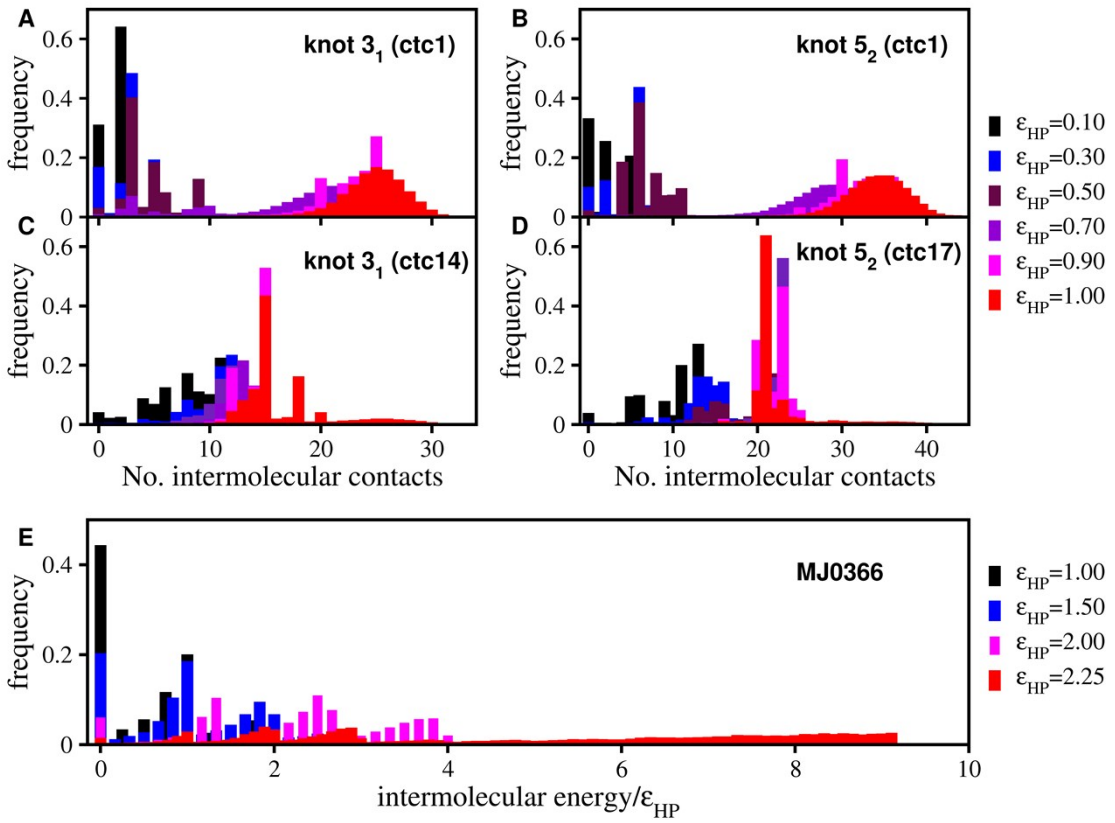
SI Figure 1 - Number of native contacts per residue in lattice knot 3_1 (A) and lattice knot 5_2 (B). The hydrophobic beads are colored red in the designed protein sequences. In sequence Ctc01 the most connected beads (establishing 3 and 4 native contacts) are the ones considered hydrophobic.



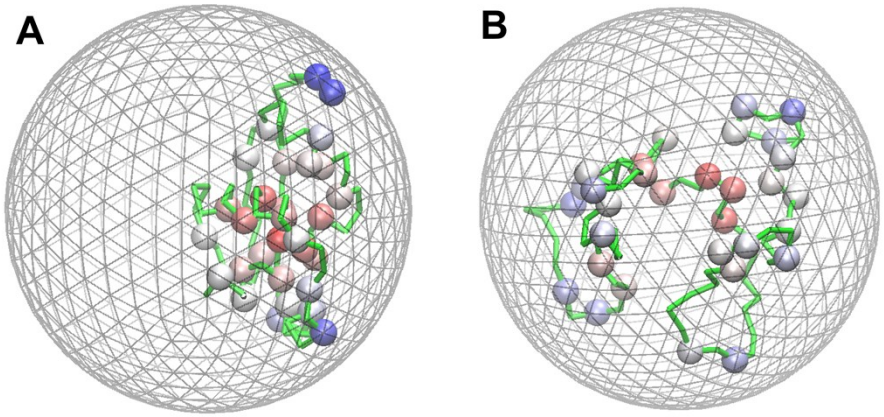
SI Figure 2 - Folding thermodynamics under steric confinement. Heat capacity as a function of temperature for knot 3_1 (A), knot 5_2 (B), and protein MJ0366 (C). The melting temperature T_m is the temperature at which the C_v peaks. The projection of the free energy on the selected reaction coordinate at T_m for knot 3_1 (D), knot 5_2 (E), and protein MJ0366 (F).



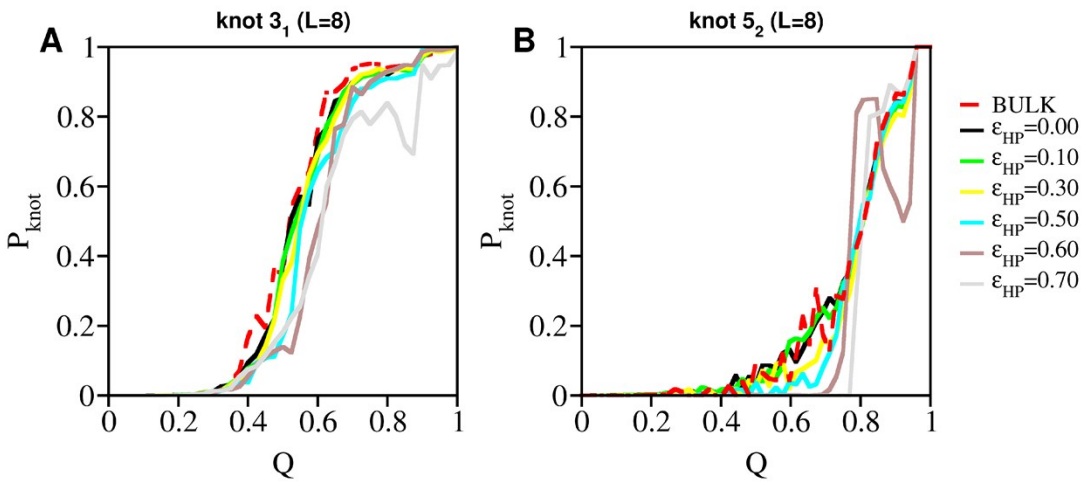
SI Figure 3 - Thermal stability under hydrophobic confinement. Dependence of the melting temperature, T_m, (normalized to the melting temperature observed in bulk conditions, T_{BULK}) on the hydrophobic intermolecular parameter, ε_{HP}, for lattice sequence Ctc01 of knot 3_1 (a), sequence Ctc01 of knot 5_2 (b), and protein MJ0366 (C) under different confinement conditions.



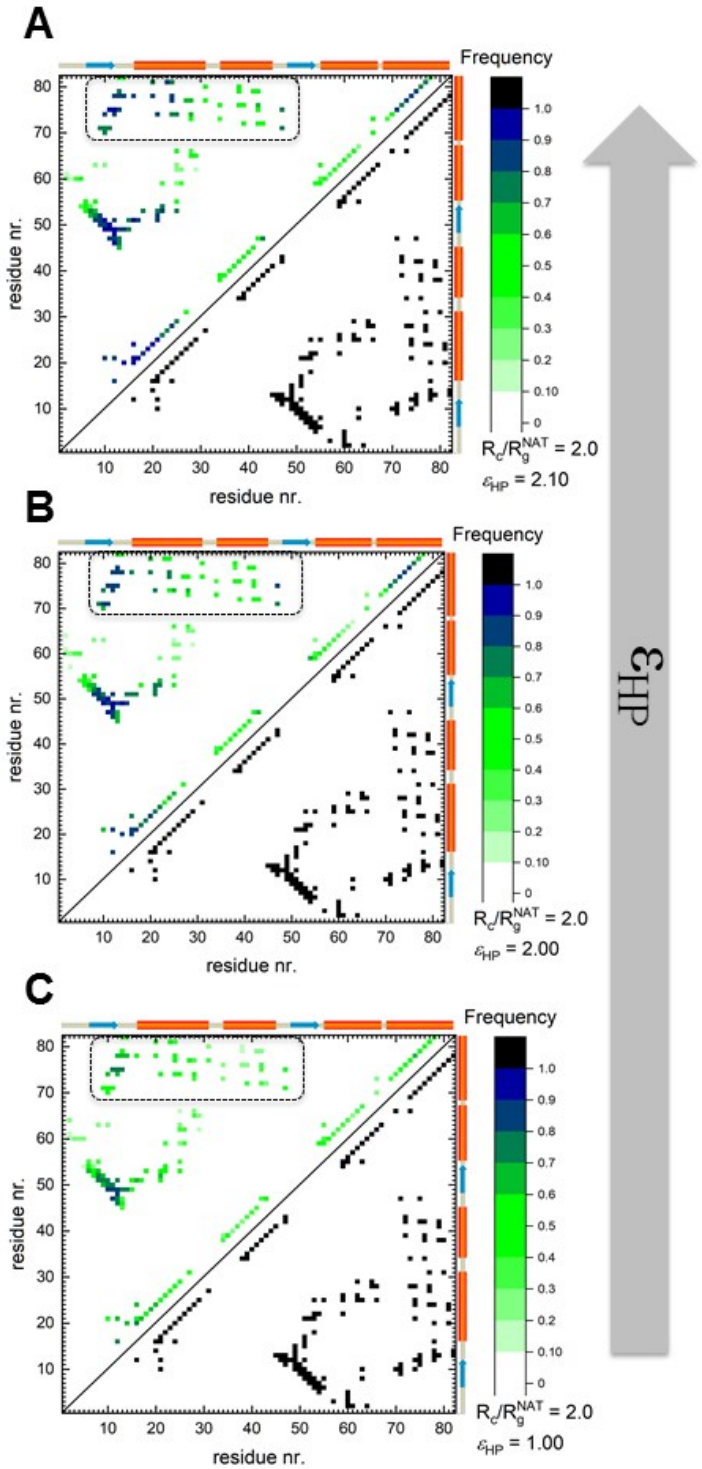
SI Figure 4 - Distribution of intermolecular interactions. Probability histograms for the distribution of the number of established intermolecular contacts at fixed temperature (T=0.6) for model sequence Ctc01 of lattice knot 3_1 (A), sequence Ctc01 of lattice knot 5_2 (B), and for sequences ctc14 (knot 3_1) (C) and ctc17 (knot 5_2) in a box of size L=8. The probability histogram for intermolecular energy for protein MJ0366 at fixed temperature (T=0.58) in a sphere of radius R_c=2R_g (E). Depending on ε_{HP}, the simulation temperature can be above or below T_m (see main text).



SI Figure 5 - Conformations populated under hydrophobic confinement. The confining sphere has radius R_C/R_g=2.0, and hydrophobic residues are represented as spheres. Residues closer to the cavity's surface are colored in blue while those further away from the surface are colored in white. The conformation (A) is populated at low T ($< T_m$) while conformation (B) is populated at high T ($> T_m$).



SI: Figure 6 - Knotting probability of lattice sequence ctc0 under hydrophobic confinement. Dependence of P_{knot} on the reaction coordinate Q for knot 3_1 (A) and knot 5_2 (B), for several strengths of the hydrophobic intermolecular parameter, ε_{HP}, in a box of size L=8 at T_m.



SI: Figure 7 – **Transition state structure**. Effect of the strength of intermolecular interactions with the cavity, ε_{HP}, on the structure of the transition state ensemble: ε_{HP}=2.1 (A), ε_{HP}=2.0 (B) and ε_{HP}=1.0 (C). The dotted region in the probability (native contact) maps indicate the native contacts establishing between the C-terminal helix 4 and its surroundings. In all cases the R_C/R_g=2.0.