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## Supplemental Information

# A Simple Model of Protein Domain Swapping in Crowded Cellular Environments

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SUPPORTING FIGURES

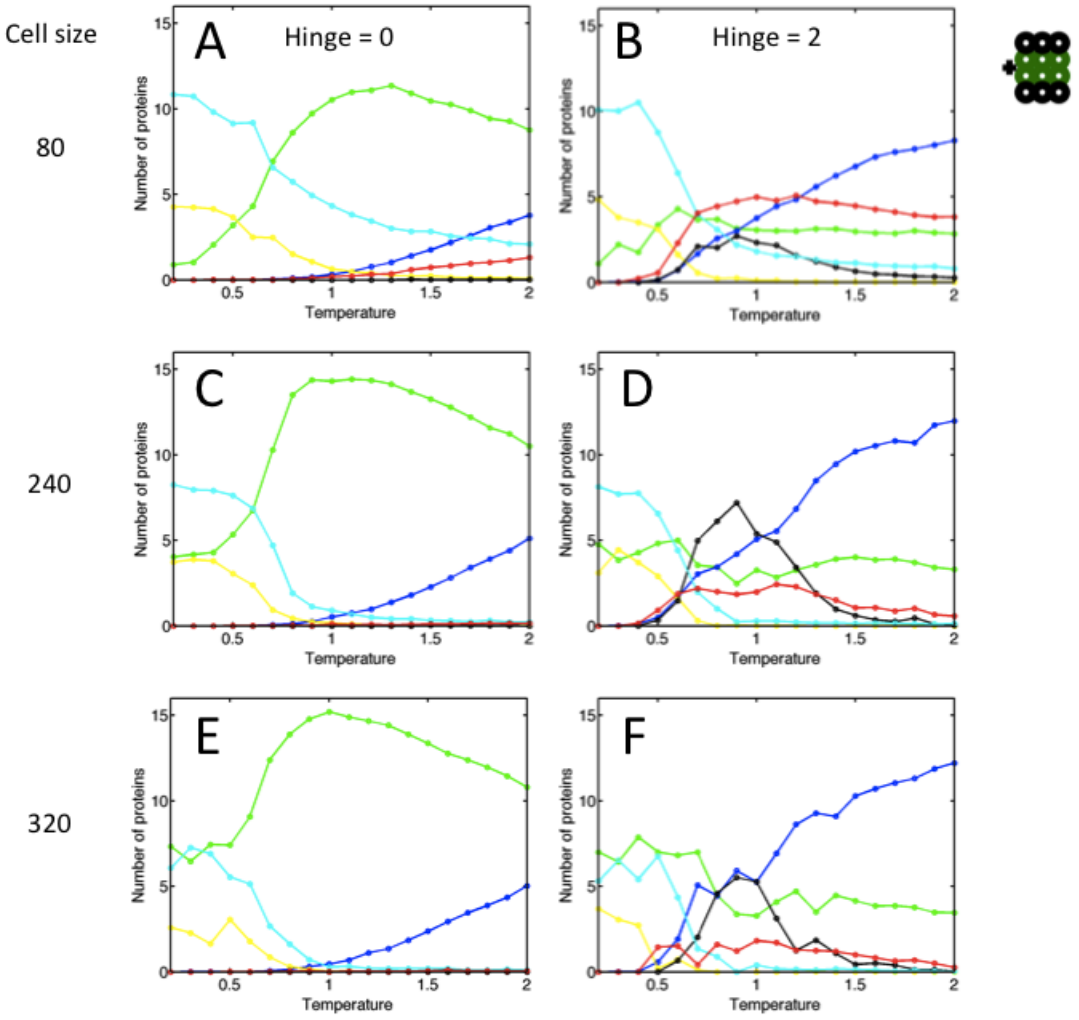


**Figure S1.** Plots displaying protein statistics as a function of temperature for sequence 0. Results are averaged over the final 200,000 frames and over 20 individual runs. The color scheme is as in Figure 3C: green: folded monomers, cyan: folded proteins exhibiting non-specific interactions, black: domain swapped dimers, yellow: functional dimers, blue: unfolded monomers, red: unfolded proteins exhibiting non-specific interactions. Cell size = 80 units for (A, B), 240 units for (C,D), and 320 units for (E, F). Hinge energy = 0 for (A, C, E) and 2 times the angle between domains for (B, D, F).

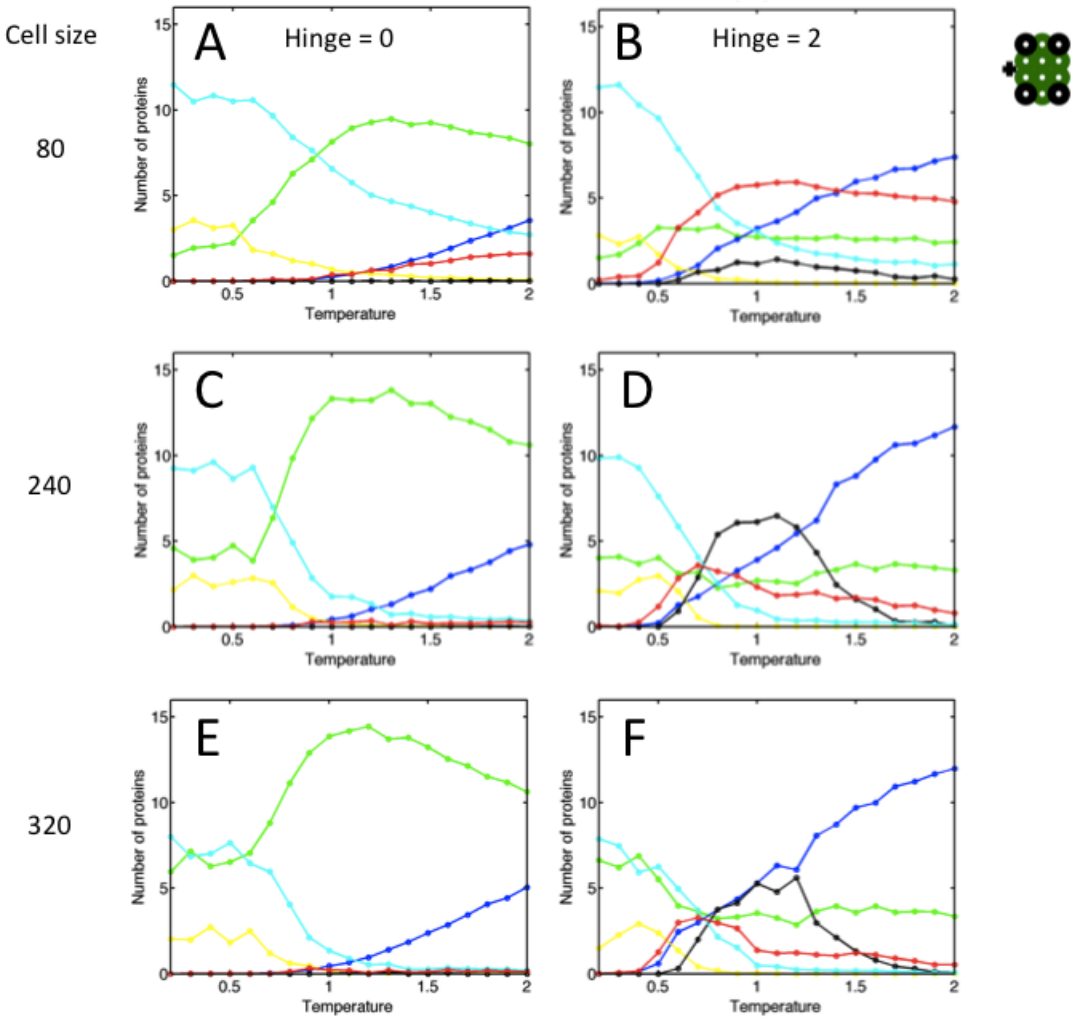


**Figure S2.** Plots displaying protein statistics as a function of temperature for sequence 1. Results are averaged over the final 200,000 frames and over 20 individual runs. The color scheme is as in Figure 3C: green: folded monomers, cyan: folded proteins exhibiting non-specific interactions, black: domain swapped dimers, yellow: functional dimers, blue: unfolded monomers, red: unfolded proteins exhibiting non-specific interactions. Cell size = 80 units for (A, B), 240 units for (C,D), and 320 units for (E, F). Hinge energy = 0 for (A, C, E) and 2 times the angle between domains for (B, D, F).

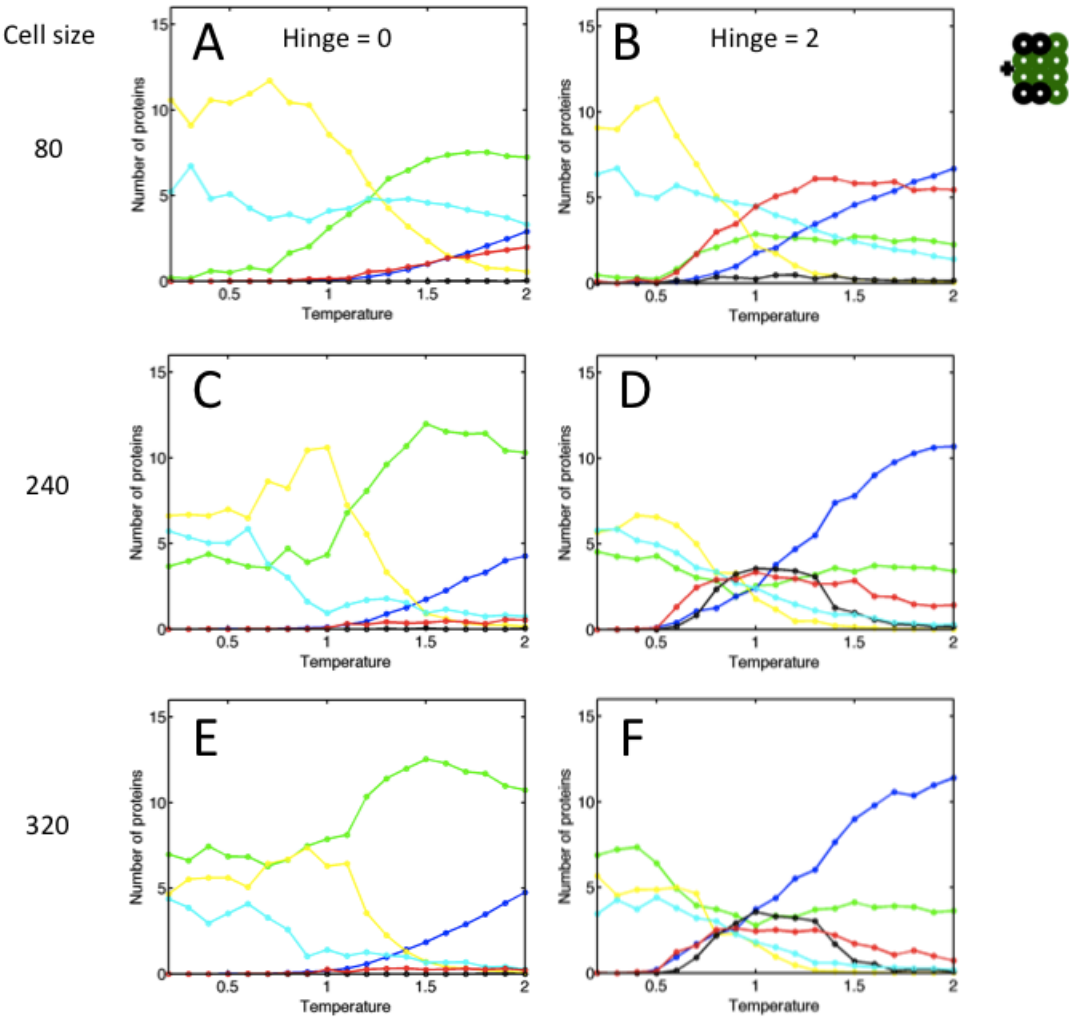


**Figure S3.** Plots displaying protein statistics as a function of temperature for sequence 2. Results are averaged over the final 200,000 frames and over 20 individual runs. The color scheme is as in Figure 3C: green: folded monomers, cyan: folded proteins exhibiting non-specific interactions, black: domain swapped dimers, yellow: functional dimers, blue: unfolded monomers, red: unfolded proteins exhibiting non-specific interactions. Cell size = 80 units for (A, B), 240 units for (C,D), and 320 units for (E, F). Hinge energy = 0 for (A, C, E) and 2 times the angle between domains for (B, D, F).

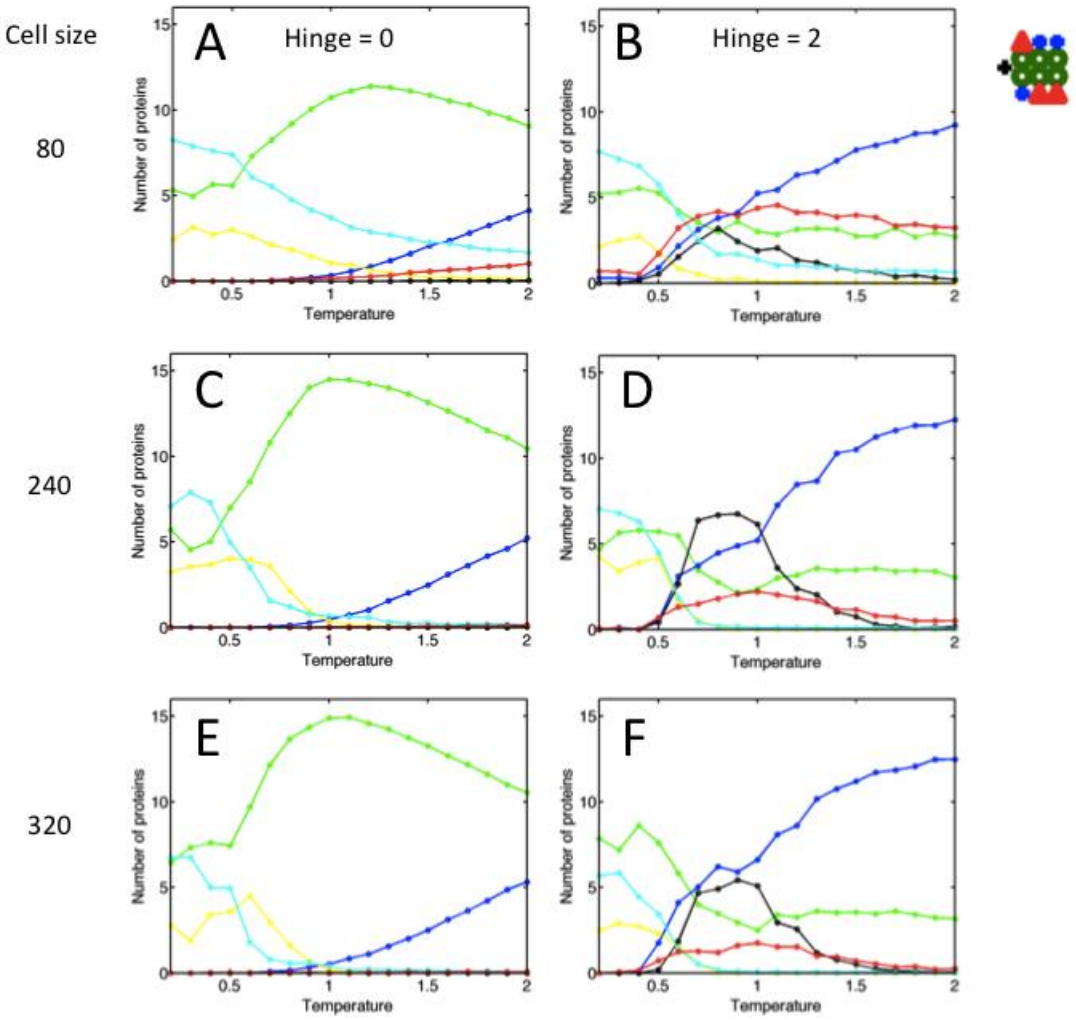


**Figure S4.** Plots displaying protein statistics as a function of temperature for sequence 3. Results are averaged over the final 200,000 frames and over 20 individual runs. The color scheme is as in Figure 3C: green: folded monomers, cyan: folded proteins exhibiting non-specific interactions, black: domain swapped dimers, yellow: functional dimers, blue: unfolded monomers, red: unfolded proteins exhibiting non-specific interactions. Cell size = 80 units for (A, B), 240 units for (C,D), and 320 units for (E, F). Hinge energy = 0 for (A, C, E) and 2 times the angle between domains for (B, D, F).

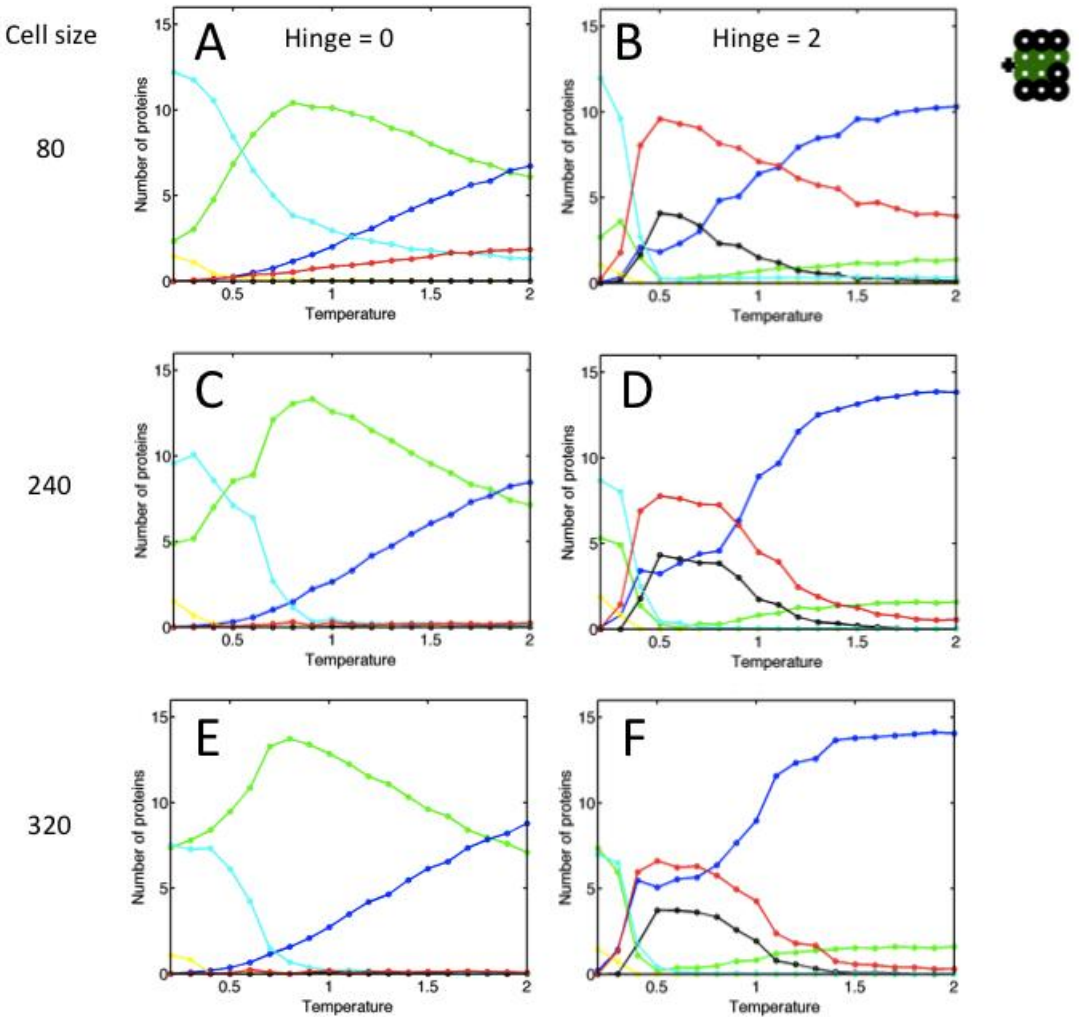


**Figure S5.** Plots displaying protein statistics as a function of temperature for sequence 4. Results are averaged over the final 200,000 frames and over 20 individual runs. The color scheme is as in Figure 3C: green: folded monomers, cyan: folded proteins exhibiting non-specific interactions, black: domain swapped dimers, yellow: functional dimers, blue: unfolded monomers, red: unfolded proteins exhibiting non-specific interactions. Cell size = 80 units for (A, B), 240 units for (C,D), and 320 units for (E, F). Hinge energy = 0 for (A, C, E) and 2 times the angle between domains for (B, D, F).

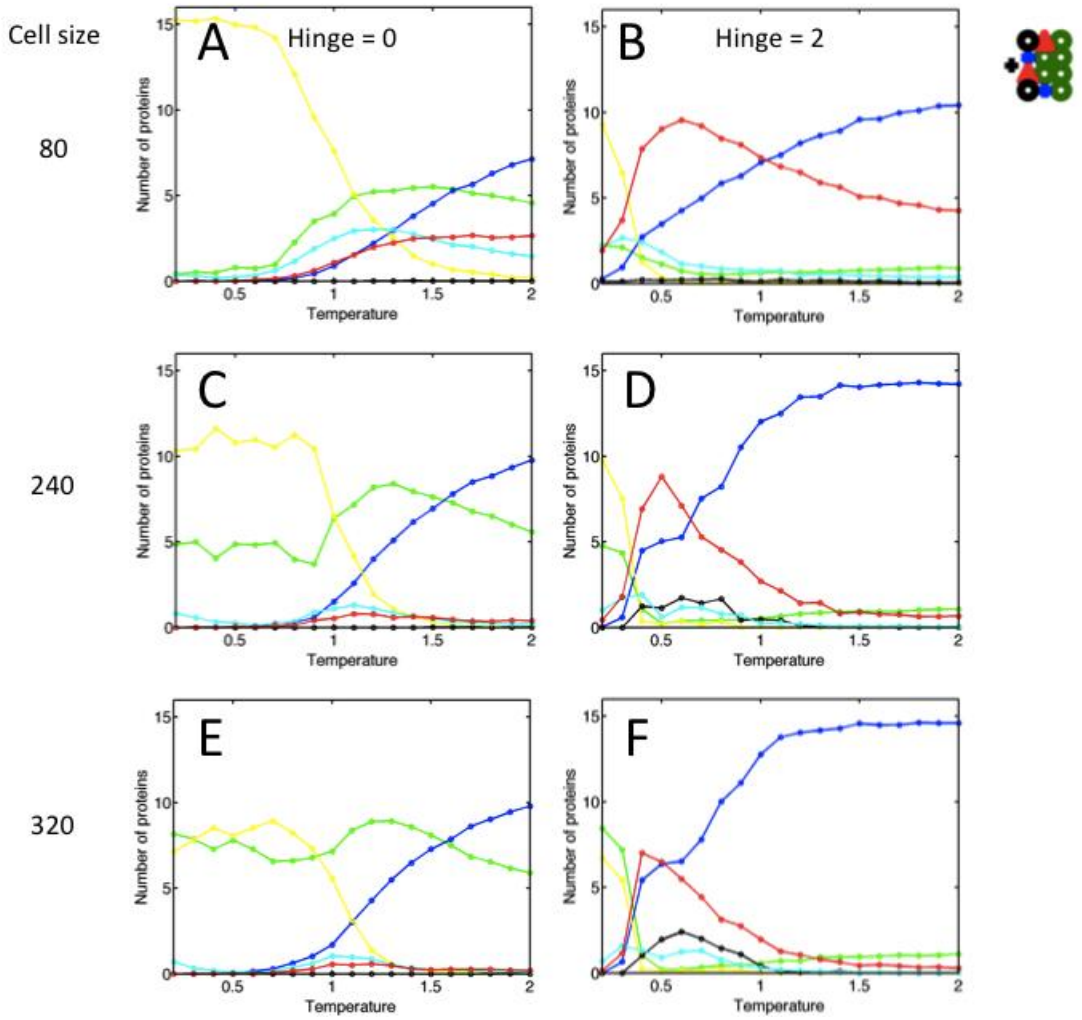


**Figure S6.** Plots displaying protein statistics as a function of temperature for sequence 5. Results are averaged over the final 200,000 frames and over 20 individual runs. The color scheme is as in Figure 3C: green: folded monomers, cyan: folded proteins exhibiting non-specific interactions, black: domain swapped dimers, yellow: functional dimers, blue: unfolded monomers, red: unfolded proteins exhibiting non-specific interactions. Cell size = 80 units for (A, B), 240 units for (C,D), and 320 units for (E, F). Hinge energy = 0 for (A, C, E) and 2 times the angle between domains for (B, D, F).

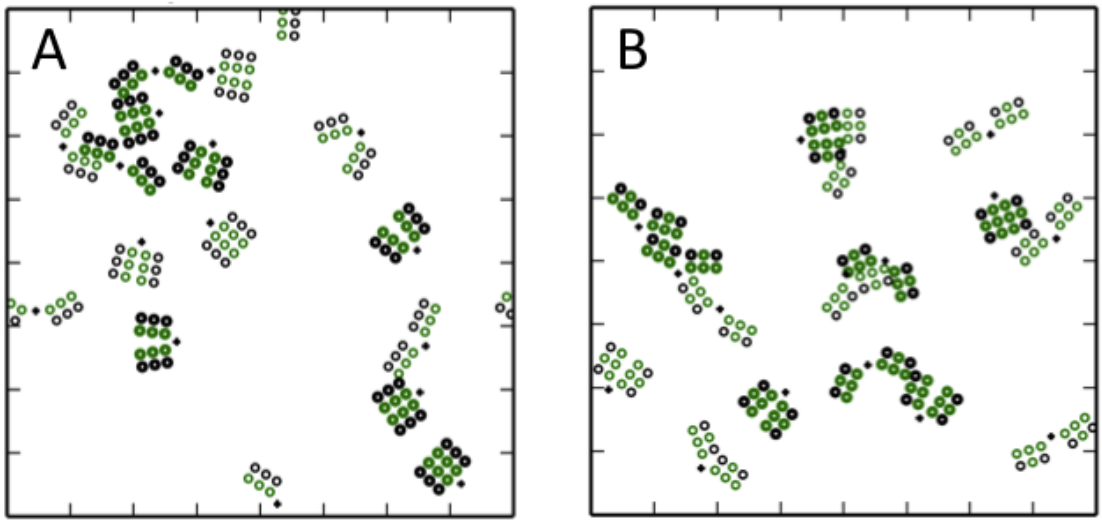


**Figure S7.** Representative frames from simulations at high concentration. A) sequence = 0, hinge = 0, cell size = 80, temperature = 2.0. B) sequence = 1, hinge = 2, cell size = 80, temperature = 1.0.

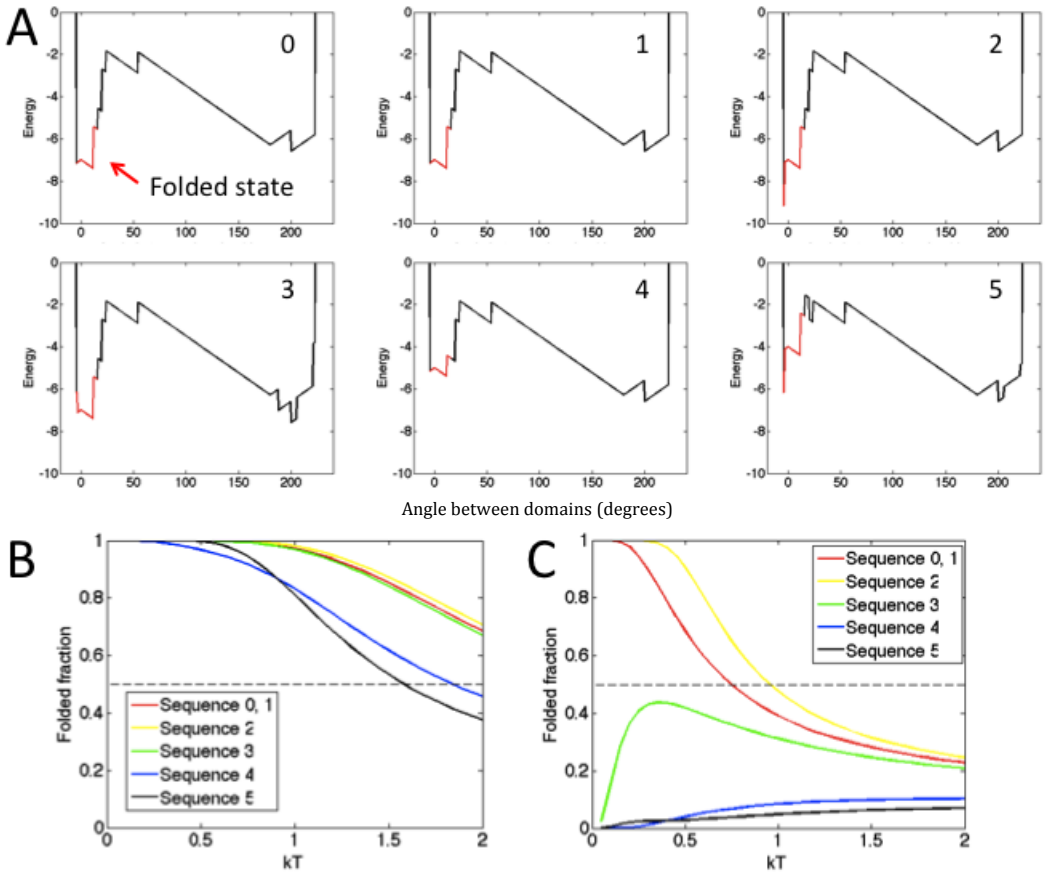


**Figure S8.** Single protein energy landscapes and temperature dependence of folded fraction. A) Domain-domain interaction energy as a function of angle between domains, for sequences 0-5, with hinge energy = 2 times angle between domains. The region defined as the folded state is colored red. B) Population of folded state, calculated from intra-protein interaction diagrams, with hinge energy = 0. The dotted line indicates an equal number of folded and unfolded proteins. C) Population of folded state, calculated from intra-protein interaction diagrams, with hinge energy = 2 (shown in (A)).

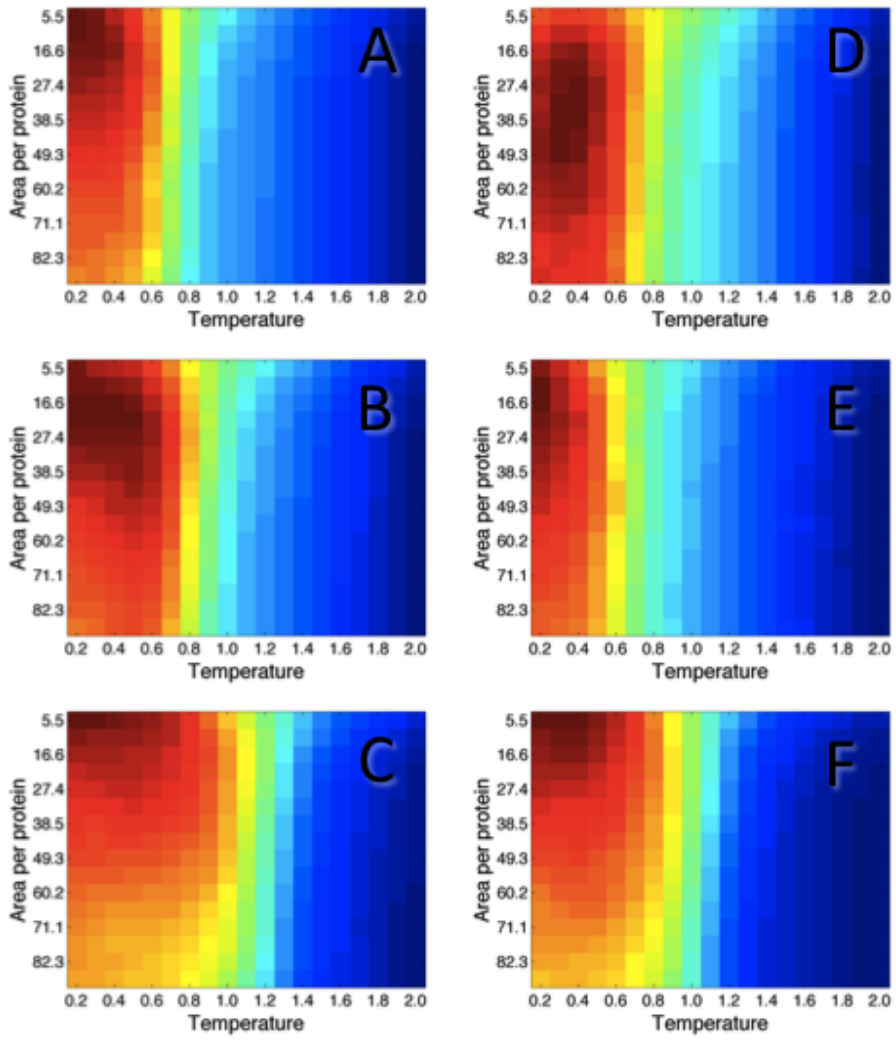


**Figure S9.** Total interaction energy from simulations as a function of cell area and temperature, with hinge = 0. Results are averaged over the final 200,000 frames and over 20 individual runs. Dark red indicates lowest energy, and dark blue indicates highest energy; color scales are normalized for each plot. A smoothing function was applied to each plot in two dimensions. A) Sequence 0. B) Sequence 1. C) Sequence 2. D) Sequence 3. E) Sequence 4. F) Sequence 5.

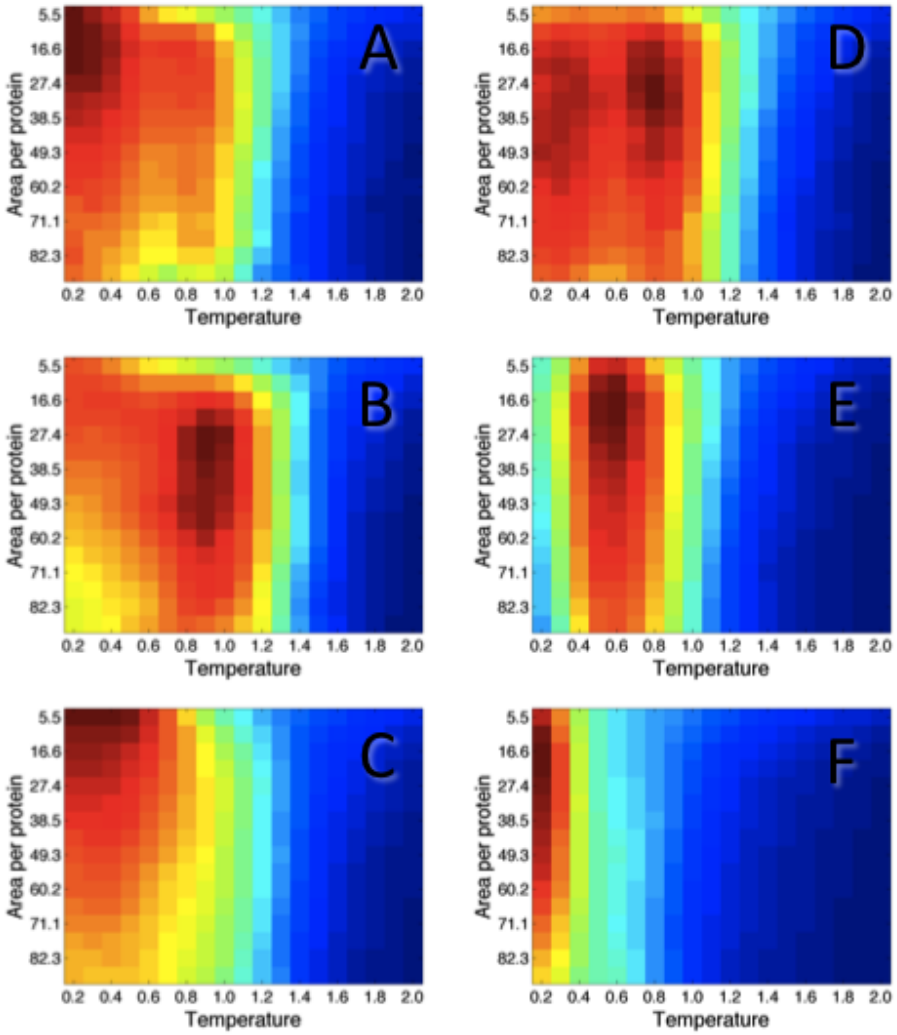


**Figure S10.** Total interaction energy from simulations as a function of cell area and temperature, with hinge = 0. Results are averaged over the final 200,000 frames and over 20 individual runs. Dark red indicates lowest energy, and dark blue indicates highest energy; color scales are normalized for each plot. A smoothing function was applied to each plot in two dimensions. A) Sequence 0. B) Sequence 1. C) Sequence 2. D) Sequence 3. E) Sequence 4. F) Sequence 5.

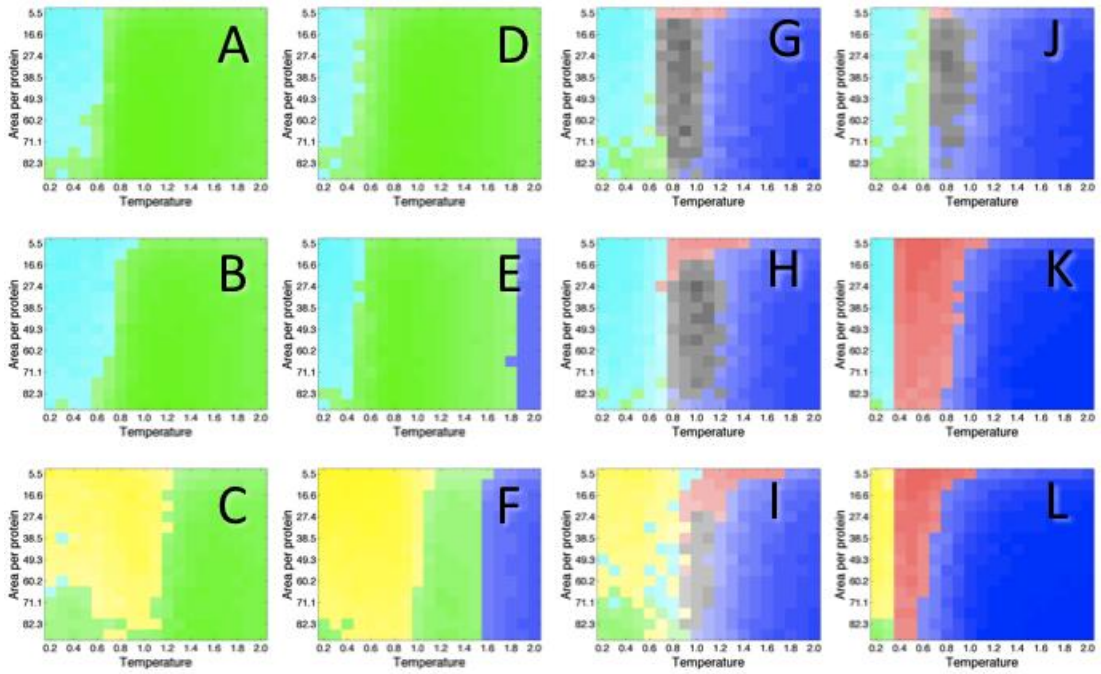


**Figure S11.** Raw phase diagrams, prior to applying smoothing function to generate Fig. 5-6. Hinge energy = 0 for (A-F). A) Sequence 0. B) Sequence 1.. C) Sequence 2. D) Sequence 3. E) Sequence 4. F) Sequence 5. Hinge energy = 2 times angle between domains for (G-L). G) Sequence 0. H) Sequence 1.. I) Sequence 2. J) Sequence 3. K) Sequence 4. L) Sequence 5.