Electronic Supplementary Material (ESI) for Molecular BioSystems

Synergistic Folding of Two Intrinsically Disordered Proteins: Searching for Conformational Selection

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Supplemental Materials

Table S1: All 76 native intermolecular contacts identified from PDB:1KBH, model 1. Residues 1-47 correspond to ACTR residues 1040-1086, and residues 48-106 correspond to NCBD residues 2059-2117.

Contacting Residues	ε_{ij} (kcal/mol)	Contacting Residues	ε_{ij} (kcal/mol)
GLU 1 ILE 52	0.514847	ALA 22 SER 68	0.316466
GLU 1 GLN 85	0.223573	THR 23 SER 69	0.308593
GLN 3 GLN 85	0.242466	LEU 25 LEU 64	1.160374
SER 4 ARG 50	0.255062	LEU 25 PHE 90	1.146204
ASP 5 ARG 50	0.360550	LEU 25 ARG 94	0.634506
ASP 5 SER 51	0.256636	GLU 27 GLN 74	0.223573
GLU 6 ARG 50	0.357402	ILE 28 VAL 76	0.952546
GLU 6 SER 51	0.233019	ILE 28 LEU 77	1.108417
LEU 9 SER 51	0.617187	ILE 28 LEU 80	1.108417
LEU 9 SER 53	0.617187	ILE 28 PHE 90	1.076928
LEU 9 LEU 57	1.160374	ASP 29 PHE 90	0.547911
LEU 10 GLN 85	0.636080	ASP 29 ARG 94	0.360550
LEU 10 LEU 86	1.160374	ASP 29 TYR 98	0.434550
LEU 10 ALA 89	0.773058	ALA 31 LEU 77	0.773058
GLN 12 LEU 57	0.636080	LEU 32 LEU 77	1.160374
GLN 12 LEU 61	0.636080	LEU 32 MET 87	1.009226
LEU 13 SER 53	0.617187	LEU 32 PHE 90	1.146204
LEU 13 ALA 56	0.773058	LEU 32 ILE 91	1.108417
LEU 13 LEU 60	1.160374	ILE 34 PHE 90	1.076928
LEU 13 LEU 61	1.160374	ILE 34 ILE 91	1.029694
LEU 13 LEU 86	1.160374	ILE 34 ARG 94	0.571528
HSD 14 LEU 86	0.714803	ILE 34 THR 95	0.634506
HSD 14 ALA 89	0.379444	ILE 34 TYR 98	0.826589
LEU 16 LEU 61	1.160374	PRO 35 TYR 98	0.502251
LEU 16 LEU 64	1.160374	LEU 37 ILE 91	1.108417
LEU 16 LYS 65	0.530592	LEU 37 THR 95	0.683314
LEU 17 LEU 60	1.160374	VAL 38 THR 95	0.544762
LEU 17 LEU 64	1.160374	VAL 38 TYR 98	0.727399
LEU 17 VAL 76	1.020248	VAL 38 VAL 99	0.869100
LEU 17 LEU 80	1.160374	ASN 39 MET 105	0.464465
LEU 17 LEU 86	1.160374	GLN 42 LYS 92	0.203105
LEU 17 PHE 90	1.146204	GLN 42 THR 95	0.299147
SER 18 GLN 93	0.234594	ALA 43 THR 95	0.365274
SER 18 ARG 94	0.255062	ALA 43 ALA 96	0.428252
ASN 19 LEU 64	0.588847	ALA 43 VAL 99	0.636080
ASP 21 ARG 94	0.360550	LEU 44 GLN 106	0.636080
ASP 21 LYS 97	0.264509	GLU 45 LYS 92	0.283402
ALA 22 LEU 64	0.773058	LYS 47 LYS 92	0.018893

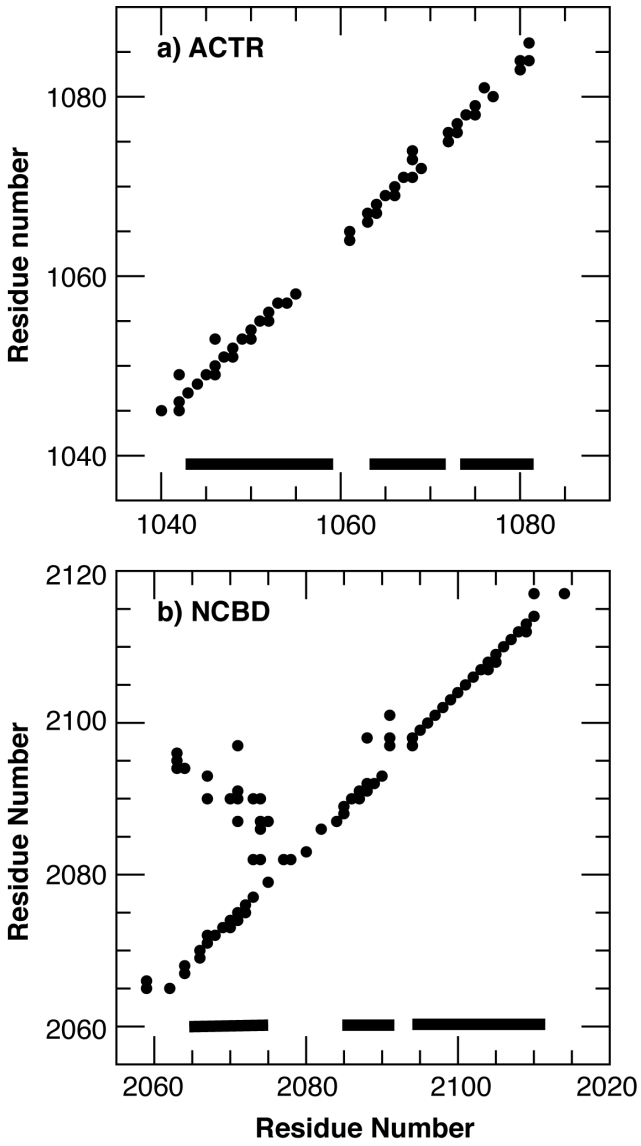

Figure S1. Residue-residue intra-molecular contact maps of ACTR and NCBD in the complex. The contact maps are derived from the PDB:1kbh model 1. The solid bars mark the locations of helical segments formed in the complex.

a)

b)

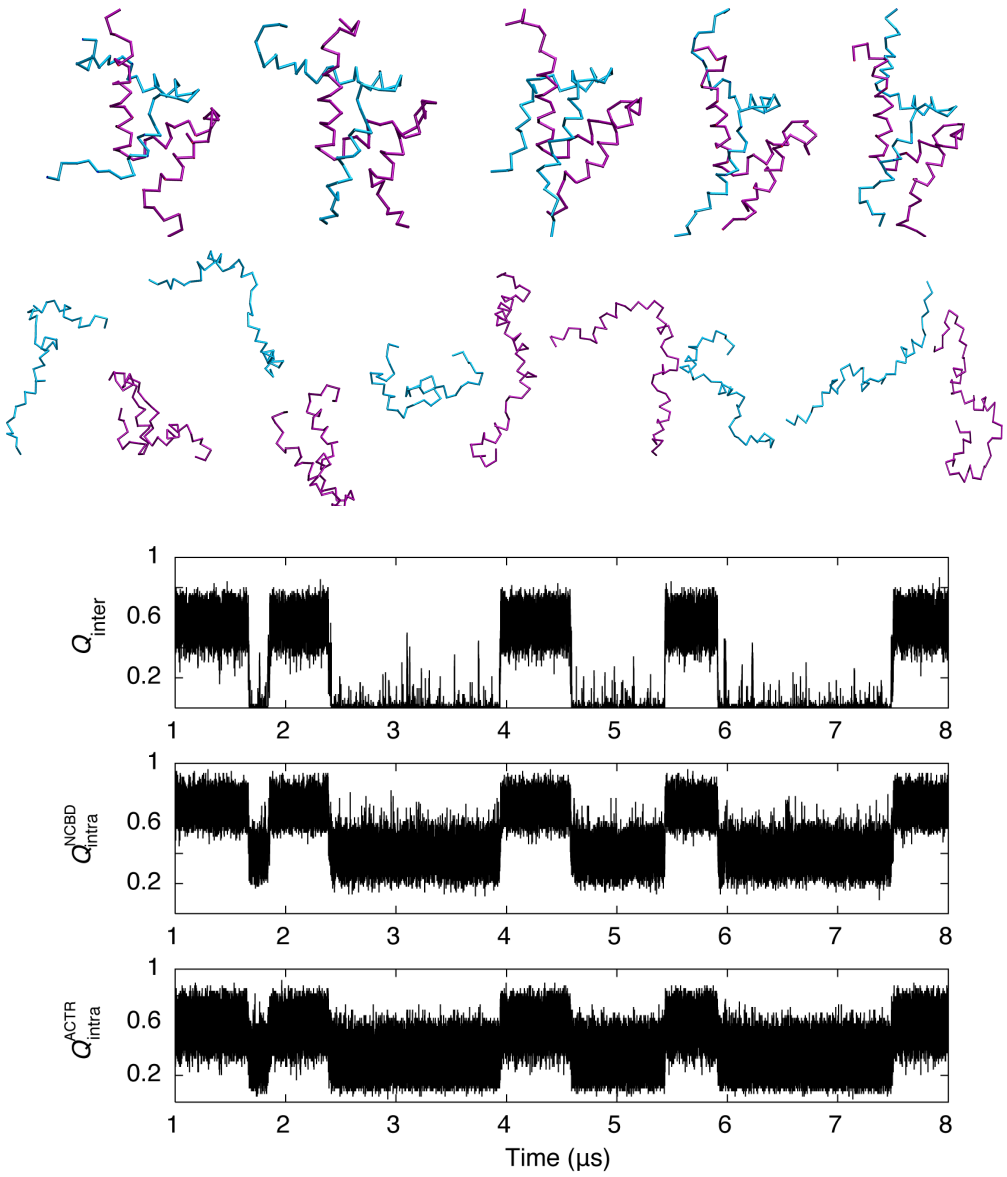

Figure S2. a) Five bound and five unbound conformations randomly selected from the REX calibration simulation using the final calibrated sequenced-flavored Gō-like model. NCBD is shown in purple trace and ACTR in cyan. b) Representative time traces of the fractions of inter- and intra-molecular contacts from one of eleven independent 30-μs production simulations at T_m = 315 K.

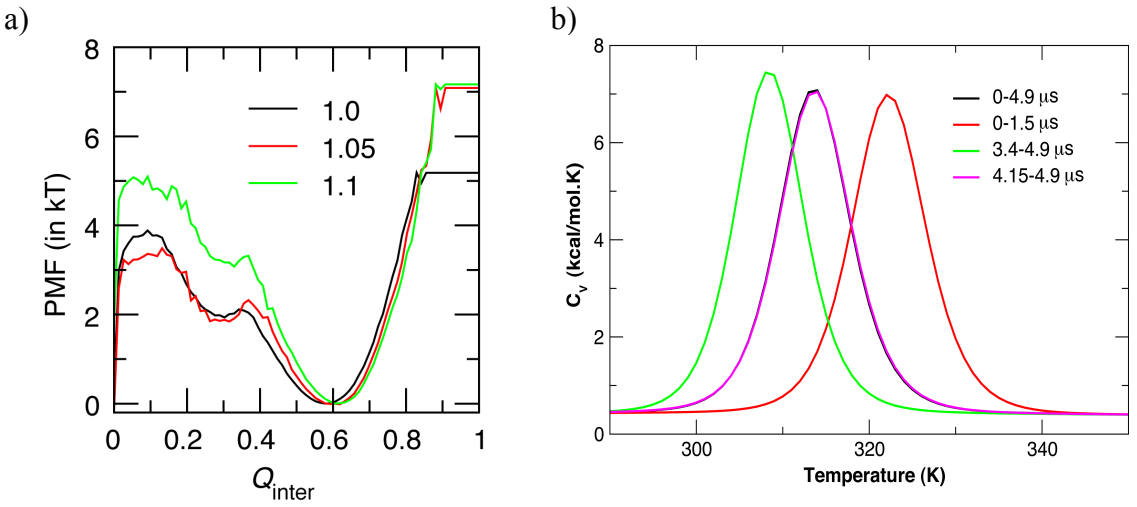

Figure S3. a) The PMFs as functions of Q_{inter} with three of scaling values of the intermolecular interaction strength searched during model calibration. b) The heat capacity as a function of temperature. The curves were calculated from various segments of a 4.9-μs REX simulation of the NCBD/ACTR complex using the final calibrated model. The simulation appears to reasonably converged after 4 μs.

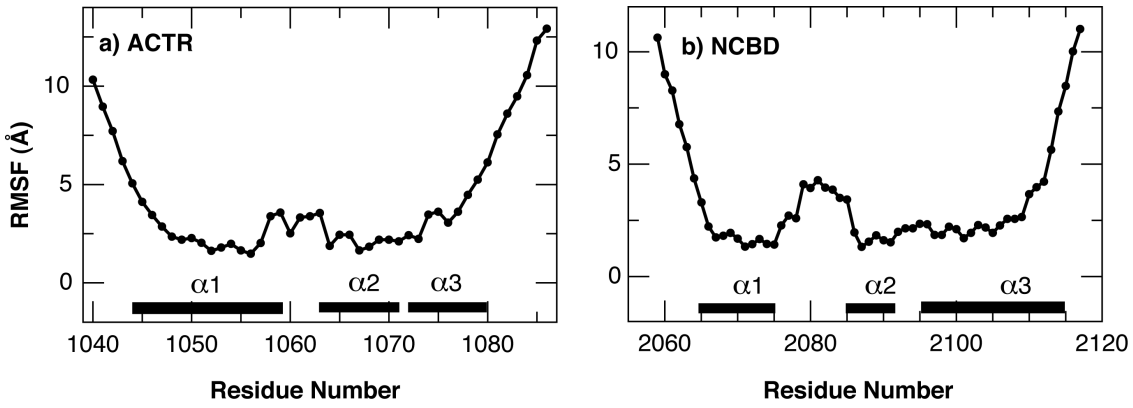

Figure S4. The RMSF profiles of NCBD and ACTR in the bound state at 300 K. These profiles were calculated from a 1-μs simulation of the folded complex using the final calibrated model.

Table S2: Summary of all 11 production simulations at 315 K. The average fraction of the unbound state is above 0.5, indicating that T_m is actually slightly below 315 K. The five initial bound (b1 to b5) and unbound (u1 to u5) conformations are shown in Fig. S2a.

Initial Conformation	**Time (μs)**	N_{trans}	P_{ub}
1KBH Model 1	30	26	0.62
1100.pdb (b1)	30	29	0.50
6200.pdb (b2)	30	23	0.73
6800.pdb (b3)	30	21	0.60
700.pdb (b4)	30	16	0.69
7200.pdb (b5)	30	26	0.55
15230.pdb (u1)	30	29	0.61
4200.pdb (u2)	30	20	0.80
2900.pdb (u3)	30	20	0.78
19113.pdb (u4)	30	30	0.65
23510.pdb (u5)	30	28	0.62
Average	**30**	**24.4**	**0.65**

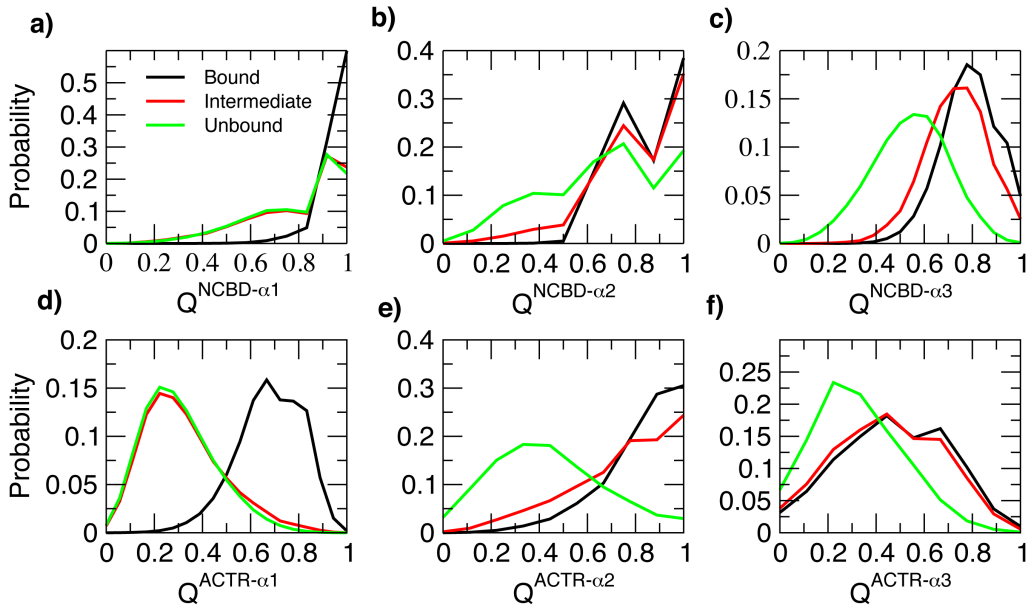

Figure S5. Distributions of the fractions of intra-molecular contacts of various ACTR and NCBD helical segments in the unbound, intermediate and bound states. See the main text for the state assignment criteria.

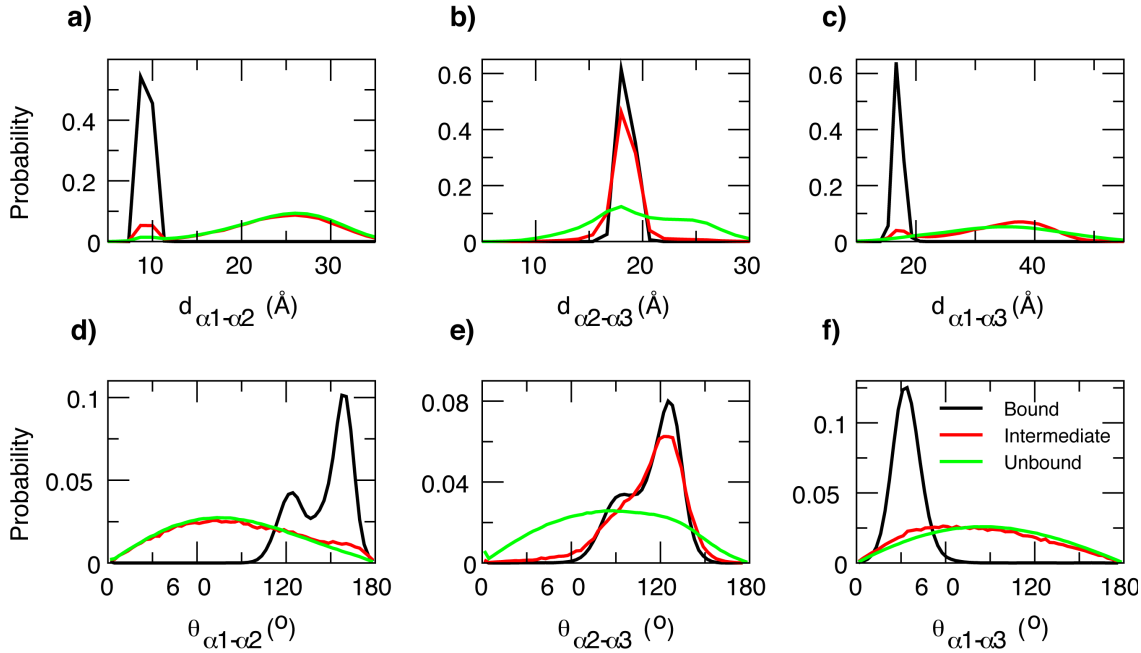

Figure S6. Distributions of the distances and cross-angles between NCBD helices in the unbound, intermediate and bound states. The helix-helix distances were calculated as the distances between the CA atoms at the middle of the helices. See the main text for the state assignment criteria.

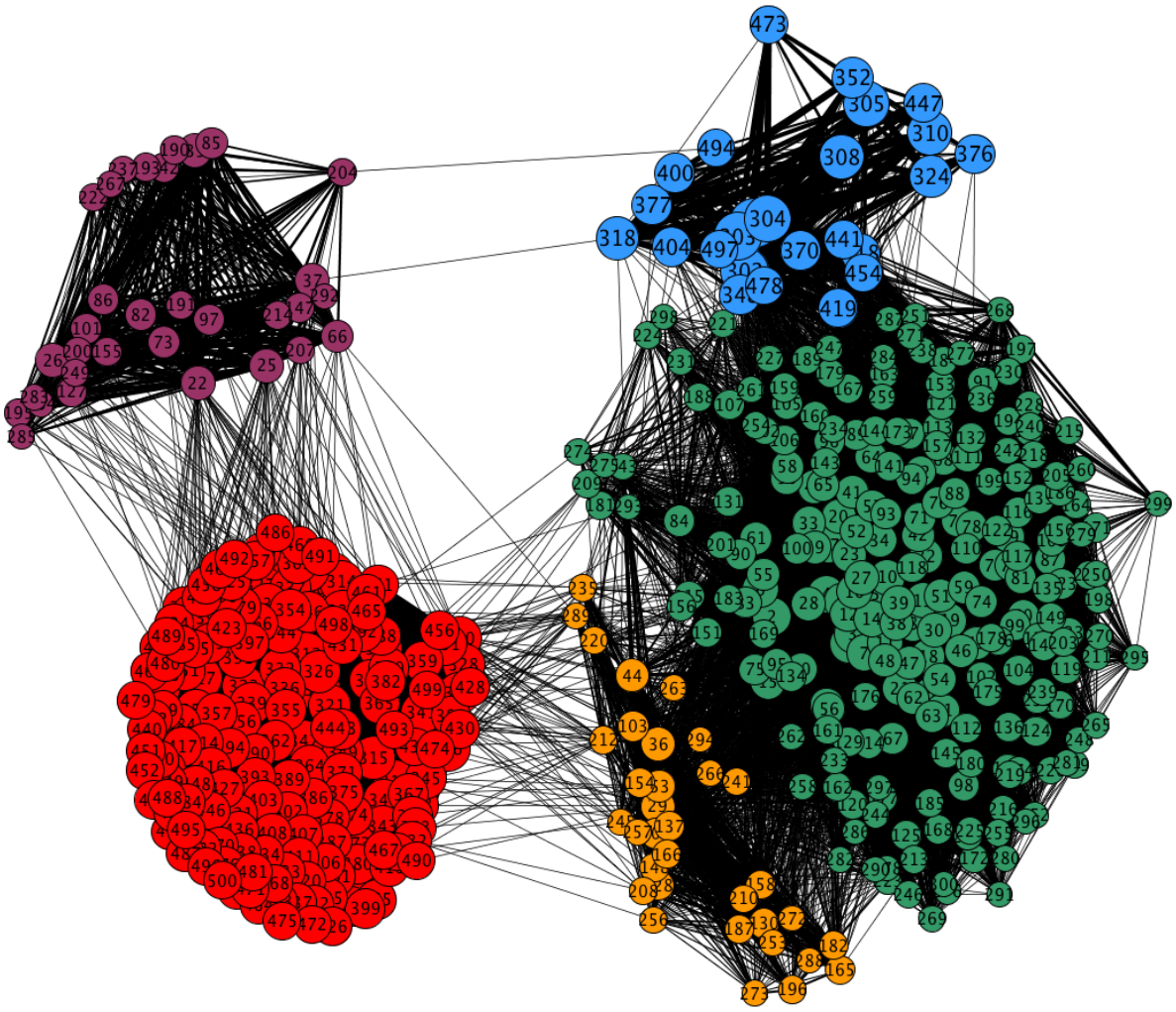

Figure S7. CSN of the synergetic folding of NCBD and ACTR, constructed by including the most populated 200 nodes and additional 300 nodes from the transition paths. The nodes are colored in the same fashion as in Fig. 9 of the main text.