Molecular Simulations of a Dynamic Protein Complex: Role of Salt-Bridges and Polar Interactions in Configurational Transitions

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SUPPORTING MATERIAL

Supplemental Movies

Transitions are evident in the trajectory started with the cluster1 configuration (movie1), but not in the trajectory started with a structure far away from the major configurations (movie2, see methods). In both movies, the SAM domain mainchain is shown in ribbon representation, and is aligned on the EphA2 SAM domain. Note that in the second movie, the configuration of the complex is with helix5 nearly antiparallel. This does not change/fluctuate over the course of the simulation (see Fig. S2b).

movie1.mpg

movie2.mpg

Supplemental Tables

Table S1. Analysis of cluster centers. Coordinate frames from the four and six trajectories were k-clustered by interface sidechain RMSD as described (cut-off 5.5 Å). Cluster center population in the trajectories and RMSD to starting structures is given (underlined value is the closest). The extent to which the experimental restraints are satisfied in these unrestrained calculations is given; Q-factors for RDCs from the two alignment media and RMS deviation from ambiguous and unambigious NOEs (experimental data from reference 5) are given. Q-factors ≥ 31% and RMS NOE ≥ 1.0 A are in bold. In clustering all trajectories, the 8 of 14 cluster center structures no longer satisfy the NMR data well, amounting to 26% of structures (another 26% of structures in cluster12 are near the cut-off). * Cluster centers are structures from the two non-converged trajectories.

Clustering of 4 trajectories and rel. population	**Q-factor RDC1**	**Q-factor RDC2**	**RMS_NOE (Å)**	**RMSD to cluster1 (Å)**	**RMSD to cluster2 (Å)**	**RMSD to cluster3 (Å)**
Cluster1 15%	28.0	29.9	0.65	1.74	4.03	4.74
Cluster2 4%	29.5	28.1	0.67	2.68	4.61	4.72
Cluster3 1%	**42.2**	**35.6**	0.44	4.14	7.50	2.46
Cluster4 17%	29.1	**31.9**	0.67	2.29	3.04	5.89
Cluster5 9%	28.1	28.7	0.67	2.07	3.89	5.10
Cluster6 53%	28.8	30.5	0.62	2.54	5.11	4.20
Clustering of 6 trajectories and rel. population	**Q-factor RDC1 (%)**	**Q-factor RDC2 (%)**	**RMS_NOE (Å)**	**RMSD to cluster1 (Å)**	**RMSD to cluster2 (Å)**	**RMSD to cluster3(Å)**
Cluster1 4%	**39.0**	**31.7**	0.70	3.20	5.00	5.00
Cluster2 6%	27.9	29.1	0.63	2.90	3.44	6.28
Cluster3 7%	29.4	30.5	0.47	3.93	4.75	6.07
Cluster4 17%	27.7	28.8	0.66	2.51	3.81	5.70
Cluster5 1%	28.2	30.3	**1.08**	7.12	5.38	9.77
Cluster6 3%	29.2	29.5	**1.20**	2.76	5.06	4.61
Cluster7* 2%	**41.9**	**43.1**	**2.01**	11.38	11.53	8.74
Cluster8* 1%	27.2	29.9	0.94	5.66	8.83	2.98
Cluster9* 5%	**31.0**	28.9	**2.50**	10.85	11.81	8.22
Cluster10* 4%	29.8	30.6	**1.26**	10.40	11.57	7.53
Cluster11 17%	29.3	28.5	0.48	3.91	5.49	5.10
Cluster12 26%	30.6	**31.0**	0.54	3.61	4.11	6.39
Cluster13 4%	**38.0**	**32.8**	0.83	5.48	3.41	8.83
Cluster14 3%	**35.1**	29.1	0.77	3.42	4.47	5.76

Supplemental Figures

Figure S1. Analysis of three trajectories (see Fig. 2 for description of parameters). Trajectories were started with a) a cluster1-like configuration (structure refined without unambiguous NOEs from reference 6), with b) cluster2 and c) the cluster3 structure. The RMSD is calculated from the starting structure (blue) and from the NMR derived cluster1 (green) as the reference.

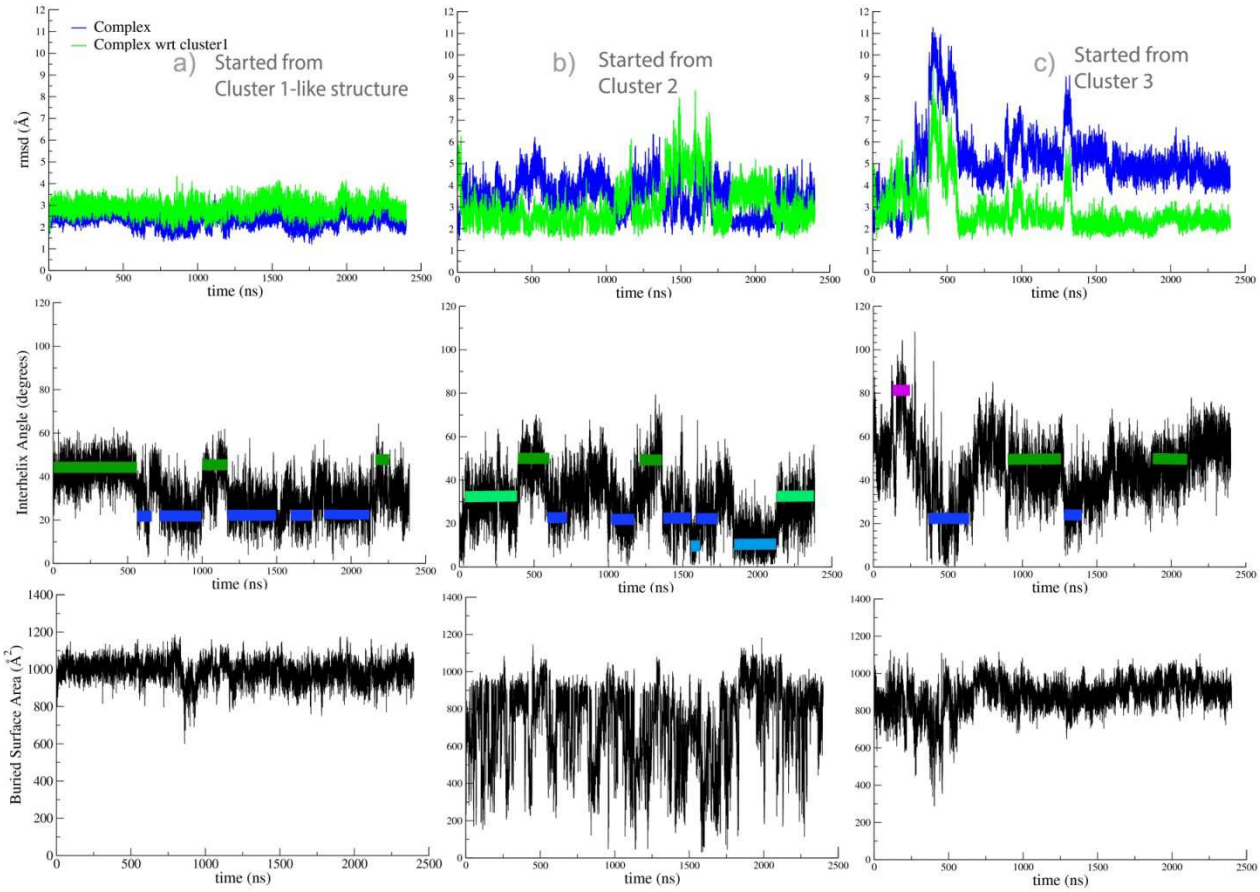


Figure S2. Analysis of two trajectories (see description for Fig. 2 and S1, above). Two trajectories that moved/stayed away from the NMR derived structures a) started with a cluster3 structure and b) started with a structure away from the three NMR derived configurations (a minor configuration in the structure determination without unambiguous restraints, ref. 6). Note the expanded scale for the inter-helix angle compared to Fig. 2 and S1.

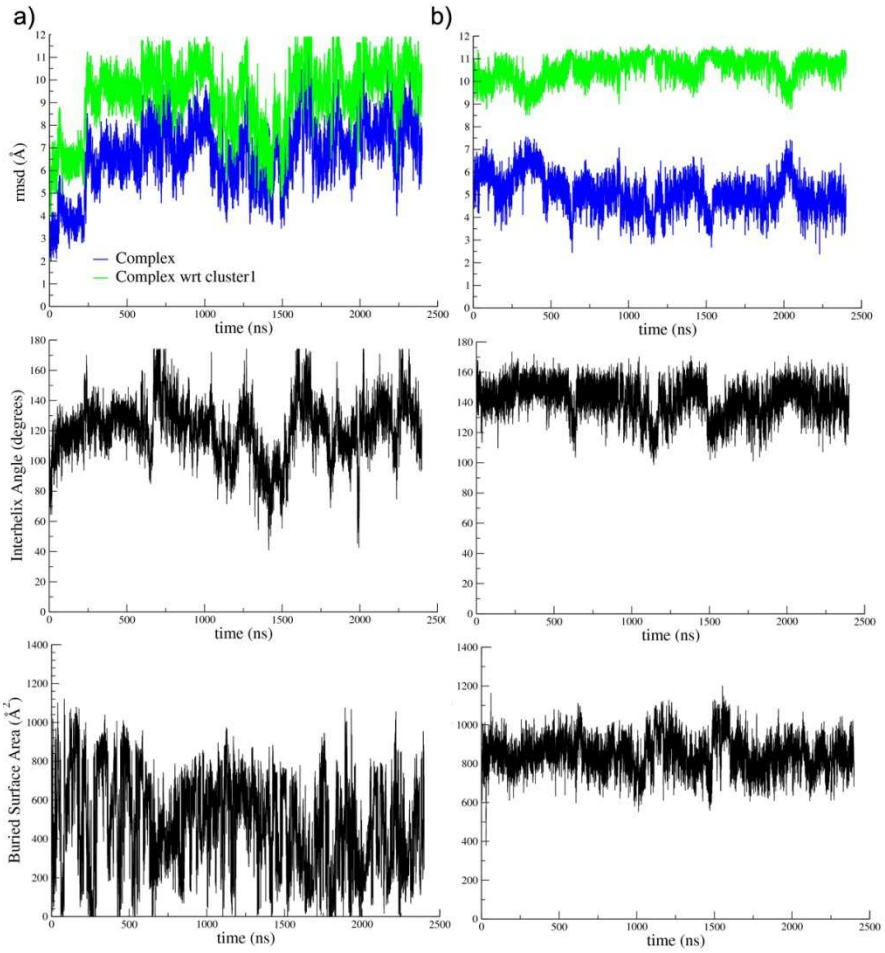
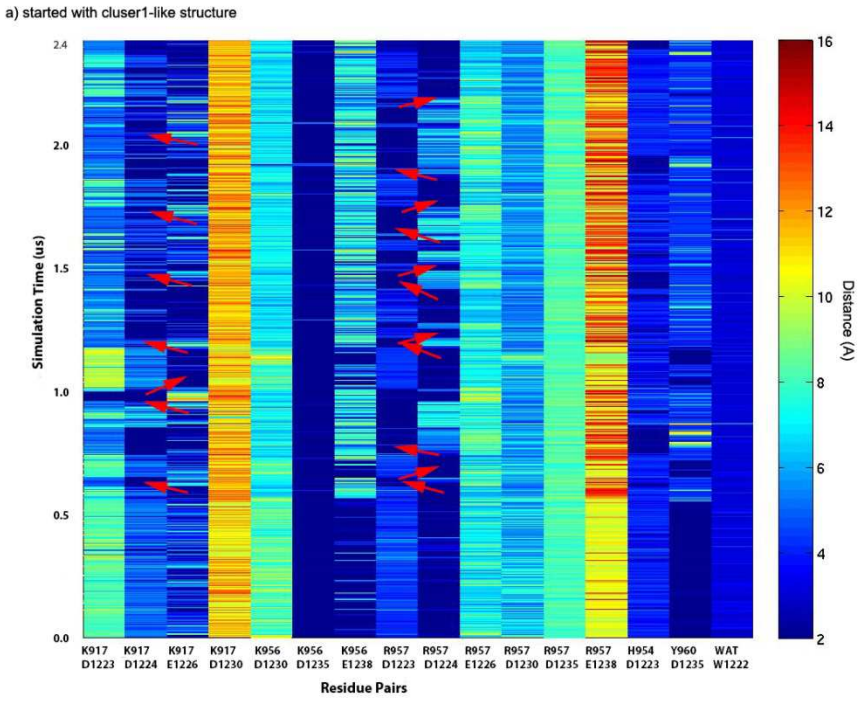
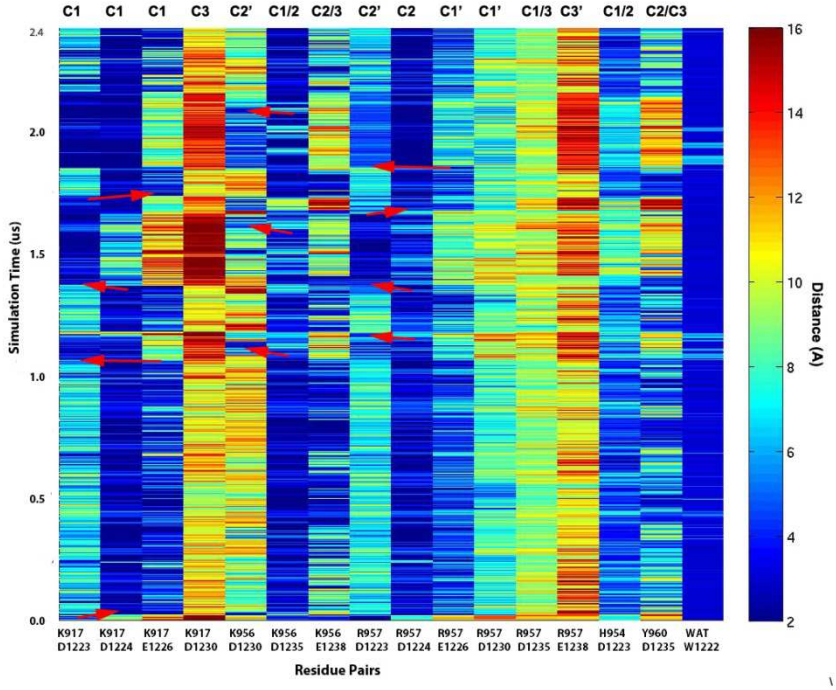


Figure S3. Distances between ion pairs/hydrogen bond donor-acceptor groups across the interface, plotted as a function of simulation time. Distances are indicated by colors (dark blue 2 Å to dark red 16 Å). The trajectories analyzed are those of Fig. S1. a) a cluster1-like configuration (see legend of Fig. S1), b) cluster2 and c) the cluster3 structure. For those contacts that match/are close to those the NMR derived clusters we use the label C1, C2, C3, whereas for those with contacts that partially match or a little away from NMR derived contact pairings we use C1'.



b) started with cluster2 structure



c) started with cluster3 structure

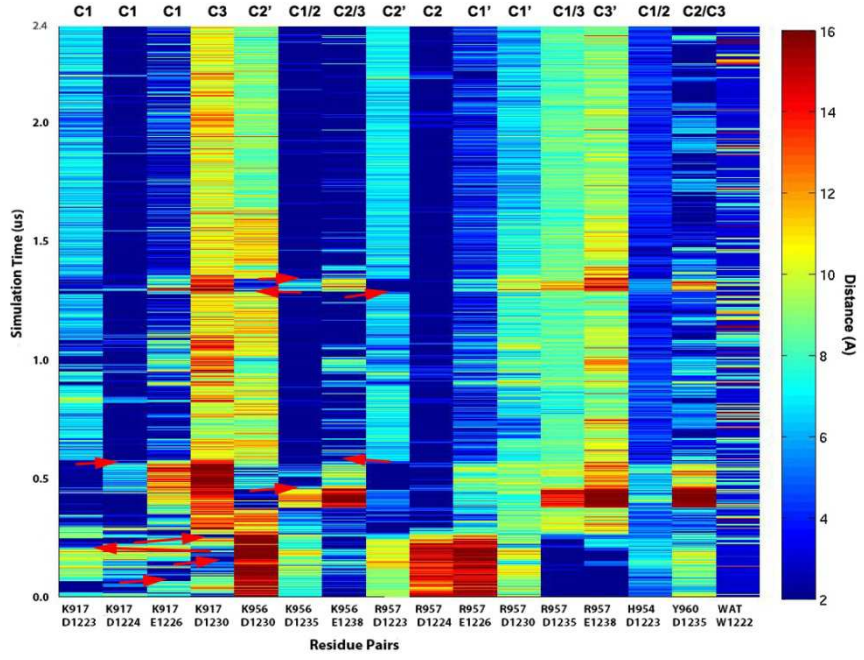


Figure S4. Same as Fig. S3, but for the two trajectories that showed few transitions (see Fig. S2).