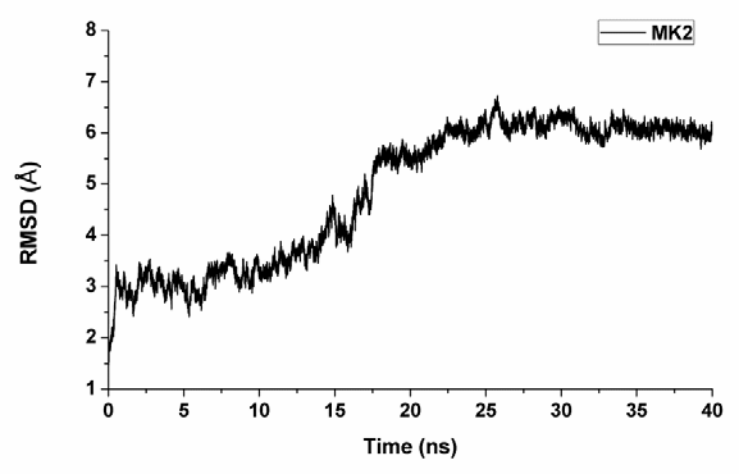
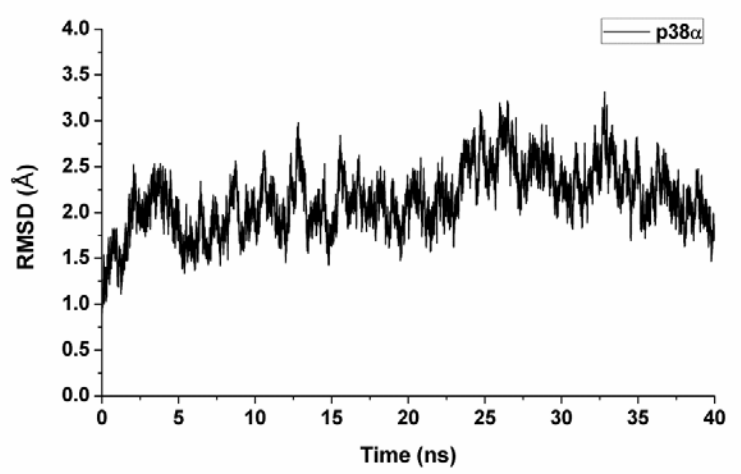
Supporting Information

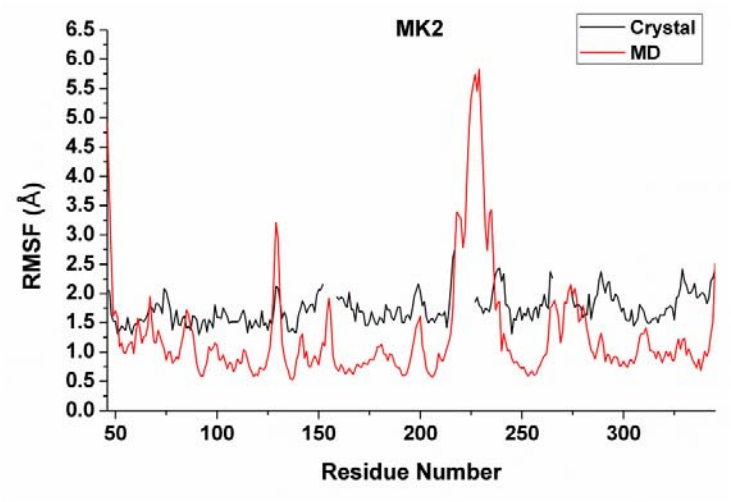


(a)

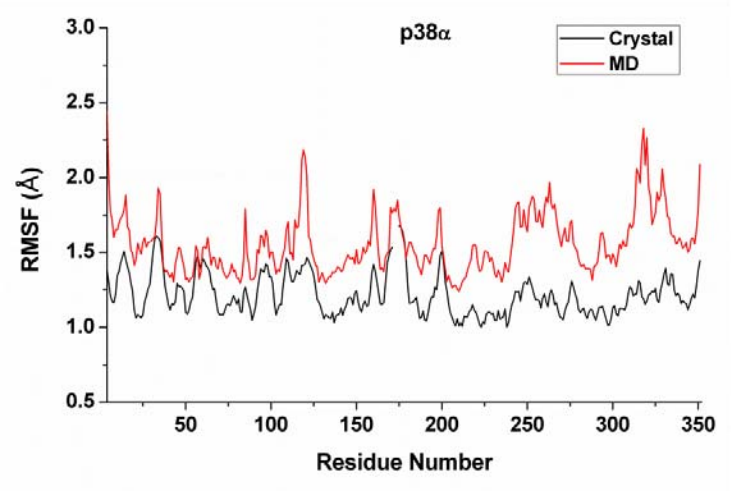


(b)

Figure S1. The RMSD plots for the protein backbone atoms of the individually crystallized MK2 (PDB: 1NY3) and p38α (PDB: 1R39) proteins relative to the initial structures over the 40-ns MD simulations.

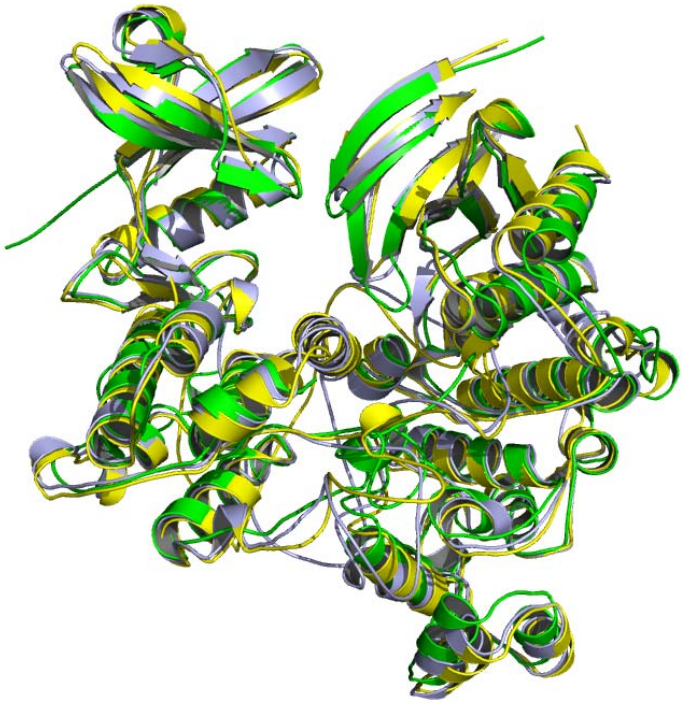


(a)

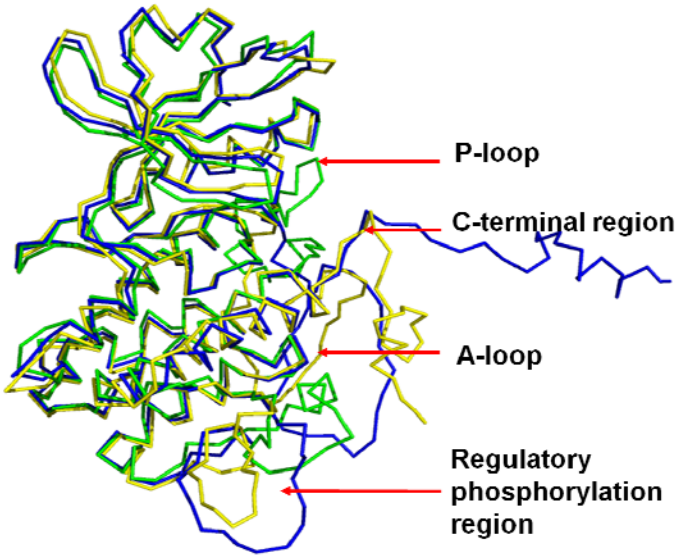


(b)

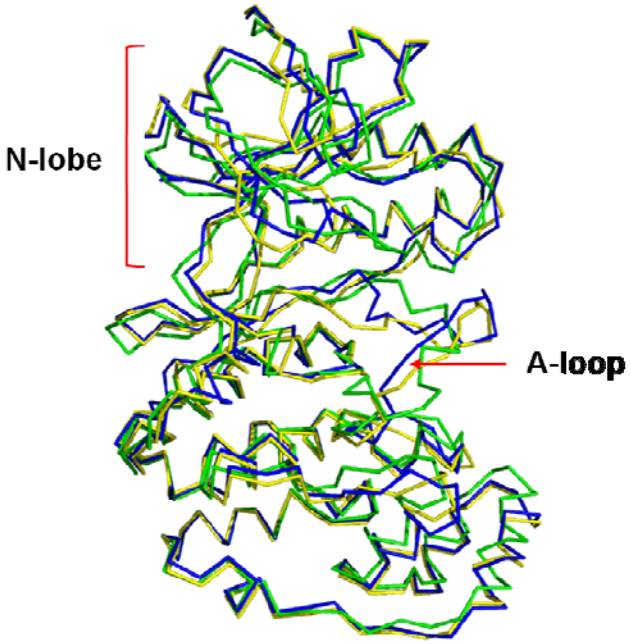
Figure S2. The RMSF plots of residue fluctuations obtained by averaging atomic fluctuations over the 40-ns MD simulation and by computing the value from the experimentally derived B factors for the individually crystallized MK2 (PDB: 1NY3) and p38α (PDB: 1R39) proteins.



(a) MK2-p38α

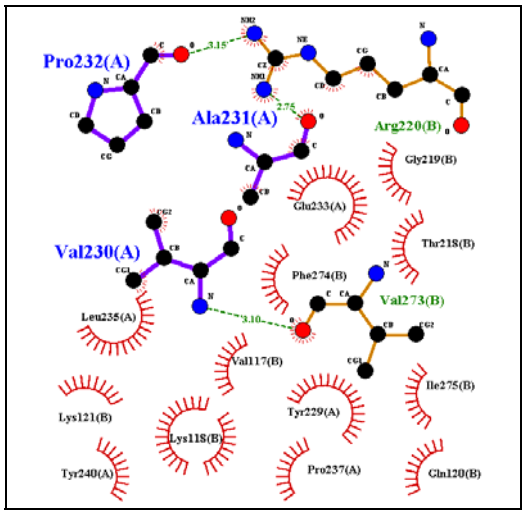


(b) MK2

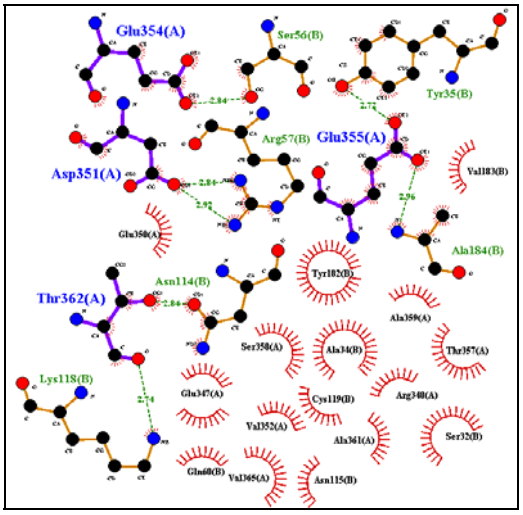


(c) p38α

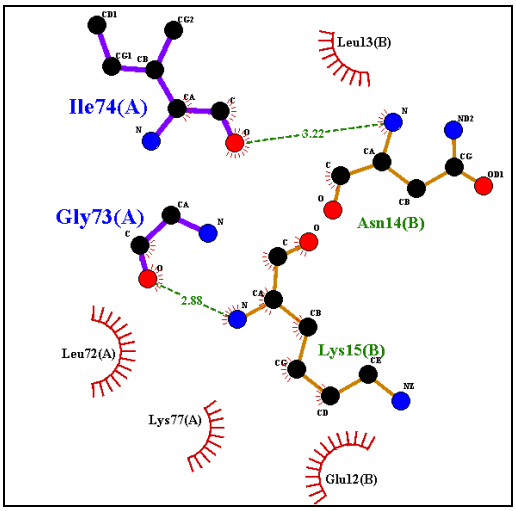
Figure S3. Superimpositions of average structures from the last 20 ns of the MD trajectories: (a) Overlay of the individually crystallized MK2 (PDB: 1NY3, green) and p38α (PDB: 1R39, green), the unbound MK2 and p38α (yellow) from the MK2-p38α complex (PDB: 2OZA), and the MK2-p38α complex (PDB: 2OZA, blue). (b) Overlay of the individually crystallized MK2 (green), the unbound MK2 (yellow), and the complex MK2 (blue). (c) Overlay of the individually crystallized p38α (green), the unbound p38α (yellow), and the complex p38α (blue).



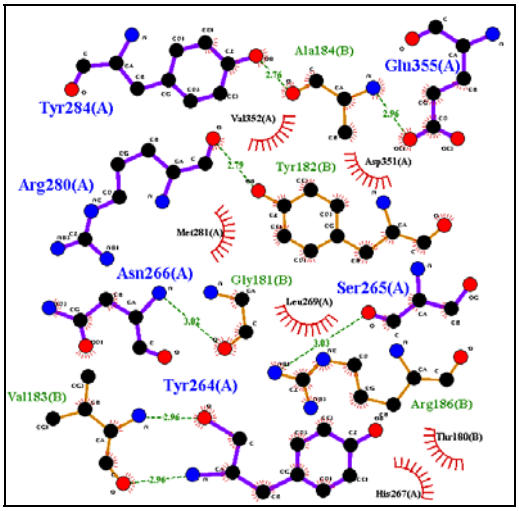
(a) Region I



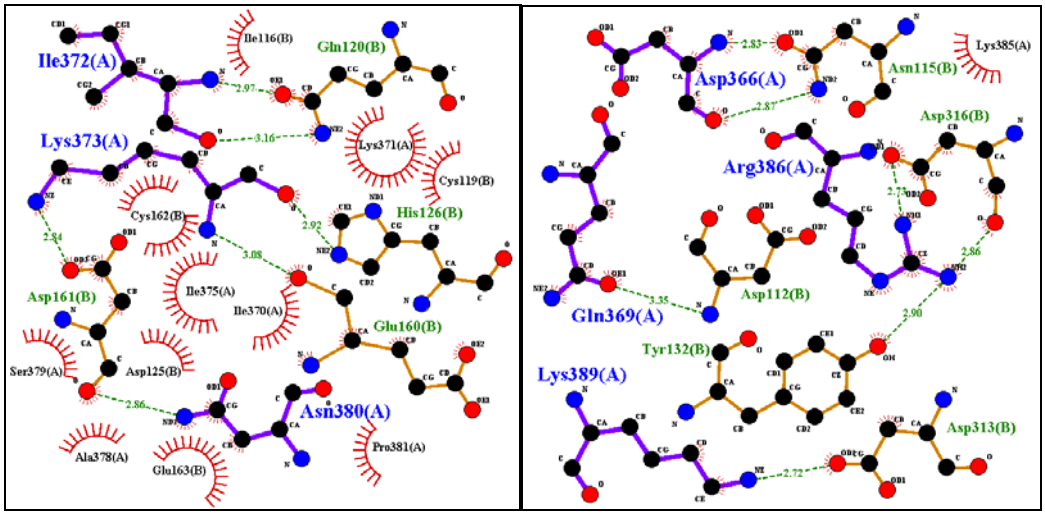
(b) Region II



(c) Region III

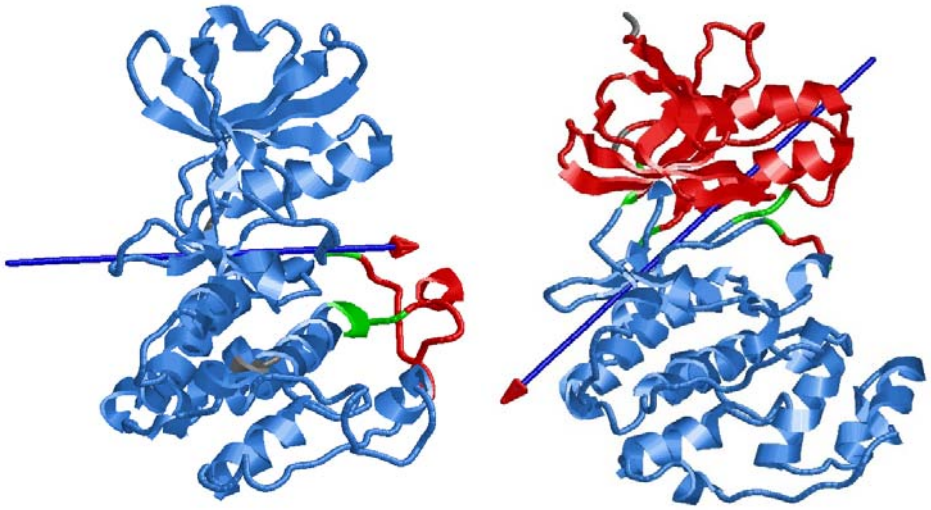


(d) Region IV



(e) Region V

Figure S4. **DIMPLOT** diagram of the residues interacting across the dimer interface of MK2-p38α complex for five interaction regions. The label A represents MK2, and B represents p38α. The interactions shown are those mediated by hydrogen bonds and by hydrophobic contacts. Hydrogen bonds are indicated by dashed lines between the atoms involved, while hydrophobic contacts are represented by an arc with spokes radiating towards the atoms they contact. The contacted atoms are shown with spokes radiating back.



(a) MK2 (b) p38α

Figure S5. The first principal component mode of motion for the individually crystallized MK2 (PDB: 1NY3) (a) and p38α (PDB: 1R39) (b). The colors of the arrows denote the particular moving domain (right-hand rule). The fixed domains are the large domains colored in blue, and the moving domains are the small domains colored in red.

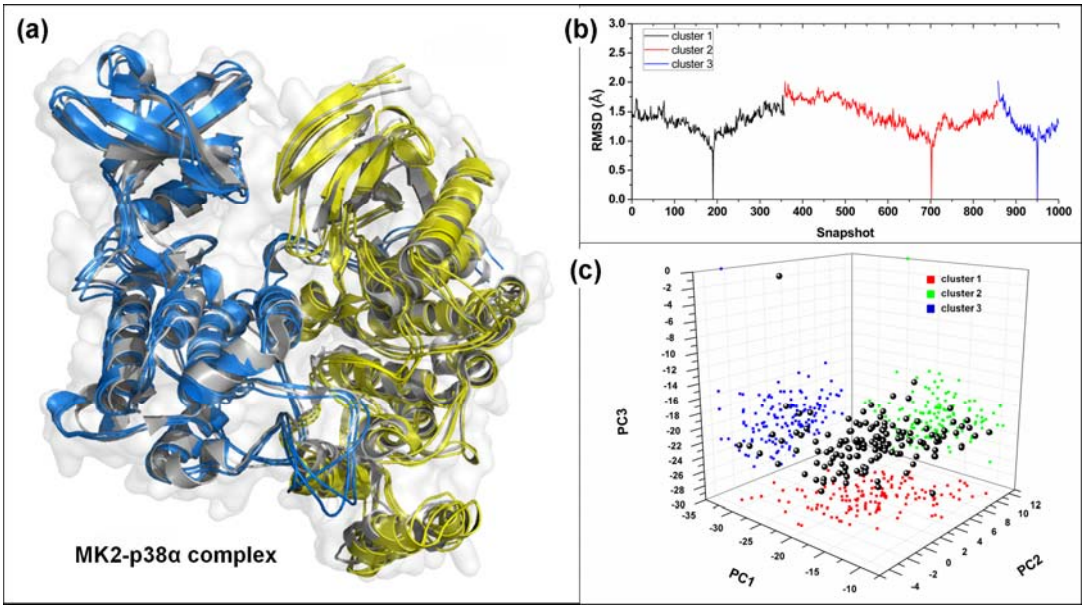
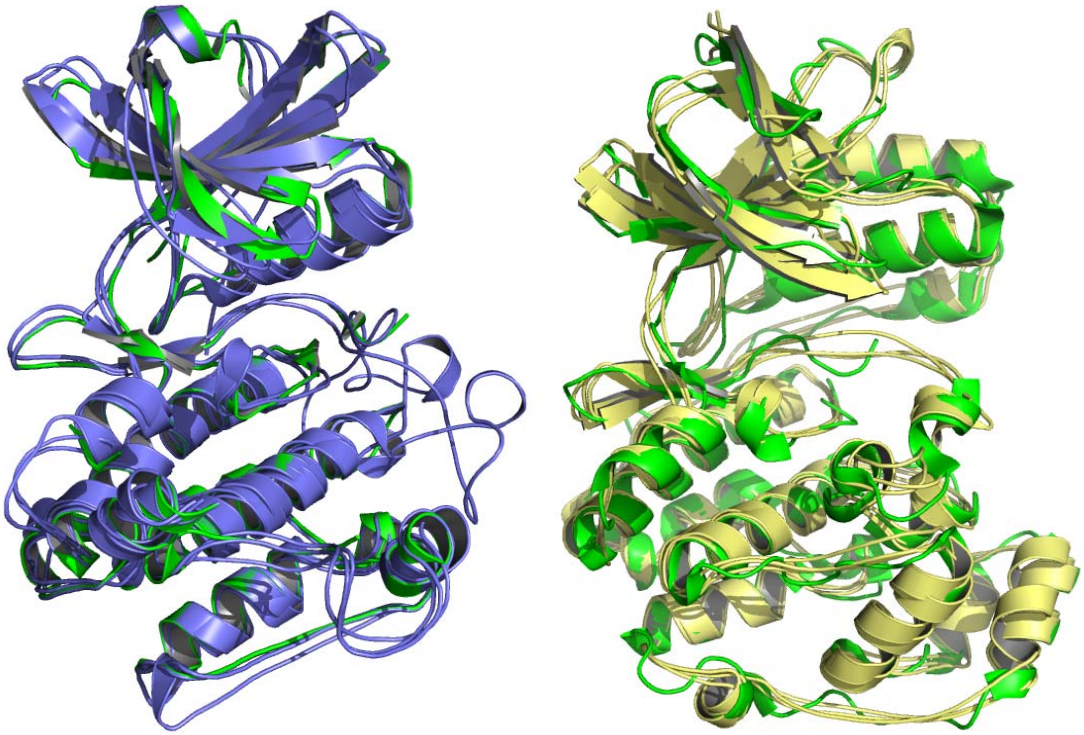
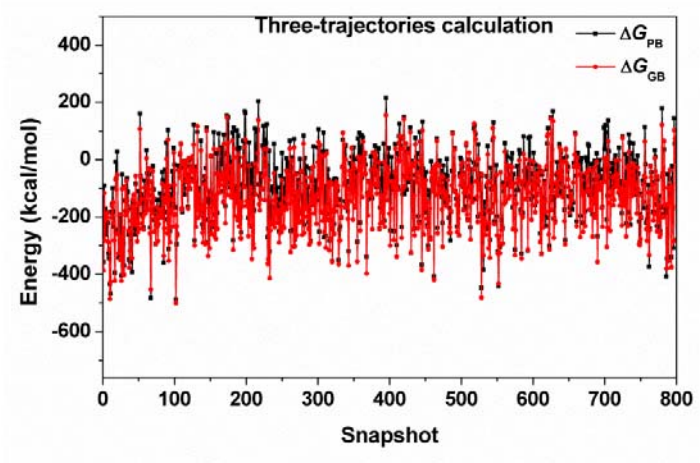


Figure S6. Representative structures of MK2-p38α from clustering. (a) Superposition of the representative conformations (MK2-blue, p38α-yellow) onto crystal structure (grey). (b) Root mean square deviation (RMSD) of the cluster members from the representative structures closed to the centroids. Different colors denote different clusters of conformations. (c) Projection PCA sorted by clusters.

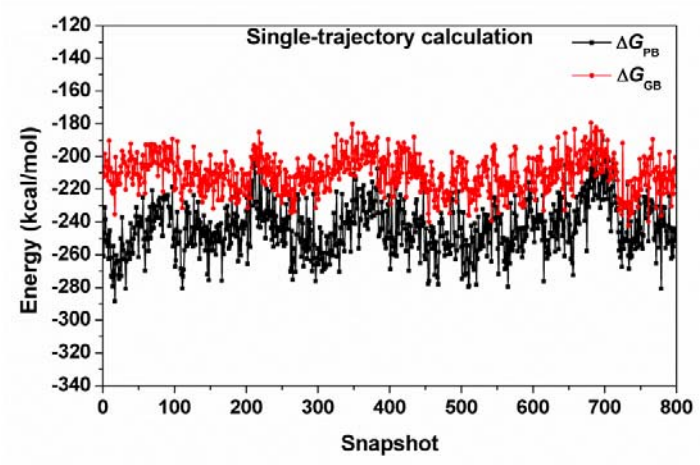


(a) MK2 (b) p38α

Figure S7. Superimposing the representative structures (MK2-blue, p38α-yellow) onto crystal structures (green). Representative structures of the individually crystallized MK2 (PDB: 1NY3) (a) and p38α (PDB: 1R39) (b) were obtained by clustering 40-ns MD trajectories.



(a)



(b)

Figure S8. The binding free energies calculated for 800 snapshots extracted at 25 ps intervals from the last 20 ns of MD simulations by MM/PBSA and MM/GBSA methods. The snapshots were taken from separate trajectories (a) and complex trajectory (b), respectively.