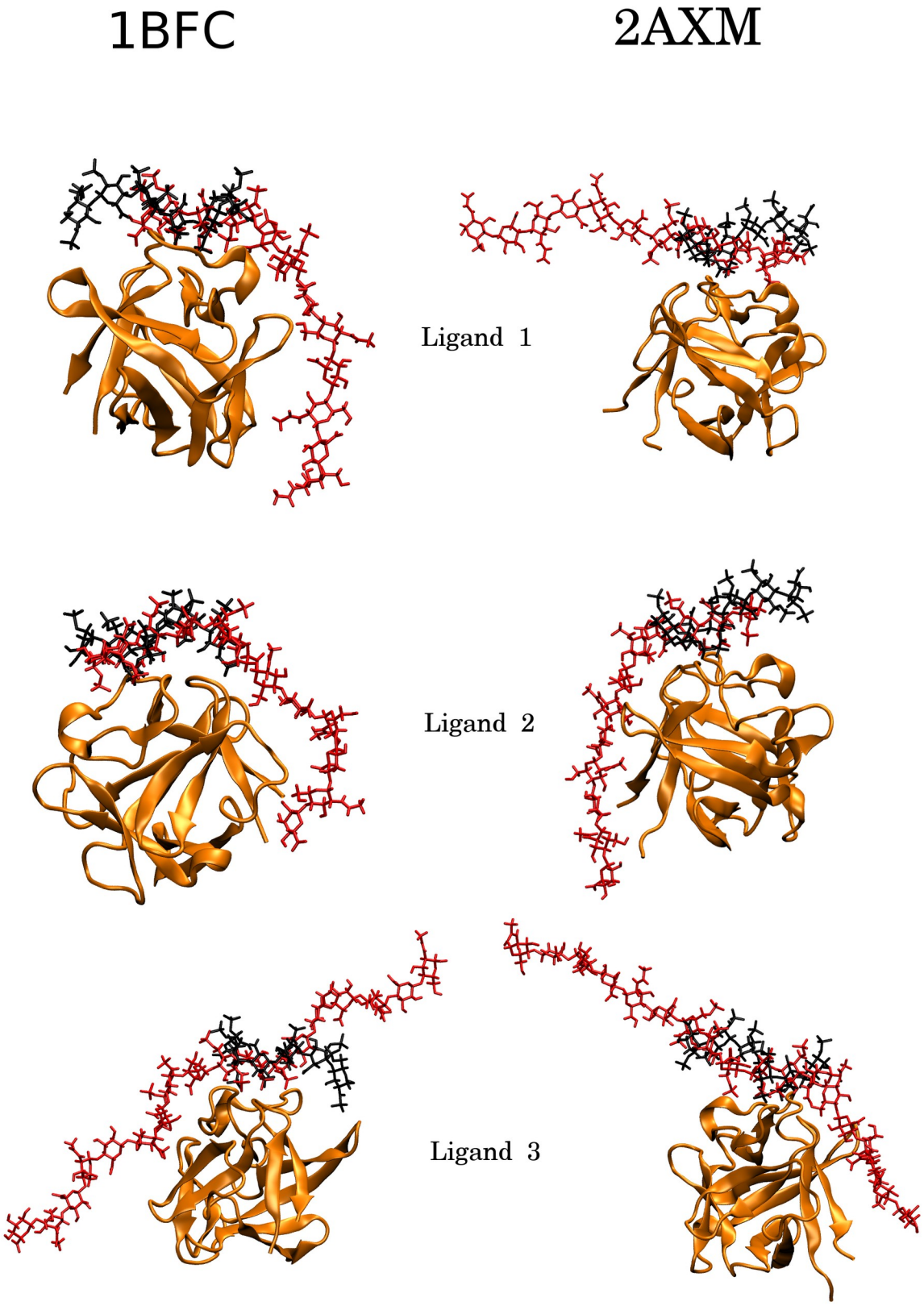
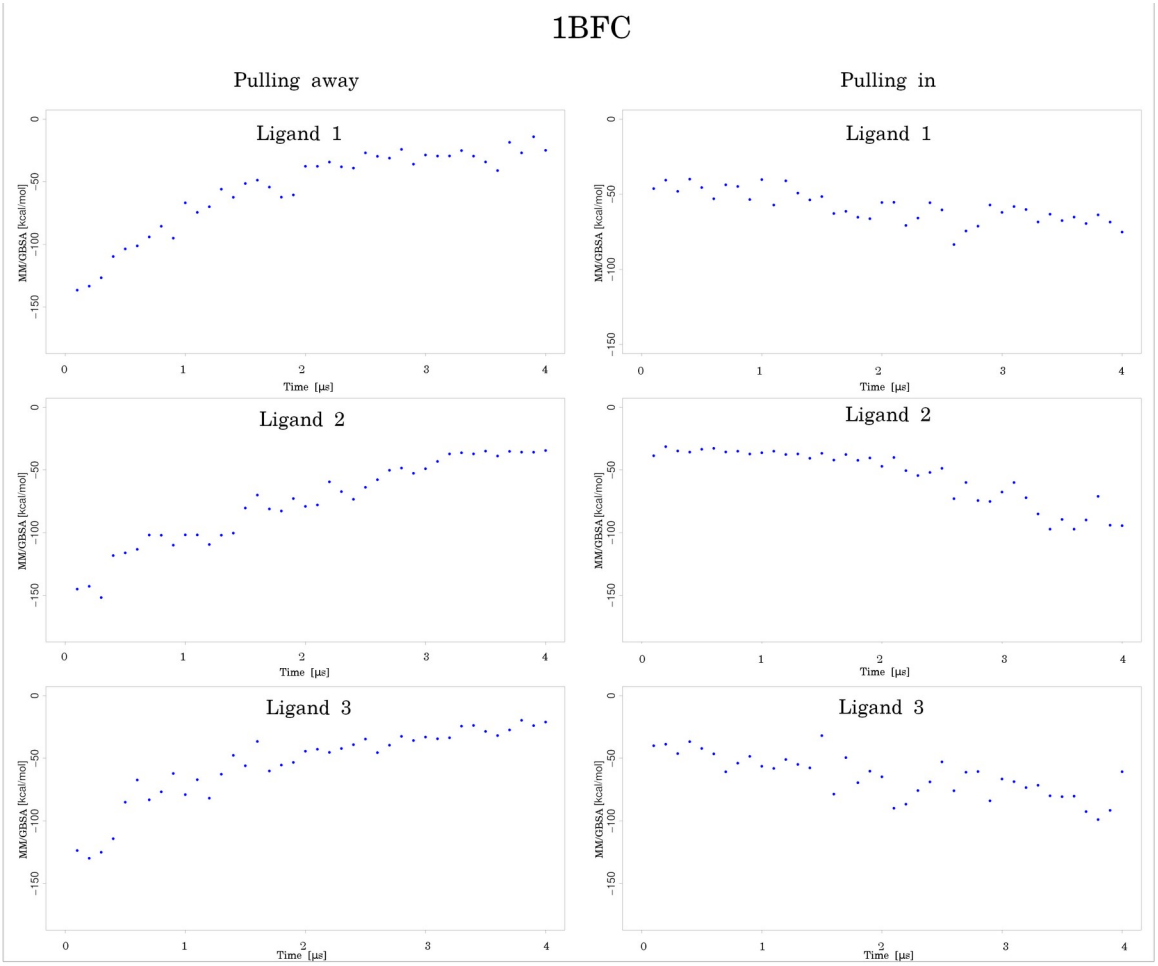
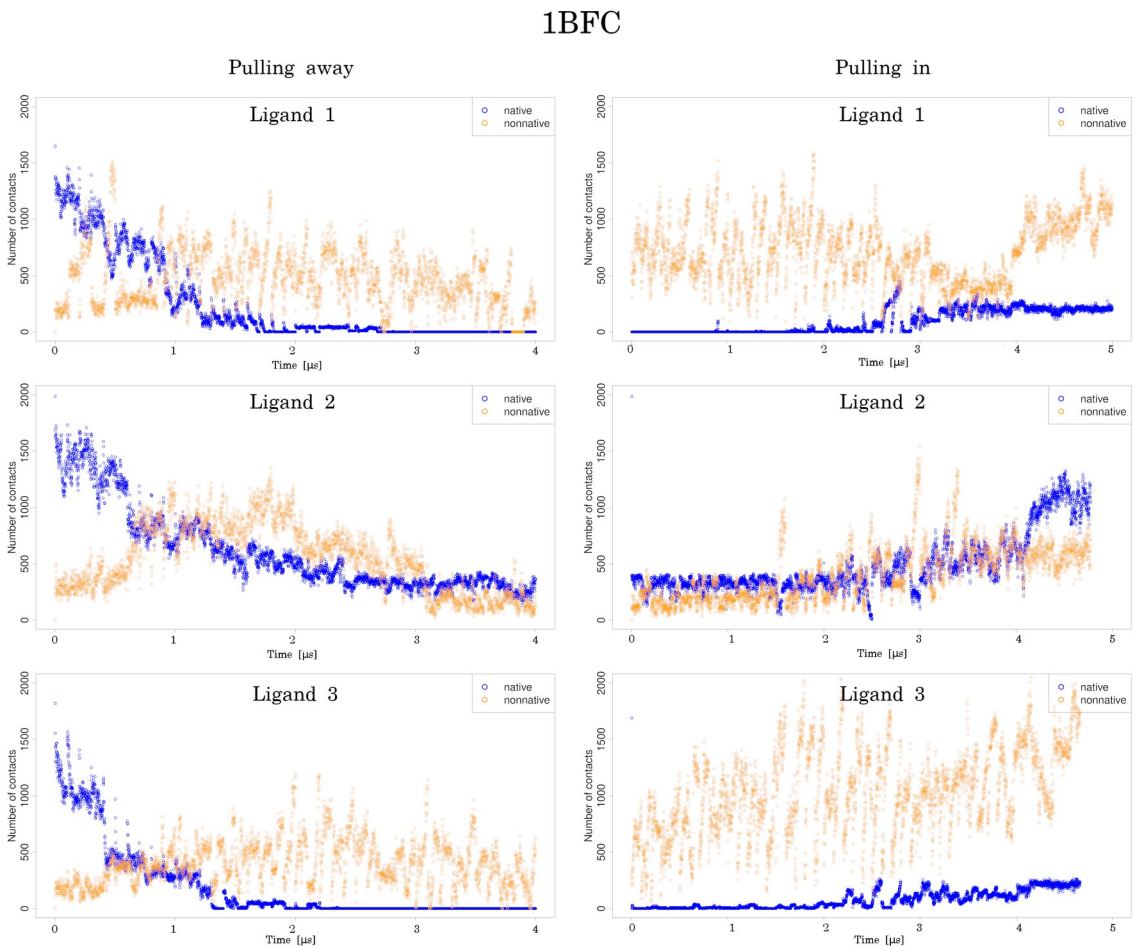


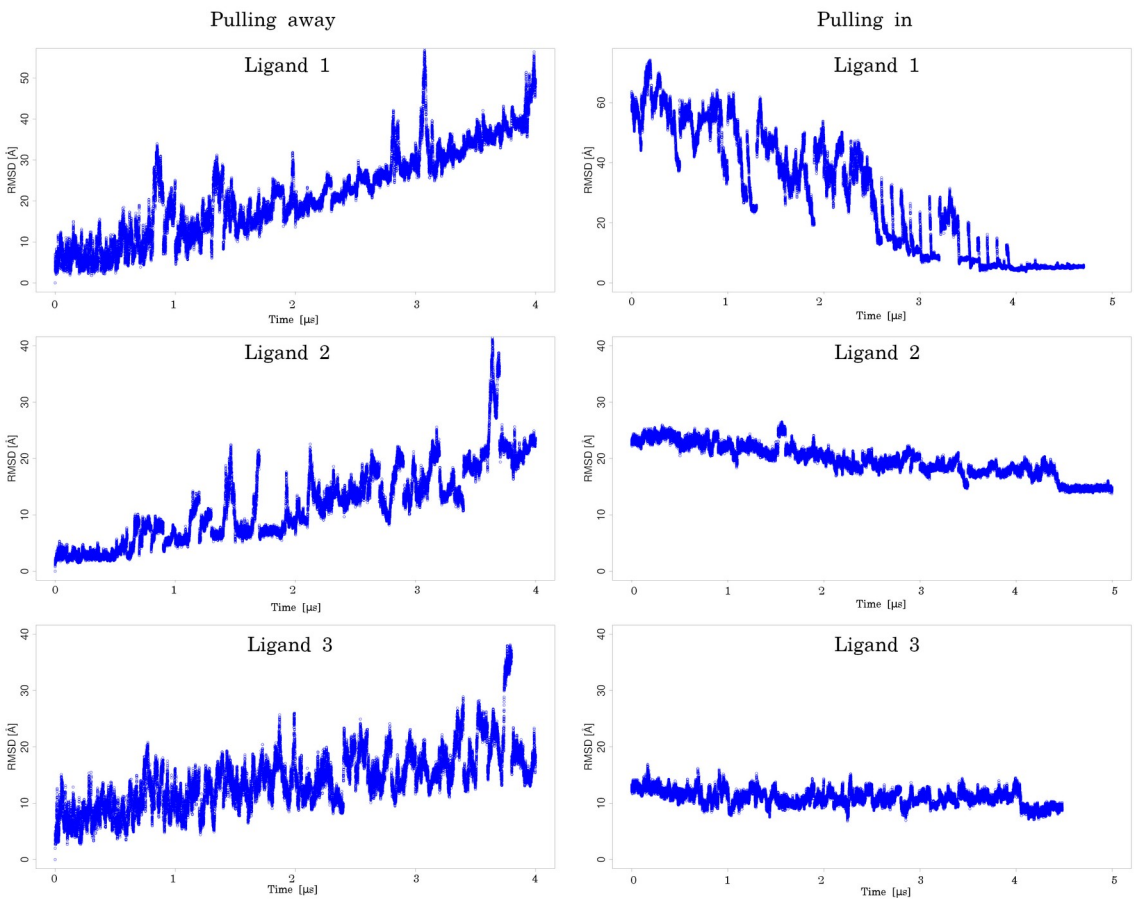
Supporting Figure 1. Graphical representation of ligands docked using RS-REMD method (licorice, in red) in comparison to the experimental structure (licorice, in black).



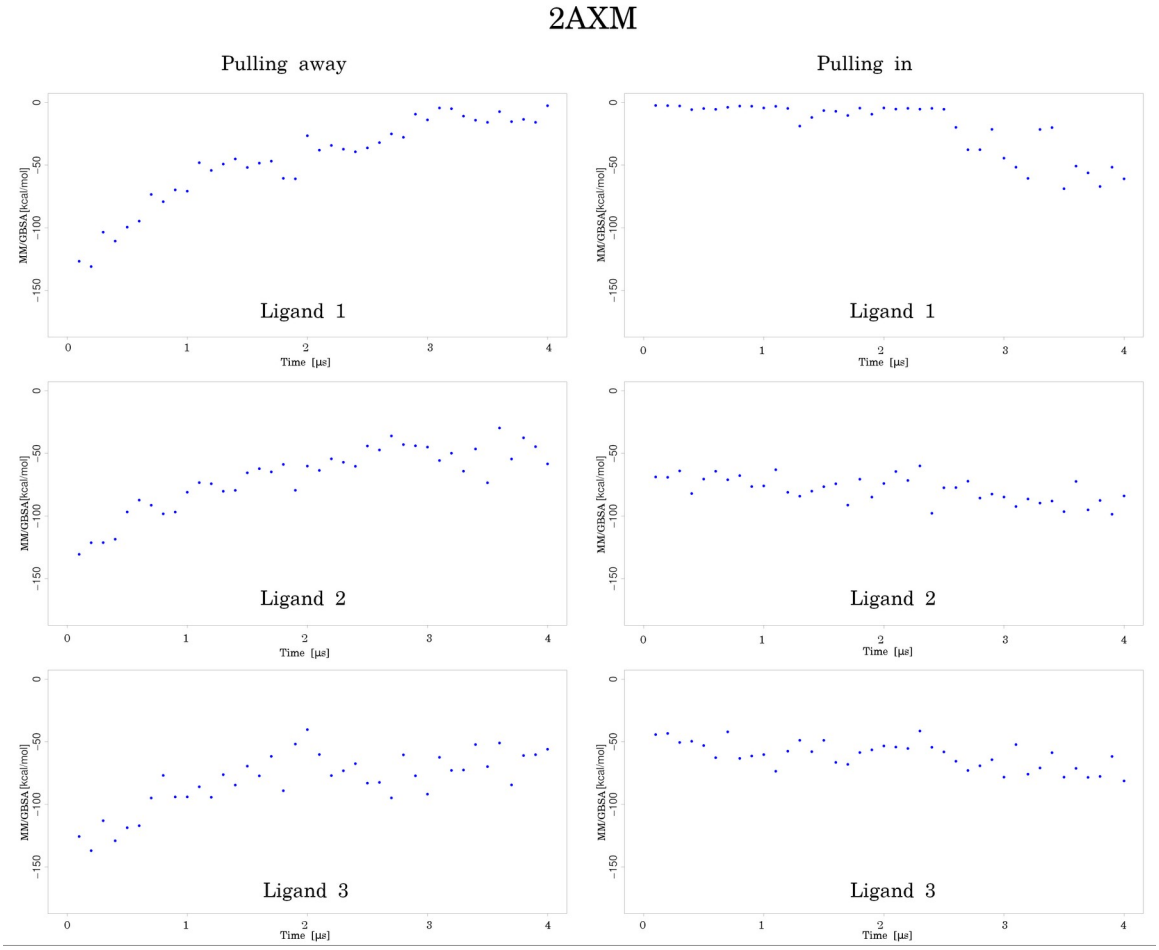
Supporting Figure 2. Energies obtained from MM/GBSA analysis for 1BFC complexes with 3 different ligands: ligand is pulled away from the binding site (left panel) and is pulled in towards the binding site (right panel).



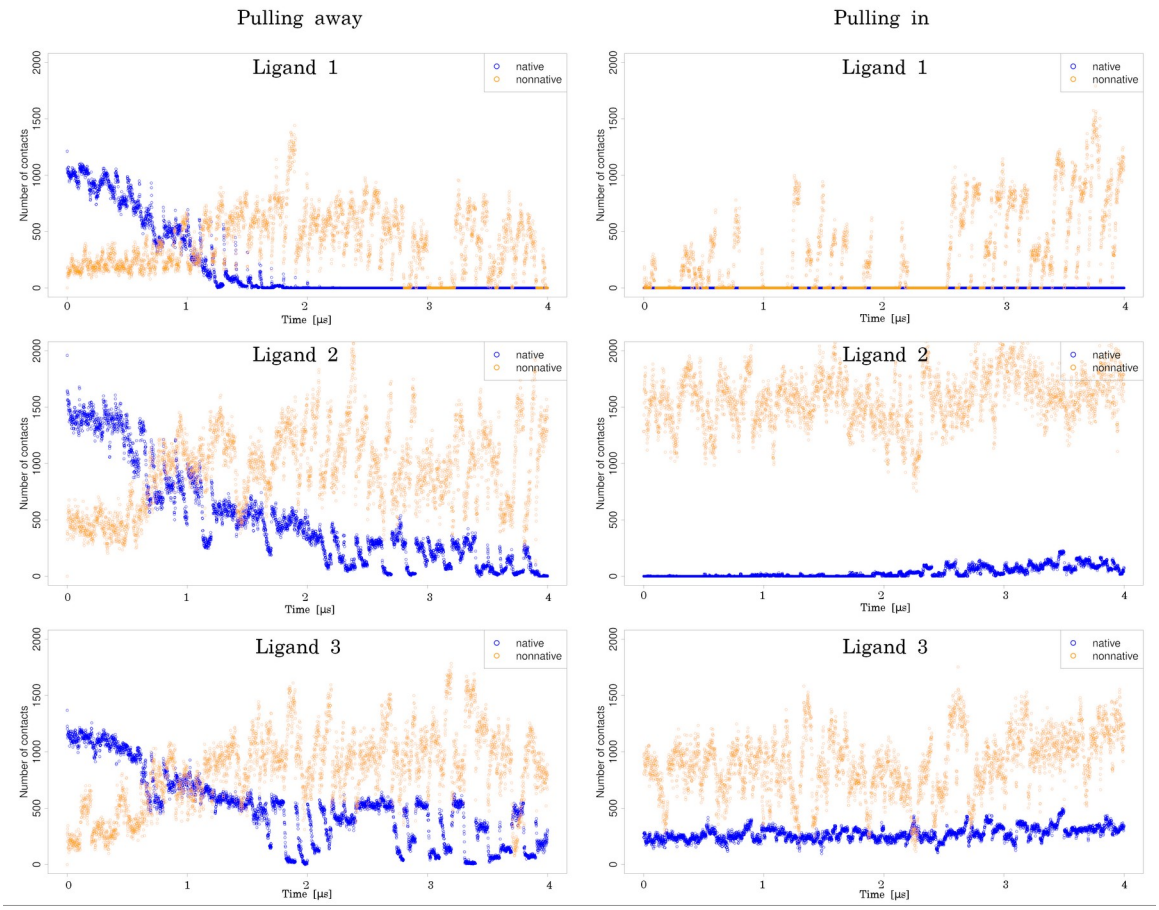
Supporting Figure 3. Number of native and non-nonative contacts obtained using cpptraj script from AMBER suite for 1BFC complexes with 3 different ligands: ligand is pulled away from the binding site (left panel) and is pulled in towards the binding site (right panel).



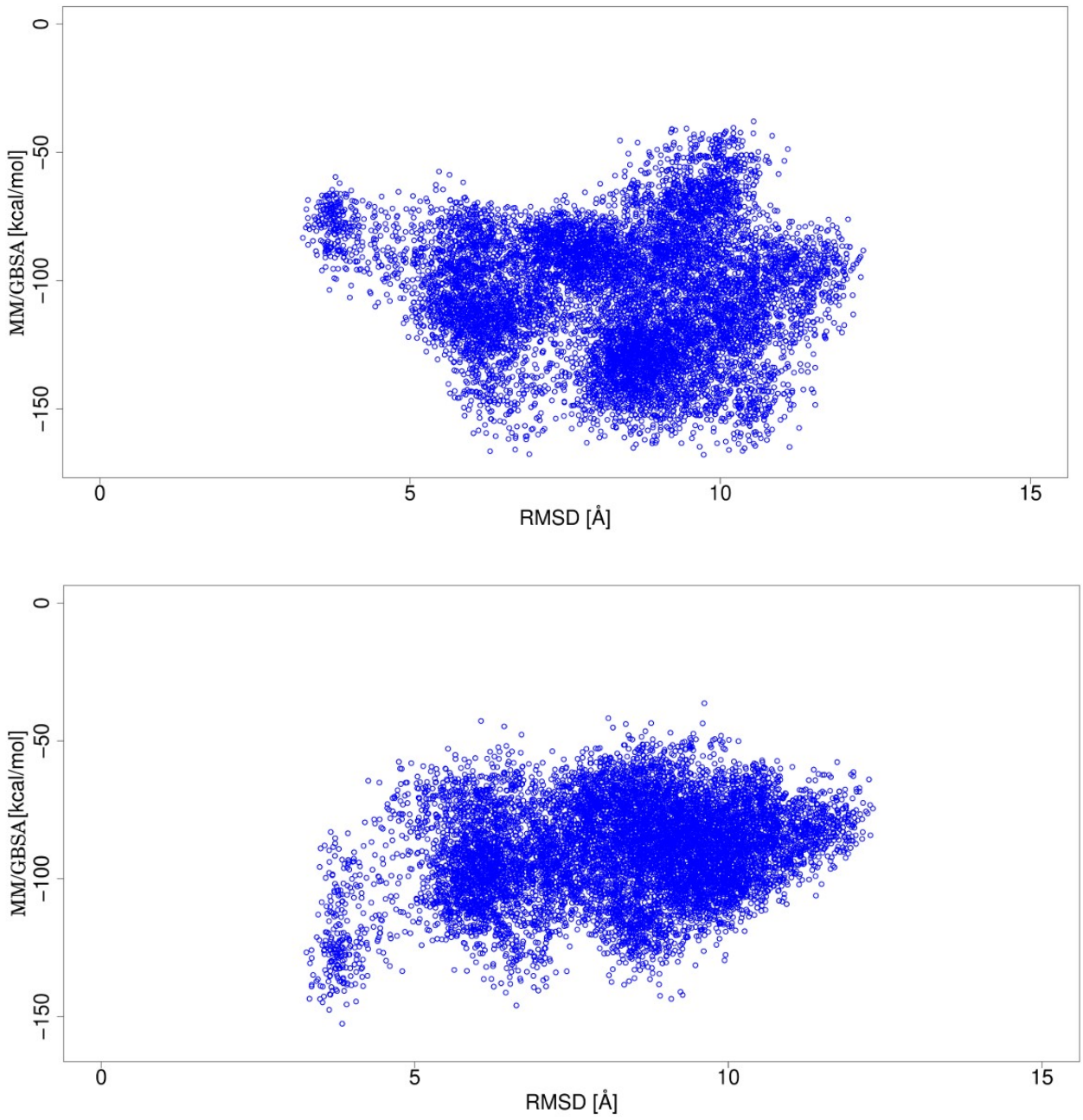
Supporting Figure 4. RMSD values obtained using cpptraj script from AMBER suite for 2AXM complexes with 3 different ligands: ligand is pulled away from the binding site (left panel) and is pulled in towards the binding site (right panel).



Supporting Figure 5. Energies obtained from MM/GBSA analysis for 2AXM complexes with 3 different ligands: ligand is pulled away from the binding site (left panel) and is pulled in towards the binding site (right panel).



Supporting Figure 6. Number of native and non-nonative contacts obtained using cpptraj script from AMBER suite for 2AXM complexes with 3 different ligands: ligand is pulled away from the binding site (left panel) and is pulled in towards the binding site (right panel).



Supporting Figure 7. MM/GBSA energy vs. RMSD for the pulling away (upper panel) and pulling in (bottom panel) by dp2. The Pearson and Spearman correlation coefficients are -0.18, -0.16 and 0.25, 0.20, respectively.

Supporting Table 1. Ligand's RMSatd in Å showing comparison of the last frame in the pulling in process with their corresponding experimental structure.

Protein	Ligand	RMSatd score
1BFC	ligand1	9.3
	ligand2	6.6
	ligand3	7.2
2AXM	ligand1	4.1
	ligand2	4.3
	ligand3	7.7
3C9E	ligand4	4.1
4N8W	ligand4	8.3

Supplementary Table 2. Ligand's RMSatd in Å showing comparison of the last frame in the pulling in process with their corresponding docked structure.

Protein	Ligand	RMSatd score
1BFC	ligand1	15.8
	ligand2	3.2
	ligand3	14.5
2AXM	ligand1	3.8
	ligand2	9.4
	ligand3	18.0
3C9E	ligand4	10.2