Molecular Recognition in a Diverse Set of Protein-Ligand Interactions Studied with Molecular Dynamics Simulations and End-Point Free Energy Calculations

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SUPPORTING INFORMATION

Table S1. Atom Types Used in Developing Knowledge-Based Pair Potentials

Atom Types		Description	Atom Types		
Protein	Ligand		Protein	Ligand	
C.3	c.3	Carbon sp3	O.3	o.3	Ox
C.2	c.2	Carbon sp2	O.2	o.2	Ox
C.AR	c.ar	Carbon aromatic, sp1	O.CO2	o.co2	Ox ar
C.CAT	c.cat	Carbocation	P.3	p.3	Ph su su
N.4	n.4	Nitrogen sp3, and sp3 positively charged	S.3	s.3	Su
N.AM	n.am	Nitrogen amide	MET	-	Al
N.PL3	n.pl3	Nitrogen trigonal	-	f	Fl
N.2	-	Nitrogen sp1, sp2 and aromatic	-	cl	Ch
-	n.2	Nitrogen sp1and sp2			
-	n.ar	Nitrogen aromatic			

Table S2. Parameters Used in MM-PBSA/MM-GBSA Calculations.

Parameters	Values
PB (free energies calculation using *pbsa*)	
Method used for solving the PB equation. (PROC)	2 (*pbsa* program)
Reference state taken for PB calculation. (REFE)	0
Dielectric constant for the solute. (INDI)	1.0 (2-10,15,20, agreed with DIELC)
Dielectric constant for the surrounding solvent. (EXDI)	80.0
Ionic strength (in mM) for the Poisson-Boltzmann solvent. (ISTRING)	0.0
Solvent probe radius in Angstrom. (PRBRAD)	1.6
Option to set up radii for PB calculation. (RADIOPT)	0
Lattice spacing in number of grids per Angstrom. (SCALE)	2
Number of iterations with linear PB equation. (LINIT)	1000
Values used to compute the nonpolar contribution G_{NP} to the desolvation according to G_{NP} = SURFTEN * SASA + SURFOFF (SURFEN/SURFOFF)	0.0072/0.00
GB (free energies calculation using GB model in *sander*)	

GB model. (IGB)	2 (Onufriev's GB)
Method used for SASA calculation. (GBSA)	2 (ICOSA)
Concentration (in M) of 1-1 mobile counterions in solution. (SALTCON)	0.00
Dielectricity constant for the surrounding solvent. (EXTDIEL)	80.0
Dielectricity constant for the solute. (INTDIEL)	1.0
Values used to compute the nonpolar contribution G_{NP} to the desolvation according to G_{NP} = SURFTEN * SASA + SURFOFF (SURFEN/SURFOFF)	0.0072/0.00
MM (gas phase energies calculation using *sander*)	
Dielectric constant for electrostatic interactions. (DIELC)	1 (2-10,15,20,)
MS (nonpolar contributions calculation using *molsurf*)	
Radius of the probe sphere used to calculate the SAS. (PROBE)	0.0
NM (entropies calculation with *nmode*)	
Distance-dependent dielectric constant. (DIELC)	4
Maximum number of cycles of minimization. (MAXCYC)	10000
Convergence criterion fro the energy gradient. (DRMS)	0.0001

Figure S1

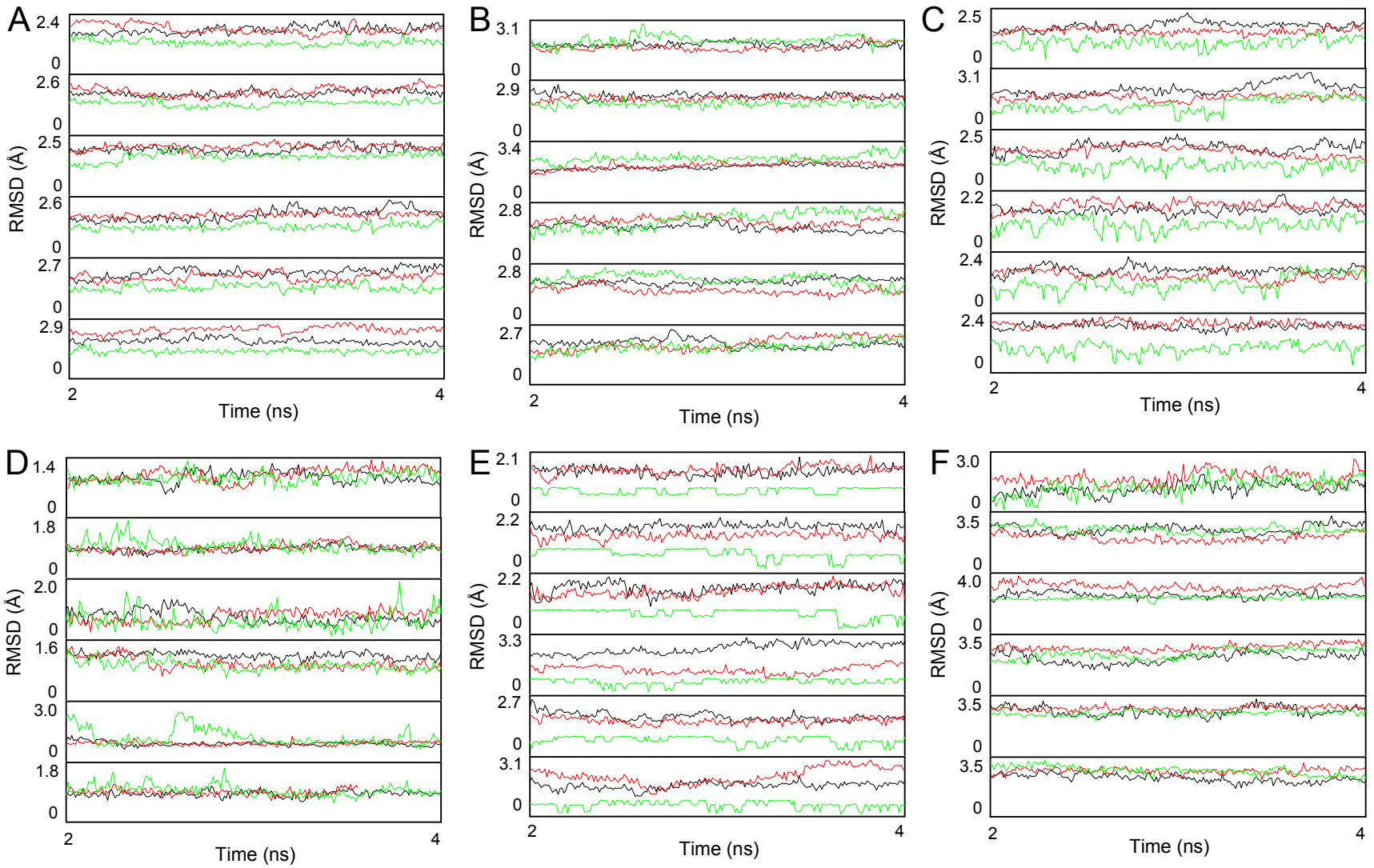

Figure S1. **Comparison of dynamics of the free ligand and protein to the protein-ligand complex**. RMSDs of atoms of MD simulations. Atoms of binding pocket (5.5 Å distance around ligand) for protein-ligand complexes are illustrated in black, atoms of binding pocket for apo proteins are illustrated in red, atoms in ligands are illustrated in green. Each MD simulation consists of six separate trajectories of 2 ns (12 ns total) from top to bottom; (A) **4** bound to HIV-1 protease (1HXW); (B) **5** bound to leukocyte function-associated antigen-1 (1RD4); (C) **7** bound to mouse major urinary protein 6 (1I06); (D) **10** bound to hen lysozyme C (1LZB); (E) **13** bound to bovine pancreatic trypsin (1S0R); and (F) **14** bound to human brain fatty acid-binding protein (1FDQ).