Supplemental Information:

Figure S1A ***(Provides the plots similar to Figure 2 but for the HXCB2 structure, 1G9M)*** *The GNM B-factors calculated in GNM for GPO1 (black), GCD1 (red), COM1 (green) and the experimental B-factors from the X-ray structure (orange).*

Figure S1B. ***(Provides the plots similar to Figure 2 but for the YU2 structure, 1G9N)*** *The GNM B-factors calculated in GNM for GPO2(black) GCD2 (red), COM2(green) and the experimental B-factors from the X-ray structure (orange).*

Figure S2. *B-factors calculated from GNM (black) of the mean structure (average over 5ns) from Molecular Dynamics (MD) simulations, the root mean square fluctuation (rmsf) (red) from MD simulations, and the B-factors from GNM of the GPO3 X-ray structure.*

Figure S3. ***GNM slow mode profiles for MD-relaxed X-ray structures*** *Mean square fluctuation calculated from GNM Slow modes for MD- snapshots, averaged over respective simulation trajectory of 5ns, for GCD2 (black curve) GCD3(red curve) and GPO3(green curve) structures.*

Figure S4. ***Minimum distances of residues communication hubs for A) outer domain (C-α atoms) and B) inner domain (C-α atoms) for a 17ns MD trajectory of GPO3.***

Table S1. **(*Gives the sequence differences for the two strains that are relevant to GNM slow mode minima described in Table 2)*** *Sequence differences listed for HXBC2 and YU2 HIV strains. File: table_s1_seqdiff_HXBC2_YU2.xls*

Table S2. ***(Gives a residue by residue list of GNM minima and maxima for each of the structures ploted in Figure 3)*** *GNM minima and maxima for residues in the three gp120s studied from HXBC2 and YU2 HIV strains. File: table_s2_GNMMinMax.xls*

Table S3. ***(List of residues that have low commute times as plotted in Figure 6)*** *Residues pairs that have low commute times, (C(i,j)) < 0.20, in the GPO1, GPO2, and GPO3 x-ray structures. File: table_s3_gpo1-gpo2-gpo3_commun.xlsx*

Table S4. ***(List of residues with low commute times for the GCD1, GCD2 and GCD3 complexes as in Table 3)*** *Common residues pairs between gp120 and protein ligand CD4 or Mini-protein that have low commute times, (C(i,j)) < 0.21, in the GCD1, GCD2, and GCD3 X-ray structures.*

Table S5. ***(List of residues with low commute times for the COM1, COM2 and COM3 complexes as in Table 3)*** Residues pairs between gp120 and FAB 17B that have low commute times, (C(i,j)) < 0.20, in the COM1, COM2, and COM3 X-ray structures.

Materials and Methods: *Molecular Dynamics Calculations*

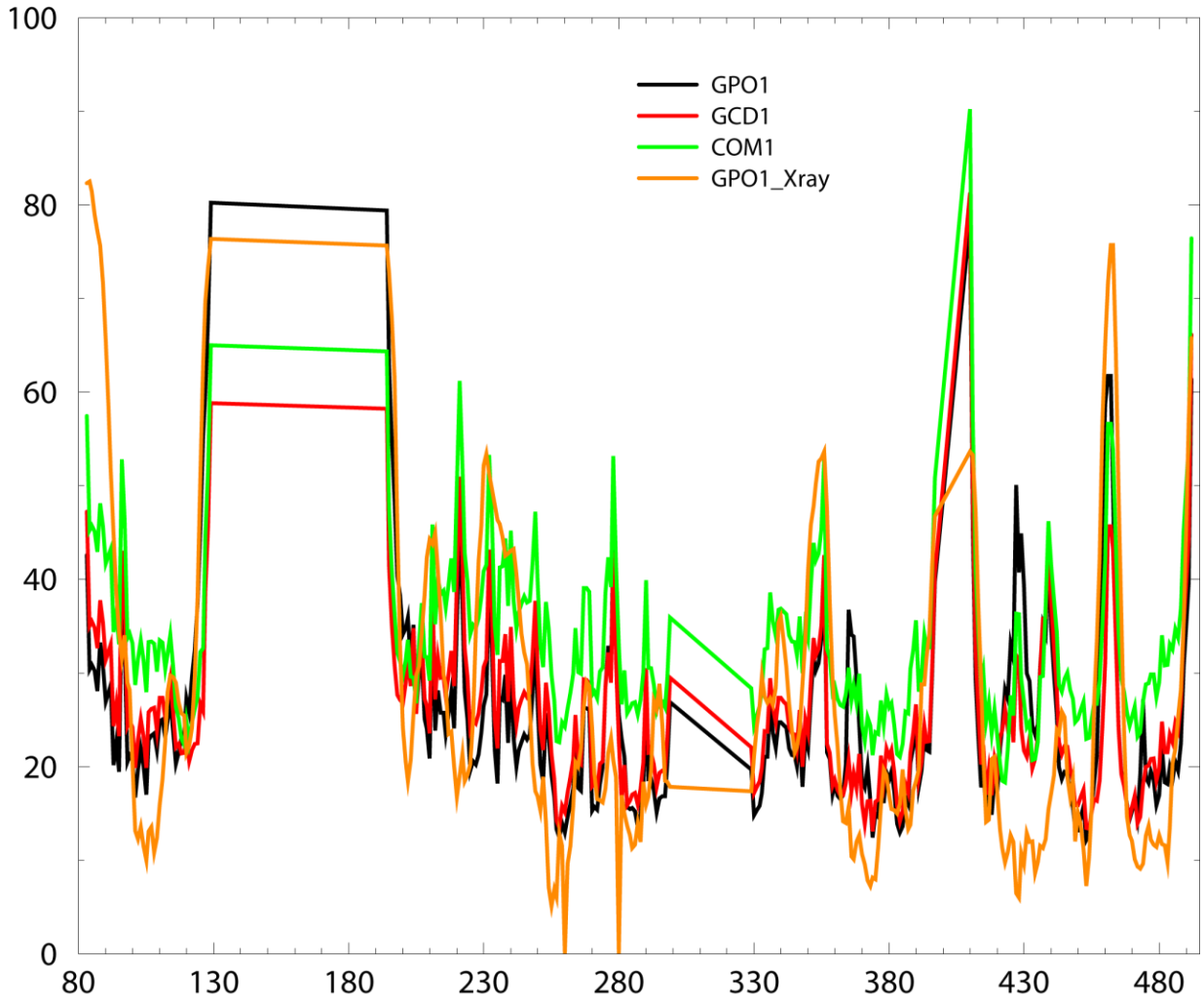


Figure *S1A* *The GNM B-factors calculated in GNM for GPO1 (black), GCD1 (red), COM1 (green) and the experimental B-factors from the X-ray structure (orange). Note that we illustrate here the GP120 part only.*

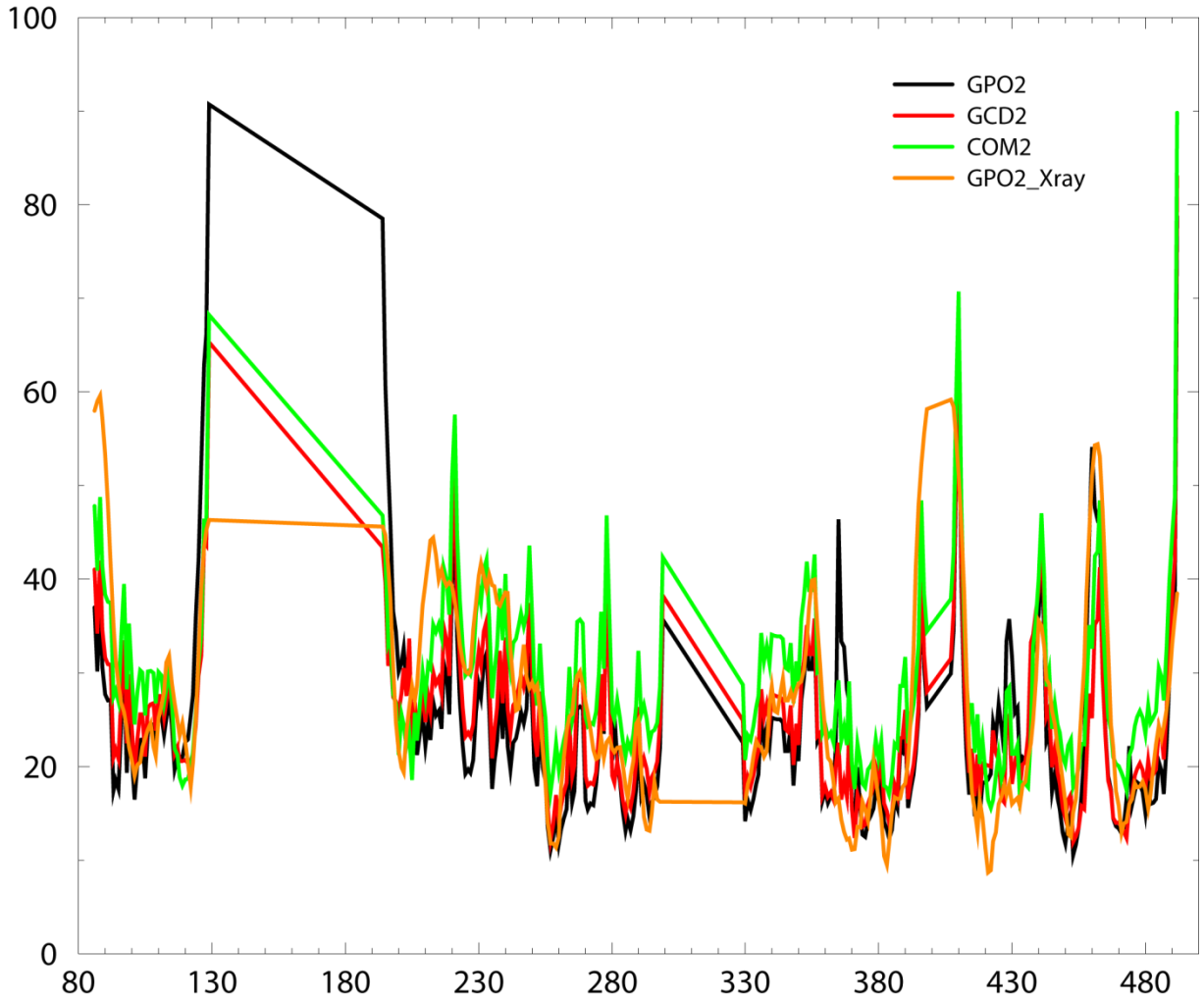


Figure S1B. *The GNM B-factors calculated in GNM for GPO2(black) GCD2 (red), COM2(green) and the experimental B-factors from the X-ray structure (orange). Note that we illustrate here the GP120 part only.*

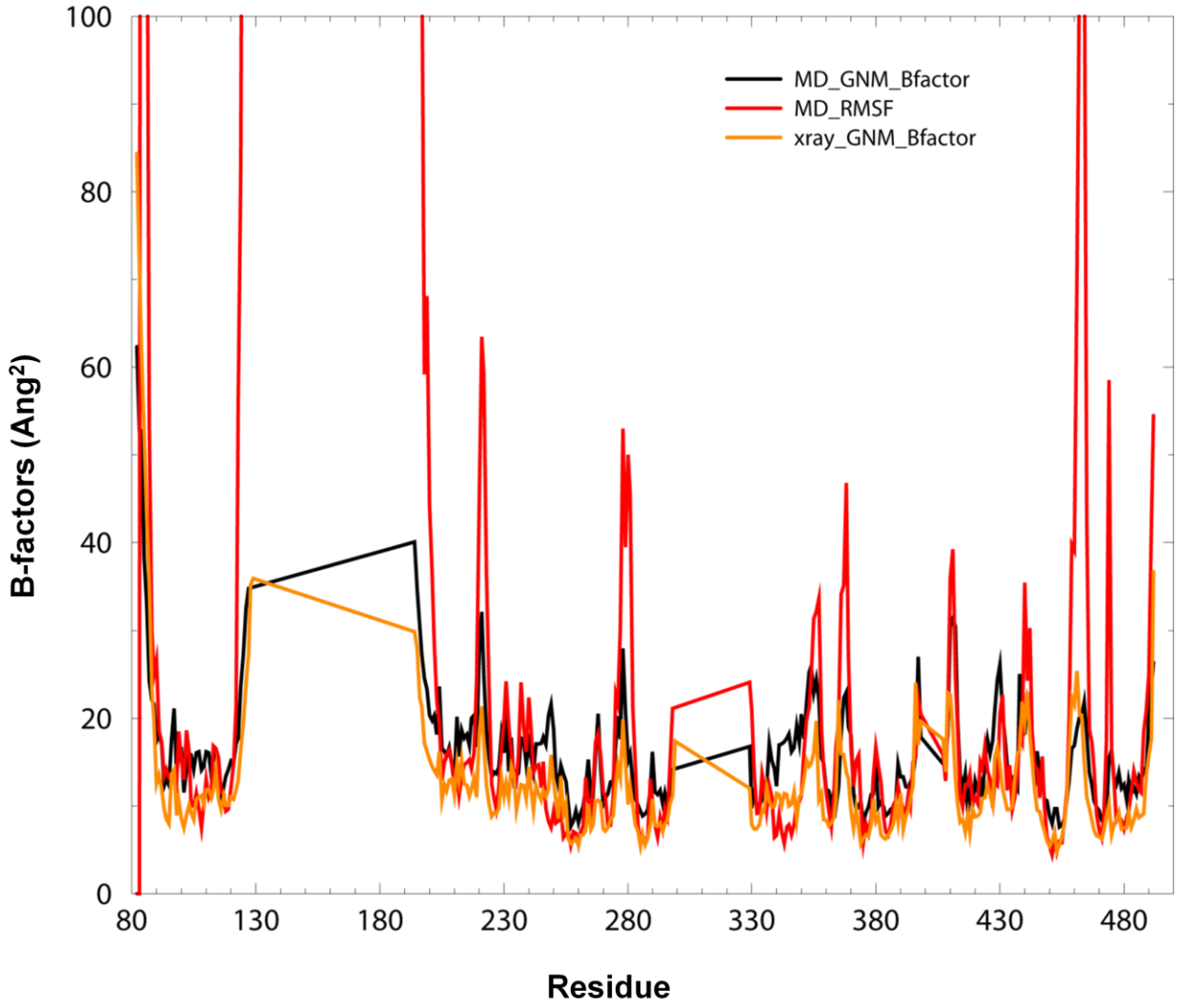


Figure *S2.* *B-factors calculated from GNM (black) of the mean structure (average over 5ns) from Molecular Dynamics (MD) simulations, the root mean square fluctuation (rmsf) (red) from MD simulations, and the B-factors from GNM of the GPO3 X-ray structure.*

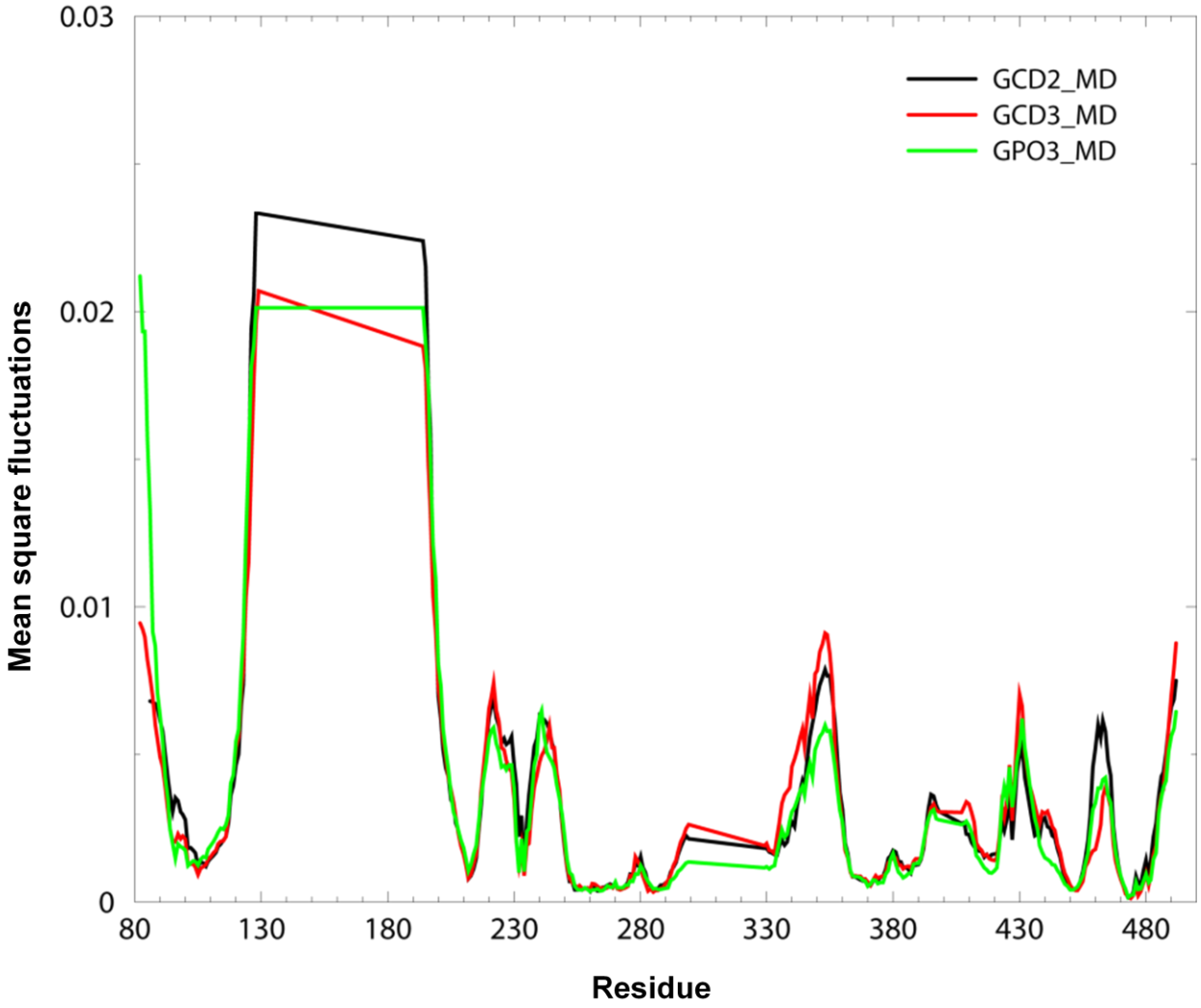
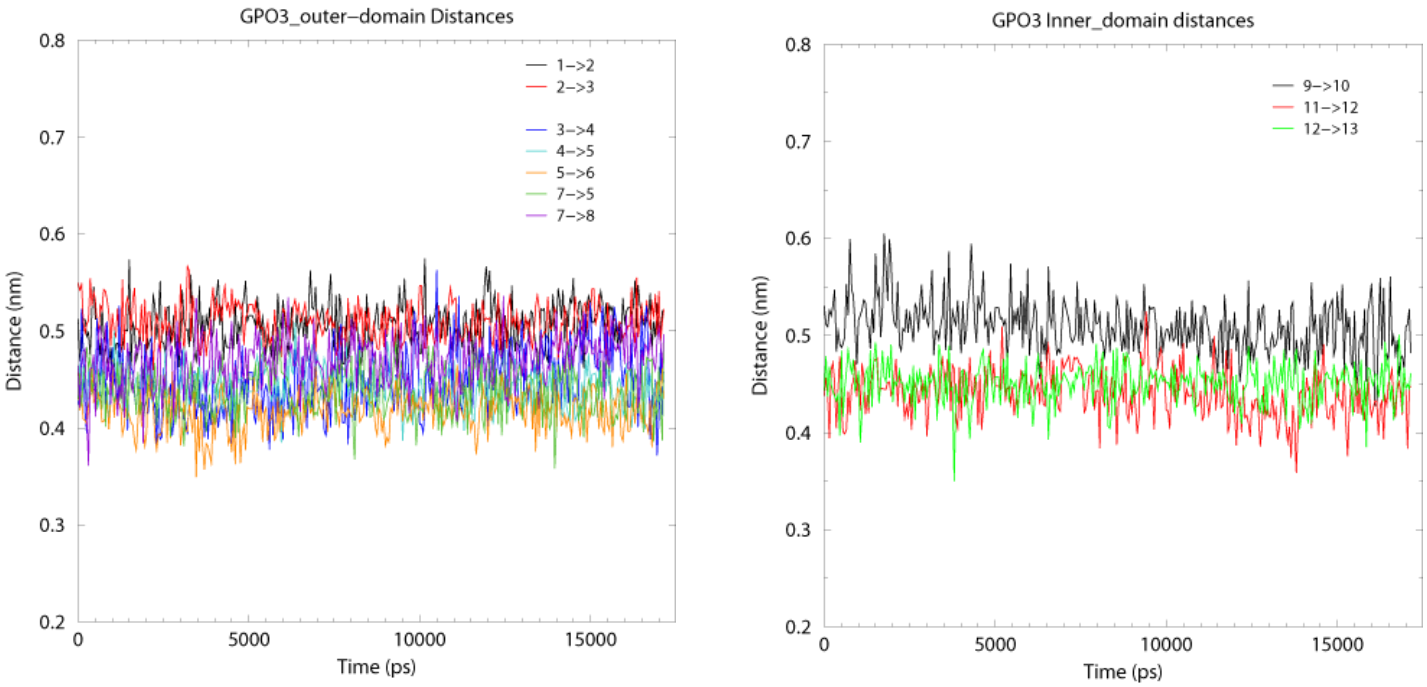


Figure S3 GNM slow mode profiles for MD-relaxed X-ray structures *Mean square fluctuation calculated from GNM Slow modes for MD- snapshots, averaged over respective simulation trajectory of 5ns, for GCD2 (black curve) GCD3(red curve) and GPO3(green curve) structures.*



A ***B***

Figure S4 Minimum distances of residues communication hubs for A) outer domain (C-α atoms) and B) inner domain (C-α atoms) for a 17ns MD trajectory of GPO3. *Outer domain hubs are numbered as follows: 1, residues 383 to 386; 2, residues 374 to 373; 3, residues 257to 262; 4, residues 265 to 266; 5, residues 284 to 289; 6, residues 270 to 272; 7, residues 447 to 455; 8, residues 470 to 472 and inner domain residues and bridging sheet hubs as 9, residues 122 to 118; 10, residues 433 to 434; 11, residues 224 to 228; 12, residues 487 to 488; 13, residues 242 to 245. The center of mass of the residue range comprising the hub was used in computing the distance between the hubs.*

Table S1. Sequence differences listed for HXBC2 and YU2 HIV strains. File: seqdiff_HXBC2_YU2.xls

Table S2. GNM minima and maxima for residues in the three gp120s studied from HXBC2 and YU2 HIV strains. File: GNMMinMax_tableS2.xls

Table S3. Residues pairs that have low commute times, (C(i,j)) < 0.20, in the GPO1, GPO2, and GPO3 X-ray structures. Residues that also exhibit GNM slow mode minima are in blue font. Residues in the inner, outer and bridging sheet domains are indicated in red, yellow and green, respectively. Residues pairs that exhibit low commute times in all 3 coordinate sets are shaded

gray. The amino-acid residue is given for YU2/GPO3 only. File:supptable3_gpo1-gpo2-gpo3_commun.xls.

GCD1		**GCD2**		**GCD3**	
gp120 (i)	**Cd4 (j)**	**gp120 (i)**	**Cd4 (j)**	**gp120 (i)**	**Mini (j)**
G366	T45	G366	T45	G366	A25
G366	K46	G366	K46	G366	C26
G367	T45	G367	T45	G367	A25
D368	T45	D368	T45	D368	A25
I371	F43	I371	F43	I371	B23
I371	T45	I371	T45	I371	A25
G473	Q40	G473	Q40	G473	A20
G473	F43	G473	F43	G473	B23

Table S4. Residues pairs between gp120 and protein ligand CD4 or Mini-protein that have low commute times, (C(i,j)) < 0.21, in the GCD1, GCD2, and GCD3 X-ray structures. B23 in GCD3 indicates the residue containing biphenyl bound in the gp120 Phe-43 pocket.

COM1		COM2		COM3	
gp120 (i)	**FAB (j)**	**gp120 (i)**	**FAB (j)**	**gp120 (i)**	**FAB (j)**
		K421	D108		
		K421	Y109		
		Q422	G107	Q422	G107
		Q422	D108	Q422	D108
		Q422	Y109	Q422	Y109
I423	G107	I423	G107	I423	G107
		I423	D108	I423	D108
		I423	Y109	I423	Y109

Table S5. Residues pairs between gp120 and FAB 17B that have low commute times, (C(i,j)) < 0.20, in the COM1, COM2, and COM3 X-ray structures.

Materials and Methods:

Molecular dynamics simulation trajectories were generated using Gromacs software package version 3.3.1(Scott W.R.P. et al., 1999; Van Der Spoel et al., 2005), using the GROMOS 43a1 force field and the SPC water model (Berendsen et al., 1987) for solvation. The solvated protein molecule was *initially* energy minimized with 1000 steps of steepest descent, followed by a short equilibration run of 200 picoseconds, during which the protein backbone atom were position restrained and the sidechain atoms and water molecules were allowed to relax. *During the production run of 5ns, all the position restraints were removed.* The simulations were all performed under constant Number of particles, Pressure and Temperate (NPT) conditions. A dielectric permittivity, ε=1 and timestep of 2 femtoseconds was used. The LINCS (Hess et al., 1997) algorithm was used to constrain all bond lengths and the Particle Mesh Ewald (PME) method (Darden et al., 1993) to compute the electrostatic term. In all simulations, the temperature was kept constant (T=310K) by coupling to an external temperature bath with a coupling constant of 0.1 ps, and isotropic pressure coupling was employed to maintain a constant pressure of 1bar. GNM calculations were performed on a structure averaged over 5ns of the simulation trajectory.