Biophysical Journal, Volume 97

Supporting Material

Comparative Molecular Dynamics Simulation Studies of Protegrin-1 Monomer and Dimer in Two Different Lipid Bilayers

Huan Rui, Jinhyuk Lee, and Wonpil Im

Supplementary Materials

Comparative Molecular Dynamics Simulation Studies of Protegrin-1 Monomer and Dimer in Two Different Membrane Bilayers

Huan Rui, Jinhyuk Lee, and Wonpil Im*

Department of Molecular Biosciences and Center for Bioinformatics,
The University of Kansas, Lawrence, Kansas

Keywords: Antimicrobial peptide; Chemical shift; Tilt angle; Conformational change; Peptide-lipid interaction

Running Title: PG-1 Interactions in Membranes

* Corresponding: wonpil@ku.edu

TABLE S1. PG-1 simulation systems.

Systems	Lipids (top/bottom)	Number of waters	Number of ions (K^+/Cl^-)	Number of total atoms
M1_DLPC	DLPC (34/34)	3140	5/12	16947
M2_DLPC	DLPC (34/34)	3162	5/12	17013
M3_DLPC	DLPC (34/34)	3170	5/12	17037
M1_POPC	POPC (32/32)	2585	5/12	16650
M2_POPC	POPC (32/32)	2591	5/12	16668
M3_POPC	POPC (32/32)	2604	5/12	16707
D1_DLPC	DLPC (39/39)	3878	4/18	20528
D2_DLPC	DLPC (39/39)	3899	4/18	20603
D3_DLPC	DLPC (39/39)	3903	4/18	20591
D1_POPC	POPC (37/37)	3273	4/18	20361
D2_POPC	POPC (37/37)	3266	4/18	20340
D3_POPC	POPC (37/37)	3275	4/18	20367

TABLE S2. PG-1 monomer intramolecular H-bond occupancies in DLPC and POPC bilayers.

Acceptor (HN)	Donor (O)	Occupancy					
		M1_DLPC	M2_DLPC	M3_DLPC	M1_POPC	M2_POPC	M3_POPC
Arg18	Gly3	0.80	-	0.87	-	-	0.45
Val16	Leu5	1.00	0.36	0.99	0.77	0.56	1.00
Val14	Tyr7	0.97	0.98	0.98	0.98	0.66	1.00
Phe12	Arg9	0.57	0.99	0.98	-	0.96	0.95
Arg9	Phe12	0.98	0.99	1.00	0.35	0.97	0.98
Tyr7	Val14	0.98	0.98	0.99	0.98	0.65	1.00
Leu5	Val16	1.00	0.36	1.00	0.60	0.48	0.98

TABLE S3. H-bond occupancies of PG-1 monomer backbone and lipid in DLPC and POPC bilayers.

Acceptor (HN)	Occupancy					
	M1_DLPC	M2_DLPC	M3_DLPC	M1_POPC	M2_POPC	M3_POPC
Gly2	-	0.50	-	0.16	-	0.39
Gly3	-	-	-	0.52	0.20	0.38
Arg4	0.24	-	0.25	-	0.39	-
Leu5	-	-	-	0.23	-	-
Cys6	0.34	-	0.92	-	-	-
Cys8	-	-	-	0.37	0.67	-
Arg10	-	-	0.66	-	0.81	-
Arg11	-	0.30	-	0.67	0.32	0.46
Phe12	-	-	-	0.46	-	-
Cys15	-	0.72	0.42	-	-	-
Gly17	-	0.42	0.57	-	0.18	0.26
Arg18	-	0.33	-	-	-	0.17

TABLE S4. Intermolecular H-bond occupancies of PG-1 dimer[§] in DLPC bilayers.

PROA		PROB		Occupancy					
Residue	Atom	Residue	Atom	D1_DLPC	D2_DLPC	D3_DLPC	D1_POPC	D2_POPC	D3_POPC
CYS13	HN	ARG11	O	0.88	0.25	0.67	0.76	0.93	0.83
CYS13	O	CYS13	HN	0.98	0.96	0.82	0.81	0.85	0.92
CYS15	HN	CYS13	O	0.99	0.99	0.98	1.00	1.00	1.00
CYS15	O	CYS15	HN	0.99	0.97	0.86	1.00	1.00	0.98
GLY17	HN	CYS15	O	-	-	-	0.38	0.89	0.98
GLY17	O	GLY17	HN	-	-	-	-	0.38	-

[§]PROA and PROB are the names of monomers in the PG-1 dimer

TABLE S5. H-bond occupancies between PG-1 dimer[§] backbone and lipid molecules.

Acceptor (HN)	Occupancy											
	D1_DLPC		D2_DLPC		D3_DLPC		D1_POPC		D2_POPC		D3_POPC	
	PROA	PROB	PROA	PROB	PROA	PROB	PROA	PROB	PROA	PROB	PROA	PROB
GLY2	0.99	-	-	0.87	0.42	-	0.25	0.58	0.53	0.42	-	-
GLY3	0.98	-	0.66	-	0.57	-	0.56	-	0.64	0.54	-	0.74
ARG4	0.95	0.77	0.63	-	0.40	-	0.51	-	0.50	0.15	0.17	0.86
LEU5	-	0.49	-	-	-	-	-	-	-	-	-	-
CYS6	-	0.44	-	-	-	0.56	-	-	0.26	-	0.29	-
CYS8	0.64	-	-	0.90	0.72	-	-	-	-	-	-	-
ARG10	-	0.23	0.18	-	0.54	-	-	-	0.62	0.20	-	0.99
ARG11	-	-	-	-	0.47	0.27	-	-	0.62	0.95	-	-
GLY17	-	-	0.36	0.75	0.87	0.99	-	-	-	-	-	-
ARG18	0.16	0.39	-	-	0.24	0.92	-	-	-	-	-	-

[§]PROA and PROB are the names of monomers in the PG-1 dimer

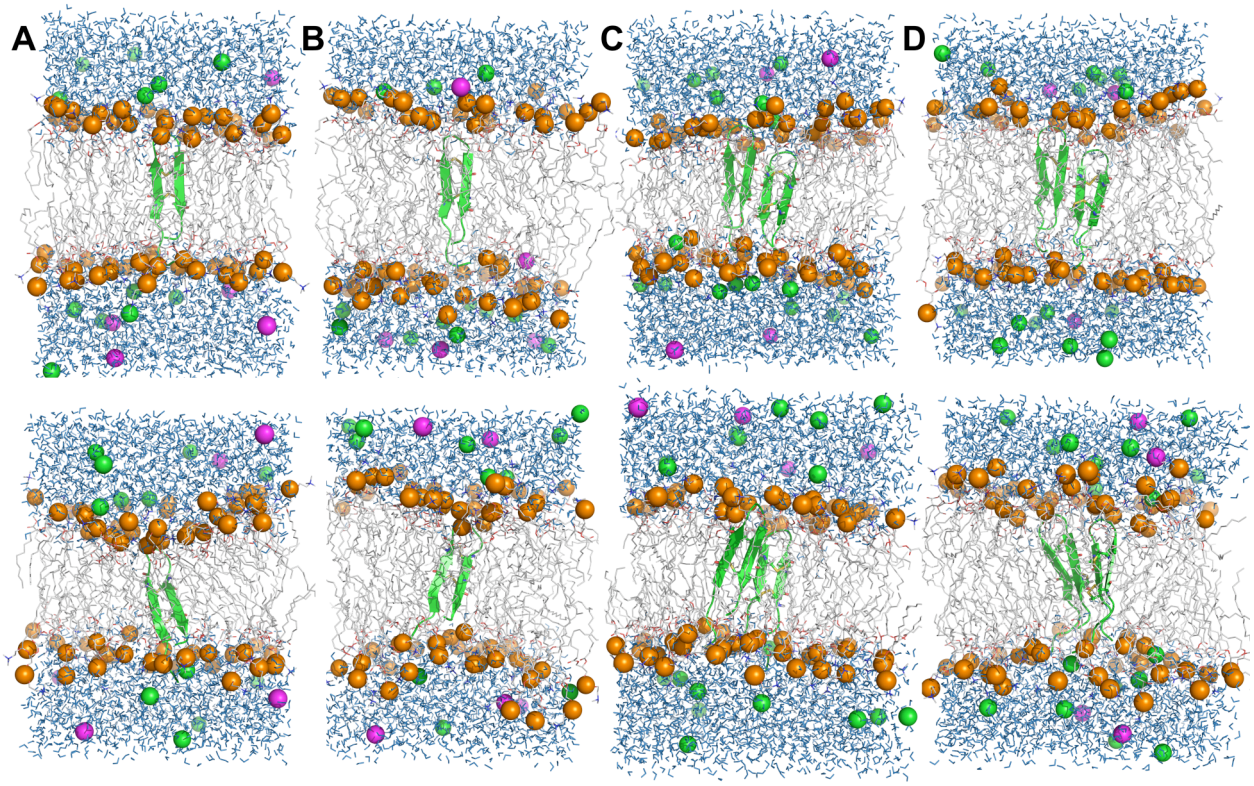

FIGURE S1. Molecular representation of the initial (top) and final (bottom) structures of PG-1 monomer and dimer in DLPC and POPC bilayers: (*A*) M1_DLPC, (*B*) M1_POPC, (*C*) D1_DLPC, and (*D*) D1_POPC. The secondary structure of PG-1 (*green*) is shown. Lipid molecules (*grey*) are illustrated by lines. Phosphate atoms (*orange*) are shown in spheres to illustrate the hydrophobic/hydrophilic interface. Water molecules (*blue*) are shown in lines. 0.2 M K^+ (*magenta*) and Cl^- (*green*) are also presented with spheres. The figure is produced with PyMOL (61).

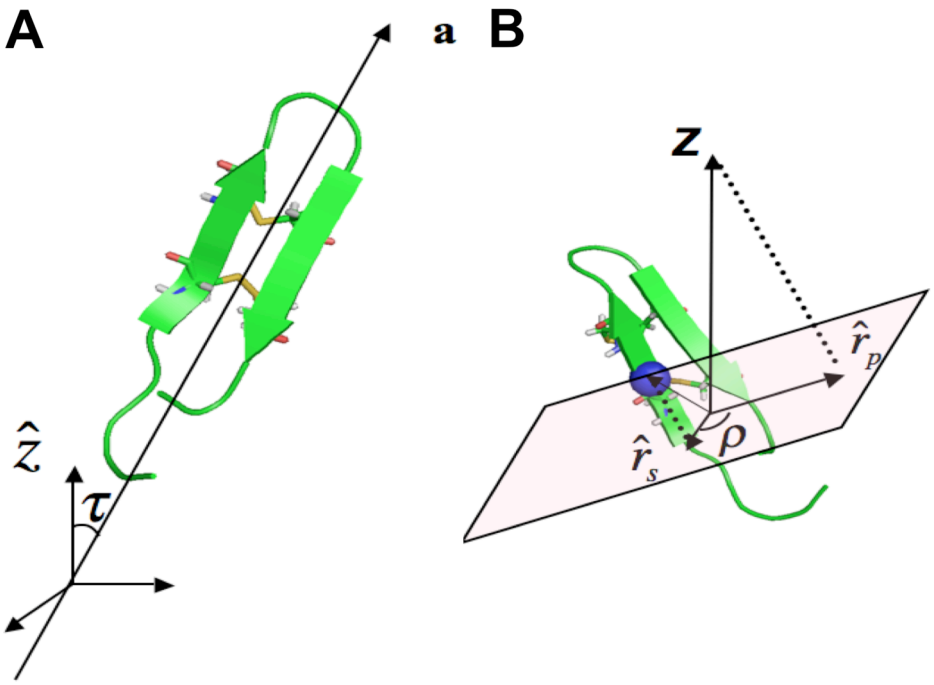

FIGURE S2. Definitions of (*A*) tilt angle (τ) and (*B*) rotation angle (ρ). PG-1 monomer (*green*) is shown in cartoon representation. The disulfide bonds (*yellow*) are shown in sticks. The hairpin axis (**a)** is the eigenvector that corresponds to the smallest eigenvalue. $\mathbf{r}_p$ is the projection of the *Z*-axis on the plane (*pink*) made by the second and third principal axes. $\mathbf{r}_s$ is the perpendicular vector from **a** to the reference atom N on Cys6 (*blue sphere*).

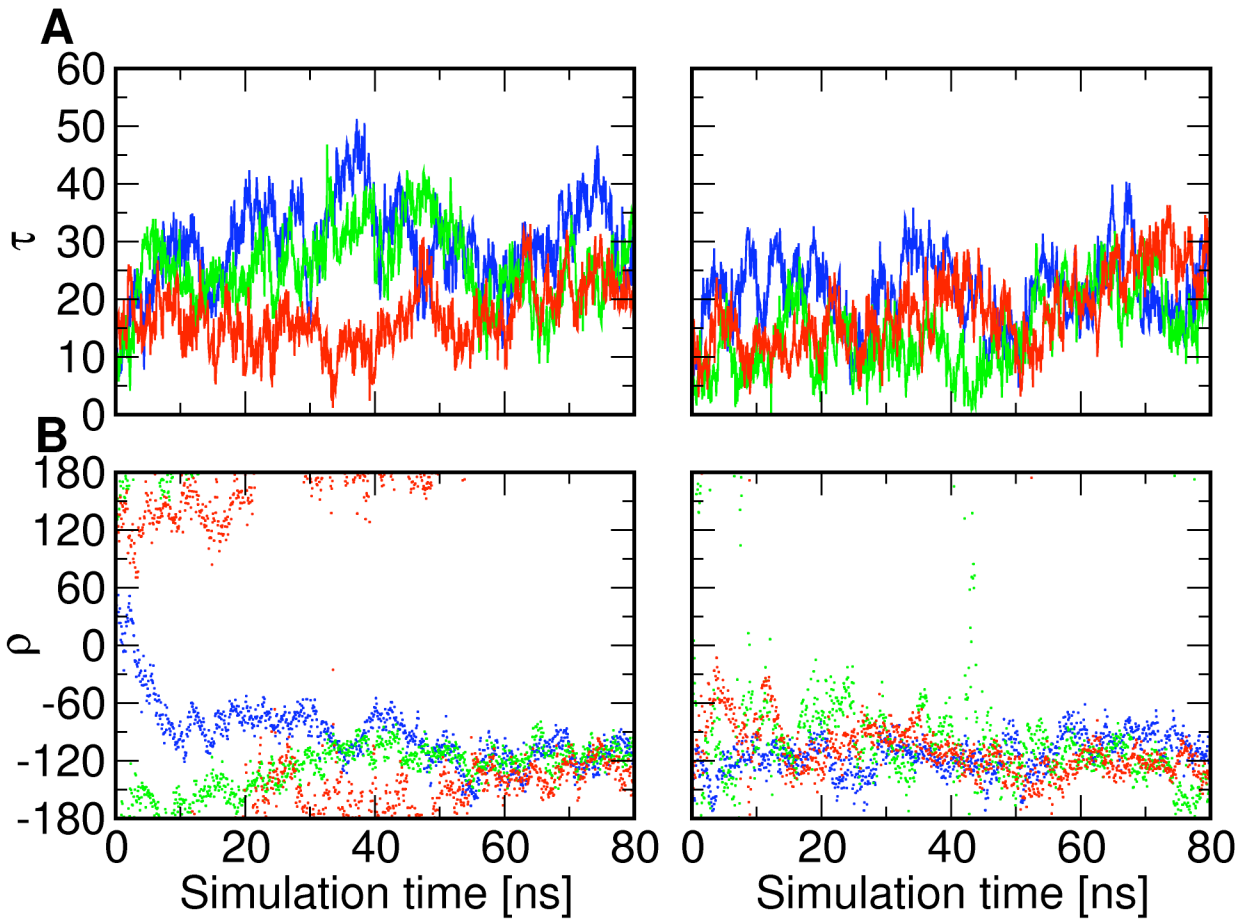

FIGURE S3. The tilt angle (τ) and rotation angle (ρ) time profile of the PG-1 monomers in different bilayers: (*A*) Tilt angles in the DLPC bilayers (*left*) and POPC bilayers (*right*). (*B*) Rotation angles in the DLPC bilayers (*left*) and POPC bilayers (*right*). Systems M1 (*blue*), M2 (*green*), and M3 (*red*) are shown in different color for a clear view. Note that ρ is not well defined when τ is very small by definition.

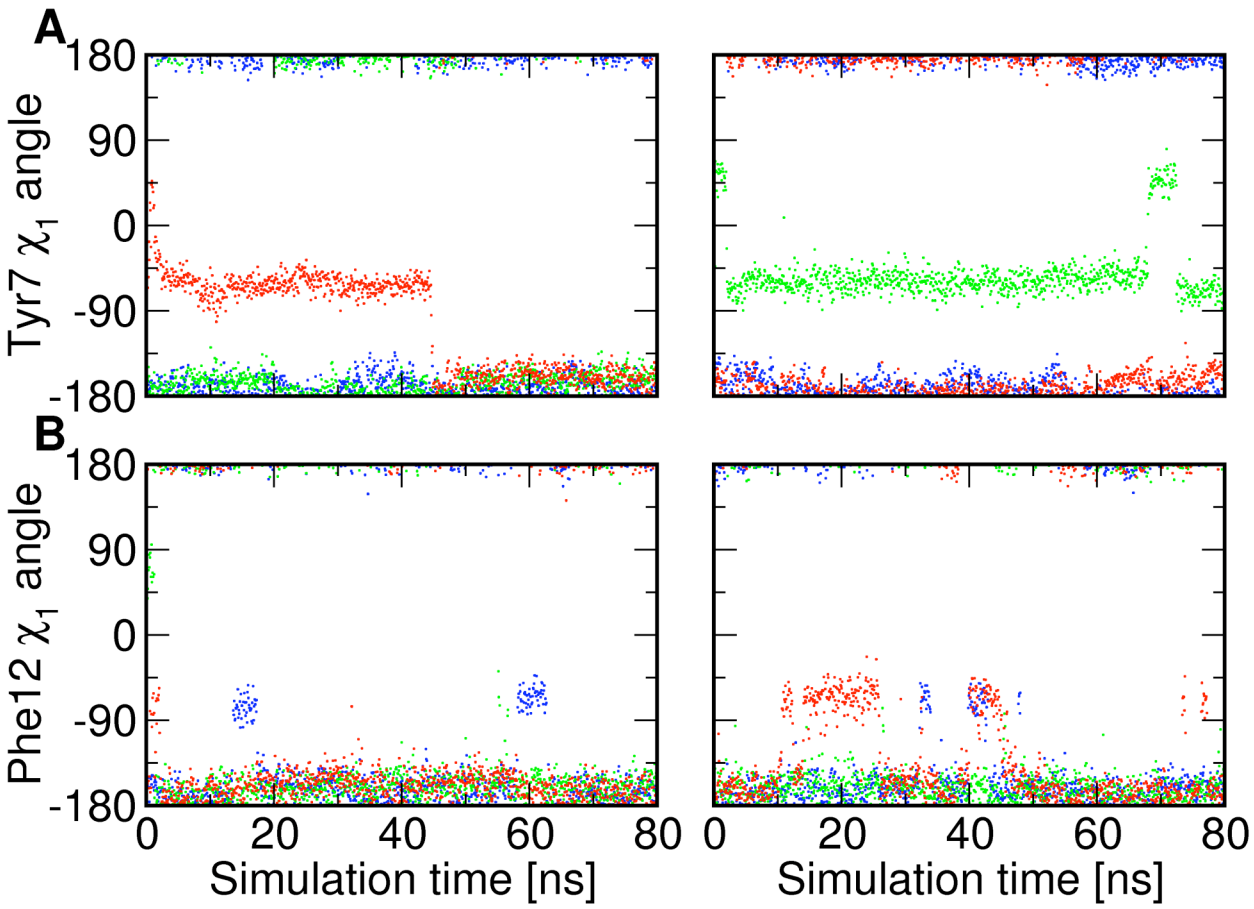

FIGURE S4. The side chain rotamer χ1 angle for (*A*) Tyr7 in systems containing DLPC (*left*) and POPC (*right*) bilayers. (*B*) Phe12 in systems containing DLPC (*left*) and POPC (*right*) bilayers. System M1 (*blue*), M2 (*green*) and M3 (*red*) are represented by different color for clarity.

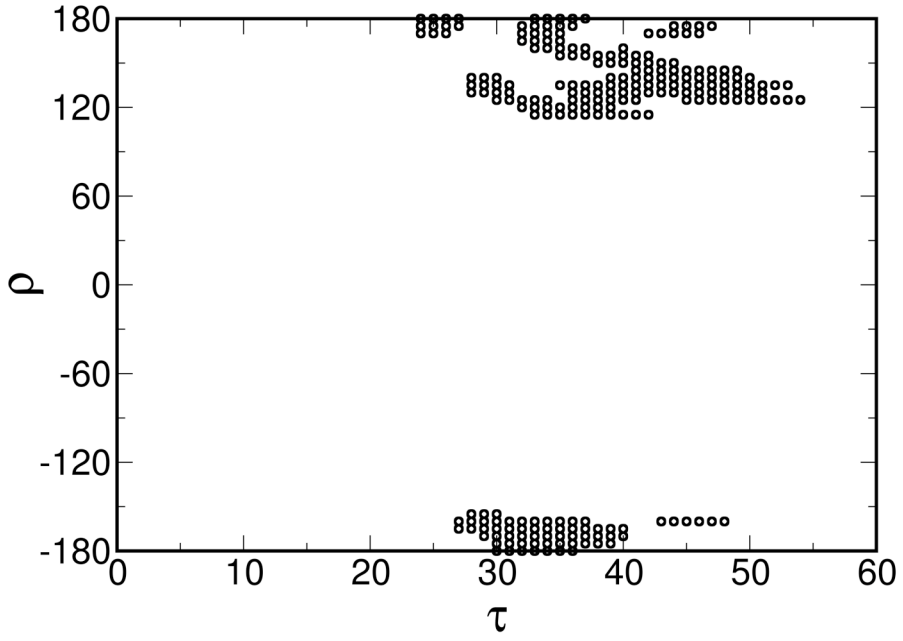

FIGURE S5. The orientation of PG-1 solution NMR structures with chemical shifts root mean-square deviation (δ_σ) less than 4 ppm.

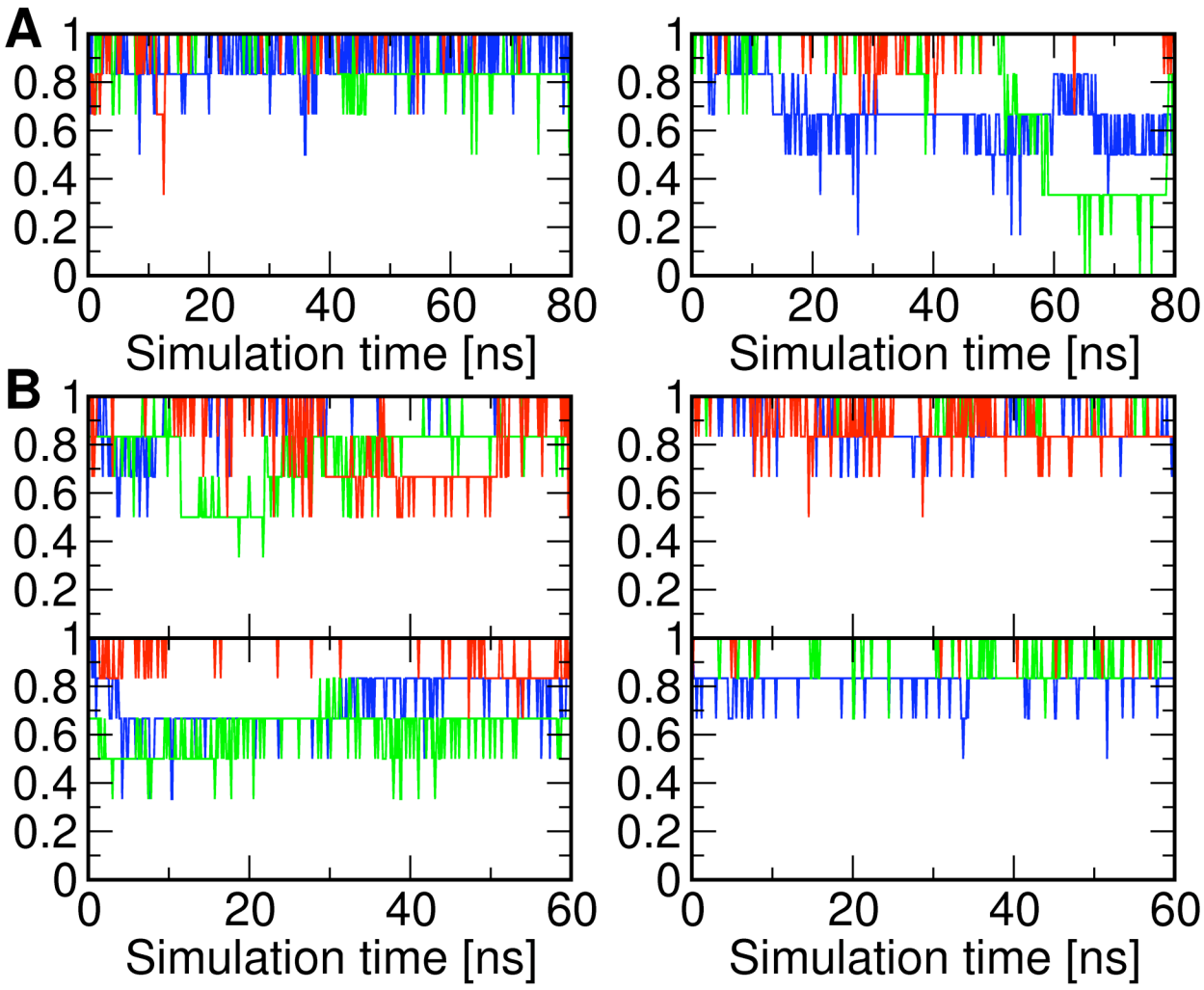

FIGURE S6. (*A*) The intramolecular H-bond fraction of PG-1 monomer in DLPC (*left*) and POPC (*right*) bilayers. (*B*) The intramolecular H-bond fraction of PG-1 dimer monomer A (*top*) and monomer B (*bottom*) in DLPC (*left*) and POPC (*right*) bilayers. Systems M1 (*blue*), M2 (*green*), M3 (*red*), D1 (*blue*), D2 (*green*), and D3 (*red*) are shown in different color for clarity.

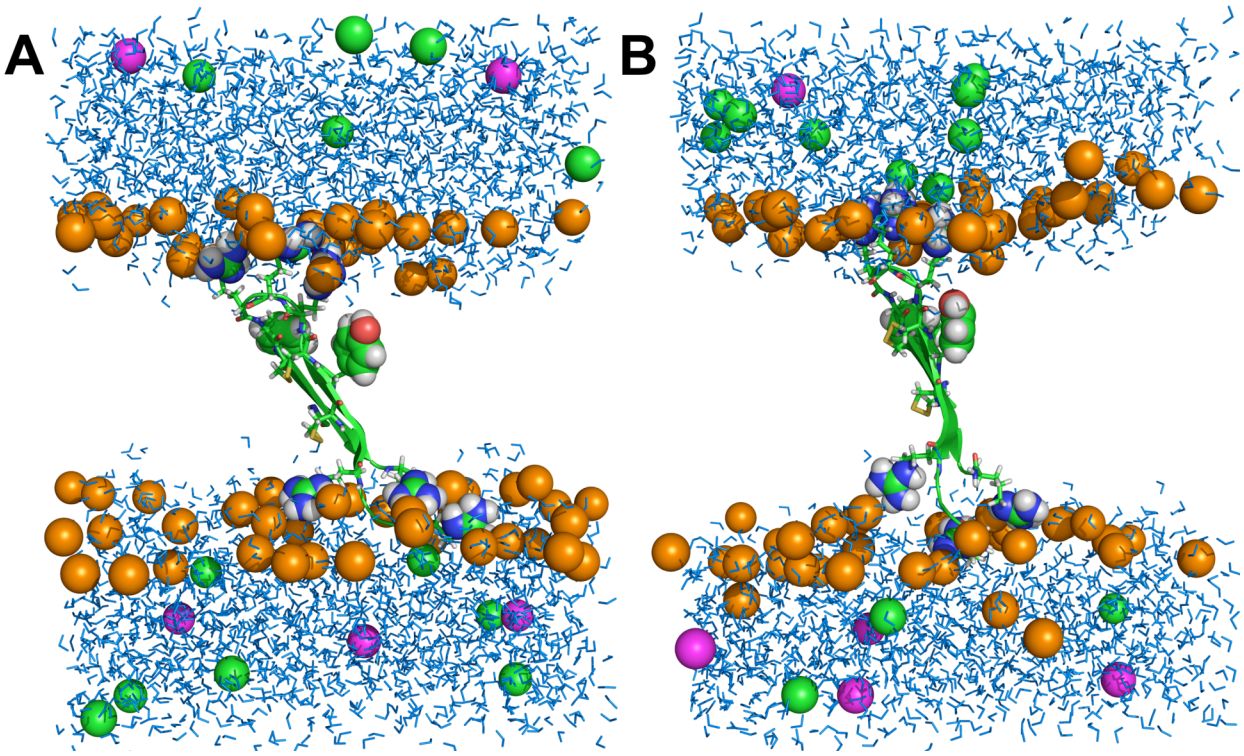

FIGURE S7. The snapshots of PG-1 monomer in system M1 in (*A*) DLPC and (*B*) POPC at 20 ns. PG-1 (*green*) is shown in cartoon representation with the N-terminal strand pointing outwards. The disulfide bonds (*yellow*) are shown in sticks. The guanidinium groups as well as side chains of Tyr7 and Phe12 are represented in spheres. The lipid tails are not shown for clarity. The phosphate atoms (*orange spheres*) are shown to illustrate the hydrophobic/hydrophilic interface. The water molecules (*blue*), K^+ (*magenta*), and Cl^- (*green*) are also shown.

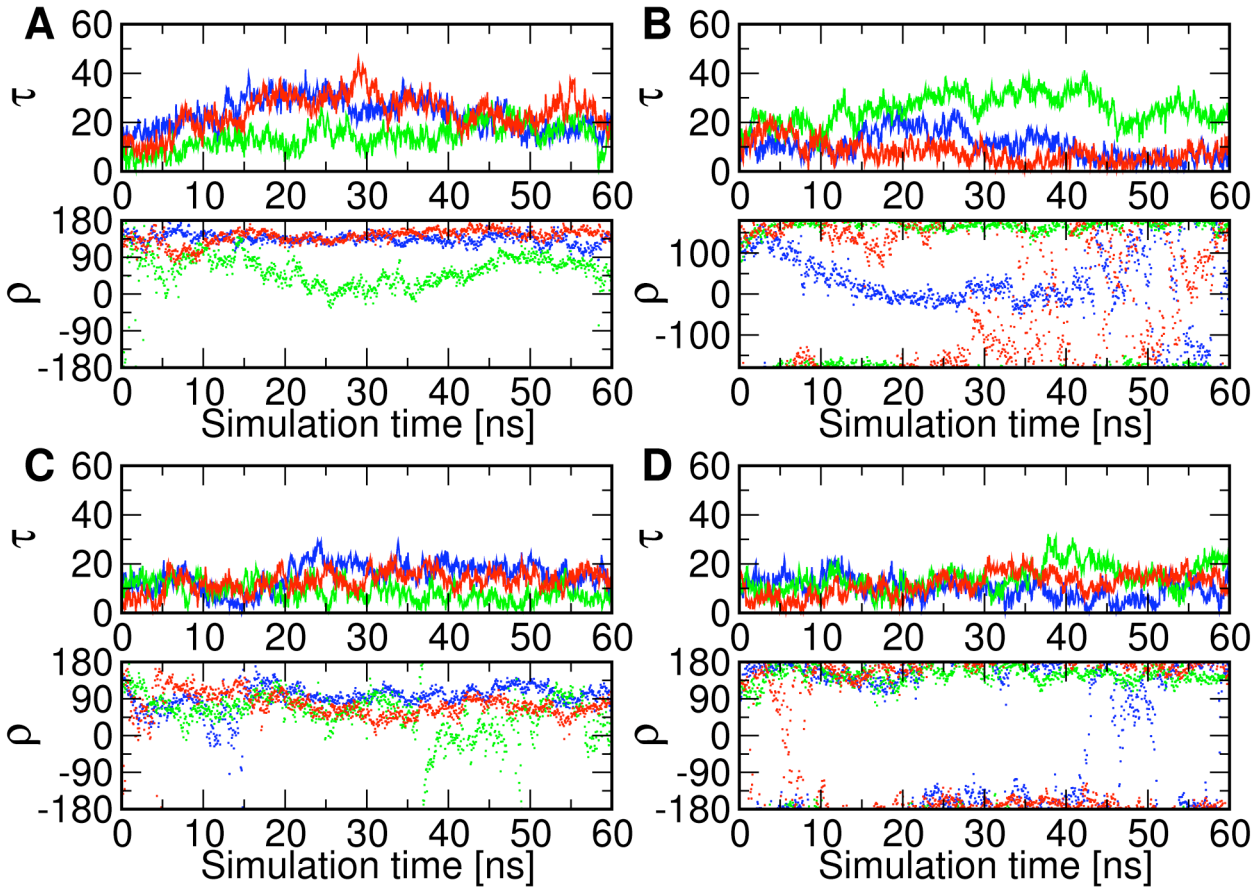

FIGURE S8. The tilt angle (τ) and rotation angle (ρ) time profile of monomers in PG-1 dimer in different bilayers: (*A*) monomer A and (*B*) monomer B in the DLPC bilayers, and (*C*) monomer A and (*D*) monomer B in the POPC bilayers. Systems D1 (*blue*), D2 (*green*), and D3 (*red*) are shown in different color for a clear view. Note that ρ is not well defined when τ is very small by definition.

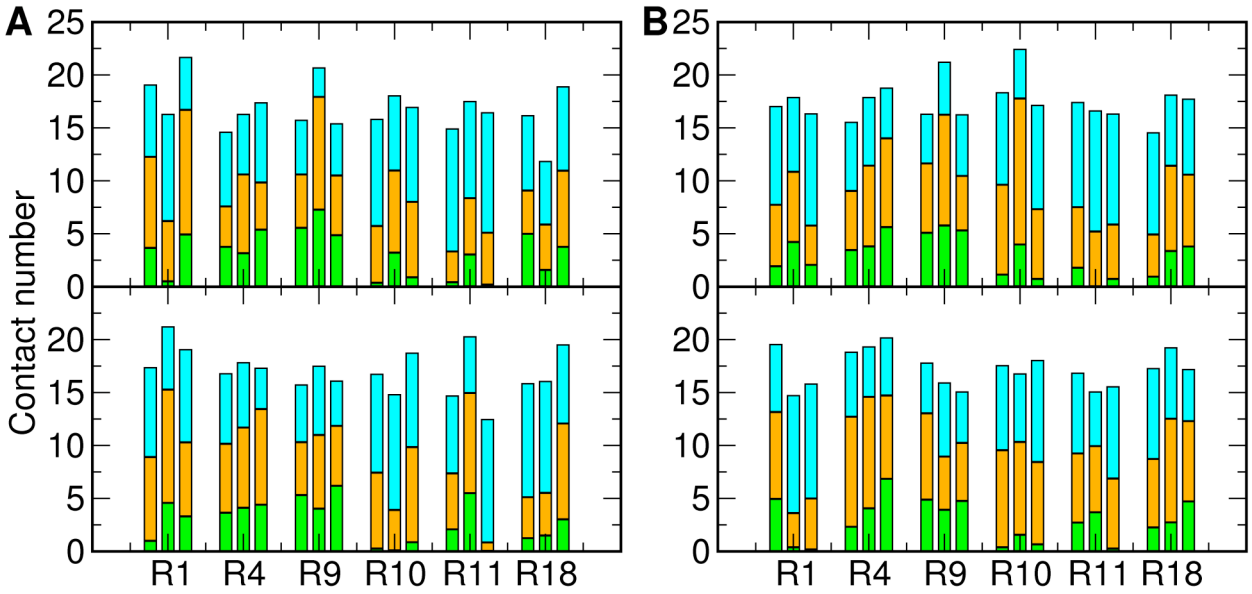

FIGURE S9. Average contact numbers of guanidinium-water (*cyan*), guanidinium-lipid head groups (*orange*), and guanidinium-lipid tails (*green*) in (*A*) monomer A (*top*) and monomer B (*bottom*) of PG-1 dimer in the DLPC bilayers, and (*B*) monomer A (*top*) and monomer B (*bottom*) of PG-1 dimer in the POPC bilayers. Atoms within 4.5 Å are counted as interacting pairs. The results from system D1 (*left*), D2 (*middle*), and D3 (*right*) are shown for each arginine residue.