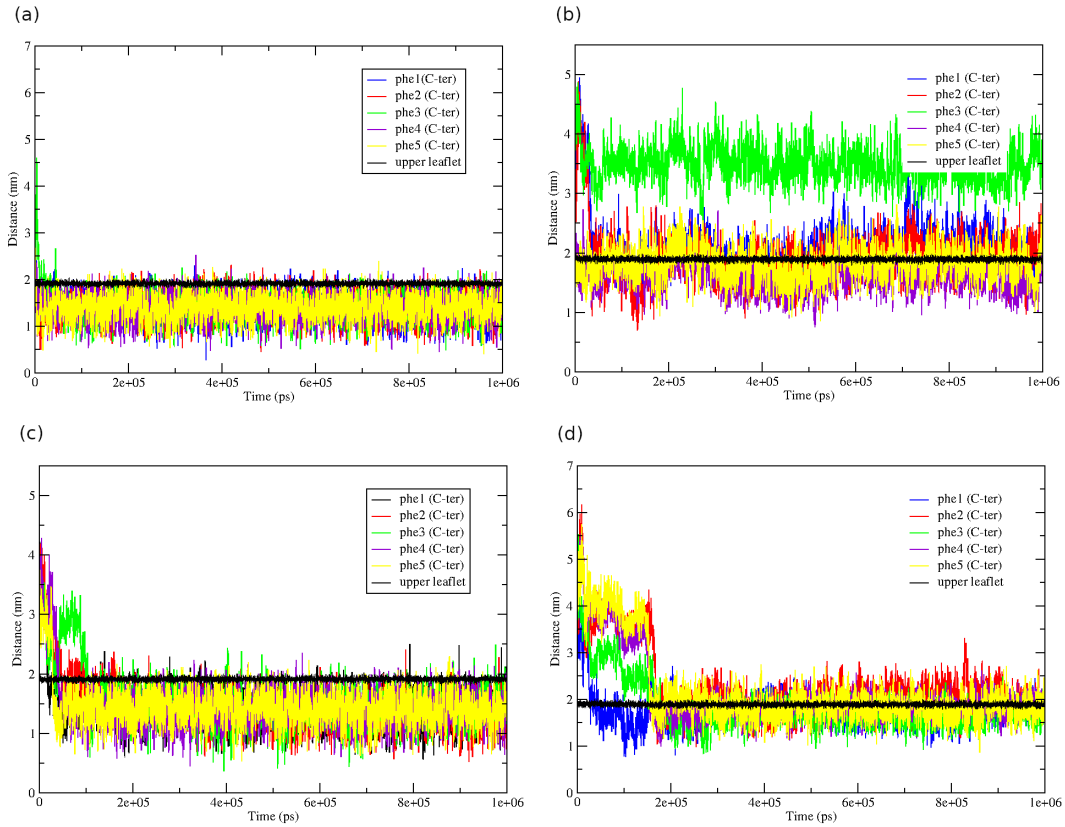

Figure 1. Distance between peptide termini and the center of mass (COM) of the membrane for systems containing five peptides. Plots are shown for aurein and LLAA with two different initial orientations. Sub-figures (a) and (b) correspond to systems with C-terminal initial orientation, while sub-figures (c) and (d) correspond to N-terminal initial orientation.

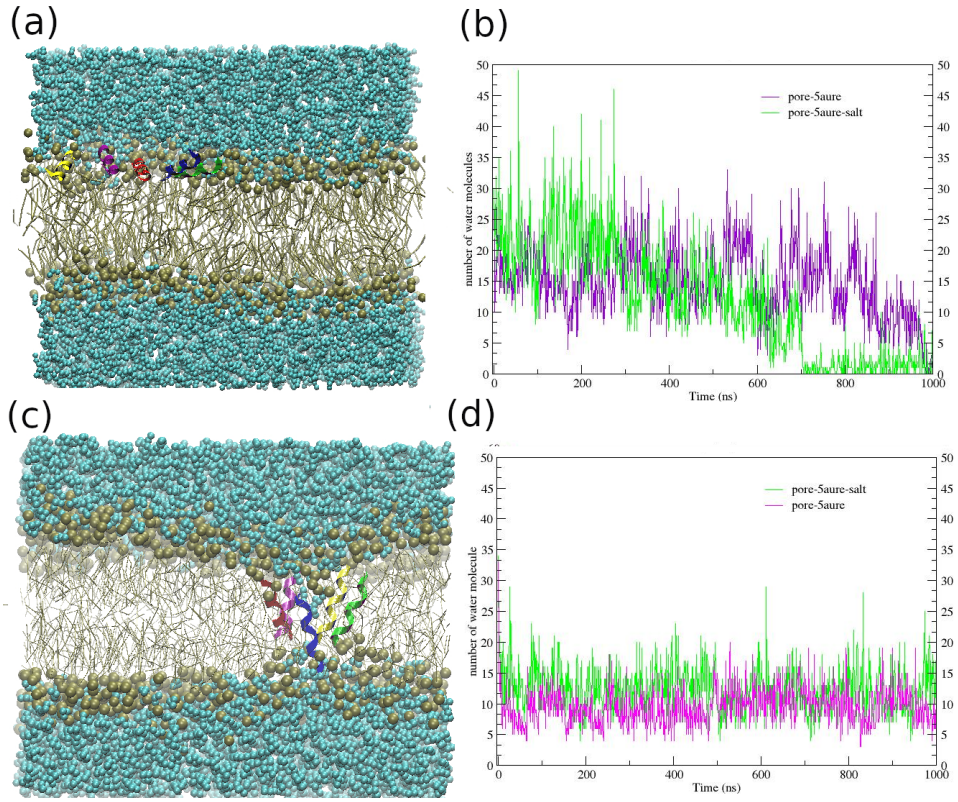

Figure 2. Simulations of pre-formed pores generated by aurein peptides in lipid bilayers. (a, b) Representative snapshot and corresponding water-occupancy profile for the Pore-5Aurein–DPPC system. (c, d) Representative snapshot and water-occupancy profile for the Pore-5Aurein–POPE/POPG (3:1) system. Plots compare simulations conducted with and without salt, while the snapshots correspond to simulations performed with salt.

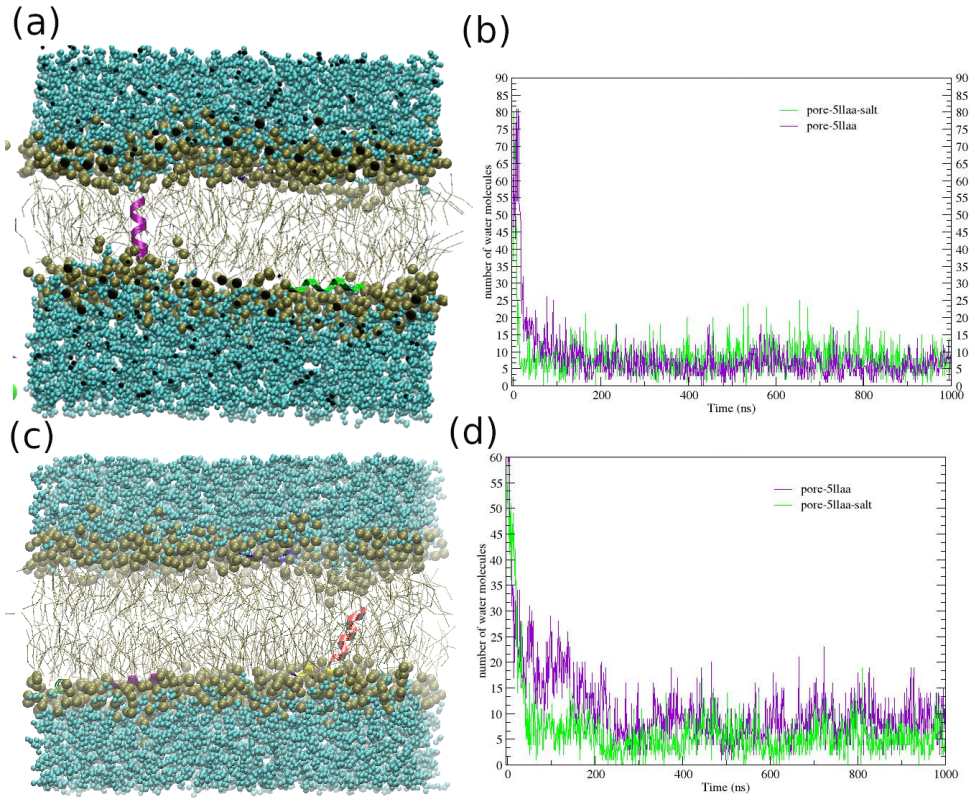

Figure 3. Simulations of pre-formed pores generated by LLAA peptides in lipid bilayers. (a, b) Representative snapshot and water-occupancy profile for the Pore-5LLAA–DPPC system. (c, d) Representative snapshot and water-occupancy profile for the Pore-5LLAA–POPE/POPG (3:1) system. Plots compare simulations conducted with and without salt, while the snapshots correspond to simulations performed with salt.

Table 1: Specifications of simulation systems used for coarse-grained (CG) and all-atom (AA) molecular dynamics simulations. Each system contains peptide(s), a lipid bilayer, and water molecules. The number of each component is provided in the table.

System Name	Peptide	Peptide	Terminus	Membrane Composition	Lipids	Water	Model
1aur-C-PEPG	Aurein	1	C-terminal	POPE:POPG (3:1)	252:84	5479	CG
1aur-N-PEPG	Aurein	1	N-terminal	POPE:POPG (3:1)	252:84	5478	CG
5aur-C-PEPG	Aurein	5	C-terminal	POPE:POPG (3:1)	252:84	5405	CG
5aur-N-PEPG	Aurein	5	N-terminal	POPE:POPG (3:1)	252:84	5259	CG
1LLAA-C-PEPG	LLAA	1	C-terminal	POPE:POPG (3:1)	252:84	5474	CG
1LLAA-N-PEPG	LLAA	1	N-terminal	POPE:POPG (3:1)	252:84	5326	CG
5LLAA-C-PEPG	LLAA	5	C-terminal	POPE:POPG (3:1)	252:84	5344	CG
5LLAA-N-PEPG	LLAA	5	N-terminal	POPE:POPG (3:1)	252:84	5216	CG
1aur-C-POPC	Aurein	1	C-terminal	POPC	338	5408	CG
1aur-N-POPC	Aurein	1	N-terminal	POPC	338	5553	CG
5aur-C-POPC	Aurein	5	C-terminal	POPC	338	5333	CG
5aur-N-POPC	Aurein	5	N-terminal	POPC	338	5484	CG
1LLAA-C-POPC	LLAA	1	C-terminal	POPC	338	5557	CG
1LLAA-N-POPC	LLAA	1	N-terminal	POPC	338	5400	CG
5LLAA-C-POPC	LLAA	5	C-terminal	POPC	338	5421	CG
5LLAA-N-POPC	LLAA	5	N-terminal	POPC	338	5301	CG
1aur-C-DPPC	Aurein	1	C-terminal	DPPC	338	5792	CG
1aur-N-DPPC	Aurein	1	N-terminal	DPPC	338	5644	CG
5aur-C-DPPC	Aurein	5	C-terminal	DPPC	338	5708	CG
5aur-N-DPPC	Aurein	5	N-terminal	DPPC	338	5710	CG
1LLAA-C-DPPC	LLAA	1	C-terminal	DPPC	338	5787	CG
1LLAA-N-DPPC	LLAA	1	N-terminal	DPPC	338	5638	CG
5LLAA-C-DPPC	LLAA	5	C-terminal	DPPC	338	5668	CG
5LLAA-N-DPPC	LLAA	5	N-terminal	DPPC	338	5520	CG
1aur-C-PEPG	Aurein	1	C-terminal	POPE:POPG (3:1)	96:32	4512	AA
1aur-N-PEPG	Aurein	1	N-terminal	POPE:POPG (3:1)	96:32	4509	AA
5aur-C-PEPG	Aurein	5	C-terminal	POPE:POPG (3:1)	96:32	3948	AA
5aur-N-PEPG	Aurein	5	N-terminal	POPE:POPG (3:1)	96:32	3938	AA
1LLAA-C-PEPG	LLAA	1	C-terminal	POPE:POPG (3:1)	96:32	4483	AA
1LLAA-N-PEPG	LLAA	1	N-terminal	POPE:POPG (3:1)	96:32	4480	AA
5LLAA-C-PEPG	LLAA	5	C-terminal	POPE:POPG (3:1)	96:32	3785	AA
5LLAA-N-PEPG	LLAA	5	N-terminal	POPE:POPG (3:1)	96:32	3819	AA

Table 2: Average electrostatic (Coulombic) interaction energies between peptides and membrane lipids, calculated over the last 300 ns of simulation.

Configuration	Coulombic energy of peptide-lipid (kJ/mol)
1aur-C-PEPG (3:1)	-49.33 ± 0.48
1aur-N-PEPG (3:1)	-49.73 ± 0.64
1LLAA-C-PEPG (3:1)	-200.53 ± 2
1LLAA-N-PEPG (3:1)	-198.51 ± 1.1
1aur-C-PEPG (5:1)	-51.05 ± 0.56
1aur-N-PEPG (5:1)	-52.47 ± 0.3
1LLAA-C-PEPG (5:1)	-197.71 ± 1.7
1LLAA-N-PEPG (5:1)	-192.95 ± 2.9
1aur-C-POPC	-48.37 ± 0.25
1aur-N-POPC	-48.21 ± 0.22
1LLAA-C-POPC	-177.59 ± 1.1
1LLAA-N-POPC	-176.89 ± 2.3

Table 3: Comparison of average distances of all amino acids from the membrane in different peptide-lipid coarse-grained systems. Distances are measured relative to the membrane COM.

(a) 1LLAA systems

Amino acids	**1LLAA-N-POPC**	**1LLAA-N-POPE/POPG 3:1**	**1LLAA-N-POPE/POPG 5:1**
1Arg	2.19	2.15	2.18
2Ile	1.65	1.59	1.62
3Phe	1.44	1.39	1.42
4Asp	1.99	1.96	1.98
5Lys	1.78	1.75	1.76
6Ile	1.37	1.33	1.35
7Arg	1.84	1.79	1.82
8Gln	1.97	1.95	1.96
9Val	1.51	1.48	1.48
10Ile	1.39	1.35	1.37
11Arg	1.91	1.87	1.90
12Lys	1.90	1.88	1.86
13Phe	1.38	1.37	1.38
headgroup	1.89	1.91	1.91

(b) 1aur systems

Amino acids	**1aur-N-POPC**	**1aur-N-POPE/POPG 3:1**	**1aur-N-POPE/POPG 5:1**
1Gly	1.90	1.90	1.89
2Leu	1.61	1.61	1.60
3Phe	1.76	1.76	1.76
4Asp	2.16	2.17	2.15
5Ile	1.77	1.78	1.76
6Ile	1.53	1.54	1.53
7Lys	2.05	2.06	2.03
8Lys	2.14	2.17	2.14
9Ile	1.56	1.58	1.57
10Ala	1.65	1.69	1.68
11Glu	2.05	2.09	2.07
12Ser	1.84	1.90	1.88
13Phe	1.54	1.53	1.53
headgroup	1.89	1.90	1.91