

A systematic approach: Molecular dynamics study and parametrization of Gemini type cationic surfactants

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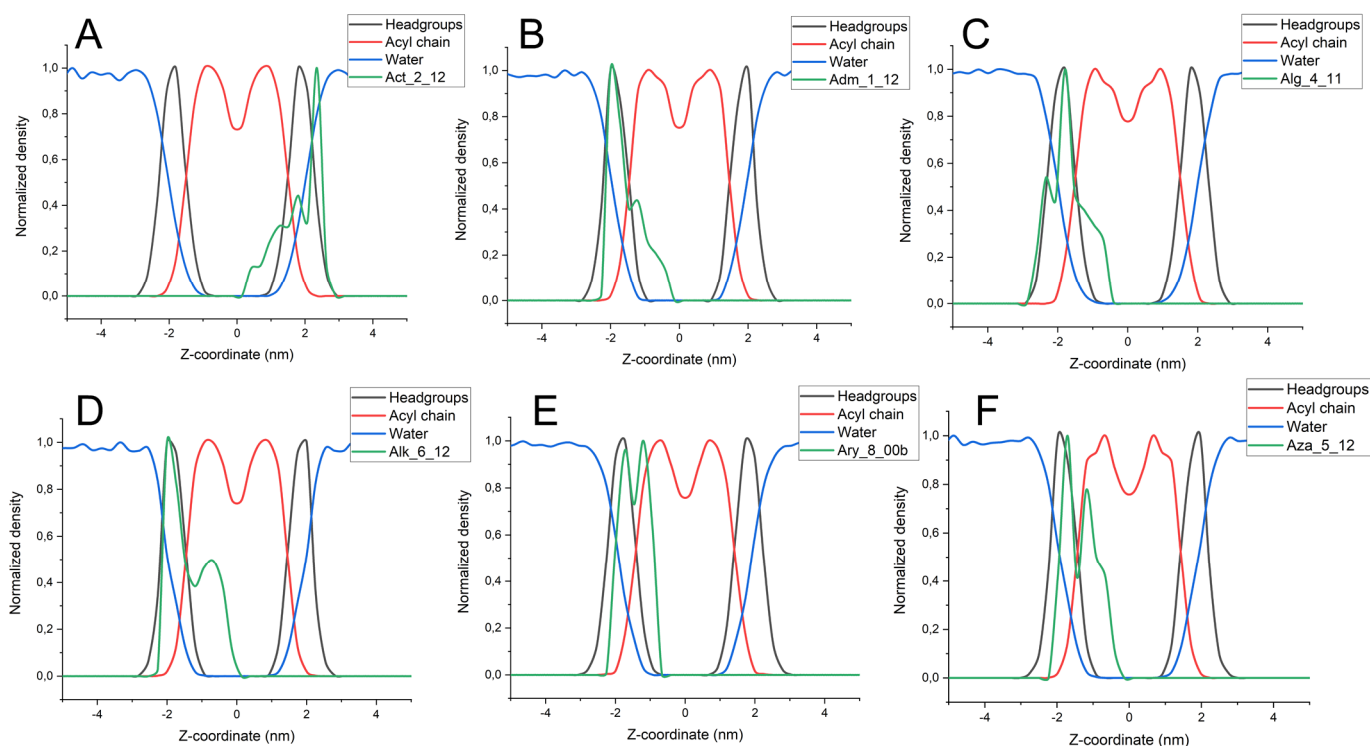


Figure S1 Density profiles of lipid bilayer regions and surfactant location along the axis normal to the membrane surface for (A) Act_2_12, (B) Adm_1_12, (C) Alg_4_11, (D) Alk_6_12, (E) Ary_8_00b, (F) Aza_5_12 Gemini agents.

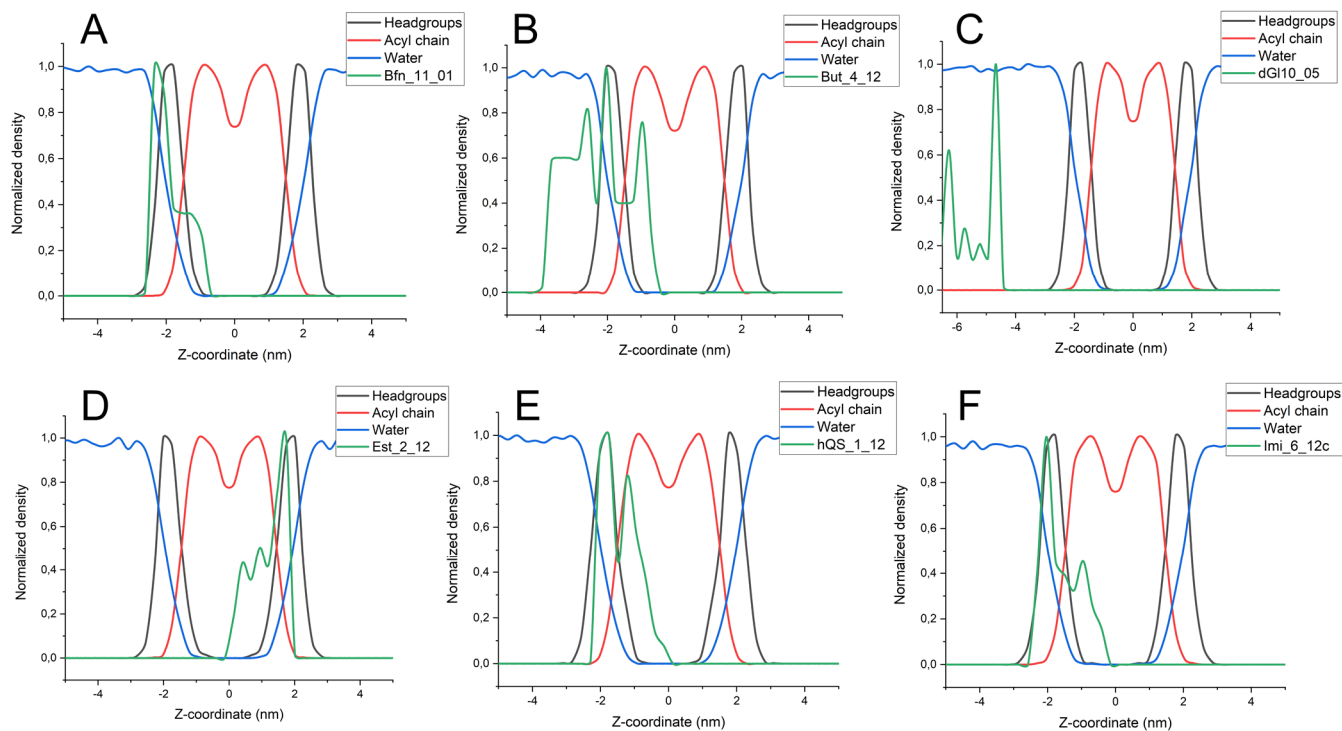


Figure S2 Density profiles of lipid bilayer regions and surfactant location along the axis normal to the membrane surface for (A) Bfn_11_01, (B) But_4_12, (C) dGI10_05, (D) Est_2_12, (E) hQS_1_12, (F) Imi_6_12c Gemini agents.

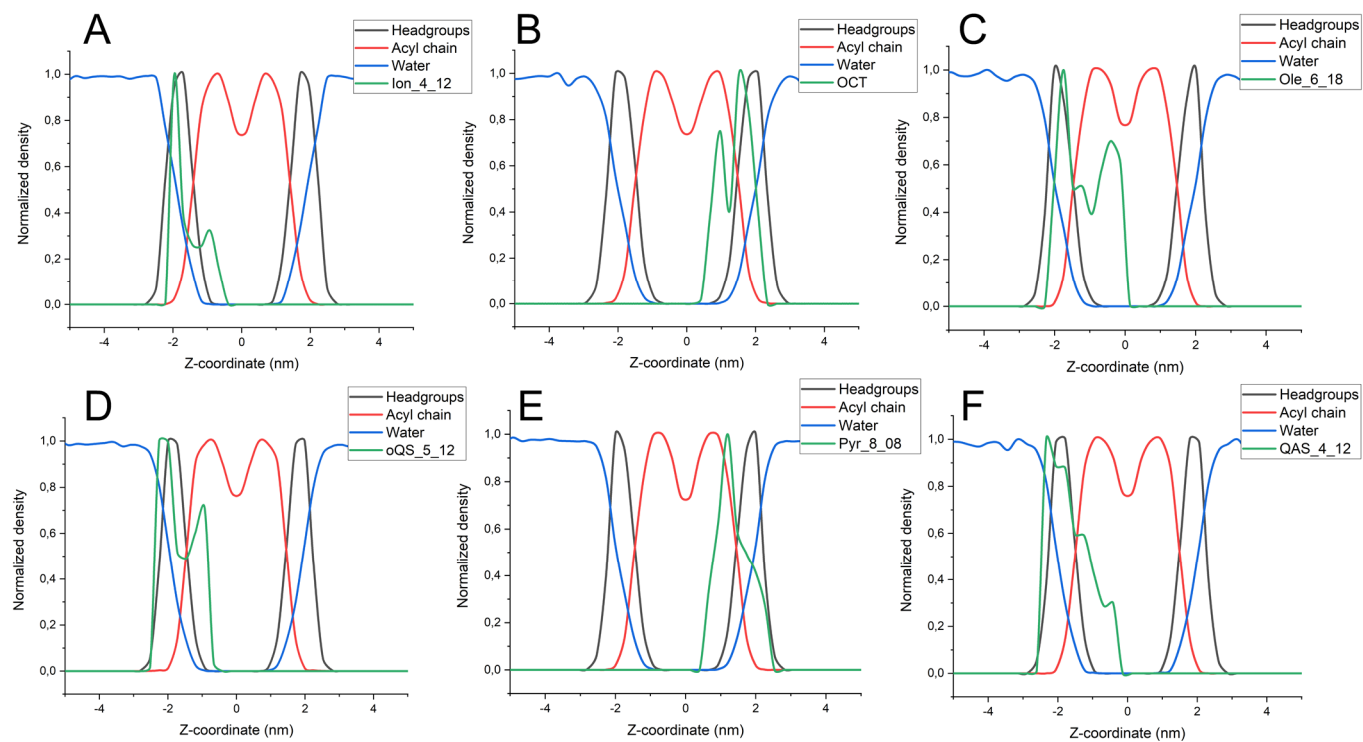


Figure S3 Density profiles of lipid bilayer regions and surfactant location along the axis normal to the membrane surface for (A) Ion_4_12, (B) OCT, (C) Ole_6_16, (D) oQS_5_12, (E) Pyr_8_08 (F) QAS_4_12 Gemini agents.

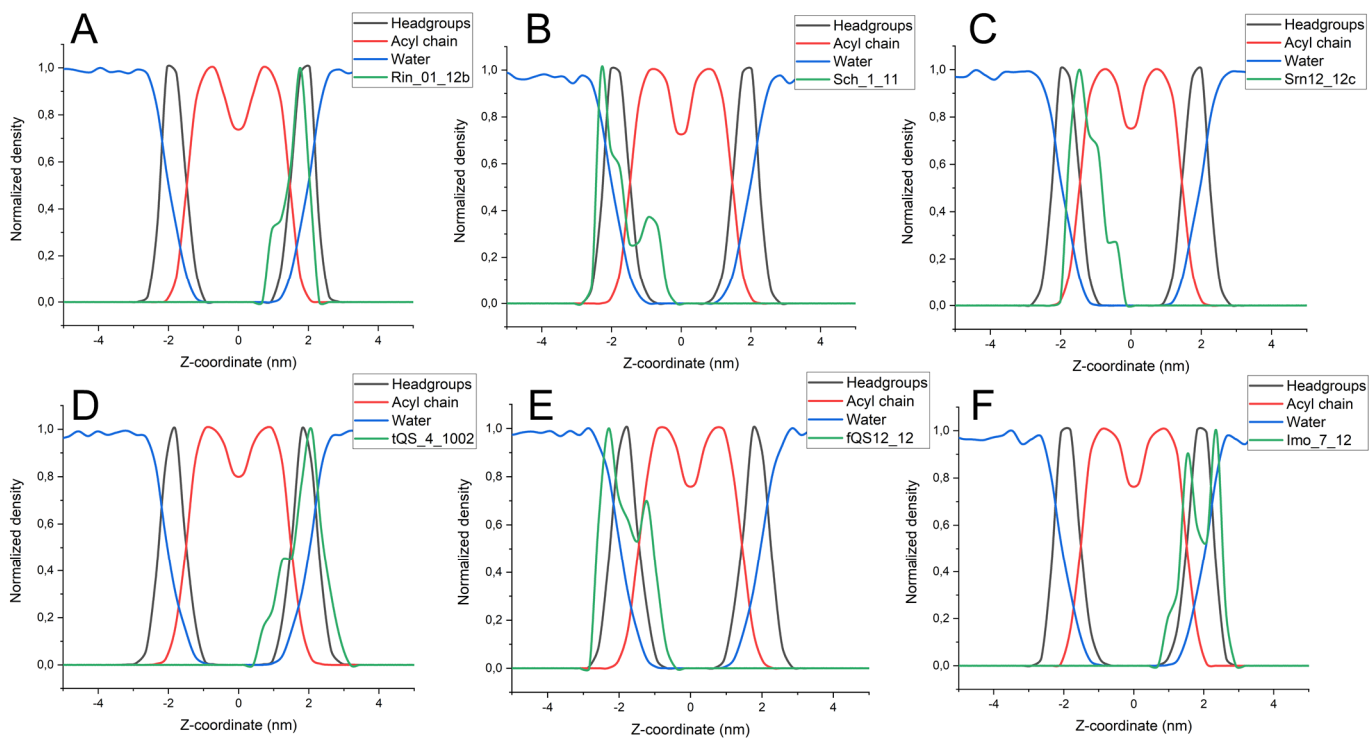


Figure S4 Density profiles of lipid bilayer regions and surfactant location along the axis normal to the membrane surface for (A) Rin_01_12b, (B) Sch_1_11, (C) Srn12_12c, (D) tQS_4_1002, (E) fQS12_12, (F) Imo_7_12 Gemini agents.

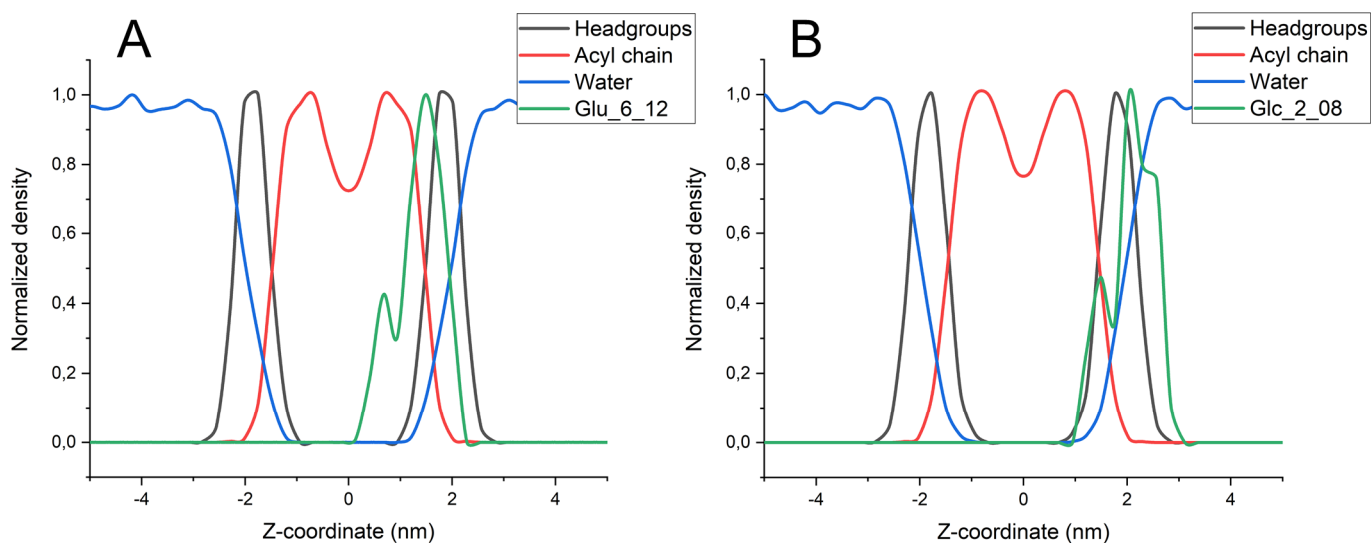
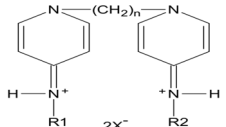
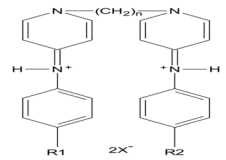
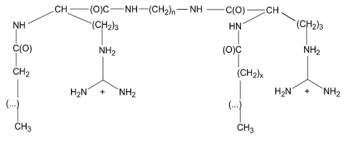
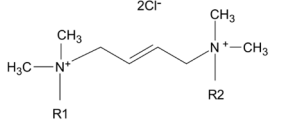
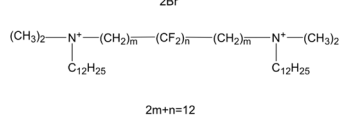
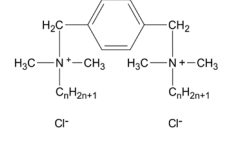
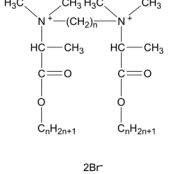
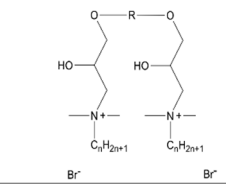
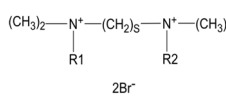
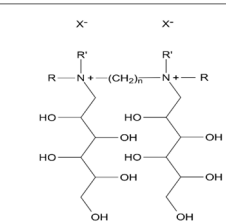
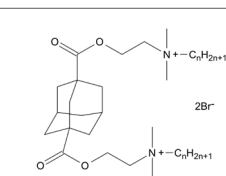
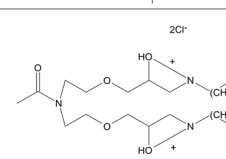
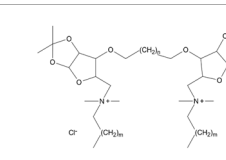
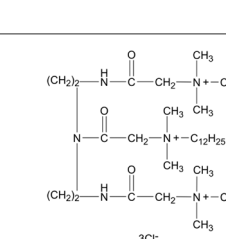
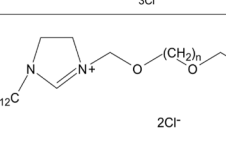


Figure S5 Density profiles of lipid bilayer regions and surfactant location along the axis normal to the membrane surface for (A) Glu_6_12, (B) Glc_2_08 Gemini agent.

Table S1 Selected and modelled Gemini surfactants used in molecular dynamics studies.

Group	Scheme	ID	Seg name	Linker	Linker length (n)	Chain compound (R1 or R2)	Number of carbons in R1/R2 (m)	Number of carbons from N+	Chemical formula	Organic salt	log10(CMC)	Ref
Alkyl Bisp		Alk_6_12	A6G	(CH ₂) ₆	6	C ₁₂ H ₂₅	12	12	C ₄₀ H ₇₂ N ₄	Br	-4,09	1
Aryl Bisp		Ary_8_00b	AC2	(CH ₂) ₈	8	F	0	6	C ₃₀ H ₃₄ F ₂ N ₄	Cl	-3,49	1
Algine		Alg_4_11	AL2	(CH ₂) ₄	4	C ₁₁ H ₂₃	11	12	C ₄₀ H ₈₂ N ₁₀ O ₄	Cl	-6,21	40
Butene		But_4_12	BU3	C ₄ H ₆	4	C ₁₂ H ₂₅	12	12	C ₃₂ H ₆₈ N ₂	Cl	-3,3	37
fQAS		fQS12_12	F0A	C ₁₂ H ₁₆ F ₈	12	C ₁₂ H ₂₅	12	12	C ₄₀ H ₇₈ F ₈ N ₂	Br-	-6,65	45
Ring		Rin_01_12b	RI1	C ₆ H ₄	1	C ₁₂ H ₂₅	12	12	C ₃₆ H ₇₀ N ₂	Cl	-3,63	46
Ester		Est_2_12	E2D	C ₂ H ₄	2	C ₁₂ H ₂₅	12	15	C ₃₆ H ₇₄ N ₂ O ₄	Br	-4,21	35

Ionic		Ion_4_12	I4C	CH ₂ CH ₂ OCH ₂ CH ₂ H ₂	4	C ₁₂ H ₂₅	12	12	C ₃₈ H ₈₂ N ₂ O ₅	Br	-4,8	10
QAS		QAS_4_12	Q4A	C ₄ H ₆	4	C ₁₂ H ₂₅	12	12	C ₃₂ H ₇₀ N ₂	Br / Cl	-2,61	27,36
tQAS		tQS_4_1002	T4F	(CH ₂) ₄	4	R1: C ₁₀ H ₂₁ R2: C ₂ H ₅	10 & 2	18	C ₄₀ H ₈₆ N ₂ O ₁₀	I	-5,82	49
Adamantane		Adm_1_12	AD1	C ₁₀ H ₁₆	1	C ₁₂ H ₂₅	12	12	C ₄₄ H ₈₄ N ₂ O ₄	Br	-6,57	41
Acetyl		Act_2_12	AC2	NC ₂ OH ₃	2	C ₁₂ H ₂₅	12	12	C ₄₀ H ₈₅ N ₃ O ₅	Cl	-5,55	42
Glucose		Glu_6_12	GL3	C ₆ H ₁₂	6	C ₁₂ H ₂₅	12	12	C ₅₂ H ₁₀₂ N ₂ O ₈	Cl	-9,44	32
hQAS		hQS_1_12	HQ1	N	1	C ₁₂ H ₂₅	12	12	C ₅₂ H ₁₀₉ N ₆ O ₃	Cl-	-8,16	45
Imidazolium		Imi_6_12c	M6B	CH ₂ O-(CH ₂) ₄ -CH ₂ O	6	CH ₂	12	15	C ₃₈ H ₇₂ N ₄ O ₂	Cl-	-4,1	28

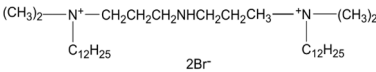
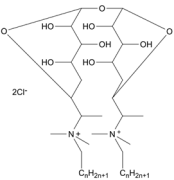
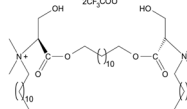
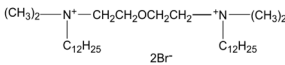
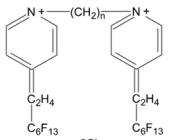
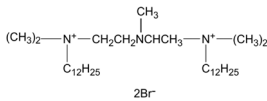
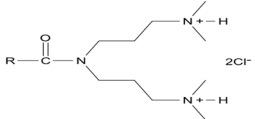
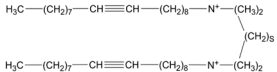
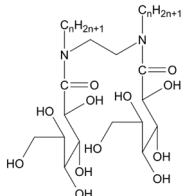
Imino		Imo_7_12	IMO	C ₇ NH	7	C ₁₂ H ₂₅	12	12	C ₃₄ H ₇₅ N ₃	Br-	-3,13	45
Sacharide		Sch_1_11	SA1	O	1	C ₁₁ H ₂₃	11	11	C ₄₄ H ₉₀ N ₂ O ₉	Cl	-7,34	7
Serine		Srn12_12c	SE3	C ₁₂ H ₂₄	12	C ₁₂ H ₂₅	12	12	C ₄₆ H ₉₄ N ₂ O ₆	CF ₃ COO	-6,17	44
O-QAS		oQS_5_12	OQS	(CH ₂) ₂ O(CH ₂) ₂	5	C ₁₂ H ₂₅	12	12	C ₃₂ H ₇₀ N ₂ O ₁	Br-	-2,78	45
Pyridine		Pyr_8_08	PY3	C ₈ H ₁₆	8	C ₈ H ₄ F ₁₃	8	13	C ₃₄ H ₃₂ F ₂₆ N ₂	Cl	-11,2	25
Aza		Aza_5_12	AZ5	C ₅ N	5	C ₁₂ H ₂₅	12	12	C ₃₃ H ₇₃ N ₃	Br-	-3,09	45
Bifunction		Bfn11_01	BF1	N-CO-C ₁₁ H ₂₃	11	C ₅ NH ₁₃	1	4	C ₂₂ H ₄₉ N ₃ O ₁	Cl-	-0,94	38
Oleyl		Ole_6_18	OL6	C ₆ H ₁₂	6	C ₁₈ H ₃₇ :1	18	18	C ₄₆ H ₉₄ N ₂	Br-	-5,04	45
Gluconamid		Glc_2_08	GU1	C ₂ H ₄	2	C ₈ H ₁₇	8		C ₃₀ H ₆₀ N ₂ O ₁₂	N/A	-4,3	33

Table S2 The effect of Gemini agents' incorporation on model membrane structural and dynamic parameters.

Name	Membrane thickness	Area per lipid (other leaflet)	Area per lipid (Gemini leaflet)	Bending rigidity	Tilt	Compressibility	Interdigitation	Penetration depth	Diffusion coefficient	Surface tension
	Å	Å ²	Å ²	fold K _B T	fold K _B T	mN*m ⁻¹	Å	Å	μm ² *s ⁻¹	mN*m ⁻¹
Membrane	39.7±0.5	58.4±2.1	58.66±2.12	13.9±0.7	10.5±0.3	78±17	4.7±0.5	-	6.49±0.02	0.13±0.02
Ctrl+ (OCT)	39.71±1.04	59.2±2.6	60.53±2.64	14.0±0.6	10.5±0.3	534±11	4.05±0.93	10.5±2.4	4.44±0.03	0.42±0.03
Adm_1_12	39.4±1.1	60.21±3.5	59.3±2.6	12.79±0.63	10.7±0.3	579±10	4.01±0.76	15.9±2.2	5.08±0.06	0.30±0.04
Act_2_12	39.5±1.1	62.0±2.5	59.1±2.4	13.8±0.6	10.58±0.25	344±13	4.56±0.64	5.4±2.2	4.53±0.07	0.41±0.04
Ary_8_00b	39.6±1.0	60.8±2.8	67.0±3.3	14.5±0.6	10.0±0.3	436±13	4.57±0.64	14.6±2.0	3.39±0.08	1.09±0.01
But_4_12	39.5±1.1	61.6±2.6	59.65±2.73	14.0±0.7	10.56±0.26	403±17	4.53±0.67	5.5±2.3	8.24±0.09	0.20±0.01
Est_2_12	40.7±0.8	59.43±2.34	60.7±2.1	13.4±0.7	10.7±0.3	502.9±15.1	4.67±0.56	5.9±2.4	3.99±0.06	0.59±0.06
Glu_6_12	39.59±1.31	62.2±3.0	64.78±2.67	14.07±0.64	10.34±0.36	283.7±16.5	4.10±0.83	6.5±2.9	2.37±0.02	0.16±0.06
hQS_1_12	40.2±1.2	59.3±2.9	62.49±3.21	13.7±0.7	10.85±0.32	517.0±10.3	4.32±0.60	5.7±2.1	3.56±0.01	0.05±0.05
Imi_6_12c	39.75±1.04	60.8±3.5	62.1±2.7	13.78±0.65	10.2±0.3	110±27	4.6±0.7	6.02±1.94	8.22±0.08	0.47±0.05
Imo_7_12	39.2±1.0	61.7±3.0	59.5±2.4	14.6±0.6	10.4±0.3	413.5±10.6	4.43±0.54	13.0±2.3	1.96±0.04	0.05±0.01
QAS_4_12	39.3±1.0	61.3±2.6	61.6±2.8	14.27±0.52	9.94±0.24	392±40	4.4±0.8	7.28±2.04	3.10±0.04	0.73±0.05
Rin_01_12b	39.51±1.03	60.9±2.8	60.8±2.4	13.68±0.54	10.3±0.3	351±20	4.5±0.8	8.6±2.1	2.48±0.02	0.25±0.04
Sch_1_11	39.8±0.9	63.9±3.1	60.41±2.24	14.35±0.64	10.39±0.26	41±29	4.4±0.6	5.6±1.8	3.76±0.01	0.20±0.01
Srn12_12c	39.0±0.9	60.6±2.5	63.3±3.2	12.36±0.83	10.2±0.3	401.5±13.7	4.6±0.6	8.1±2.8	4.93±0.01	0.61±0.01
tQS_4_1002	39.51±1.12	61.87±2.71	59.6±2.8	13.6±0.6	10.6±0.3	423.8±10.4	4.3±0.8	7.06±1.74	3.28±0.01	0.39±0.08
fQS12_12	39.4±1.0	60.89±2.34	60.7±2.9	12.9±0.6	10.3±0.3	368±11	4.6±0.6	8.66±2.23	4.22±0.08	0.20±0.01
oQS_5_12	40.0±1.0	61.65±2.44	59.45±2.72	14.4±0.6	10.46±0.32	505.4±16.1	4.51±0.64	6.9±1.9	1.95±0.03	0.18±0.03
Pyr_8_08	39.6±0.9	62.2±2.2	60.3±3.0	14.0±0.7	10.29±0.26	507.4±20.2	4.8±0.6	7.92±2.54	7.62±0.04	0.03±0.03
Alg_4_11	39.9±0.9	60.0±3.1	61.45±2.54	14.1±0.5	10.2±0.3	362±12	4.4±0.6	7.8±2.0	5.47±0.02	0.55±0.04
Aza_5_12	39.5±0.8	60.9±3.4	61.69±3.42	13.38±0.63	10.3±0.3	371.5±10.3	4.8±0.7	7.2±2.3	3.01±0.01	0.95±0.03
Bfn11_01	40.1±1.0	63.8±2.8	60.20±2.53	13.5±0.7	10.3±0.3	309.0±21.4	4.2±0.9	20.4±2.2	3.06±0.03	0.37±0.03
Ion_4_12	39.4±0.9	63.2±3.0	60.6±2.8	14.05±0.61	10.6±0.3	412.9±9.2	4.51±0.53	7.9±2.1	3.59±0.02	0.52±0.02
Ole_6_18	39.7±0.8	57.9±2.8	61.14±2.64	13.2±0.7	10.5±0.3	386±15	4.41±0.65	4.7±3.8	3.30±0.07	0.15±0.03
Glc_2_08	40.0±1.1	61.2±2.6	61.5±2.53	14.7±0.6	10.2±0.3	328.2±9.7	4.45±0.61	11.5±2.5	2.99±0.2	0.16±0.09
Alk_6_12	39.4±1.0	62.22±3.04	58.87±3.34	13.57±0.63	10.4±0.3	22.6±29.4	4.41±0.54	5.4±2.2	3.39±0.02	0.78±0.03

File preparation for GROMACS users

In this work, we prepared a database with a significant number of ready-to-use Gemini surfactants structures and topologies. Provided files are intended for NAMD software, however may be easily translated to fit GROMACS users. On that purpose we recommend using Python 2 tool made by Reza Salari called *PyTopol: A Library For Converting Molecular Topologies*. Further, we present a brief tutorial on how to deal with delivered NAMD force fields.

Firstly, ensure that you have Python 2.7 installed. You can clone the git repo or simply download it from the Reza Salari GitHub page <https://github.com/resal81/PyTopol/wiki/PyTopol-Installation> or use the pip installer. Afterward, copy desired topology files into the main PyTopol directory and use the following command to generate .top and .itp files.

```
psf2top.py -p psf_file.psf -c parameter_file.par
```

Further, comment redundant and overlapping headings in the .top file if needed. (in general first three lines, otherwise GROMACS will prompt when calling *gmx grompp* function). All the details and test section are available on the GitHub page.