Supplementary data

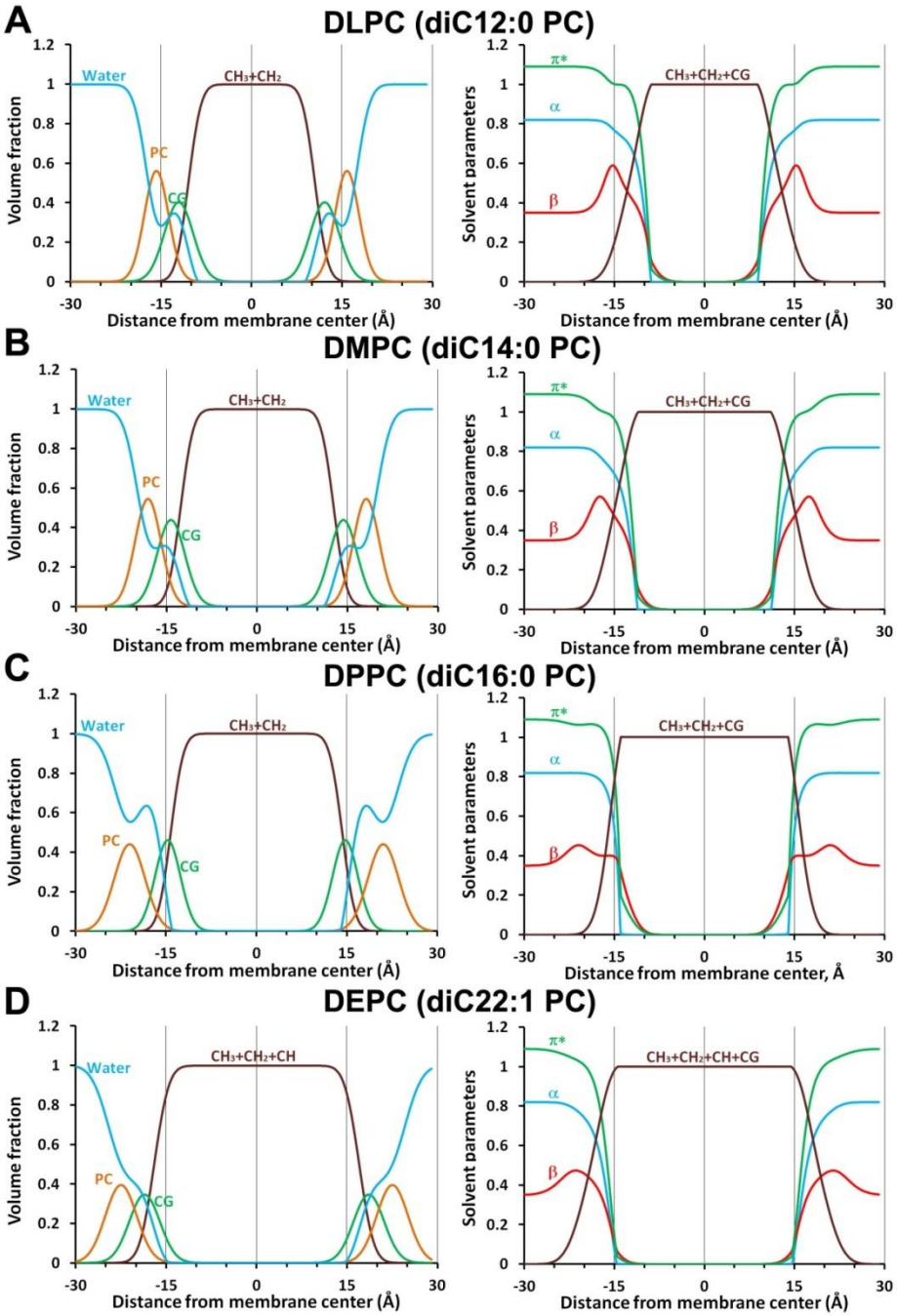

Figure S1. Structures of DLPC (**A**), DMPC (**B**), DPPC (**C**), and DEPC (**D**) bilayers with different lengths of acyl chains. Distributions of lipid segments determined from X-ray scattering data (left pannels). Changes of polarity parameters (α, β, and π^*) along the membrane normal (right pannels). Parameters used for calculation of these profiles and references are provided in Tables 2, S3 and S4.

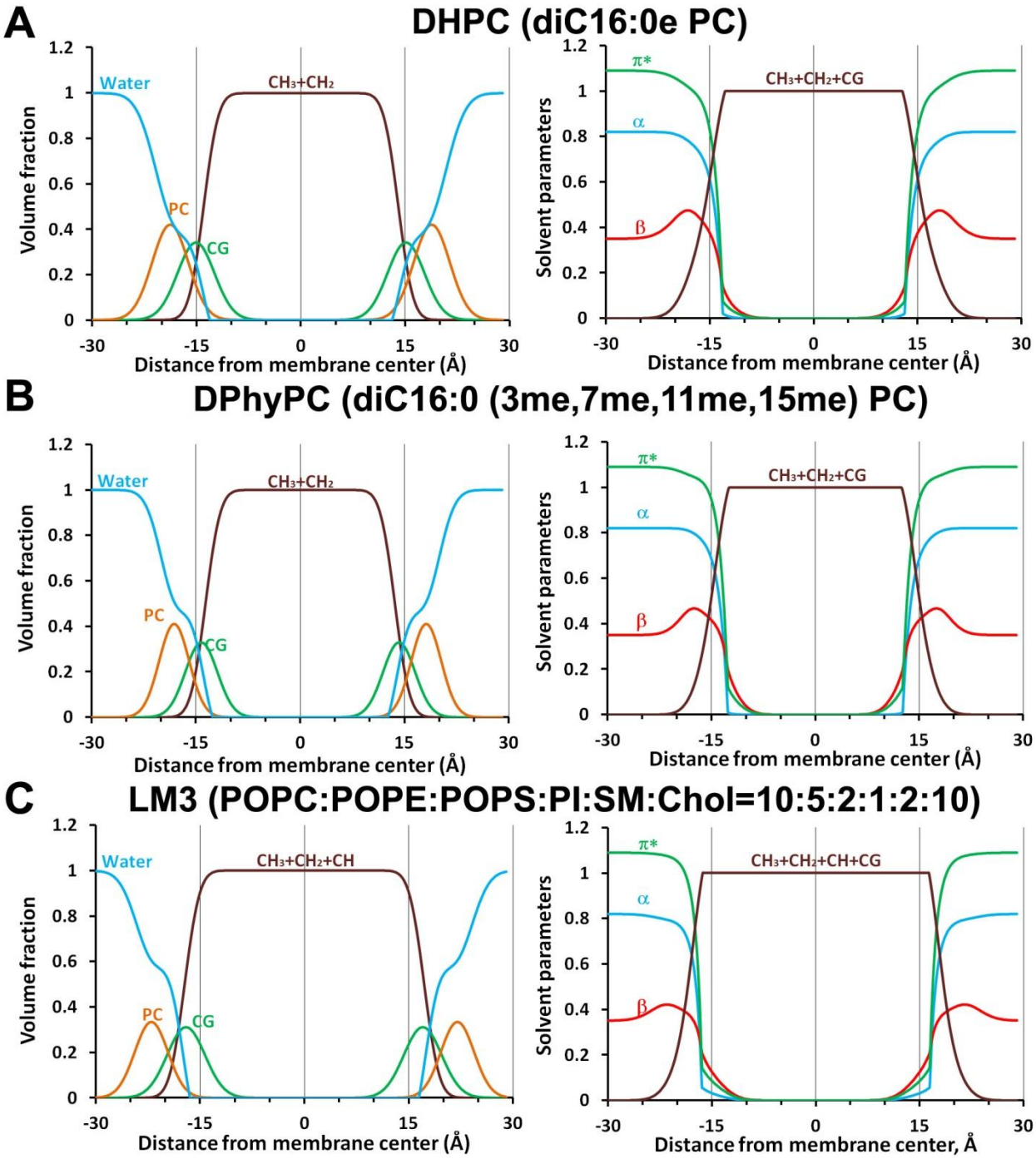

Figure S2. Structures of DHPC (**A**), DPhyPC (**B**) bilayers with ether linkages between head groups and acyl chains, and of an eularyotic PM mimic, LM_3 bilayer composed of POPC, POPE, POPS, PI, SM, and cholesterol at molar ratio 10:5:2:1:2:10 (**C**). Distributions of lipid segments determined from X-ray scattering data (left panels). Changes of polarity parameters (α, β, and π^*) along the membrane normal (right panels). Parameters used for calculation of these profiles and references are provided in Tables 2, S3 and S4.

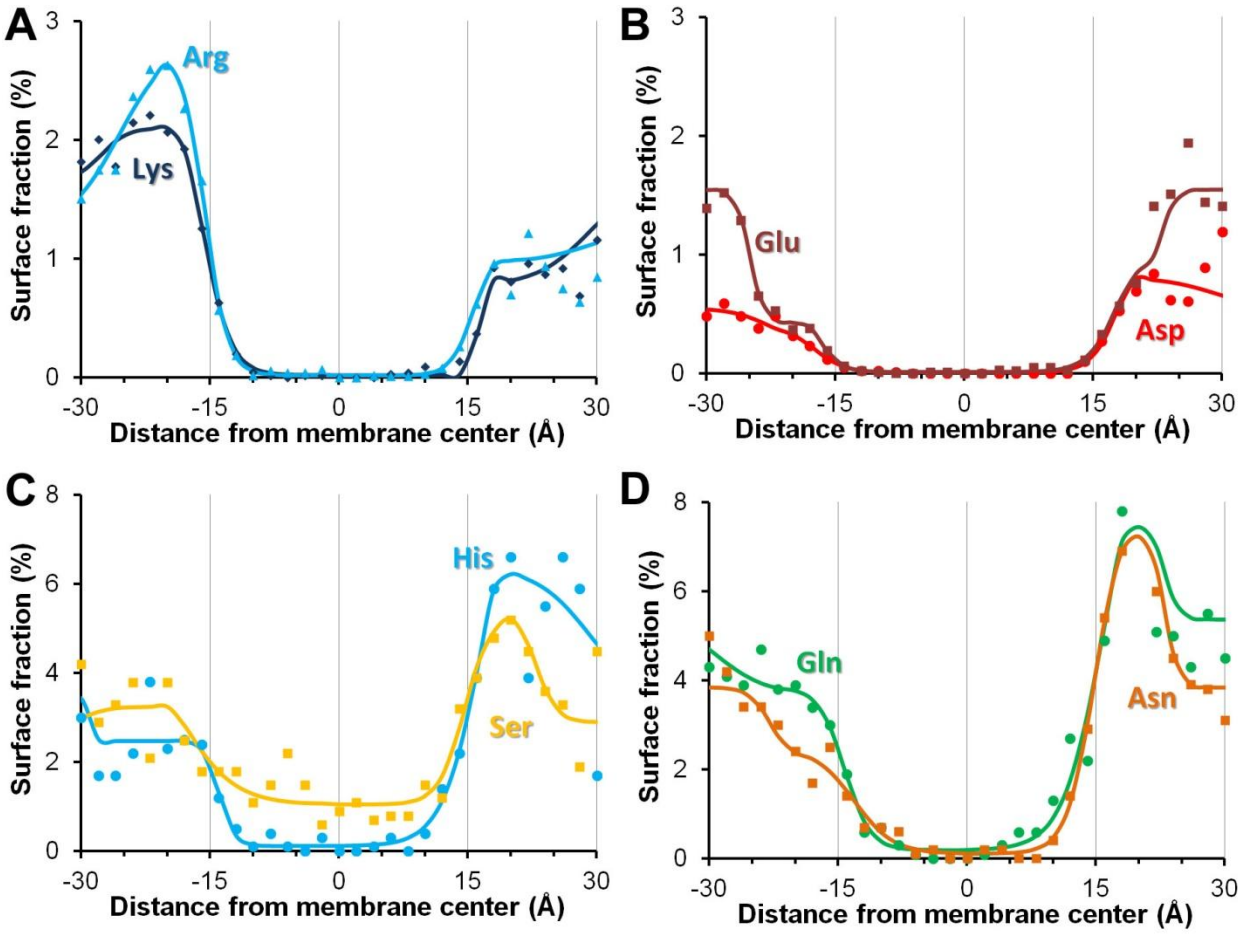

Figure S3. Distributions of lipid-facing polar and charged atoms in structures of 77 TM α-helical protein from six membrane types (PMs of archaebacteria, Gram-positive and Gram-negative bacteria, eukaryotic PM and ER, MIM). Distribution across the membrane were analyzed for polar atoms (N, O) of Arg and Lys (A), Asp and Glu (B), His and Ser (C), and Gln and Asn (D) residues.

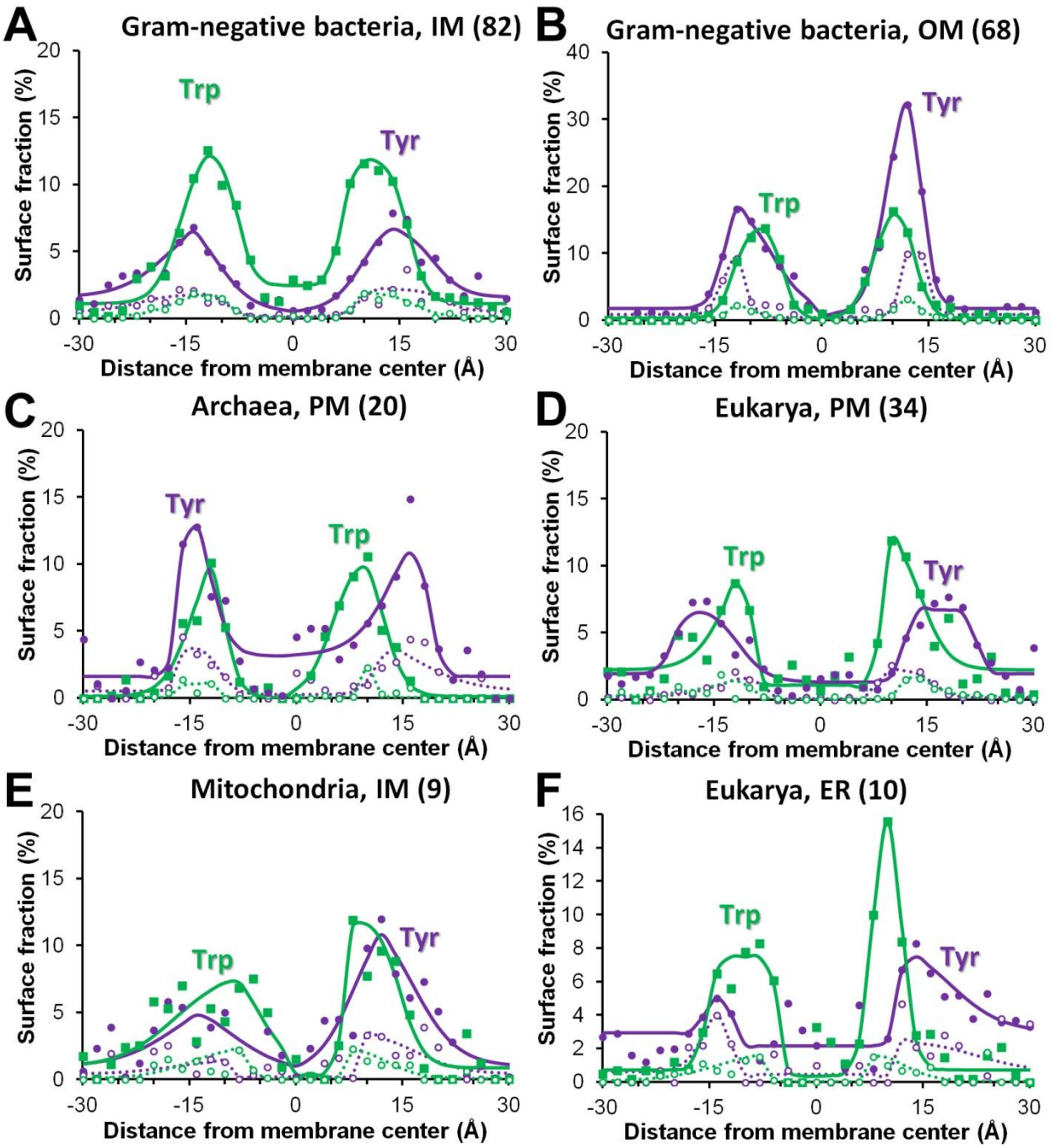

Figure S4. Transbylayer distributions of lipid-facing atoms of Trp (green) and Tyr (purple) residues in structures of TM α-helical protein from six membrane types: IM (A) and OM (B) of Gram-negative bacteria, archaebacterial PM (C), eukaryotic PM (D), MIM (E), and eukaryotic ER (F). Distributions of aromatic atoms (C-atoms of indole ring of Trp and benzene ring of Tyr) are shown by solid lines, closed circles and squares; distributions of polar groups ($N^{\varepsilon}H$ of Trp and $O^{\eta}H$ of Tyr) are shown by dashed lines and open circles. The numbers of proteins for each membrane type are shown in paranthesis.

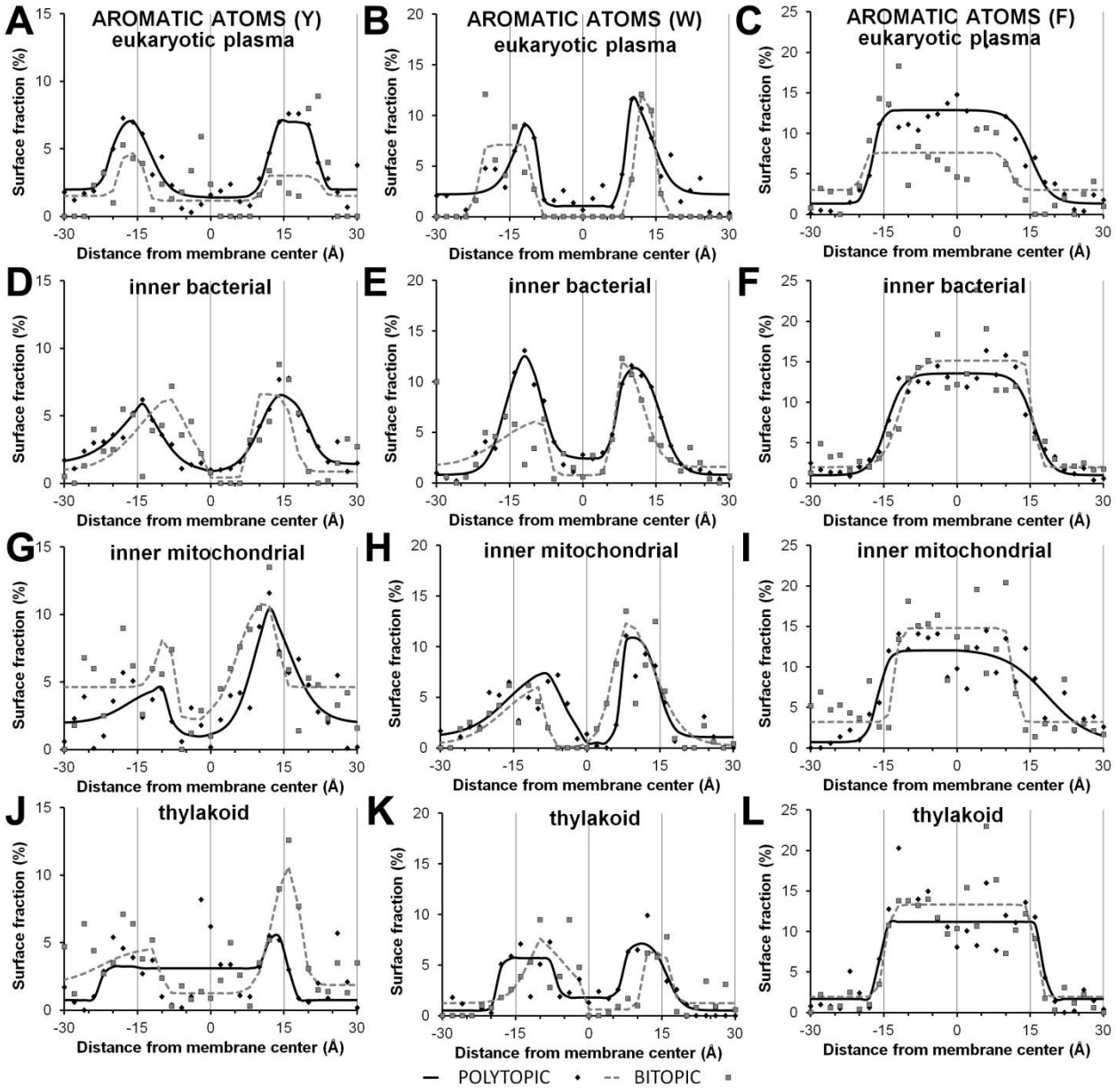

Figure S5. (**A-I**) Comparison of distributions of lipid-facing aromatic atoms of Tyr (**A, D, G, J**) Trp (**B, E, H, K**), and Phe (**C, F, I, L**) in structures of polytopic (black solid line and black diamonds) and bitopic (grey dashed line and grey squares) TM α-helical protein from four membrane types. The numbers of structures for polytopic and bitopic proteins for different membranes were the following: eukaryotic PM (34 and 21, respectively, **A-C**), IM of Gram-negative bacteria (82 and 19, respectively, **D-F**), IM of mitochondria (9 and 24, respectively, **G-I**), and thylakoid membranes (8 and 39, respectively, **J-L**). Aromatic atoms are C-atoms from rings of Tyr, Phe, Trp residues.

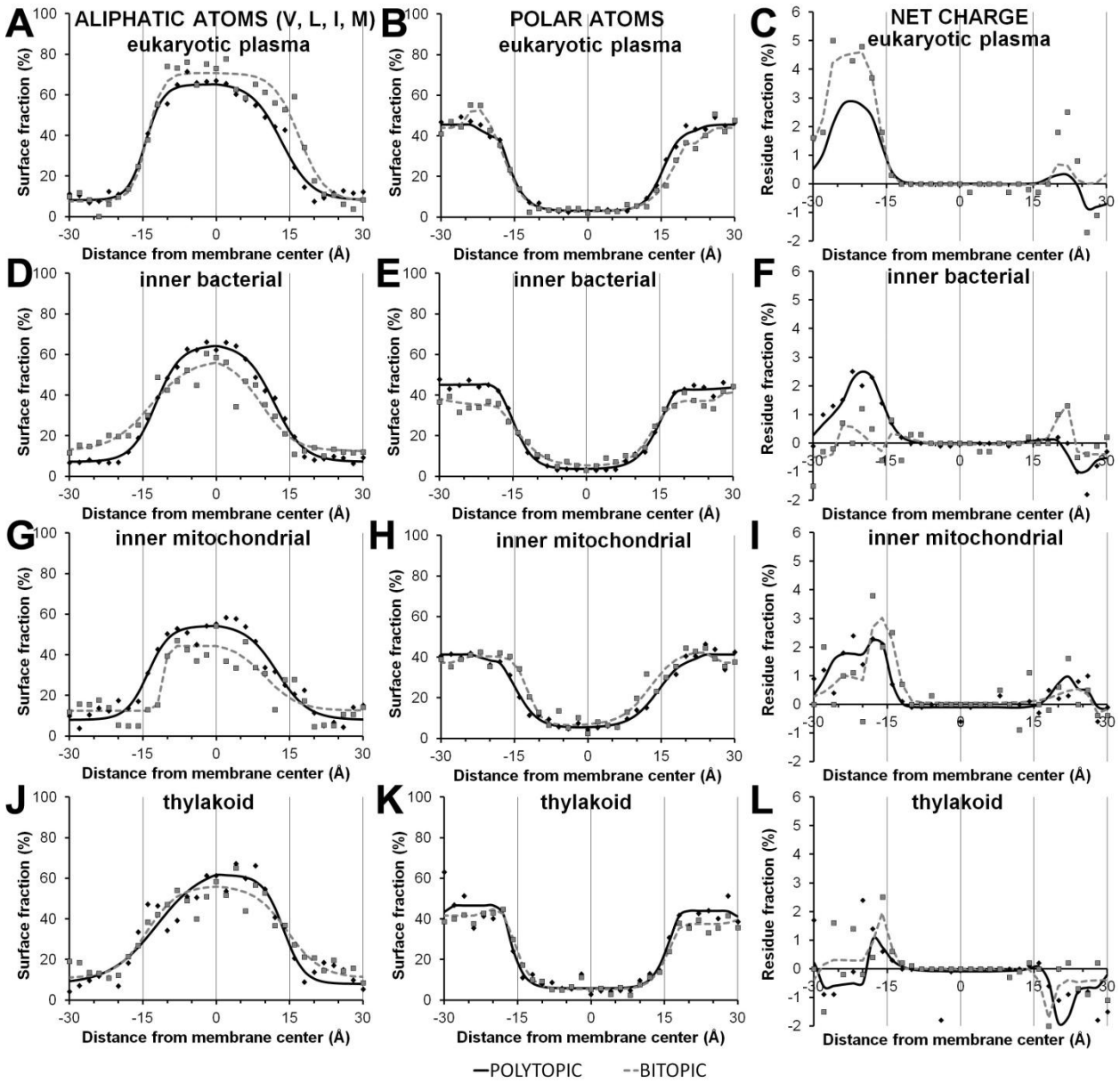

Figure S6. (**A-I**) Comparison of distributions of lipid-facing aliphatic atoms (**A, D, G, J**) polar atoms (**B, E, H, K**), and net charge (**C, F, I, L**) in structures of polytopic (black solid line and black diamonds) and bitopic (grey dashed line and grey squares) TM α-helical protein from four membrane types. The numbers of structures for polytopic and bitopic proteins for different membranes were the following: eukaryotic PM (34 and 21, respectively, **A-C**), IM of Gram-negative bacteria (82 and 19, respectively, **D-F**), IM of mitochondria (9 and 24, respectively, **G-I**), and thylakoid membranes (8 and 39, respectively, **J-L**). Distribution across the membrane were analyzed for aliphatic atoms (C from side chains of Val, Leu, Ile, Met), polar atoms (N, O), and net charge as difference between positively (amine group of Lys, guanidinium group of Arg) and negatively (carboxyl group of Asp and Glu) charged groups.

Table S1. TM proteins from different membrane types used for the analysis.

Membrane type	Number of Structures	Protein type	PDB codes (number of subunits)
Eukaryotic PM	34	Polytopic α-helical	1J4N(4), 2B6O(4), 2D57(4), 3C02(4), 2ZZ9(4), 3D9S(4), 2QTS (3), 2R9R(4), 3SPG(4), 3UKM(2), 3UM7(2), 2ZXE(2), 3KDP(2), 2X72(2), 2Z73(2), 4EIY(1), 2Y02(1), 3SN6(1), 3OE6(1), 3PBL(1), 3RZE(1), 4DAJ(1), 4EA3(1), 4EJ4(1), 4DKL(2), 4DJH(2), 3V2Y(1), 3KG2(4), 2ZW3 (6), 3HD6(3), 4EZC(3), 3RHW(5), 2BG9(5), 3G5U(1)
Eukaryotic PM	16	Bitopic α-helical	3HD7 (2), 1IIJ(1), 2JWA(2), 2K1K(2), 2K9Y(2), 2L2T(2), 2L6W(2), 2L9U(2), 2K1A(1), 2L8S(1), 2K9J(2), 2HAC(2), 2KLU(1), 1AFO(2), 2L34(2) 2LOH(2)
Eykaryotic ER	10	α-helical	2UUH(3), 2H8A(3), 2Q7R(3), 3DWW (3), 3DWW (1), 3TLM(1), ZBD(1), 1P49 (1), 1JDM(1), 2LAT(1)
Archaebacterial PM	20	α-helical	2ZZL(3), 1H2S(4), 1E12(3), 3A7K(3), 2EI4(3), 2B2F (3), 2NWL(3), 3GIA(1), 2ONK(2), 3D31(2), 3V5U(1), 2F2B(4), 3NE2(4), 3LDC (4), 1ORS(1), 1RH5(3), 3MP7(2), 3S0X(1), 3B4R(1), 4A2N(1)
PM of Gram-positive bacteria	12	α-helical	2HYD(2), 3VMR(1), 3P5N(1), 3RLB(1), 2AHY(4), 3QNQ(2), 3AYF(1), 3TDP(5), 1R3J(4), 2OAR(5), 2JLN(1), 4DOJ(3)
IM of Gram-negative bacteria	82	α-helical	2L6X(1), 1XIO(1), 3DDL(1), 3RKO(6), 1KQF(6), 1Q16(2), 1KF6(2), 2BS2(2), 1NEK(6), 2VPZ(2), 2QJY(6), 1M56(4), 3S8G(3), 2YEV(3), 3MK7(3), 1FFT(3), 3O0R(2), 2J7A(2), 1EYS(3), 2J8C(3), 3T6E(3), 1IJD(18), 1LGH(16), 1NKZ(18), 1XRD(1), 2WLH(4), 2WLL(4), 3BEH(4), 2QKS(4), 3RVY(4), 3PJZ(2), 1L7V(2), 2NQ2(2), 3TUI(2), 3PUW(2), 3QF4(2), 3B60(2), 2GFP(1), 1PW4(1), 2CFQ(1), 3O7Q(1), 2XUT(1), 1ZCD(1), 3NE5(3), 2GIF(3), 2V50(3), 3AQP(1), 1LDF(4), 1RC2(4), 3KCU(4), 3LLQ(4), 3KLY(5), 1U7G(3), 3B9W(3), 3K3F(3), 2BBJ(5), 2YVX(2), 1OTS(2), 1KPL(2), 3ND0(2), 3RQW(5), 3EAM(5), 3H90(2), 2A65(2), 3HQK(2), 3DH4(2), 4DJI(1), 3HFX(3), 2ZJS(2), 3M73(3), 3ZUY(1), 3MKT(1), 3TX3(1), 3TIJ(3), 3RCE(1), 2XTV(1), 1YEW(9), 3CHX(15), 3RFR(10), 3KP9(1), 2BL2(10), 1YCE(11)
OM of Gram-negative bacteria	68	β-barrel (β-I)	1QJP(1), 2K0L(1), 3QRC(1), 1QJ8(1), 1P4T(1), 2F1V(1), 2X27(1), 2QOM(1), 1UYN(1), 3KVN(1), 3QQ2(1), 3AEH(1), 4E1S(1), 4E1T(1), 3GP6(1), 2ERV(1), 3FID(1), 1I78(1), 2X55(1), 1K24(1), 1TLY(1), 2FGQ(3), 2J1N(3), 3POX(3), 1OSM(3), 1PHO(3), 3A2S(3), 3NSG(3), 2O4V(3), 2POR(3), 3PRN(3), 1A0S(3), 1AF6(3), 2MPR(3), 2GSK(1), 1FEP(1), 1KMP(1), 1QFG(1), 1XKW(1), 2IAH(1), 2HDI(1), 3CSL(1), 3EFM(1), 3FHH(1), 3QLB(1), 3V8X(1), 1QD6(2), 1T16(1), 3BRY(1), 3DWO(1), 3BS0(1), 2IWV(1), 2QDZ(1), 2ODJ(1), 3JTY(1), 2Y0L(1), 3SYB(1), 2Y0H(1), 3SZD(1), 3T24(1), 2QTK(1), 2Y0K(1), 3SY9(1), 3RBH(1), 2WJR(1), 2VQI(1), 3RFZ(1), 3DZM(1)
OM of Gram-negative bacteria	5	β-barrel (β-II)	1EK9(3), 1YC9(3), 1WP1(3), 3PIK(3), 2GR7(3)
OM of Gram-	2	α-helical	2J58 (8), 3JQO (14)

negative bacteria			
Thylakoid membranes	8	α-helical	1JB0(9), 3LW5(14), 3ARC (32), 1RWT(3), 3PL9(1), 1Q90(16), 2E74(16), 2ZT9(16)
Mitochondrial IM	9	α-helical	1YQ3(2), 1ZOY(2), 3VR8(2), 1L0L(12), 3H1J(10), 3CX5(10), 1V55(20), 1OKC(1), 4AYT(2)
Mitochondrial OM	2	β-barrel	3EMN(1), 2JK4(1)
Mitochondrial OM	3	α-helical	2KA2(2), 2L5B(1), 1O5W(1)

Table S2. Values of polarity parameters (α, β and π^*) for different protein atoms and groups used in calculations.

Atom/Group	Parameter		
	α	β	π^*
C_{sp3}	0	0	0
C_{sp2}	0	0.14	0.59
-NH (peptide group)	0.38	0	0.85
$-NH_2$ (Asn, Gln, Arg)	0.56	0	0.95
$-N^+$ (Lys)	0.87	0	0.95
=O (peptide group)	0	0.72	0.85
-OH (Ser, Thr)	0.37	0.48	0.40
-OH (Tyr)	0.60	0.17	0.72
$=O^-$ (COO^-, Asp, Glu)	0	1.25	0.95
-S- (Met)	0	0.32	0.35
-SH (Cys)	0	0.16	0.35

Table S3. Molecular volumes (V, Å^3), and polarity parameters (α, β, and π^*) for "CG" and "P" lipid segments.

Lipid segment	Parameter	Lipid bilayer		
		DOPC[a]	DHPC	LM_3[b]
"CG"	V	152	148	152
"CG"	α	0	0	0.19
"CG"	β	0.88	0.45	0.76
"CG"	π^*	0.55	0.27	0.52
"P"	V	178	178	143
"P"	α	0.83	0.83	0.59
"P"	β	1.74	1.74	1.36
"P"	π^*	0.73	0.73	1.02

[a] These parameters were used for DOPC, DEPC, POPC, DPPC, DPhyPC, DMPC, and DLPC.

[b] Values for lipid mixture (LM_3) were evaluated based on the lipid composition LM_3.

Table S4. Parameters of POPG bilayer[a]

Parameter	Group			
	$(CH)_2$	CG	PG1	PG2
V_m, Å^3	40	150	46	93
Z_m, Å	7.8	14.4	18.9	21.1
S_m, Å	3.2	2.48	2.45	3.3
α	0	0	0	0.74
β	0.07	0.86	1.74	0.96
π^*	0.34	0.55	0.73	0.62

[a] Experimental data based on 3G SDP model [Kučerka et al., J. Phys. Chem. B 116 (2012) 232-239]. V_m is the molecular volume of the fragment, and Z_m and S_m define the locations and widths of corresponding Gaussians, respectively. "PG1" is PO_4 fragment, "PG2" is -CH_2-CHOH-CH_2-OH fragment. Parameters of Gauss error function for total aliphatics were Z_{HDC} =13.85 Å, S_{HDC} =2.8 Å.