ESI

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Table S1 Ensembles and force constants used during the equilibration steps on head group positions and chain dihedrals.

step	time / ps	ensemble	P atom z pos. (kJ/mol)	chain dih. ang. (kJ/mol)
1	25	NVT	1000	1000
2	25	NVT	1000	400
3	25	NVT	400	200
4	100	NpT	200	200
5	100	NpT	40	100
6	100	NpT	0	0

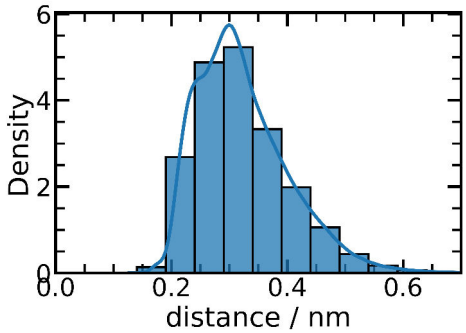

Fig. S1 Distribution of minimum distances between protein residue and lipid molecule atom pairs of the TMD monomer in the asymmetric bilayer system.

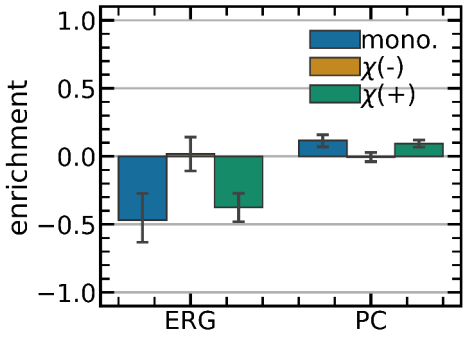

Fig. S2 Enrichment of ERG and PC lipids in the cytosolic leaflet of the different symmetric bilayer setups (monomeric, or dimeric in $\chi(-)$ and $\chi(+)$ configuration) around the TMD. The enrichment is defined as the number of the respective lipid species divided by the total number of neighbors and the total concentration of the species minus 1 such that 0 indicates no enrichment or depletion.

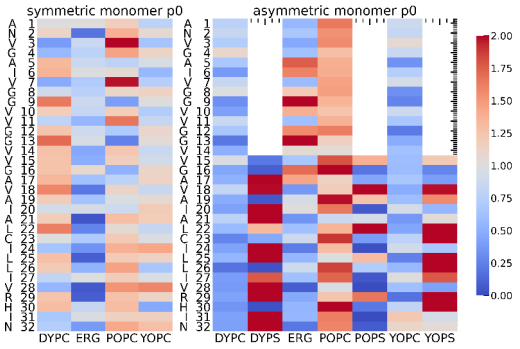

Fig. S3 Enrichment and depletion maps of lipid neighbors around the TMD monomer residues in the symmetric (left) and asymmetric (right) bilayer. The number of lipid type neighbors is normalized with respect to the total number of neighbors and the respective fraction of the lipid type within the leaflet, such that values above unity indicate enrichment and values below unity indicate depletion of the lipid type. Red indicates values of 2 or higher.

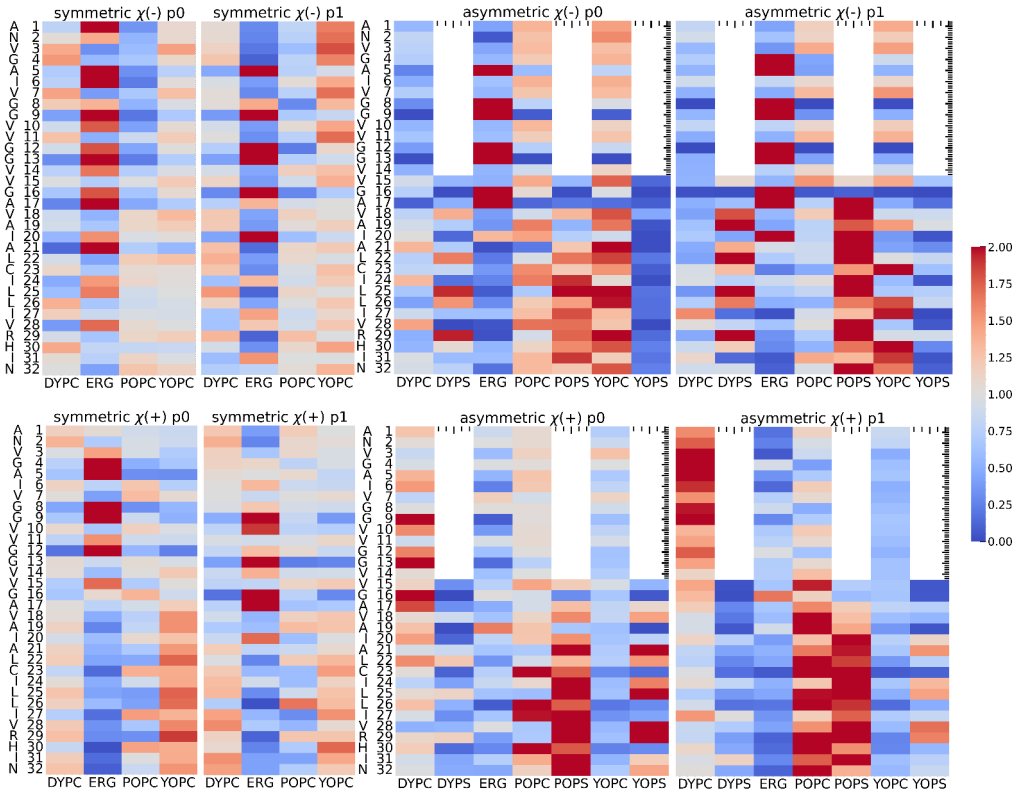

Fig. S4 Enrichment and depletion maps of lipid neighbors around each TMD (p0 and p1) in the dimer configurations with negative crossing angle, $\chi(-)$ (top), and positive crossing angle, $\chi(+)$ (bottom), in the symmetric (left) and asymmetric (right) bilayers. The number of lipid type neighbors is normalized with respect to the total number of neighbors and the respective fraction of the lipid type within the leaflet, such that values above unity indicate enrichment and values below unity indicate depletion of the lipid type. Red indicates values of 2 or higher.

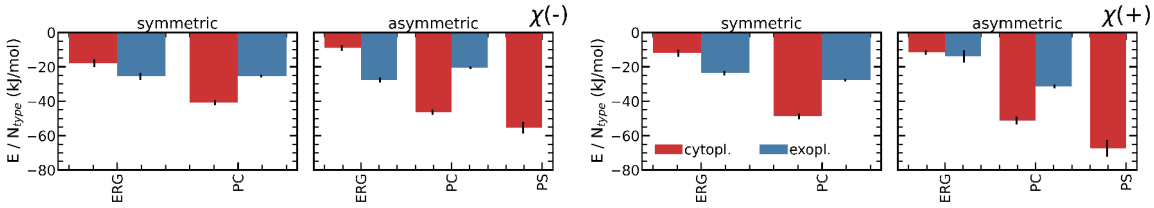

Fig. S5 Pair interactions between the cytoplasmic (red) and exoplasmic (blue) side of the TMDs and its lipid neighbors. The data was averaged for time frames of 1 µs and the bars indicate the corresponding unbiased standard error.

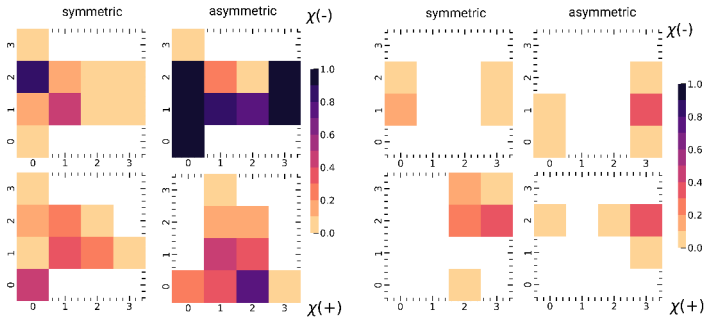

Fig. S6 The TMD-TMD contact map of the extracellular (left) and cytosolic (right) TMD faces. Indexes 0 and 1 indicate the TMD face including motifs a) and b) and indexes 2 and 3 indicate the other TMD faces. The color code represents the fraction of contacts (distances of less than 7Å) formed per simulation such that a value of 1 represents a contact that was maintained throughout the whole simulation. The distance cutoff was chosen such that at least one contact pair in all bilayer systems exhibits a contact fraction of 0.9.

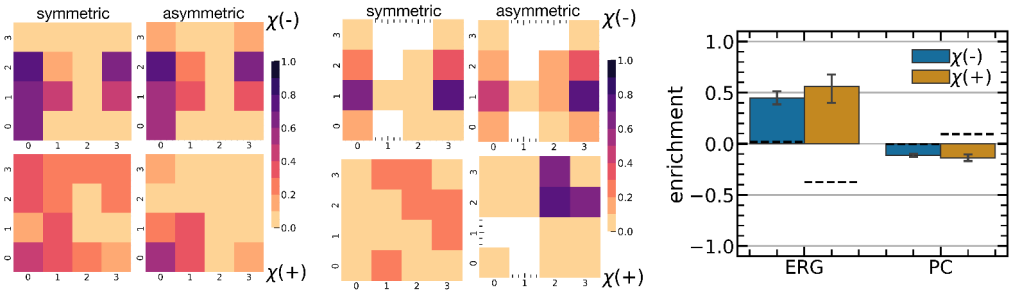

Fig. S7 The evaluated data from the atomistic simulations (dashed lines) compared to the corresponding data from coarse-grained (Martini) simulations, namely, enrichment of lipids in the cytosolic leaflet of the symmetric bilayer (left), and the protein contact map of the cytosolic TMD side (right).

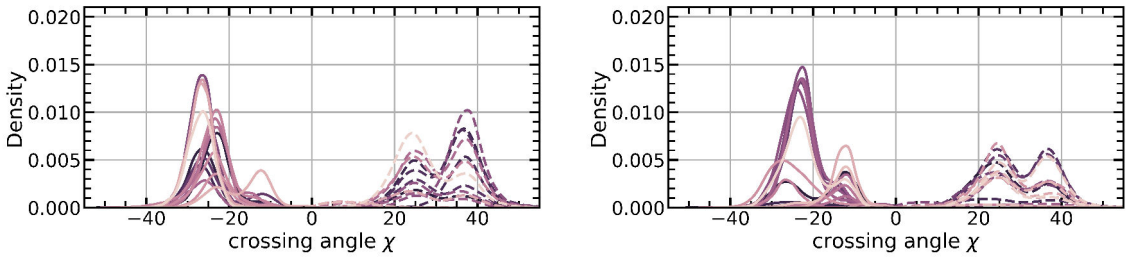

Fig. S8 Crossing angle distributions of the TMD dimers with positive (dashed) and negative (solid) crossing angle in the bilayers with an asymmetric (left) and a symmetric (right) bilayer composition of the 25 independent simulations distinguished by shades of purple.

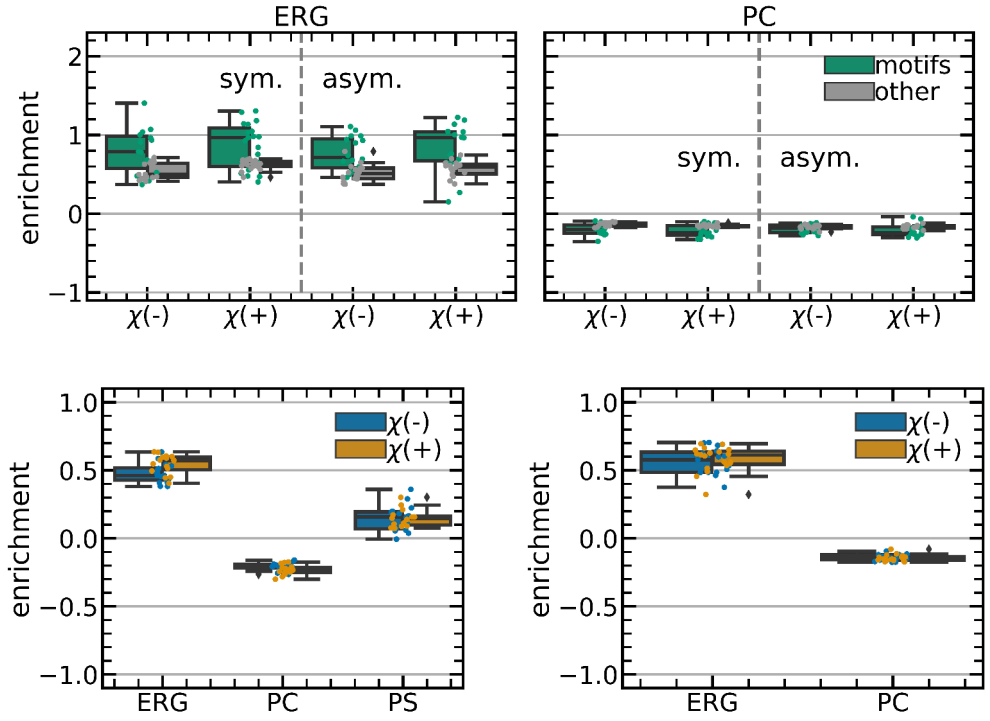

Fig. S9 Variation of the mean values of enrichment between the independent CG samples in standard box plot representation. Only those samples were considered that had at least 5 time blocks (1.5 μs of total sampling time). The top figures shows enrichment data of ERG and PC (left to right) in the extracellular leaflet and the bottom figures show enrichment data of ERG, PC, and PS lipids in the cytosolic leaflet for the symmetric and asymmetric bilayers (left to right).