Supporting Materials

Effects of Flanking Loops on Membrane Insertion of Transmembrane Helices: A Role for Peptide Conformational Equilibrium

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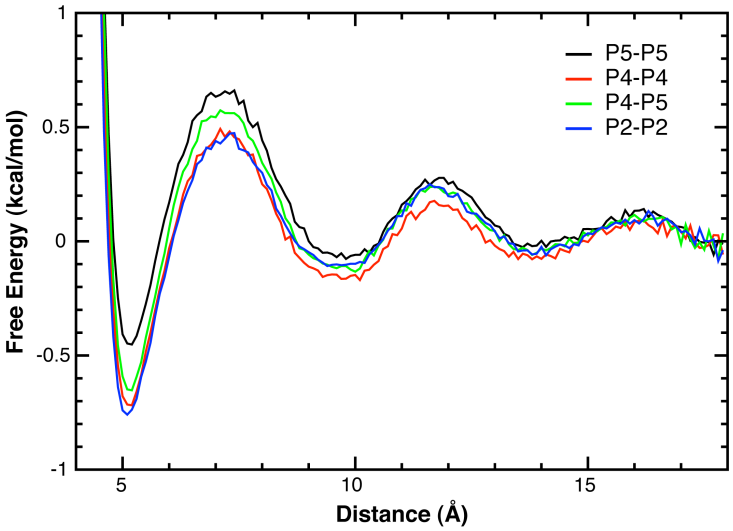

FIGURE S1. PMFs of pair-wise interactions between various MARTININ polar particle types in water. Note that the MARTINI water is represented by particle type P4.

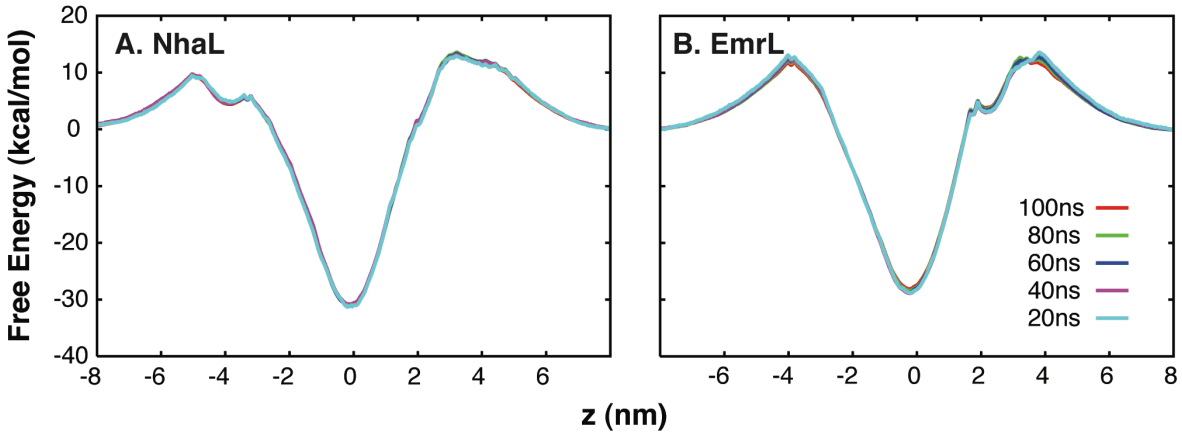

FIGURE S2. PMFs of membrane insertion of A) NhaL and B) EmrL calculated using the last 20, 40, 60, 80 and 100 ns of the umbrella sampling trajectories.

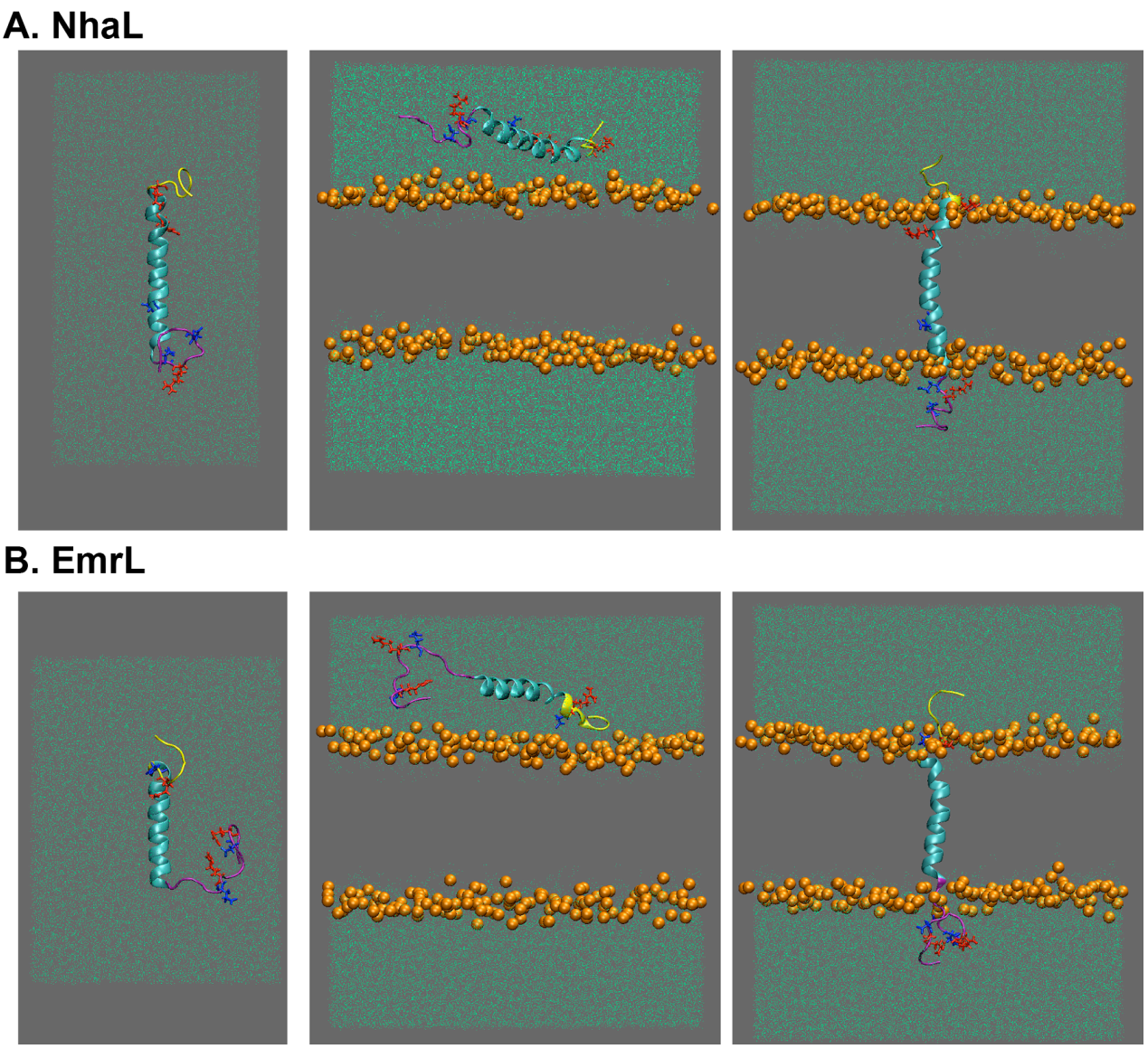

FIGURE S3. Snapshots of the initial conformations of A) NhaL and B) EmrL under the aqueous (water), interfacial (IF) and transmembrane (TM) conditions (from left to right). See the caption of Fig. 8 for additional description the molecular representations.

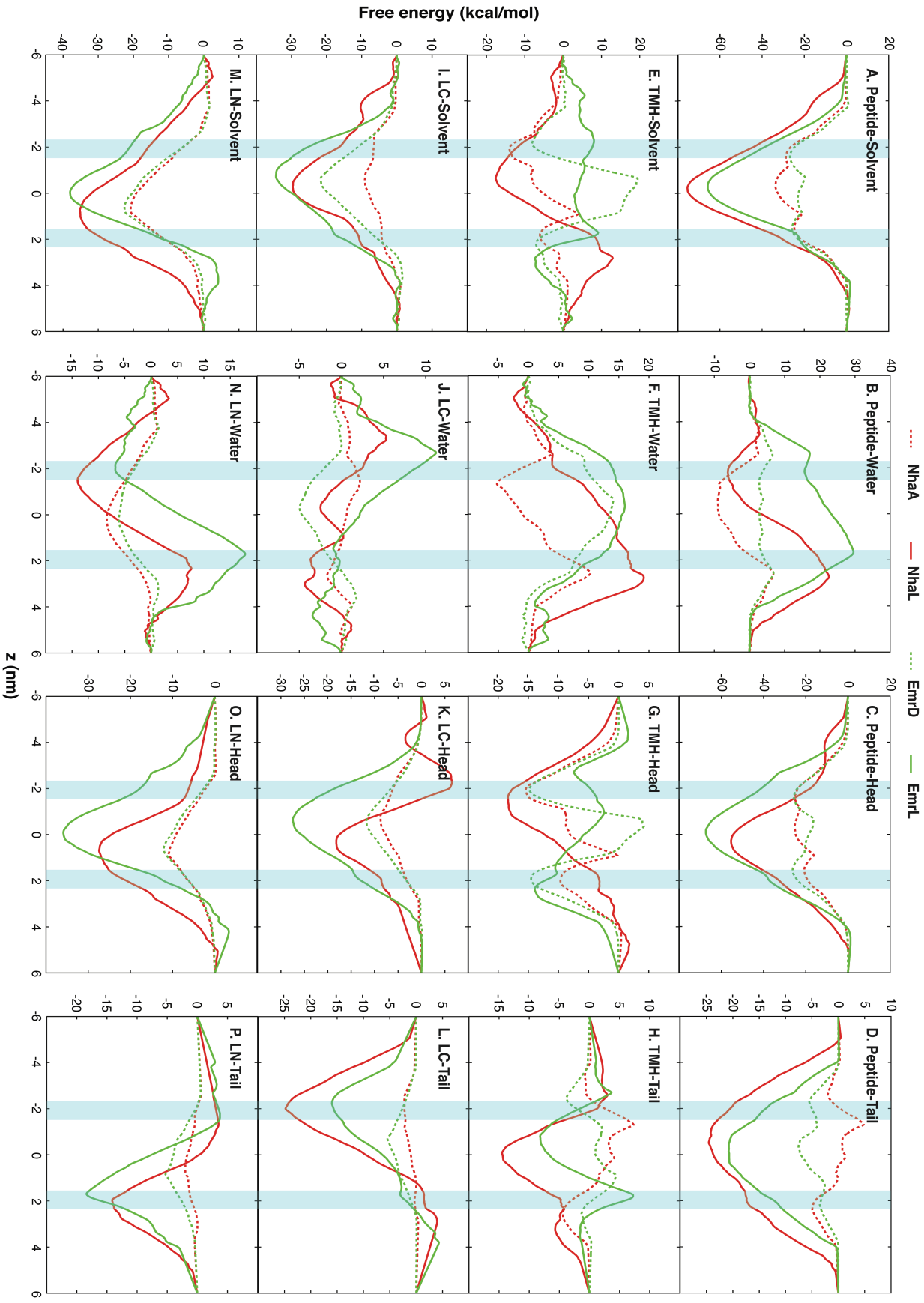
Free energy (kcal/mol)
NhaA
NhaL
EmrD
EmrL
A. Peptide-Solvent
B. Peptide-Water
C. Peptide-Head
D. Peptide-Tail
E. TMH-Solvent
F. TMH-Water
G. TMH-Head
H. TMH-Tail
I. LC-Solvent
J. LC-Water
K. LC-Head
L. LC-Tail
M. LN-Solvent
N. LN-Water
O. LN-Head
P. LN-Tail
z (nm)

FIGURE S4. Free energy contributions arising from the interactions of the TMH segment (TMH), C-terminal loop (LC) and N-terminal loop (LN) with water molecules (Wat) and DPPC head (Head) and tail groups (Tail). The head group includes choline, phosphate and glycerol groups, and the rest of the DPPC molecule is defined as the tail. "Solvent" include all water and lipid molecules (Wat + Head + Tail), and "Peptide" include the whole peptide (TMH + LC + LN). The results were derived from force decomposition analysis using the last 40 ns of the umbrella sampling trajectories. The cyan stripes indicate the approximate locations of the membrane/water interface. Note that the overall contributions to the total free energy from peptide-solvent interactions do not include the (compensating) contributions from perturbations to the intra-peptide and solvent-solvent interactions.

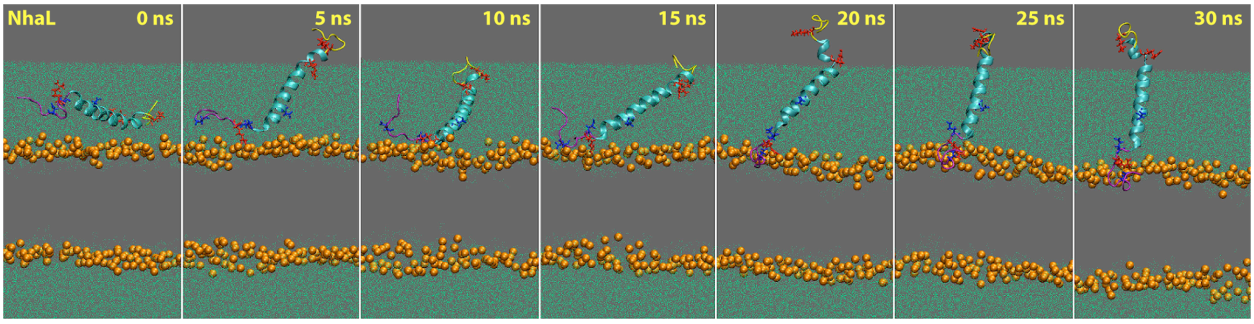

FIGURE S5. Snapshots taken every 5 ns during the 30-ns atomistic simulation of peptide NhaL initiated from an interfacial-like state. Note that the simulation boxes are not shown in full to allow better view of the peptide and adjacent lipid head groups. See the caption of Fig. 8 for additional description the molecular representations.

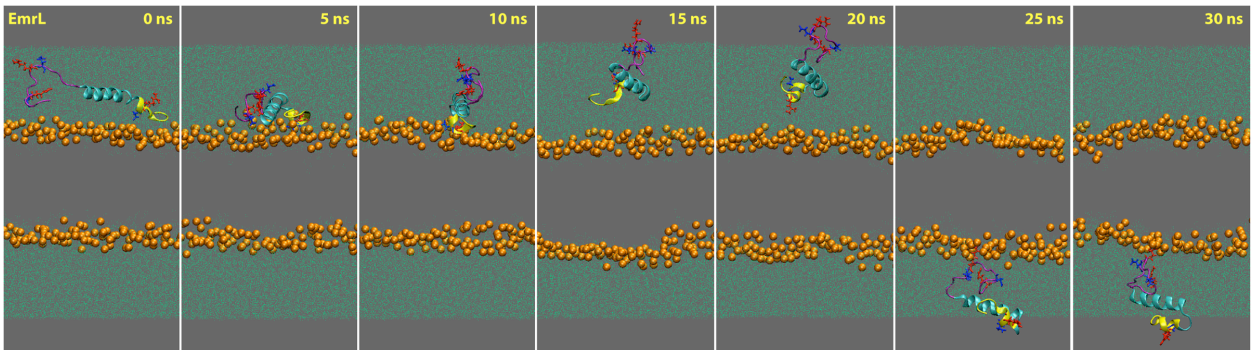

FIGURE S6. Snapshots taken every 5 ns during the 30-ns atomistic simulation of peptide EmrL initiated from an interfacial-like state. Note that the simulation boxes are not shown in full to allow better view of the peptide and adjacent lipid head groups. During the simulation, the peptide first dissociated from the membrane (between 10-15 ns) before diffusing to the other side of the bilayer (due to periodic boundary) and re-absorbing See the caption of Fig. 8 for additional description the molecular representations.