

# Supplementary Information

## **Polyproline Modulates Membrane Translocation of Arginine-Rich Cell-Penetrating Peptides: Insights from Molecular Dynamics Simulations**

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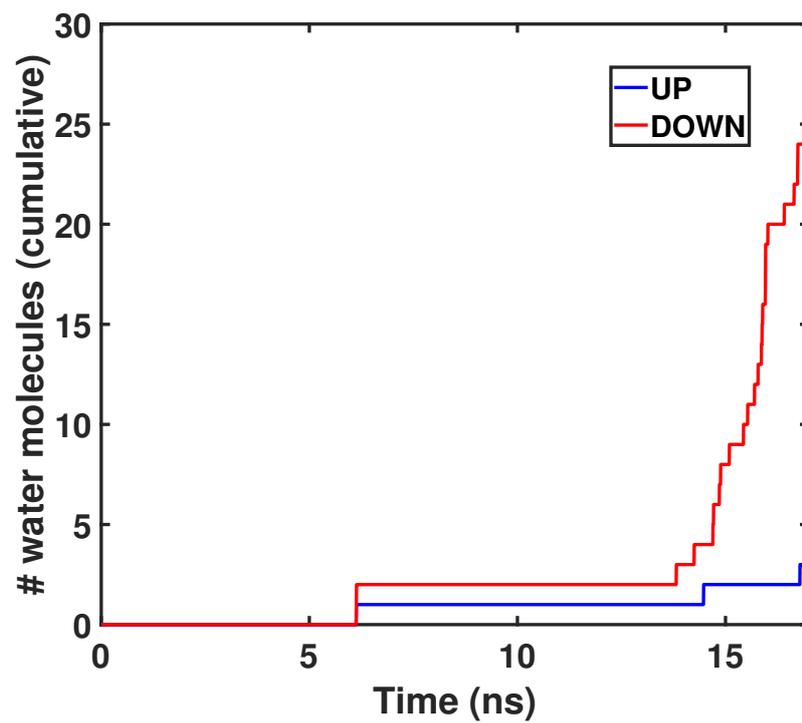
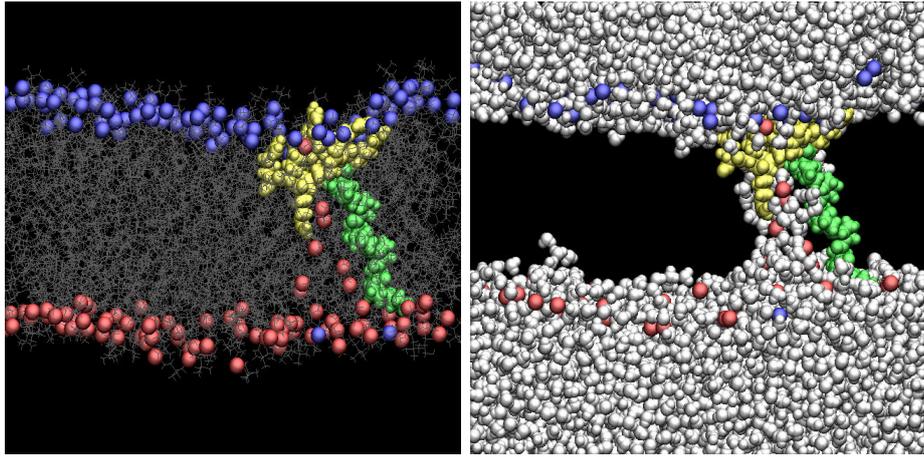
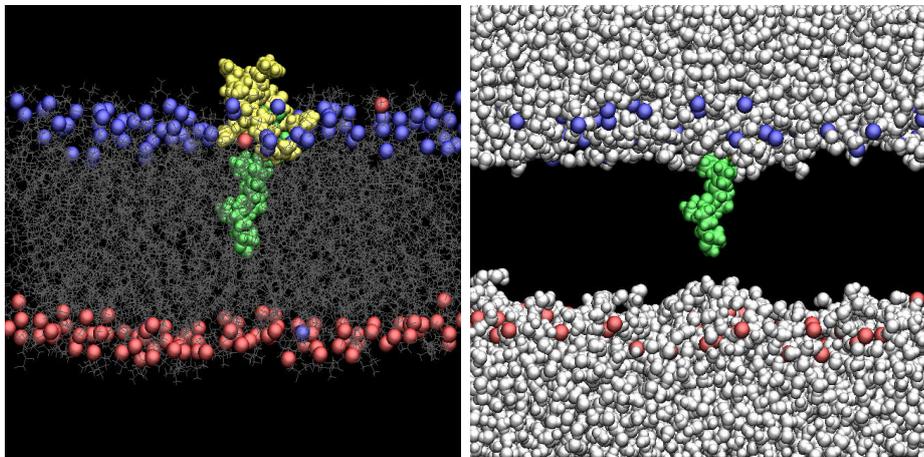


FIG. S1: Cumulative number of water molecules transported across the membrane in both directions during the WE MD simulation.



(a) 500 ns



(b) 1000 ns

FIG. S2: Representative snapshots of S4 during the additional MD simulation. Arginine residues are shown in yellow, proline residues in green, phosphorus atoms in the upper and lower leaflets in blue and red, respectively, lipids in gray, and water in white.

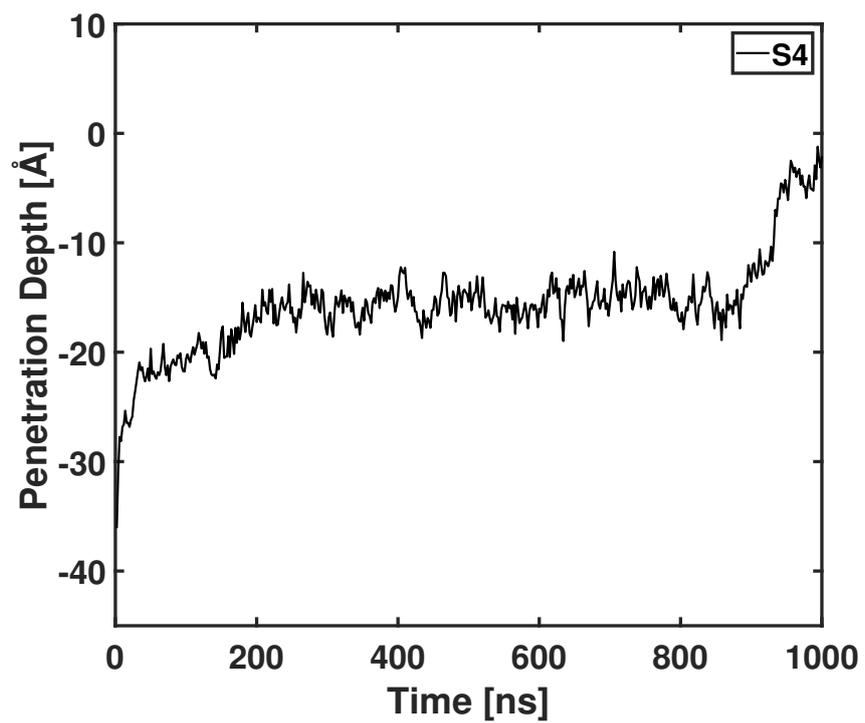


FIG. S3: Time evolution of the penetration depth of S4 during the additional MD simulation.

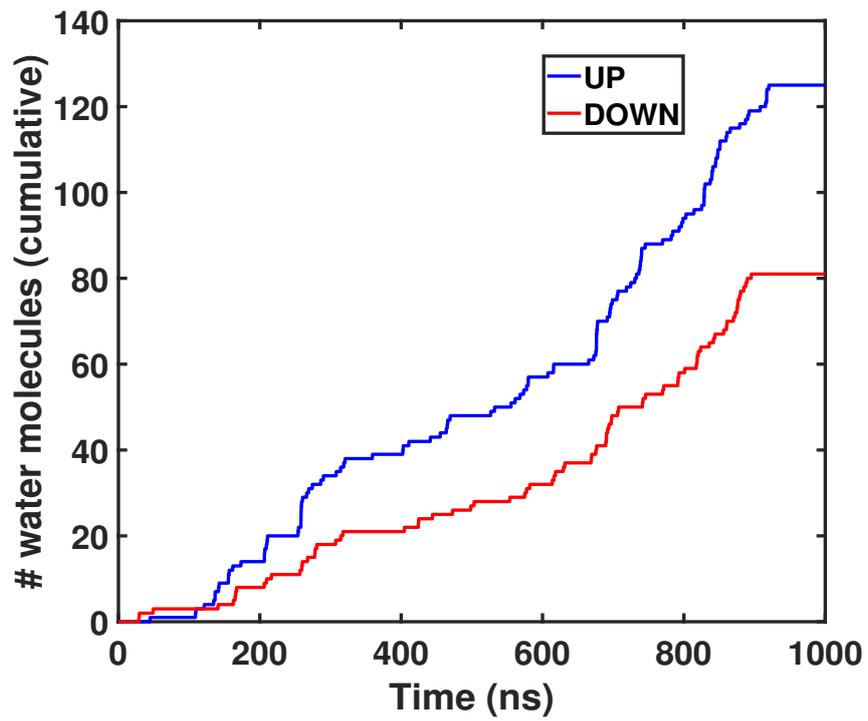


FIG. S4: Cumulative water transport during the additional MD simulation.

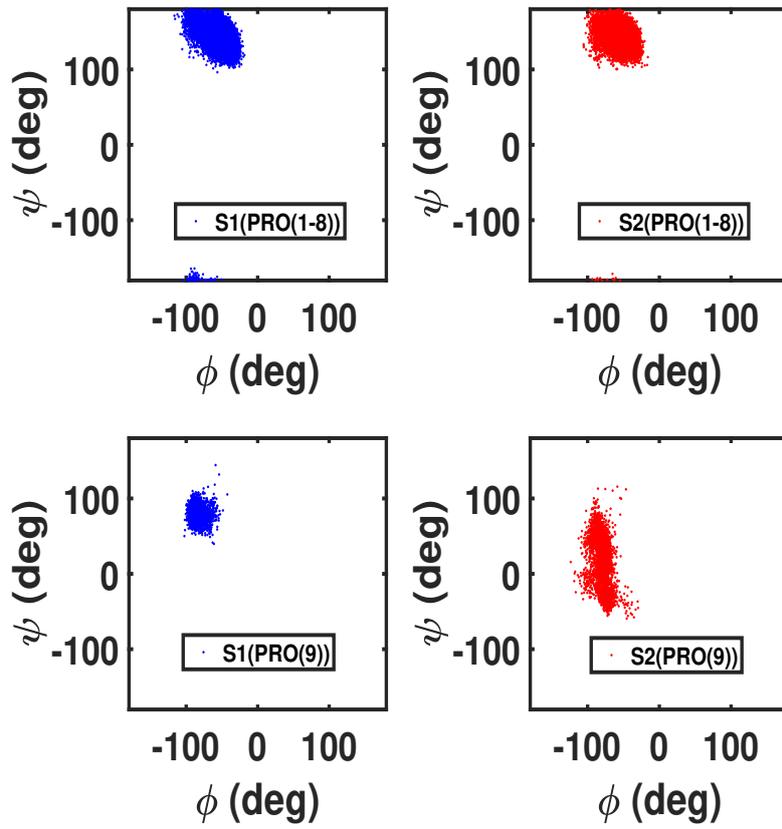
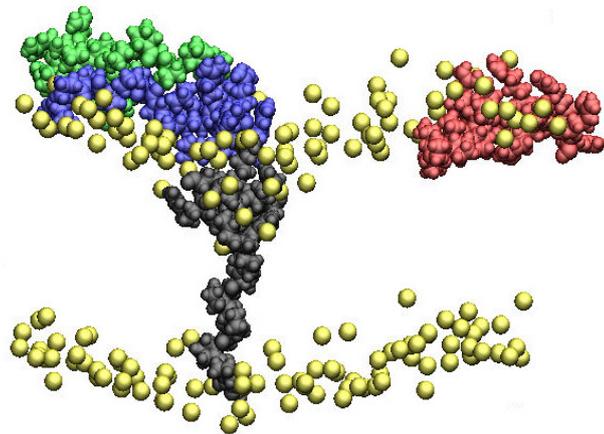
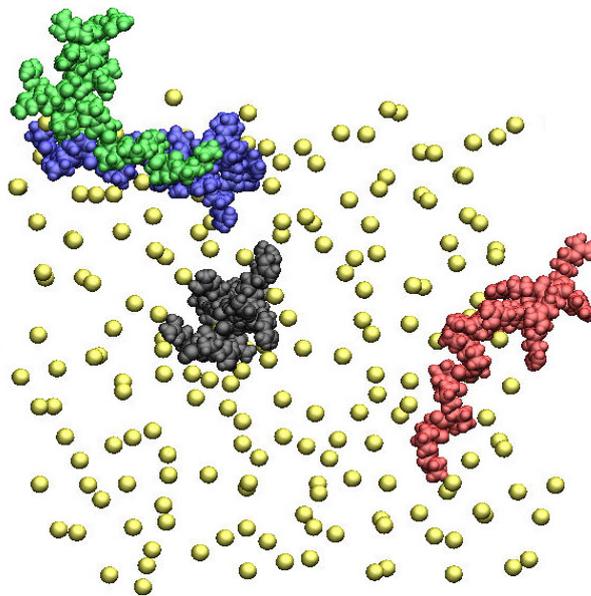


FIG. S5: Ramachandran plots of Pro residues 1–8 and Pro9 during translocation. S1 and S2 denote the two P9R9 peptides in the system.



(a) side view



(b) top view

FIG. S6: Formation of the S1–S3 dimer during translocation. S1 is shown in blue, S2 in red, S3 in green, S4 in black, and phosphorus atoms in the bilayer in yellow.

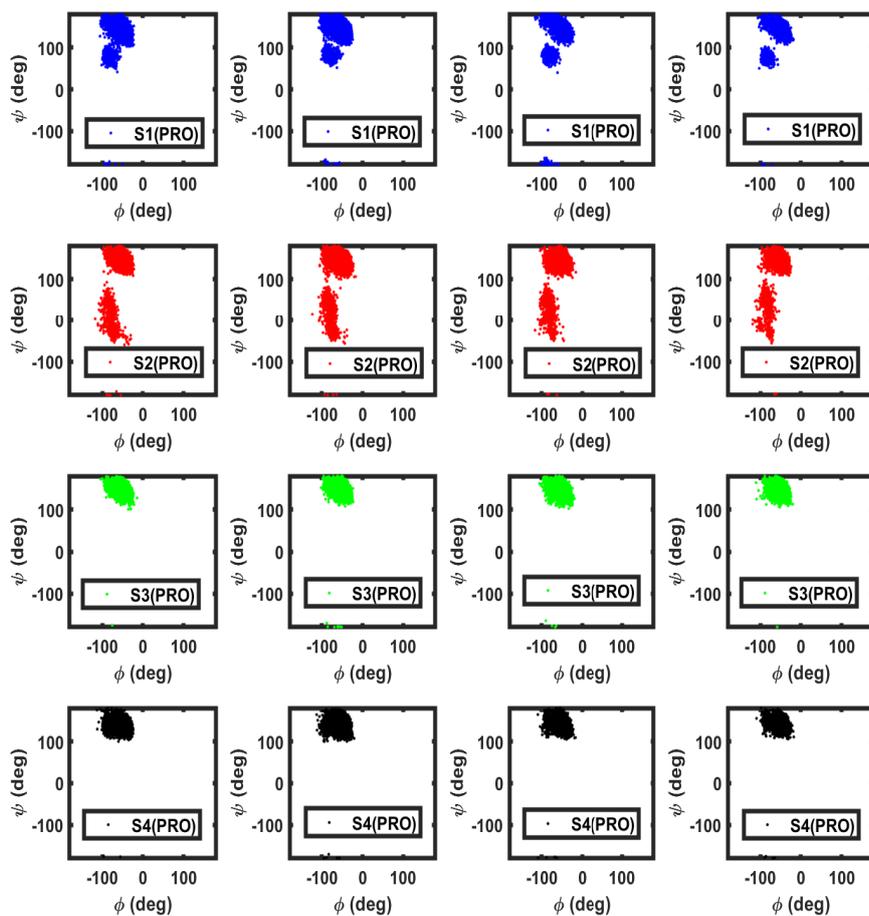
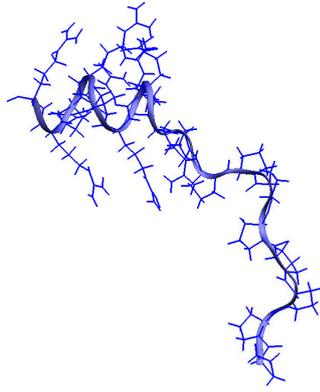
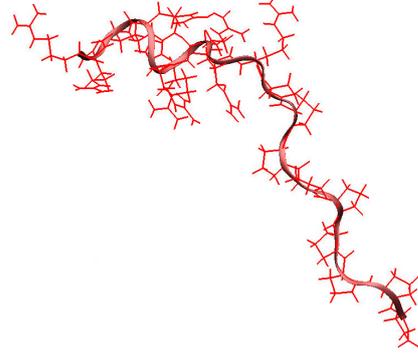


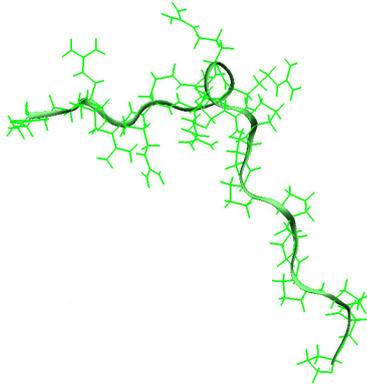
FIG. S7: Ramachandran plots of the polyproline (P9) segment during translocation. S1–S4 denote the four P9R9 peptides in the system.



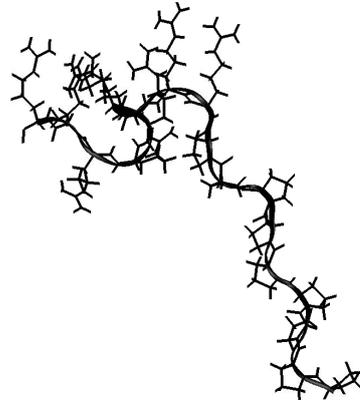
(a) S1



(b) S2



(c) S3



(d) S4

FIG. S8: Final conformations of the peptides at the end of translocation. S1–S4 denote the four P9R9 peptides in the system.

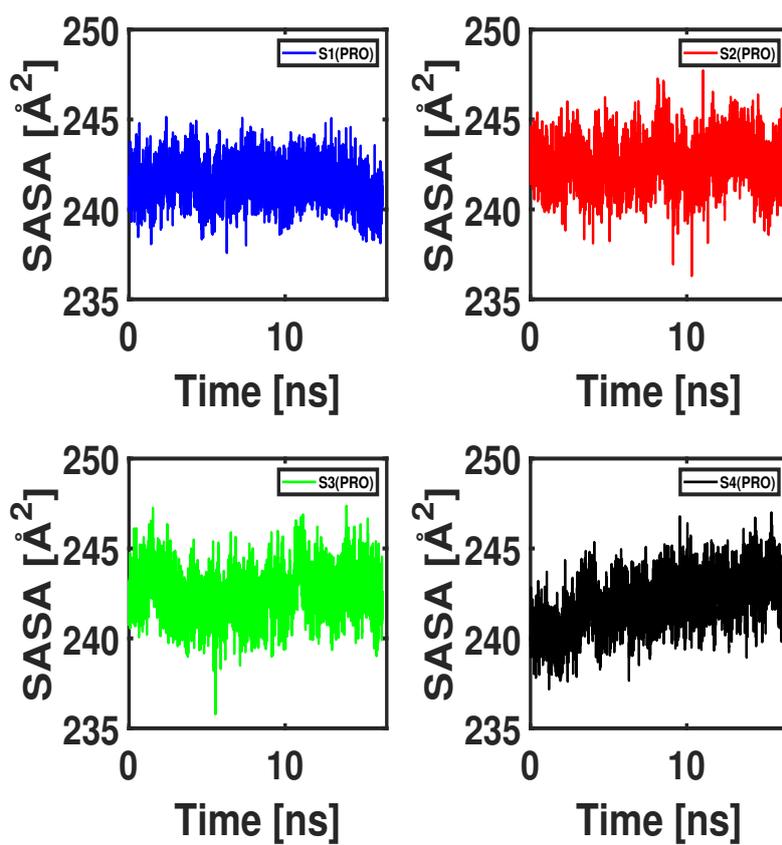


FIG. S9: Solvent-accessible surface area (SASA) of the polyproline (P9) segment during translocation. S1–S4 denote the four P9R9 peptides in the system.

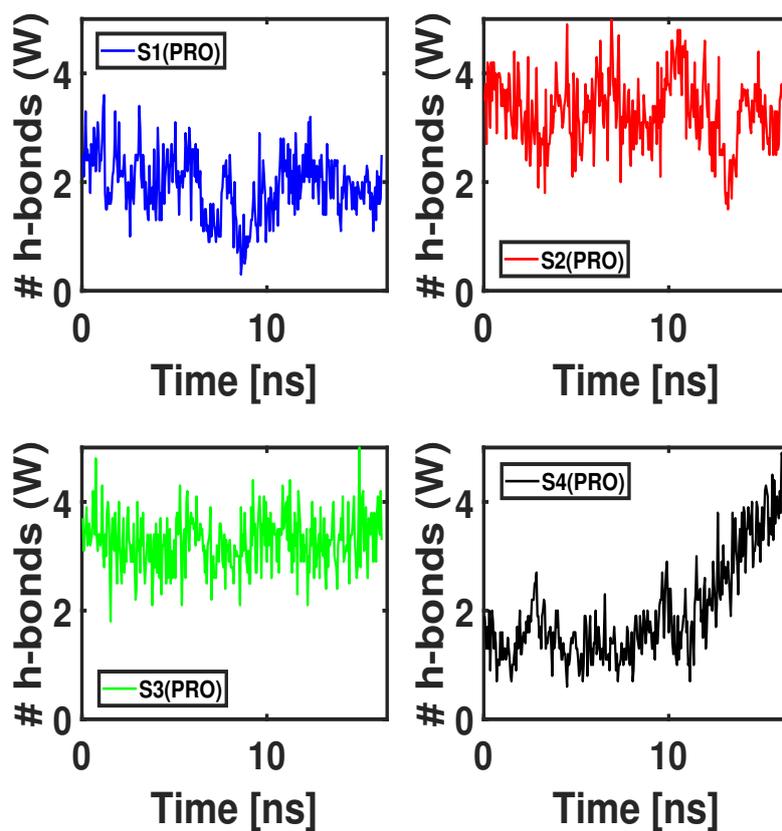


FIG. S10: Hydrogen bonds between the polyproline (P9) segment and water during translocation. S1–S4 denote the four P9R9 peptides in the system.

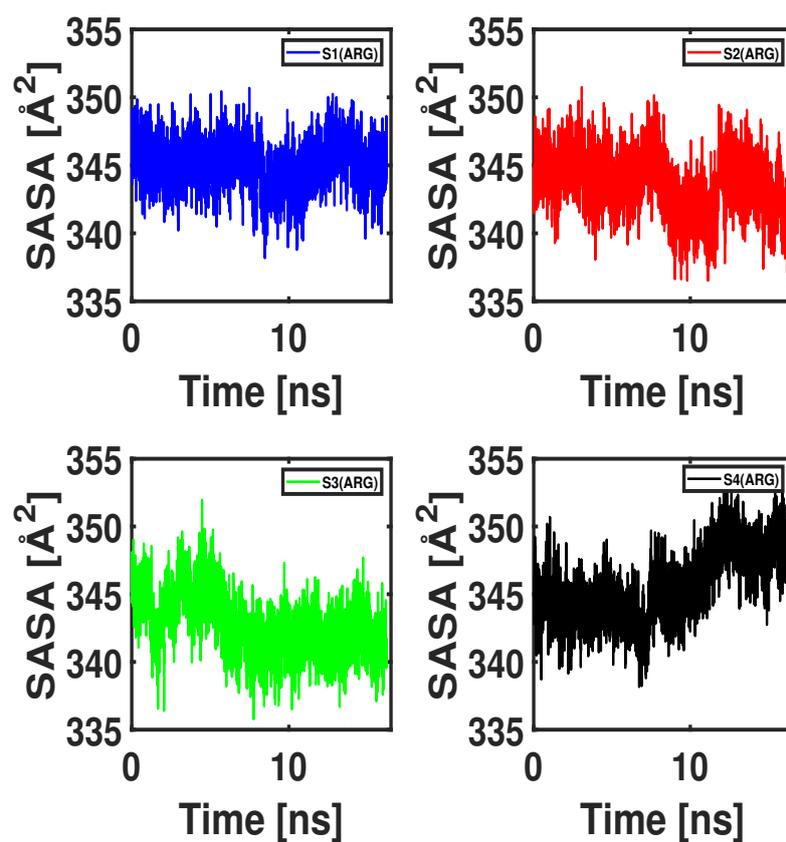


FIG. S11: Solvent-accessible surface area (SASA) of the polyarginine (R9) segment during translocation. S1–S4 denote the four P9R9 peptides in the system.

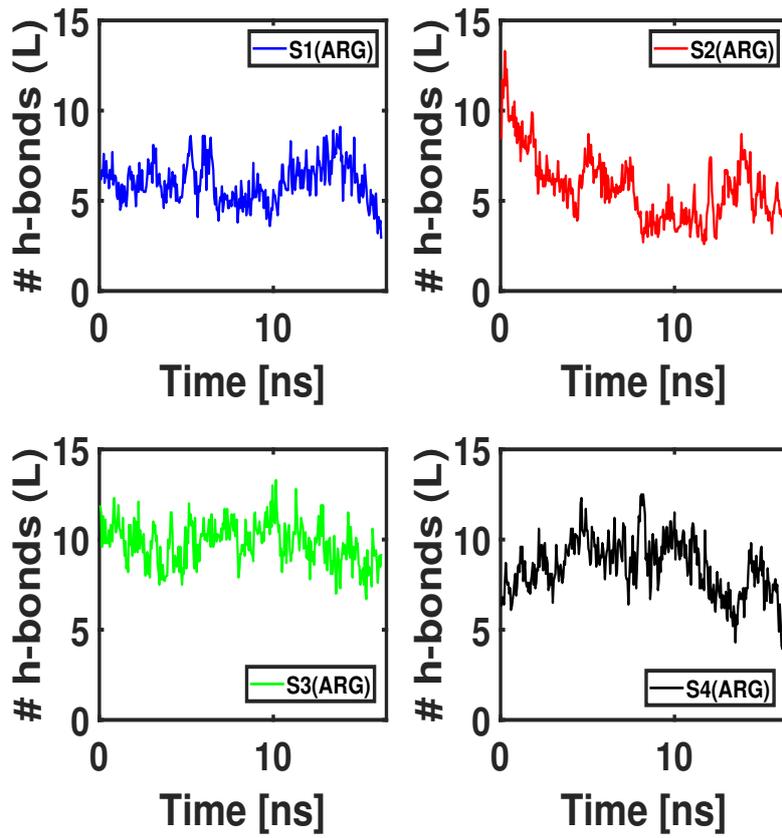


FIG. S12: Hydrogen bonds between the polyarginine (R9) segment and lipids during translocation. S1–S4 denote the four P9R9 peptides in the system.