Molecular Dynamics Study of Interfacial Interaction Between Perfluoroalkyl Substances and the Lipid Bilayer Membrane

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Per- and polyfluoroalkyl substances (PFAS) are synthetic chemicals widely used in consumer products like non-stick cookware and food packaging since the 1950s. Due to their strong carbon-fluorine bonds, they persist in the environment and accumulate in living organisms, posing serious health risks, including cancer and organ damage. This study employs molecular dynamics simulations to investigate the interactions of three PFAS—perfluorobutanoic acid (PFBA), perfluorooctanoic acid (PFOA), and perfluorododecanoic acid (PFDoA)—with lipid bilayer membranes, key biological interfaces. Models were constructed using CHARMM-GUI, with force fields applied via Moltemplate and simulations conducted in LAMMPS. The system was equilibrated for 50 nanoseconds (ns) before running productive simulations for over 100 ns. Umbrella sampling and the weighted histogram analysis method (WHAM) were used to determine free-energy profiles. Results show that PFAS first attach to the membrane via their charged head groups before rotating and embedding their hydrophobic tails. PFOA and PFDoA successfully penetrate the membrane, transitioning from dominant Coulombic to van der Waals interactions. PFBA, however, remains near the surface and does not fully insert. PFDoA exhibits the highest energy barrier for membrane entry, while PFBA has the lowest. PFOA and PFDoA show similar insertion behavior, while PFBA's effect is weaker. These findings provide molecular-level insights into PFAS interactions with biological membranes, improving our understanding of their potential health impacts and informing strategies to mitigate PFAS-related risks.

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