Lipid bilayers are central in the study and understanding of biological membranes. Their structure, function, and activity are directly related to the composition and molecular properties of the membrane constituents. In an effort to understand the antimicrobial activity of a new class of dendritic amphiphiles (3CAm19)—potentially safe, effective, acceptable, and affordable topical microbicides with anti-HIV, anti-STD pathogens, antibacterial, and antifungal activities [1], we combine experimental and computational techniques to obtain insight into how these amphiphiles interact with lipid bilayers. Because 3CAm19 are lipid-like compounds, their interactions with the lipid bilayer of biological membranes result in biophysical changes in the structure and dynamics of the membranes. Wide-angle (XAXD) and small-angle (SAXD) X-ray diffraction on model DPPC membranes show systematic changes to the membrane structure and, consequently, the phase transition due to interaction with these dendritic amphiphiles. Molecular dynamics simulations of these structures reveal the specific molecular mechanisms associated with the changes to the membrane structure. This study represents a multi-scale modeling approach to design, develop, and understand the biological activities of this homologous series of dendritic amphiphiles that include very long chains.


**Experimental: Materials and Methods**

Long chained amphiphile and DPPC (Avanti) were mixed in desired molar ratio in chloroform + methanol, the solvent was evaporated under a stream of gaseous nitrogen and its traces removed by an oil vacuum pump. Redistilled water was added at the H2O/DPPC = 5/1 weight ratio and the mixture was homogenized mechanically at 60 °C. SAXD and WAXD experiments were performed at beam A2 in HASYLAB at DESY using a monochromatic radiation of wavelength 0.15 nm. During temperature scans, the samples were heated from 20 to 60 °C in 40 min, and the diffractograms were recorded for 10 sec. every min. Data reduction, normalization and analysis were done with the programs STAF0, OTOKO, PEAKFIT and GRAPHER.

**Simulation Methods**

- NPT simulations
- Berendsen thermostat
- Berendsen barostat
- 2 ns time-step
- Over 80 ns of simulation time
- Short-range cutoff: 1.0 nm
- PME for long-range electrostatics
- All-bonds constrained (LINCS and SHAKE)

All systems contained 40 water per total 3CAm19 + DPPC

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