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Peptide-induced Asymmetric Distribution of Charged Lipids in a Vesicle Bilayer Revealed by Small-Angle Neutron Scattering¹ WILLIAM HELLER, SHUO QIAN, Oak Ridge National Laboratory — Cellular membranes are complex mixtures of lipids, proteins and other small molecules that provide functional, dynamic barriers between the cell and its environment, as well as between environments within the cell. The lipid composition of the membrane is highly specific and controlled in terms of both content and lipid localization. Here, small-angle neutron scattering and selective deuterium labeling were used to probe the impact of the membrane-active peptides melittin and alamethicin on the structure of lipid bilayers composed of a mixture of the lipids dimyristoyl phosphatidylglycerol (DMPG) and chain-perdeuterated dimyristoyl phosphatidylcholine (DMPC). We found that both peptides enriched the outer leaflet of the bilayer with the negatively charged DMPG, creating an asymmetric distribution of lipids. The level of enrichment is peptide concentration-dependent and is stronger for melittin than alamethicin. The enrichment between the inner and outer bilayer leaflets occurs at very low peptide concentrations, and increases with peptide concentration, including when the peptide adopts a membrane-spanning, pore-forming state.

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