Thermodynamics of Drug-Lipid Interactions Studied by Nonlinear Optical Methods

Using the laser-based surface-specific method, second harmonic generation (SHG), we directly monitored adsorption of therapeutically-relevant aqueous concentrations of small molecule drugs and “drug-like” organics to supported lipid bilayers without the use of extrinsic labels. We studied phospholipids of varying phase, cholesterol content, and head group charge at a range of physiological pH conditions. Thermodynamic driving forces were quantified to provide a molecular link between variations in plasma membrane composition and drug adsorption. The small molecules we studied included the non-steroidal anti-inflammatory drug (NSAID) indomethacin and protein-mimicking, water-soluble peptoids (N-substituted glycine oligomers) of varying lengths and sequences. We aim to provide a quantitative model, which can be used to predict how variations in primary and secondary structural features impact interactions with plasma membranes.