**Modeling membranes in ADME: predicting distribution, intracellular concentrations, and drug absorption**

Tissue partitioning is an important component of drug distribution and half-life. Protein binding and lipid partitioning together determine drug distribution. This lecture will review our recent work on predicting membrane partitioning and volume of distribution of drugs. Next, prediction of the impact of transporters on unbound intracellular concentrations will be discussed. These predictions utilize explicit membrane compartmental models. We have developed models based on in situ single-pass liver perfusions as well as systemic concentration-time data to predict intracellular hepatic concentration-time profiles. Published studies with atorvastatin as well as new work with preclinical bosentan pharmacokinetics will be presented. Finally, the incorporation of explicit membrane compartmental models into a novel continuous intestinal absorption model will be discussed.