



COLLEGE OF PHARMACY  
PHARMACEUTICAL SCIENCES  
UNIVERSITY OF MICHIGAN

The Pharmaceutical Sciences Department  
is pleased to announce the  
Ph.D. Dissertation Defense Seminar of



**Alex Yu**

Pharmaceutical Sciences, Ph.D. Candidate  
(Mentor: Dr. Duxin Sun)

Friday, March 23, 2018  
3:00 pm  
2548 C.C. Little Building

**“A Novel Mechanistic and Physiologically-Based Pharmacokinetic  
Model with Dynamic Gastrointestinal Fluid Transport”**

Abstract: Quantification of *in vivo* gastrointestinal (GI) dissolution rate and extent for oral drug products can provide an invaluable perspective in the drug development process. However, *in vivo* dissolution rate is extremely challenging to experimentally measure. To obtain an indirect measurement of *in vivo* dissolution, fasted human volunteers were dosed with 800mg of immediate release ibuprofen and post-dose drug concentrations were acquired by sampling directly from the human gastrointestinal tract. To translate the *in vivo* measurements into a prediction of regional dissolution rates, we developed a physiologically based mechanistic oral absorption model comprised of a series of mathematical compartments with distinctions for transit, fluid volume, and drug phases. Deconvolution of the model estimated an *in vivo* dissolution rate which was validated based on comparison with clinically observed *in vivo* GI concentrations. From the model design, we found GI fluid volume, mucus, and gastric emptying to be important considerations in modeling drug transport. From the ibuprofen simulation results, we found the primary site of dissolution to be the jejunum, dissolution rates to be similar amongst individuals, and the major period of dissolution to be complete within 3 hours.

*Defenses are open to the public.*