

Physiologically-Based Modeling

PHA 6131, Section TBA

Class Periods: Monday 9:00-10:00AM

Location: Zoom (link will be posted on Canvas)

Academic Term: Spring 2023

Course Faculty:

Dr. Stephan Schmidt

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Office Hours: Upon request

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Teaching Partners:

A team of internationally-renown PBPK experts

Teaching Assistant:

TBA

Program coordinator:

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Course Description

"Physiologically-Based Modeling" is a 3-credit course that provides students and trainees with the theoretical concepts as well as hands-on applications in physiologically-based modeling and its use in drug development and regulatory evaluation with focus on physiologically-based pharmacokinetic (PBPK) modeling.

Course Pre-Requisites / Co-Requisites

none

Course Objectives

1. Understand the role of physiologically-based models at different stages of drug development and regulatory evaluation with focus on physiologically-based pharmacokinetic (PBPK) models.
2. Identify key PBPK model components and parameters
3. Understand and apply PBPK model building and verification processes
4. Identify the data needed to inform PBPK models
5. Parametrize clearance, volume of distribution, and absorption processes using different *in vitro* and *in vivo* data sources
6. Identify factors impacting clearance, volume of distribution, and oral drug absorption
7. Understand the role of transporters and parametrize them in PBPK models
8. Develop and verify models for major PBPK applications (i.e., absorption, drug-drug interactions, and special patients' populations) in different software platforms
9. Have a basic understanding of additional major PBPK applications (e.g., virtual bioequivalence and non-oral routes of absorption)
10. Understand the setup of PBPK models for large molecules and how they differ from small molecules

Course Schedule

Every week, two lectures will be assigned and made available on Canvas. These lectures can be watched by the students at any time. Students will be able to ask question on the course material and attend software tutorials during live zoom sessions on Monday mornings (9:00-10:00AM). In addition, reading assignments will be made available on Canvas under the respective course modules. Please routinely check your campus calendar and the Canvas course site for any messages about changes in the schedule and deadlines.

The following topics will be covered:

Week/Date	Module	Instructor	Topics
Week 1 Jan 9 - Jan 13	1	Stephan Schmidt	Introduction ✓ Course overview & Setup ✓ Introduction to physiologically-based modeling
Week 2 Jan 17 - Jan 20	2	Stephan Schmidt	Physiologically-Based Modeling Approach in Drug Development and Regulatory Evaluation
Week 3 Jan 24 - Jan 27	3	Stephan Schmidt	PBPK Model Development and Verification ✓ PBPK model components ✓ Development and verification workflow ✓ Variability
Week 4 Jan 31 - Feb 3	4	Rodrigo Cristofolletti	Clearance ✓ In vitro-in vivo extrapolation (IVIVE) ✓ Factors affecting drug metabolism ✓ <i>In vitro</i> models for hepatic clearance ✓ Transporters in clearance ✓ Renal clearance
Week 5 Feb 6 - Feb 10	5	Rodrigo Cristofolletti	Volume of Distribution ✓ Factors affecting tissue distribution ✓ <i>In silico</i> models for tissue partition coefficients ✓ Perfusion & permeability limited distribution
Week 6 Feb 13 - Feb 17	6	Rodrigo Cristofolletti	Physiological Models for Oral Absorption ✓ Factors affecting drug absorption and gut bioavailability ✓ <i>In vitro</i> models for drug release ✓ Permeability, solubility, luminal stability ✓ Transporter mediated kinetics
Midterm exam			
Week 7 Feb 20 - Feb 24	7	Simulations Plus team	Software Application 1: Absorption ✓ Introduction to GastroPlus™ ✓ Guided hands-on tutorial ✓ Software assignment 1
Week 8 Feb 28 - Mar 3			
Week 9 Mar 6 - Mar 10	8	Simcyp team	Software Application 2: DDI ✓ Introduction to Simcyp ✓ Guided hands-on tutorial ✓ Software assignment 2
Week 10 Mar 20 - Mar 24			
Spring Break Mar 13-17			
Week 11 Mar 27 - Mar 31	9	esqLABS team	Software Application 3 Special Populations ✓ Introduction to PK-Sim ✓ Guided hands-on tutorial ✓ Software assignment 3
Week 12 Apr 3 - Apr 7			
Week 13 Apr 10 - Apr 14	10	All teaching partners	Additional Major PBPK Applications ✓ Metabolites ✓ PBPK/PD ✓ Virtual Bioequivalence ✓ Additional dosage routes ✓ Machine learning + PBPK in discovery
Week 14 Apr 17 - Apr 21			
Week 15 Apr 24 - Apr 26	11	esqLABS team	Large Molecules
Final Exam			

Recommended Reading

1. Derendorf H and Schmidt S (ed.) *Rowland and Tozer's Clinical Pharmacokinetics and Pharmacodynamics: Concepts and Applications*. Fifth Edition. Wolters Kluwer, Alphen aan den Rijn, Netherlands, 2019, 1-939.
2. Peters SA. *Physiologically-Based Pharmacokinetic (PBPK) Modeling and Simulation: Principles, Methods, and Applications in the Pharmaceutical Industry*. John Wiley & Sons, Inc., Hoboken, New Jersey, 2012.

Additional reading material will be made available on the Canvas course site.

Course Software

Software needed to complete the course will be made available by the instructors throughout the course.

Attendance Policy, Class Expectations, and Make-Up Policy

Students must finish the problem sets and exams within the one-week window indicated in the syllabus. Students who missed the quiz window will get a zero for that quiz without an excused reason. Students need to contact the course coordinator through email for any emergency situation that prevents the student from taking the problem set and explain the situation immediately when the situation resolved. The student will either take a make-up problem set or choose other options determined by the coordinator.

Students are required to watch lectures within the period that is indicated in the syllabus. Conflict with work schedules is not an excused absence for not watching the lectures.

Makeup assignment(s) will be made for any excused absence(s) and must be submitted **within one-week of the missed session(s)**. If the situation leads to missing multiple class sessions and makeup becomes difficult, the student and course coordinator will discuss with the administration to explore options such as a remediation plan or course withdrawal. Class attendance requires full engagement of activities including problem sets, assignments and course reflection.

Excused absences must be consistent with university policies in the [Graduate Catalog](#) and require appropriate documentation. Additional information can be found in [Attendance Policies](#).

Evaluation of Grades

Assignment	Percentage of Final Grade
Exam 1	20%
Exam 2	20%
Software Assignments (3)	60%
Total	100%

Grading Policy

Percentage Range	Grade
92.50-100%	A
89.50-92.49%	A-
86.50-89.49%	B+
82.50-86.49%	B
79.50-82.49%	B-
76.50-79.49%	C+
72.50-76.49%	C
69.50-72.49%	C-
66.50-69.49%	D+
62.50-66.49%	D
59.50-62.49%	D-
< 59.50%	E

More information on UF grading policy may be found at:

[UF Graduate Catalog](#)
[Grades and Grading Policies](#)

Students Requiring Accommodations

Students with disabilities who experience learning barriers and would like to request academic accommodations should connect with the [Disability Resource Center](#). It is important for students to share their accommodation letter with their instructor and discuss their access needs, as early as possible in the semester.

Course Evaluation

Students are expected to provide feedback on the quality of instruction in this course by completing [online evaluations](#). Evaluations are typically open during the last two or three weeks of the semester, but students will be given specific times when they are open. Summary results of these assessments are available to students on the [Gator Evals page](#).

University Honesty Policy

UF students are bound by The Honor Pledge which states, "We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honor and integrity by abiding by the Honor Code. On all work submitted for credit by students at the University of Florida, the following pledge is either required or implied: "On my honor, I have neither given nor received unauthorized aid in doing this assignment." [The Honor Code](#) specifies a number of behaviors that are in violation of this code and the possible sanctions. Furthermore, you are obligated to report any condition that facilitates academic misconduct to appropriate personnel. If you have any questions or concerns, please consult with the instructor or TAs in this class.

Software Use

All faculty, staff, and students of the University are required and expected to obey the laws and legal agreements governing software use. Failure to do so can lead to monetary damages and/or criminal penalties for the individual violator. Because such violations are also against University policies and rules, disciplinary action will be taken as appropriate. We, the members of the University of Florida community, pledge to uphold ourselves and our peers to the highest standards of honesty and integrity.

Student Privacy

There are federal laws protecting your privacy with regards to grades earned in courses and on individual assignments. For more information, please see the [Notification to Students of FERPA Rights](#).

Campus Resources:

Health and Wellness

U Matter, We Care: If you or a friend is in distress, please contact umatter@ufl.edu or 352 392-1575 so that a team member can reach out to the student.

Counseling and Wellness Center: counseling.ufl.edu/cwc, and 392-1575; and the University Police Department: 392-1111 or 9-1-1 for emergencies.

Sexual Assault Recovery Services (SARS): Student Health Care Center, 392-1161.

University Police Department at 392-1111 (or 9-1-1 for emergencies), or police.ufl.edu.

Academic Resources

[E-learning technical support](#), 352-392-4357 (select option 2) or e-mail to Learning-support@ufl.edu.

[Career Resource Center](#), Reitz Union, 392-1601. Career assistance and counseling.

[Library Support](#), Various ways to receive assistance with respect to using the libraries or finding resources.

[Teaching Center](#), Broward Hall, 392-2010 or 392-6420. General study skills and tutoring.

[Writing Studio](#), 302 Tigert Hall, 846-1138. Help brainstorming, formatting, and writing papers.

[Student Complaints Campus](#)

[On-Line Students Complaints](#)