DEPARTMENT: Environmental Health

COURSE NUMBER: EH 590R  SECTION NUMBER:  4
CREDIT HOURS:  2  SEMESTER: Spring 2019

COURSE TITLE: Introduction to Physiologically-Based Toxicokinetic (PBTK)/Pharmacokinetic (PBPK) Modeling
CLASS HOURS: 3:00-4:50 PM Wednesday
CLASS LOCATION: TBD

INSTRUCTOR NAME: Qiang Zhang

INSTRUCTOR CONTACT INFORMATION

EMAIL: qiang.zhang@emory.edu
PHONE: 404-727-0154
SCHOOL ADDRESS OR MAILBOX LOCATION: 1518 Clifton Rd, Mailstop 1518-002-2BB
OFFICE HOURS: By appointment

Teaching Assistant(s): None

COURSE DESCRIPTION

The health effects of environmental or pharmaceutical chemicals depend on the concentrations of the chemicals and their metabolites in the target tissues of the human body. Given an exposure to a chemical, understanding and predicting its internal concentrations (tissue dosimetry) requires a physiologically-based toxicokinetic (PBTK) or pharmacokinetic (PBPK) modeling approach. Based on human physiology and anatomy, PBTK/PBPK models mechanistically simulate the absorption, distribution, metabolism, and elimination (ADME) processes that collectively affect the fates of exogenous chemicals in the human body, producing as model output temporal changes in chemical tissue concentrations. PBTK/PBPK modeling has be increasingly applied in chemical health risk assessment and drug discovery and development.

This introductory course will allow students to learn what happens to chemicals in the human and animal bodies after chemical exposures and the physiological and
biochemical determinants for chemical fate, and how to use numerical simulation tools to model what the body does to the chemicals. The course covers:

- The fundamental concepts underlying PBTK/PBPK modeling
- Mathematical description of the ADME of chemicals using mass-balance differential equations
- Building PBTK/PBPK models to simulate tissue dosimetry using the Berkeley Madonna software
- Application of PBTK/PBPK models in human health risk/safety assessment of environmental chemicals and in drug discovery

**Target students:**
- Environmental health science students interested in chemical tissue dosimetry, internal exposure, interpretation of biomarkers of exposures, *in vitro* to *in vivo* extrapolation (IVIVE) of chemical dosimetry
- Pharmacology/toxicology students interested in quantitative simulation of tissue-specific drug dosimetry beyond traditional compartmental PK.
- Students and researchers in biosciences, nutritional science, anesthesiology and biomedical engineering, and chemical engineering interested in computational approaches to predicting tissue concentrations of environmental, industrial, dietary, and pharmaceutical chemicals.

**Semester offered:** Spring

**Prerequisite:** None

Note: Some basic concepts related to this course, such as mammalian systemic blood circulation, chemical ADME, and numerical computer simulation will be introduced in this course, so it is not necessary that students have prior courses in these subjects.

**MPH/MSPH FOUNDATIONAL COMPETENCIES:**

- Evidence-based Approaches to Public Health
  Analyze quantitative and qualitative data using biostatistics, informatics, computer-based programming and software, as appropriate
CONCENTRATION COMPETENCIES:

• Apply the principles of toxicology to assess health effects of environmental exposures
• Evaluate the risks posed by environmental hazards using risk assessment methods
• Describe the role of toxicology in evaluating health effects of environmental exposures

COURSE LEARNING OBJECTIVES:

• Quantitative concepts associated with chemical ADME.
• General structure of a PBTK/PBPK model
• How to build a PBTK/PBPK model
• How to parameterize a PBTK/PBPK model
• How to use numerical simulation programs such as Berkeley Madonna to model TK and PK processes

EVALUATION

Students will be evaluated based upon attendance and three homework assignments. Since there is no required textbook (optional ones are recommended), class attendance is utmost important for students to understand and learn the course material. Homework assignments will involve primarily using numerical simulation methods learned in class to build models for various chemicals and exposure scenarios. The weight of the homework points progressively increases through the semester as the students become more competent and are able to work on more challenging homework projects.

<table>
<thead>
<tr>
<th>Attendance</th>
<th>10%</th>
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<tbody>
<tr>
<td>Homework #1</td>
<td>25%</td>
</tr>
<tr>
<td>Homework #2</td>
<td>30%</td>
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<tr>
<td>Homework #3</td>
<td>35%</td>
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</tbody>
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A: >=95, A-: >=90, B+:>=85, B:>=80, B-:>=75, C>=60, F<60

COURSE STRUCTURE

The course comprises lectures and hands-on computer simulation exercises. Each student will be required to bring a laptop computer to simulation sessions.

About 5 literature papers will be assigned for reading after some sessions to further solidify the concepts taught in class.

Three homework assignments.
### MPH/MSPH Foundational Competency assessed

<table>
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<tr>
<th>Competency</th>
<th>Representative Assignment</th>
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| Analyze quantitative data using biostatistics, informatics, computer-based programming and software, as appropriate | 1. Literature paper reading assignment  
2. Computer simulation homework |

### EH Concentration Competencies assessed

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<tr>
<th>Competency</th>
<th>Representative Assignment</th>
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</thead>
</table>
| Apply the principles of toxicology to assess health effects of environmental exposures | 1. Literature paper reading assignment  
2. Computer simulation homework |
| Evaluate the risks posed by environmental hazards using risk assessment methods | 1. Literature paper reading assignment  
2. Computer simulation homework |
| Describe the role of toxicology in evaluating health effects of environmental exposures | 1. Literature paper reading assignment  
2. Computer simulation homework |

Attendance is required and counts toward 10% of the final score. Each student is expected to complete the homework assignments independently. Reading assignment will also be prescribed through the semester. There is no required textbook, but the following can be used as optional reference textbooks:


Reading material: to be provided.

As the instructors of this course we endeavor to provide an inclusive learning environment. However, if you experience barriers to learning in this course, do not hesitate to discuss them with me and the Office for Equity and Inclusion, 404-727-9877.

### COURSE POLICIES

As the instructor of this course I endeavor to provide an inclusive learning environment. However, if you experience barriers to learning in this course, do not hesitate to discuss them with me and the Office for Equity and Inclusion, 404-727-9877.

### RSPH POLICIES

#### Accessibility and Accommodations

Accessibility Services works with students who have disabilities to provide reasonable accommodations. In order to receive consideration for reasonable accommodations,
you must contact the Office of Accessibility Services (OAS). It is the responsibility of the student to register with OAS. Please note that accommodations are not retroactive and that disability accommodations are not provided until an accommodation letter has been processed.

Students who registered with OAS and have a letter outlining their academic accommodations are strongly encouraged to coordinate a meeting time with me to discuss a protocol to implement the accommodations as needed throughout the semester. This meeting should occur as early in the semester as possible.

Contact Accessibility Services for more information at (404) 727-9877 or accessibility@emory.edu. Additional information is available at the OAS website at http://equityandinclusion.emory.edu/access/students/index.html

Honor Code

You are bound by Emory University’s Student Honor and Conduct Code. RSPH requires that all material submitted by a student fulfilling his or her academic course of study must be the original work of the student. Violations of academic honor include any action by a student indicating dishonesty or a lack of integrity in academic ethics. Academic dishonesty refers to cheating, plagiarizing, assisting other students without authorization, lying, tampering, or stealing in performing any academic work, and will not be tolerated under any circumstances.

The RSPH Honor Code states: “Plagiarism is the act of presenting as one’s own work the expression, words, or ideas of another person whether published or unpublished (including the work of another student). A writer’s work should be regarded as his/her own property.” (http://www.sph.emory.edu/cms/current_students/enrollment_services/honor_code.html)

COURSE CALENDAR

Week 1 (1/16/2019)
Background and introduction to PBTK/PBPK modeling (Guest lecturer: Moiz Mumtaz)

Week 2 (1/23/2019)
General introduction to chemical ADME (Guest Lecturer: Edward Morgan)

Week 3 (1/30/2019)
Construction of PBTK/PBPK models

Week 4 (2/6/2019)
Application of PBPK models (Guest Lecturer: Moiz Mumtaz)
Week 5 (2/13/2019)
Introduction to Berkeley Madonna simulation software

Week 6 (2/20/2019)
Describing individual tissue compartments

Homework #1 assignment

Week 7 (2/27/2019)
Building a full PBPK model (PCB)

Week 8 (3/6/2019)
Building a PBPK model for Styrene

Homework #1 due

Week 9
Spring break no class

Week 10 (3/20/2019)
Modeling inducible metabolism and specific binding
- A PBPK model for dioxin

Homework #2 assignment

Week 11 (3/27/2019)
Modeling life-stage body weight/body composition changes for persistent compounds

Week 12 (4/3/2019)
Modeling a pharmaceutical compound

Homework #2 due
Homework #3 assignment

Week 13 (4/10/2019)
Modeling population variability and uncertainty

Week 14 (4/17/2019)
Using biomonitoring data in PBTK modeling (Guest Lecturer: Dana Barr)

Week 15 (4/24/2019)
In vitro to in vivo extrapolation (IVIVE) modeling
Homework #3 due