**Models for Understanding and Controlling Global Infectious Diseases**

**HUMBIO 154D/HRP 204**

**Spring Quarter 2020**

**Instructors**: Jason Andrews, MD, SM; jandr@stanford.edu

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**Course Description:** This course introduces students to the dynamics of infectious diseases of global health importance, focusing on the use of mathematical models to characterize their transmission in populations. Relevant case examples of pathogens with differing natural history and transmission routes include tuberculosis, HIV, malaria, typhoid, and cholera, as well emerging infectious diseases such as Ebola and the 2019 novel coronavirus. Lectures will emphasize the theoretical basis underlying infectious disease dynamics and link them to in-class workshops and problem sets that will emphasize public health applications and will provide students with hands-on experience in creating and coding models. Students will learn the mathematical underpinnings of key topics in infectious disease transmission including herd immunity, the basic reproductive number, vaccine effects, social contact structure, host heterogeneities, and pathogen fitness. The course will teach students how to approach new questions in infectious disease transmission, from model selection, tradeoffs in model complexity or parsimony, parameterization, sensitivity and uncertainty analyses. Students will practice building models, evaluating the influence of model parameters, making predictions about disease trajectories, and projecting the impact of public health interventions.

**Prerequisites:** MATH 51 or CME 100; BIO 141 or BIOHOPK 174H

We recommend (but do not require) some familiarity with epidemiology including infectious diseases epidemiology, covered in courses such as HRP 231. For those without a background in this area, additional short readings will be provided in the first week to help familiarize students with aspects of infectious disease and epidemiology that will be referred to throughout the course.

**Class Schedule:**

* Lectures and Labs: Tuesdays & Thursdays, 10:30-11:50a
* Graduate Section: Thursdays, 5:15-6:15p (weeks 2-9)

**Teaching Assistant:** Tess Ryckman; ryckmant@stanford.edu

Office Hours: Wednesdays 3:30-5:30 pm (Zoom on Canvas)

**Class Website:** <https://canvas.stanford.edu/courses/119707>

**Course Numbers and Graduate Section:** Undergraduates should enroll in HUMBIO 154D. Enrollment in the graduate version of the course, HRP 204, requires prior permission of the course instructors.

**Graduate Section:** A weekly one-hour session will be offered for graduate students enrolled in HRP 204 (optional for advanced undergraduates with permission of the instructor), in which more advanced topics in infectious disease modeling will be discussed. This will involve additional readings from the modeling literature, examination of sophisticated techniques in model design, parameterization and analysis, and discussion of challenges in generating robust models with public health significance.

**Evaluation:** All grading will be S/NS and assignments will be submitted on Canvas.

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| 4 ungraded problem sets | 40% (for submission, graded only for completeness) |
| 1 midterm problem set | 30% (graded) |
| Final exam | 30% (graded) |

For those enrolled in the graduate section, requirements above count for 80% of the graduate grade in their proportions, and the remaining 20% come from presentation and weekly participation in the section.

**Remote Learning:** All lectures, labs, sections, and office hours will be held via Zoom. Use the “Zoom” menu on the Canvas course website to join. We encourage students to attend lectures live as much as possible for your own learning, but we are also cognizant of the different circumstances everyone is facing this quarter. We won't be grading based on lecture attendance and all lectures will be recorded and posted on Canvas. Please contact the instructors if you are enrolled in HRP 204 and will have difficulty regularly attending the graduate section, as presenting and participating in discussions will be an integral part of the section.

**Learning Objectives:**

* Translate specific infectious disease epidemiologic questions into appropriate formal models
* Develop familiarity with how biological, epidemiological, and clinical data and theory are used to estimate input parameters for formal models of infectious diseases and reciprocally how such models can help us better understand the biology and epidemiology of these diseases
* Interpret outputs from formal models of infectious diseases in terms of impacts on incidence, prevalence, severity
* Describe how outputs from formal models of infectious diseases and interventions can be assessed in terms of their robustness and uncertainty
* Develop familiarity with the mathematical underpinnings of the dynamics of transmission of various infectious diseases, including the roles of susceptibility, immunity, herd immunity, and pathogen characteristics including reproductive numbers and serial intervals
* Understand the conditions under which infectious diseases may die out, remain endemic, become epidemic, or reach other equilibria in a particular population, useful for designing and assessing effective public health control strategies and health interventions.
* Explore the links between realistic demography (birth, death, age structure, migration, household structure) and infectious disease models and their implications for epidemiologic outcomes and intervention effects
* Evaluate critically how particular models represent common infectious disease treatment, control and prevention policies and how these representations may influence findings of model-based analyses

**Textbook:** Keeling M, Rohani P. Modeling infectious diseases in humans and animals.

Princeton University Press, 2007.

Available freely through JSTOR: https://www.jstor.org/stable/j.ctvcm4gk0

**Use of R Software:** As part of the course labs (held during lecture) and homework, we will be doing hands-on modeling in R, a free software environment for statistical computing and graphics. Please make sure you have R and RStudio downloaded on your computers (instructions below). We will demonstrate the use of R for modeling during in-class labs and will provide you with the code used during class (we do not expect you to construct complex infectious disease models in R from scratch). For those of you without prior R experience, we strongly encourage you to learn some of the basics before the first lab (on April 21) and recommend this tutorial: <http://kingaa.github.io/R_Tutorial/>. Come to office hours if you have trouble installing R and RStudio or have questions about the tutorial materials.

**Installing R, RStudio, and Packages:** Instructions for installing R can be found here: <http://kingaa.github.io/R_Tutorial/#installing-r-on-your-computer>

After installing R, we also recommend you install RStudio, which makes writing and running R scripts, downloading packages, graphing, viewing data, and troubleshooting more user-friendly. To download RStudio, go to <https://rstudio.com/products/rstudio/download/#download>.

Also install the deSolve and ggplot2 packages by typing *install.packages(c("ggplot2","deSolve"))* into the RStudio console or using the Packages menu on the bottom-right.

**Students with Documented Disabilities:** Students who may need an academic accommodation based on the impact of a disability must initiate the request with the Office of Accessible Education (OAE). Professional staff will evaluate the request with required documentation, recommend reasonable accommodations, and prepare an Accommodation Letter for faculty dated in the current quarter in which the request is being made. Students should contact the OAE as soon as possible since timely notice is needed to coordinate accommodations. The OAE is located at 563 Salvatierra Walk (phone: 650-723-1066, email oae-contactus@stanford.edu, URL: http://oae.stanford.edu).

**Lecture/Lab Schedule and Readings**

*Please note: Readings may be modified during the quarter as needed to better tailor material to remote learning, student needs, and the evolving public landscape.*

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| Date | Lecture | Readings |
| 4/7 | Lecture 1: Introduction to infectious disease modeling | None |
| 4/9 | Lecture 2: Dynamics 1 - First Models | Keeling and Rohani, Chapter 1 and Chapter 2.1.1 |
| 4/14 | Lecture 3: Dynamics 2 - SIR models with demography | Keeling and Rohani, Chapter 2.1.2-2.4 |
| 4/16 | Lecture 4: Dynamics 3 - Reproductive Number, Thresholds, Equilibria | Keeling and Rohani, Chapter 2.5-2.9 |
| 4/21 | Lab 1: Dynamic Models in R | Course primer on coding models in R (Canvas) |
| 4/23 | Lecture 5: Heterogeneous mixing and temporal modeling | Keeling and Rohani, Chapter 3.1-3.2  Keeling and Rohani, Chapter 5.1-5.2  Mossong et al. Social contacts and mixing patterns relevant to the spread of infectious diseases. *PLoS Medicine,* 2008.  (***Ungraded Lab 1 Writeup Due)*** |
| 4/28 | Lecture 6: Emerging infections: takeoff, growth, extinction  / Lab 2 | Lloyd-Smith JO, Schreiber SJ, Kopp PE, Getz WM. Superspreading and the effect of individual variation on disease emergence. *Nature* 2005; 438: 355-9.    Wallinga J, Teunis P. Different epidemic curves for severe acute respiratory syndrome reveal similar impacts of control measures. *Am J Epidemiol.* 2004;160(6):509-16. |
| 4/30 | Lecture 7: Multihost models, vector, zoonoses, environmentally transmitted | Keeling and Rohani, Chapter 4.1-4.2  (***Ungraded Lab 2 Writeup Due Friday 5/1)*** |
| 5/5 | Lecture 8: Stochastic dynamics | Keeling and Rohani, Chapter 6.1-6.3  ***(Graded Midterm Problem Set released 5/4, due 5/11)*** |
| 5/7 | Lecture 9: Spatial models, networks | Keeling and Rohani, Chapter 7.1-7.2  Keeling and Rohani, Chapter 7.6-7.9 |
| 5/12 | Lecture 10: Interventions and sensitivity analyses | Keeling and Rohani, Chapter 8.1-8.2 |
| 5/14 | Lab 3: Interventions and sensitivity analyses | Course notes on interventions and sensitivity analyses (Canvas) |
| 5/19 | Lecture 11: Competition and evolutionary models | Nowak M. Evolutionary Dynamics. p.9-24  (***Ungraded Lab 3 Writeup Due Wednesday 5/20)*** |
| 5/21 | Lecture 12: Within host evolution | Nowak M. Evolutionary Dynamics. p.167-186 |
| 5/26 | Lab 4: Model Parameterization, calibration, and uncertainty | Course notes on model parameterization, calibration, and uncertainty (Canvas) |
| 5/28 | Lecture 13: Health policy and economic evaluation models | Jit M, Brisson M. Modelling the epidemiology of infectious diseases for decision analysis: a primer. *Pharmacoeconomics*. 2011 May;29(5):371-86.  Winetsky DE, Negoescu DM, DeMarchis EH, Almukhamedova O, Dooronbekova A, et al. Screening and Rapid Molecular Diagnosis of Tuberculosis in Prisons in Russia and Eastern Europe: A Cost-Effectiveness Analysis. *PLOS Medicine*, 2012 9(11): e1001348  (***Ungraded Lab 4 Writeup Due Friday 5/29)*** |
| 6/2 | Lecture 14: Uses and abuses of models and Course Wrap-up | Meltzer M, et al. Estimating the number of cases in the Ebola epidemic -- Liberia and Sierra Leone, 2014-2015. *MMWR* 2014. 63(3):1-14.  King AA, et al. Avoidable errors in the modelling of outbreaks of emerging pathogens, with special reference to Ebola. *Proc Royal Soc* 2015; 282(1806)  ***(Graded Take Home Final Distributed)*** |
| 6/4 | Last Class: TBD | TBD - possible review session |
| 6/9 | No Class | No class - work on take home final |

**Additional Readings for Graduate Student Section (Thursdays wks 2-9)**

The expectation for the graduate student section is that all students will have read the assigned article of the week prior to the section. Groups of 3-4 students will prepare a presentation covering what scientific questions the article addressed, what methods were used, what the study found, and strengths and weaknesses of the approach. Students should prepare several questions for discussion with the section, and the latter portion of the session will involve group discussion of these topics. See the separate graduate section info sheet on Canvas for details.

Week 1 (4/9) – no section

Week 2 (4/16)

Blower SM, Small PM, Hopewell PC. Control strategies for tuberculosis: new models for old problems. *Science* 1996; (5274), 497-500.

Week 3 (4/23)

Pitzer et al, Demographic variability, vaccination and the spatiotemporal dynamics of rotavirus epidemics. *Science*, 2009; 325(5938): 290-294.

Week 4 (4/30)

Leung K, Wu JT, Liu D, Leung GM. First-wave COVID-19 transmissibility and severity in China outside Hubei after control measures, and second-wave scenario planning: a modelling impact assessment. *Lancet.* 2020.

Week 5 (5/7)

Christakis and Fowler. Social network sensors for early detection of contagious outbreaks. *PLoS One,* 2010; 5(9): e12948.

Week 6 (5/14)

Bauch CT. Imitation dynamics predict vaccinating behaviour. *Proc Biol Sci.* 2005 Aug 22;272(1573):1669.

Week 7 (5/21)

Cohen and Murray. Modeling epidemics of multidrug-resistant tuberculosis of heterogeneous fitness. *Nature Medicine,* 2004. 10(10) 1117-1121.

Week 8 (5/28)

TBD – likely Professors Andrew and Goldhaber-Fiebert will present their recent work on modeling COVID-19 for the State of California

Week 9 (6/4)

Corey M. Peak, Lauren M. Childs, Yonatan H. Grad, Caroline O. Buckee. Comparing nonpharmaceutical interventions for containing emerging epidemics. *Proceedings of the National Academy of Sciences* Apr 2017, 114 (15) 4023-4028

Week 10 – no section