

Distinguished Lecture in Mathematical Biology
UCR Interdisciplinary Center for Quantitative Modeling in Biology
Mathematics Colloquium



4pm, Wednesday, March 3, 2021

Zoom Meeting:

<https://ucr.zoom.us/j/99179266453?pwd=MzJBVnJvWTVYSjh1WFZFYWJ4T3JPdz09>

Meeting ID: 991 7926 6453, Passcode: 396836

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Title: A systems biology approach to understanding the immunobiology of tuberculosis infection and treatment

Abstract: Tuberculosis (TB) is one of the world's deadliest infectious diseases. Caused by the pathogen *Mycobacterium tuberculosis* (Mtb), the standard regimen for treating TB consists of treatment with multiple antibiotics for at least six months. There are a number of complicating factors that contribute to the need for this long treatment duration and increase the risk of treatment failure. The structure of granulomas, lesions forming in lungs in response to Mtb infection, create heterogeneous antibiotic distributions that limit antibiotic exposure to Mtb. We can use a systems biology approach pairing experimental data from non-human primates with computational modeling to represent and predict how factors impact antibiotic regimen efficacy and granuloma bacterial sterilization. We utilize an agent-based, computational model that simulates granuloma formation, function and treatment, called *GranSim*. A goal in improving antibiotic treatment for TB is to find regimens that can shorten the time it takes to sterilize granulomas while minimizing the amount of antibiotic required. With the number of potential combinations of antibiotics and dosages, it is prohibitively expensive to exhaustively search all combinations to achieve these goals. We present a framework to search for optimal regimens using GranSim. Overall, we present a computational tool to evaluate antibiotic regimen efficacy while accounting for the complicating factors in TB treatment to strengthen our ability to predict new regimens that can improve clinical treatment of TB.

Bio: Dr. Kirschner received her Bachelors, Masters and PhD in applied mathematics from Tulane University. She did graduate work also at Los Alamos National Labs and a postdoctoral fellowship at Vanderbilt University joint with the departments of Mathematics and Infectious Diseases. Over the past 25 years Dr. Kirschner has focused on questions related to models of host-pathogen interactions in infectious diseases. Her main focus has been to build models of persistent infections (e.g. *Helicobacter pylori* and *Mycobacterium tuberculosis* and HIV-1). Her goal is to understand the complex dynamics involved, together with how perturbations to this interaction (via treatment with chemotherapies or immunotherapies) can lead to prolonged or permanent health. For the past 20 years, her research focus has been on building multi-scale models to describe the host immune response to *M. tuberculosis* at multiple spatial and time scales and in multiple physiological compartments including lung, lymph nodes and blood. To date she have worked and collaborated with experimentalists generating data on TB with mouse, non-human primate and human studies. Denise has over 150 publications in top journals describing this work that spans topics from methodological to biological advancement. Dr. Kirschner currently serves (and has for the past 17 years) as Editor-in-Chief of the *Journal of Theoretical Biology*. She serves as the founding co-director of The Center for Systems Biology at the University of Michigan, an interdisciplinary center at the University of Michigan aimed to facilitate research and training between wet-lab and theoretical scientists. In 2016 she was elected as President-elect of the Society for Mathematical Biology and has served as its president from 2017-2020. Denise's passion for mentoring students, postdoctoral fellows and junior faculty has been a major focus of her career, and her key mission is to promote both mathematics and family values in the scientific community.