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Identifying Optimal Antibiotic Regimens for Tuberculosis Treatment

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4:40PM in 1123 LBME**

Tuberculosis (TB) is one of the world's deadliest infectious diseases. In 2015, 1.8 million people died from TB, presenting an enormous burden on global health systems. Current therapy for TB requires at least six months of multiple antibiotics. Although antibiotics are considered a successful therapy for drug-susceptible TB, the length of therapy and its associated side effects make it difficult for patients to properly adhere to the antibiotic regimen. The emergence of multi-drug resistant TB presents an additional complication. New antibiotics are being developed or repurposed for TB therapy to address these problems. However, with the number of antibiotics and dosing regimens possible, it is impossible to test each combination in clinical trials or animal models to find an optimal antibiotic regimen.

In this talk, I will describe our approach to solving this optimization problem. First, we developed a computational model of the immune response to infection with *Mycobacterium tuberculosis*. Our multi-scale computational model simulates the formation of granulomas, the characteristic lung lesions of TB, based on data collected from in vitro and animal models. Next, we simulated antibiotic delivery to and sterilization of granulomas, so that we can predict the efficacy of antibiotic regimens. However, it is still infeasible to test each antibiotic and dosing regimen combination based on the computational time required to run our computational model. Thus we built a surrogate model to predict the efficacy of any regimen in the design space, and use the surrogate model to locate optimal regimens. Using this methodology, we aim to find combinations of antibiotics to help guide new experiments and clinical trials.

Joseph Cicchese is a doctoral candidate in the Department of Chemical Engineering at the University of Michigan. Joseph completed his undergraduate studies at Iowa State University, where he obtained his Bachelor of Science in Chemical Engineering. As a student in the Linderman Research Group, he is working on pharmacokinetic/pharmacodynamic modeling of antibiotics for tuberculosis treatment. Using a multi-scale computational model of granuloma formation and treatment, he works on ways to incorporate optimization algorithms to search for better antibiotic regimens.

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