1136-92-517 **Joseph M. Cicchese*** (cicchese@umich.edu), **Denise E. Kirschner** and **Jennifer J. Linderman**. *Multi-scale modeling of granuloma formation and surrogate-assisted optimization aid in optimizing antibiotic therapy of tuberculosis.*

Tuberculosis (TB) is one of the world's deadliest infectious diseases. Caused by infection with Mycobacterium tuberculosis, cellular lesions in lung tissue (granulomas) form as the immune system responds to fight the infection. The immune response that forms granulomas involves events that occur over multiple length and time scales. Although granuloma formation helps contain the infection, it also prevents antibiotic penetration during therapy. The length and complexity of antibiotic therapy – months of treatment with multiple antibiotics - and the emergence of drug-resistant TB indicate a need for enhanced antibiotic regimens. However, given an increasing number of potential antibiotics and dosing regimen combinations, the 'regimen design space' for TB therapy is too large to search exhaustively. We have developed a multi-scale, agent-based model that can simulate the formation of a granuloma and treatment with antibiotics. By combining our granuloma model with surrogate-assisted optimization, we can efficiently screen the regimen design space for optimal therapies. This method has been used to estimate optimal regimens for therapies of one or two antibiotics that compare reasonably to already established regimens. (Received January 22, 2018)