



2015 Summer Research Experiences (SRE) for Undergraduates and Teachers

Abstract

MUMMAH, R., SASHIDHAR, D., WEI, J., RICE, H., PARKER, L., MAREK, A., EDA, S. and V.V. GANUSOV. Discriminating between alternative mechanisms mycobacterial granuloma formation in vitro. National Institute for Mathematical and Biological Synthesis, Knoxville, TN; The Pennsylvania State University, University Park, PA; North Carolina State University, Raleigh, NC; University of Minnesota, Minneapolis, MN; University of Tennessee, Knoxville, TN.

Johne's disease is a costly chronic enteric disease which affects ruminants worldwide. Caused by *Mycobacterium avium* subspecies *paratuberculosis*, Johne's disease forms iconic granulomatous structures in the intestinal tract. Using experimental data, with deterministic and stochastic simulations of two models based on ordinary differential equations, we examine alternative mechanisms of granuloma formation. Through image analysis, granuloma areas were measured. The experimental granuloma size distributions best resemble lognormal distributions, with the mean number of granuloma cells increases linearly over time at a rate of 2.2 cells per day. From the first model, the accumulation of infected macrophages is not the primary mechanism driving granuloma formation. Rather, as seen in the deterministic component of Model II, there are other factors involved that are instrumental to granuloma growth such as migration of macrophages to the granulomatous structure. Model II demonstrated similar increases in average size and lognormal distributions, but failed to generate the increase in variability found in the data. In contrast, the stochastic component of Model II displays the linear increases in average size and variability, but not distributions of the data. Thus, further studies include honing the model so that encompasses both parametric variability as well as stochasticity.