Multicellular and Multiscale Models of Microbes and Host Systems

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Infection, host response and the occurrence of disease can be modeled as an emergent process resulting from the interaction of multiple cellular systems. Computational and experimental models enable concurrent spatiotemporal and biochemical modeling, monitoring and characterization of microbe-microbe and microbe-host interactions to understand bacterial communities and infection dynamics and outcome. We developed multiple in silico intracellular and multicellular models to probe the contribution of physiological, structural and biochemical processes in control, resolution or dissemination of bacteria in models of bacterial communities and mycobacterium infection. Using multiscale, agent-based models (ABM), we explored stress and various conditions that modulate the host immune response to infection. Informed by empirical characterization studies, models accounted for changes in the physiological environment of the host as well as the host intracellular environment. We highlight multiscale models including models of Mycobacterium tuberculosis (Mtb), an intracellular pathogen, that can adapt to changing environments within host phagocytic cells enabling persistence and proliferation during infection and onset of disease. Models are expanded to explore response in individuals with comorbidity such as chronic obstructive pulmonary disease (COPD) and tuberculosis. Computational studies demonstrated the importance of host comorbidities, physiology, microenvironment, and biochemical dynamics in modeling infection outcome.

References

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