Multiscale Models of Tissue Growth and Remodeling

Shayn M. Peirce-Cottler
Department of Biomedical Engineering, University of Virginia, Charlottesville, VA 22908, USA

Tissue growth and remodeling requires the dynamic interplay between intra- and inter-signaling, various cell behaviors, and tissue-level changes that feedback on one another. As high-quality and high-throughput biological data at multiple different levels of spatial scale (gene through tissue) become increasingly available, we are tempted to define the cause-and-effect biological relationships that span across spatial scales with greater mechanistic detail. Doing so provides an opportunity to probe, for example, how receptor-ligand interactions in the membrane of one cell impact the migratory behaviors of a neighboring cell, and, ultimately the mechanical properties of a remodeling tissue—and vice versa. Because these relationships are often complex, dynamic, and spatially heterogeneous, it becomes useful to employ multiscale computational modeling approaches that integrate biological phenomena in experimentally relevant ways. Agent-based modeling (ABM) can simulate the behaviors of individual cells within a tissue and has recently been positioned as a linker to continuum models at both lower and higher levels of spatial scale. In this talk, we will discuss some of the recent multiscale models that have coupled ABM with continuum modeling approaches at lower and higher levels of biological scale, including molecular level kinetics models of growth factor-ligand interactions and constrained mixture models of blood vessel biomechanics, respectively. We will focus on the conceptual methodologies that have underpinned how ABM were linked to other types of models, the technical challenges of interfacing other models with ABM, the types of simulation experiments that can offer insight, and the model validation approaches used in these examples.