Abstract:

When engineers design a solution to a problem, they start by making a model that can be used to test, refine, and optimize their solution. Models are especially helpful when designing for complex systems that change over time and have multiple components interacting at different length scales. The microcirculation is a complex and dynamic network of the body's smallest blood vessels that adapts to physiological and pathological stimuli. Physiological adaptations of the microcirculation include expanding (and regressing) to deliver more (or less) oxygen and nutrients to accommodate the changing metabolic demand of tissues. Disease can also invoke these adaptations and trigger other responses of the microcirculation that contribute to fibrosis. How the microcirculation changes in health and disease is governed by biochemical and biomechanical signals sensed by the cells that comprise the microcirculation–endothelial cells and pericytes. When cells are activated by these signals, they undergo phenotypic state changes such as differentiation, migration, and/or apoptosis. Our lab builds computational models to predict how molecular signals cause cell state changes that lead to expansion or regression of the microcirculation and/or contribute to tissue fibrosis. We validate our models with experiments and use them to design therapeutic interventions that can prevent disease progression–towards the ultimate goal of engineering the microcirculation back to a healthy state.