Skeletal muscles are extraordinarily adapted motors that enable us to perform many important functions, from walking to sight to speech. Thus, muscle dysfunction arising from muscle injury, atrophy, degeneration, fatty infiltration, and fibrosis present major health care problems. From a basic science perspective, we have a sophisticated understanding of the fundamental biology and mechanics of skeletal muscle. However, how these fundamentals relate to in vivo function and whole muscle adaptation is complex and remains poorly understood, which limits the translation of basic biological understanding to the development of effective treatments for muscle dysfunction. The goal of the Multi-Scale Muscle Mechanophysiology (“M3”) Lab’s research is to develop and experimentally validate multi-scale computational models of skeletal muscle that allow us to relate structure, biology, and function across a range of scales. We aim apply these models to answering questions related to the role of complex muscle biology and mechanics in a variety of contexts, including muscular dystrophy, muscle injury, and muscle regeneration. In this presentation, I will describe these approaches and present some recent examples of how computational models of muscle have led to new ideas and insights.