Abstract:

Muscles contract when the millions of myosin molecules contained within interact with actin filaments to generate filament sliding and force. Single molecule mechanical measurements made with optical traps provide detailed insights into the mechanics and chemistry of single actin-myosin interactions. However, the link between the discrete mechanics of single molecules and the smooth mechanics of muscle remains unclear. In contrast to conventional models of muscle mechanics, recent studies indicate that the basic mechanical behaviors of muscle emerge from cooperative and collective behaviors of the myosin molecules in muscle. We are developing continuous and Monte Carlo computer simulations of cooperative force generation to establish the unique predictions of this model. Using a combination of biochemical techniques and in vitro force and motility assays, we are experimentally testing these predictions. Our data support the collective force generation hypothesis and provide a new perspective on the basic mechanisms of muscle contraction in normal and disease states.