Biomolecular Site Dynamics
William S. Hlavacek
Theoretical Biology and Biophysics Group, Theoretical Division
Los Alamos National Laboratory

Biomolecules, such as proteins, generally comprise multiple functional components or sites. These sites, which are responsible for biomolecular interactions and their effects, undergo various types of state transitions. Understanding the dynamics of these state transitions is key to understanding cellular information processing and decision-making. Site dynamics can be captured using the emerging theoretical framework of rule-based modeling. In this talk, I will briefly review the principles and advantages of rule-based modeling and then discuss two examples of how rule-based modeling has been used to obtain insights into cellular regulatory systems. In the first example, a rule-based model was used to interpret mass spectrometry (MS)-based temporal phosphoproteomic data that characterize some of the earliest events in T cell receptor (TCR) signaling. The model and data together indicate that T cells use bang-bang control, fast activation followed by fast inhibition, to respond to TCR/CD28 co-stimulation through at least two distinct mechanisms. In the second example, a rule-based model was used to study the effects of APC truncation on function of the CTNNB1 (β-catenin) destruction complex in colorectal cancer cells. Analysis of the model indicates that inhibition of CSNK1E (CK1ε) could potentially reverse the oncogenic effect of APC truncation.