

Qualitative/Quantitative Analysis of Biomolecular Network Dynamics
Eduardo Sontag
Rutgers University

Abstract: Biomolecular networks, while exhibiting a rich variety of behaviors in signalling and regulation, would appear to be fairly well behaved as dynamical systems. Their (mathematical) models have solutions that tend to settle into well-defined steady states or periodic, but not "chaotic", behavior. This presents one major challenge to theoreticians: what is special about such networks, vis a vis general dynamical systems? A second challenge arises in the mathematical analysis itself: while on the one hand good qualitative, graph-theoretic, knowledge is frequently available, on the other hand it is often hard to experimentally validate the form of the nonlinearities used in reaction terms, and even when such forms are known, to accurately estimate coefficients (parameters, such as kinetic constants). This "data-rich/data-poor" dichotomy seems to be pervasive in systems biology. This theory talk is concerned with both challenges. We approach the problem through the standard paradigm in control theory and signal processing, that of viewing larger systems as interconnections of input/output subsystems: provided that these subsystems are individually well-behaved, more complex behaviors arise from the global interconnection structure. This brings up a host of issues, from basic issues of modularity, retroactivity, and input and output "impedance", to the characterization of classes of appropriately "simple" components, to the question of what type of quantitative information suffices for obtaining precise conclusions regarding dynamics (such as the existence of multiple stable steady states, or oscillations).

As one specific example, we consider order-preserving (monotone) components, which enjoy particularly nice dynamical properties as well as robust responses to perturbations. Their interconnections may be, in principle, studied through a blend of qualitative and (relatively sparse) quantitative information, allowing one to draw conclusions about global dynamical behaviour and the location of steady states. The talk will also present evidence suggesting that natural signaling and transcriptional regulation networks may be close to monotone, and that networks that are close to monotone are statistically better behaved than more arbitrary ones.

The website <http://www.math.rutgers.edu/~sontag> has references and online copies of papers with technical details.

MAIN PAPERS WITH UNDERLYING THEORY:

D. Angeli and E.D. Sontag. Monotone control systems. *IEEE Trans. Automat. Control*, 48(10):1684-1698, 2003.
http://www.math.rutgers.edu/~sontag/FTP_DIR/angeli-sontag-monotone-TAC03.pdf

D. Angeli and E.D. Sontag. Multi-stability in monotone input/output systems. *Systems Control Lett.*, 51(3-4):185-202, 2004.
http://www.math.rutgers.edu/~sontag/FTP_DIR/angeli_sontag_multistability_SCL04.pdf

G.A. Enciso and E.D. Sontag. Global attractivity, I/O monotone small-gain theorems, and biological delay systems. *Discrete Contin. Dyn. Syst.*, 14(3):549-578, 2006.
http://www.math.rutgers.edu/~sontag/FTP_DIR/enciso_sontag_DCDS06_galleys.pdf

