DEPARTMENT OF MATHEMATICAL SCIENCES

Colloquium

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Dynamic response phenotypes in systems biology: Scale-invariance and monotone I/O systems

ABSTRACT: Among the central questions in systems biology are those of understanding the roles of, and interactions among, signal transduction pathways and feedback loops. This talk focuses on "dynamic phenotypes" characterized by input/output responses to external inputs in addressing such issues, using fold-change detection and monotone architectures as case studies.

An ubiquitous property of sensory systems is "adaptation": a step increase in stimulus triggers an initial change in a biochemical or physiological response, followed by a more gradual relaxation toward a basal, pre-stimulus level. Adaptation helps maintain essential variables within acceptable bounds and allows organisms to readjust themselves to an optimum and non-saturating sensitivity range when faced with a prolonged change in their environment. It has been recently observed that some adapting systems, ranging from bacterial chemotaxis pathways to signal transduction mechanisms in eukaryotes, enjoy a remarkable additional feature: scale invariance or "fold change detection" meaning that the initial, transient behavior remains approximately the same even when the background signal level is scaled. This talk will review the biological phenomenon, and formulate a theoretical framework leading to a general theorem characterizing scale invariant behavior by equivariant actions on sets of vector fields that satisfy appropriate Lie-algebraic nondegeneracy conditions. The theorem allows one to make experimentally testable predictions, and the presentation will discuss the validation of these predictions using genetically engineered bacteria and microfluidic devices, as well their use as a "dynamical phenotype" for model invalidation. The talk will also include some speculative remarks about the role of the shape of transient responses in immune system self/other recognition and in cancer immunotherapy, as well as a brief discussion of how control-theoretic structures such as differential positivity (monotonicity) have been experimentally employed together with experimental data in order to elucidating mechanisms for stress responses and chemosensing.

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