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Multistationarity and Oscillations in Biochemical Reaction Networks

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ABSTRACT

This project focuses on two of the most important behaviors in biological dynamics, playing key roles at all scales, from molecular to cellular, to tissues and organisms. Multistationarity refers to the capacity of a system to operate at alternative steady-states, and is observed experimentally as irreversible switch-like behavior; oscillatons are periodic variations in the concentration of interacting elements (genes, metabolites, enzymes, etc). The interplay of multistationary and oscillatory behavior underlies crucial physiological processes: cellular division, differentiation and apoptosis, cellular signaling, enzyme regulation, circadian rhythms, and membrane potential activity in neurons and heart cells are only a few examples. Many diseases involve disturbances of these processes as a result of deregulation of multistationary and oscillatory behaviors in specific gene networks or biological pathways. A better understanding of the two behaviors may lead to developments in the study of such diseases. In this project, the investigator will create mathematical tools and software that will allow biochemical and biomedical scientists to analyze dynamical features of relevant biological systems.

The emergence of multistationarity and oscillation is intimately linked to the existence of feedbacks and to other subtle features of the structure (i.e. wiring diagram) in the underlying reaction network of interacting elements. Design principles associated to multistationarity and oscillations have long been proposed and refined over the years, but there is not yet a complete picture of the relationship between structure on one hand and multistationary or oscillatory behavior on the other. In this project, the investigator develops new mathematical theory and expand existing results to strengthen our understanding of this connection. In particular, algorithms will be developed to identify key structural properties of biochemical reaction networks that give rise to multistationarity and oscillation. These developments will be implemented in user friendly, open source software, to assist and complement theoretical and experimental work in biochemical and biomedical fields. For example, in a joint effort with experimental collaborators, the investigator will analyze the ERBB network of receptor tyrosine kinases whose multistable behavior is involved in early events in cancer onset. This work also opens up exciting possibilities in bioengineering for the design of reaction networks with prescribed properties, relevant to research in cellular differentiation and with applications to tissue engineering and drug development.