Hamilton Institute

Systems Approaches to Robustness Analysis of Circadian Oscillators

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Tuesday, August 22nd, 2006

Abstract: Our research is focused on unraveling the regulatory architectures of complex biological systems. As gene-level architectures become known, the open challenge is to assign predictable behavior to a known structure, the so-called "genotype-to-phenotype" problem. In response to this challenge, the discipline of systems biology has emerged with an integrative perspective towards determining complex systems behavior. A property of particular interest is the /robustness /of the biophysical network: the ability to maintain some target level of behavior or performance in the presence of uncertainty and/or perturbations. In biological systems, these disturbances can be environmental (heat, pH, etc.) or intrinsic to the organism (changes in kinetic parameters). While preliminary results are available for simple (low-dimensional, deterministic) biological systems, general tools for analyzing these tradeoffs are the subject of active research.

In this talk, a number of quantitative tools from systems theory will be presented as enabling methodologies for unraveling robust biological regulatory systems, with an emphasis on sensitivity analysis. Our work on the regulatory architecture responsible for robust maintenance of 24h cycles is used to motivate the approaches. At the gene regulatory level, it is shown that performance attributes, notably phase timing, are controlled in a robust manner. At the next level in the hierarchy, it is shown that synchrony is achieved in populations of neurons to enable clock precision. Finally, at the level of the organism, it is shown that an optimal control approach can be used to reset the clock using a light stimulus.

Venue: Seminar Room, Hamilton Institute, Rye Hall, NUI Maynooth

Time: 2.00 - 3.00pm (followed by tea/coffee)

Travel directions are available at www.hamilton.ie

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