BIOINFORMATICS SEMINAR

Metabolic pathway analysis for assessing network complexity, robustness and control

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Abstract:

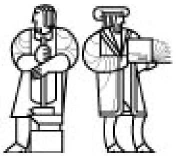
A major current challenge in biology is to clarify the relationship between structure, function and regulation in complex cellular networks. Metabolic pathway analysis offers the possibility to discover and analyse meaningful routes in metabolic networks. It thus implies a transition from a reaction-based perspective of metabolism to system-wide investigation of structural network properties.

In the first part of the talk, concepts and tools for pathway analysis will be discussed, in particular the characteristics and determination of elementary flux modes. Elementary flux modes can be defined as the smallest sub-networks enabling the metabolic system to operate in steady state. These entities enable one to investigate the space of all physiological states that are meaningful for the cell. Determination of elementary modes is a highly combinatorial problem, and requires sophistic computational tools. The FluxAnalyzer, which is a user-friendly software package facilitating integrated pathway and flux analysis for metabolic networks within a graphical user interface, will be presented.

The second part of the talk will focus on applications of elementary-mode analysis. An integrative analysis of elementary modes can be used to reconstruct key aspects of cellular behaviour from metabolic network topology, namely to reliably classify the effects of gene deletions, to analyse network robustness and flexibility, and to quantitatively predict functional features of genetic regulation. More generally, it could be shown that robustness of metabolic networks is linked to redundancy, and that hierarchical genetic control supports this robustness by finding a trade-off between network efficiency and flexibility.

Thus, elementary-mode analysis can provide a suitable method for the analysis of organization and functionality of metabolic networks requiring - in contrast to dynamic mathematical modelling - only network topology, which is well-known in many cases. Implications of the biological findings for purpose-driven manipulation of metabolic network functionalities, for instance by drugs, will be discussed as well as potential applications of metabolic pathway analysis in finding (and understanding) suitable targets for manipulation.

Monday May 19, 2003
11:00 a.m. – 1:00 p.m.
(Talk starts at 11:30)
Building NE43, Room 941
Refreshments at 11am in NE43-941 *(LCS, 200 Tech Square, Cambridge, MA)*



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