3.24 What does it cost to be flexible? A constraint based approach to modelling a micro-organism in a changeable environment

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Constraint based modelling is a widely used methodology used to analyse and study biological networks on both a small and whole organism (genome) scale. Typically these models are underdetermined and constraint based methods (e.g. linear, quadratic optimization) are used to optimise specific model properties. This is assumed to occur under a defined set of constraints (e.g. stoichiometric, metabolic) and bounds (e.g. thermodynamic, experimental and environmental) on the values that the solution fluxes can obtain.

Perhaps the most well known (and widely used) analysis method is Flux Balance Analysis (FBA) where for a model a target flux is maximised (typically a flux to biomass) where the other input/output fluxes have been bound to simulate a single set of defined environmental conditions. However, in the wild, such an organism may experience continuous changes in state that arise from sources either externally (e.g. a change in nutrient supply) or internally such as a mutation (deletion) in a particular gene which leads to a concomitant loss of (or large change in) cellular function.

In this presentation I will be discussing how we are attempting to extend established constraint based approaches to include micro-organisms living in a changeable environment. The question of what an organism can do in order to become more (or less flexible) in such an environment has necessitated the development of new theory, models, software tools and even a proposed standard for model exchange.

3.25 Rule-based modeling and application to biomolecular networks

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Modelers of molecular signaling networks must cope with the combinatorial explosion of protein states generated by post-translational modifications and complex formation. Rule-based models provide a powerful alternative to approaches that require an explicit enumeration of all possible molecular species of a system. Such models consist of formal rules stipulating the (partial) contexts for specific protein-protein interactions to occur. These contexts specify molecular patterns that are usually less detailed than molecular species. Yet, the execution of rule-based dynamics requires stochastic simulation, which can be very costly. We briefly introduce some recent results on a formal abstract interpretation-based method to convert a rule-based model into a reduced system of differential equations and highlight actual research directions.