Daniel Kahn: The MetaGenoReg project

The MetaGenoReg project Speaker Daniel Kahn (INRIA HELIX) Slides PDF

Abstract Most biological responses involve both metabolic regulation, depending on enzyme kinetic properties, and gene regulation, resulting in adjustments of enzyme concentrations. Gene regulation is affected by metabolite concentrations and, conversely, changes in gene expression affect metabolic activities. Therefore a genuine understanding of cellular regulation requires the embedding of gene regulatory networks in cellular metabolism. However we are missing a scalable methodological framework for precisely understanding how gene and metabolic regulation cooperate in a biological response. Here I will give an outline of a project that we have just initiated towards such a methodology. In a first stage, we will construct a benchmark model based on ordinary differential equations reflecting classical enzyme kinetics. Usually different types of approximations are employed for metabolic and gene regulation. While the characteristic response of the former is generally gradual and can be approximated by various linearisations, the responses of the latter are often much steeper, implying an approximation with step functions. We will therefore investigate the feasibility of composite models combining these approximations, integrating both types of regulation into a simplified model. The benchmark model will serve to assess the quality of these reduction methods and approximations. Methods validated on the benchmark model will be further applied to model a well-defined adaptation, the glucose-acetate diauxie in E. coli, for which both metabolic data and gene expression data will be collected. The resulting simplified model should allow us to evaluate the contributions of metabolic and gene regulation, both qualitatively in terms of dynamical behaviour and quantitatively in terms of regulation coefficients. It will provide insight into the biological rationale underlying the distribution of regulation between metabolic and gene regulation. We thus hope to predict to what extent metabolic and gene regulation may or may not be interchangeable.