

Validating Inferred Gene Networks using ODE Models of Regulation Dynamics

Kamil Erguler, Paul Kirk, Sophie Lèbre, Tina Toni, Michael Stumpf

Inferring gene regulatory networks from expression data remains one of the most important and challenging problems in bioinformatics and systems biology. Traditionally, validation of inferred networks is performed by comparison with experimentally identified true networks: if the inferred network (or, more generally, one of its subnets) accurately describes known biological behaviour, then we will have a greater degree of belief in its validity. However, inferred networks typically predict many new interactions that have not previously been observed.

Verifying each of these predictions experimentally would be a difficult, time-consuming, expensive, and ultimately tedious, task. We here present a data-driven method for validating inferred gene regulatory networks. In the first stage of our work, we infer a regulatory network from time-course mRNA expression data. Assuming the inferred network to be correct, we propose a parametric ODE model to link the observed mRNA expression levels with the hidden transcription factor activity. In the second stage, we infer the parameters of our ODE system and then assess how well the resulting model describes the dynamic behaviour of the observed expression data. A good description of the data would lend support to the validity of both the inferred network and the ODE model, while a poor fit would suggest a reformulation of the model at some level. The value of this approach is illustrated by applying it to yeast gene expression data.