Inferring Stable Genetic Networks from Steady-State Data

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Gene regulatory networks capture the interactions between genes and other cell substances, resulting from the fundamental biological process of transcription and translation. In some applications, the topology of the regulatory network is not known, and has to be inferred from experimental data. The experimental data consist of expression levels of the genes, which are typically measured as mRNA concentrations in microarray experiments. In a so called genetic perturbation experiment, small perturbations are applied to equilibrium states and the resulting changes in expression activity are measured. This paper develops novel algorithms that identify a sparse and stable genetic network that explains data obtained from noisy genetic perturbation experiments. Our identification algorithm is based on convex relaxations of the sparsity and stability constraints and can also incorporate a variety of possible prior knowledge of the network structure. Such knowledge can be either qualitative, specifying positive, negative or no interactions between genes, or quantitative, specifying a range of interaction strengths. Our approach is applied to both synthetic and experimental data, obtained for the SOS pathway in Escherichia coli, and the results show that the stability specification not only ensures consistency with the steady-state assumptions, but also significantly increases the identification performance. Due to its convex nature, our method can be efficiently applied to large scale networks.

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