Recognizing the Relevance of Change: Analysis and Control of Time-evolving Networks in Epidemiology and Evolutionary Medicine

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Analysis of Time-evolving Networks by Sequential Monte Carlo

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Abstract

Most current methods used for gene regulatory network identification are dedicated to inference of steady state networks which are prevalent over all time instants. However, gene interactions evolve over time. Information about the gene interactions in different stages of a life cycle is of high importance for biology in understanding of protein production, human diseases and in designing personalized treatment plans.
A large amount of gene expression data measured at a single time instant can be found in the literature. Only a limited amount of sources present experimental data on temporal sequences for gene expression, for example during the yeast cell cycle and the life cycle of Drosophila Melanogaster. However, for most of them only one temporal sequence dataset is available for each gene. Moreover, all experimental data are measured for a short time period. This lack of experimental data significantly limits the success of inference on network topology.
In the statistical graphical models literature one can find a number of methods for studying steady-state network structures while the study of time varying networks is rather recent. A sequential Monte Carlo method namely particle filtering (PF) provides a powerful tool for dynamic time series analysis. In this work, the PF technique is proposed for dynamic network inference and its potentials in time varying gene expression network tracking is demonstrated. The data used for validation are synthetic time series data available from the DREAM4 challenge, generated from known network topologies and obtained from transcriptional regulatory networks of S. cerevisiae. We model the gene interactions over the course of time with multivariate linear regressions where the parameters of the regressive process is changing over time The proposed model tracks the interactions not only from the one step past but also interactions with a delay of n-time steps which is a realistic scenario for gene interactions in general.
We would like to stress that the proposed methodology is applicable in any type of time varying network including various other biological processes where variables evolve in relation to each other. The method is easily extendable to model nonlinear interactions.