NETGEM: Network Embedded analysis of Temporal Gene Expression using Mixture models

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Associate Editor: XXXXXXX

ABSTRACT

Motivation Temporal analysis of gene expression data has been limited to identifying genes whose expression varies with time and/or correlation between genes what have similar temporal profiles. Often, the methods do not consider the underlying network constraints that connect the genes. In addition to identifying changes in the genes, it is becoming increasingly evident that interactions change substantially. Thus far, there is no systematic method to relate the temporal changes in gene expression to the dynamics of interactions between them in the context of a regulatory network. The availability of this data opens up possibilities for discovering new mechanisms of regulation and provides valuable insight into identifying time-sensitive interactions. Furthermore, such a framework would also allow for studies on the effect of a genetic perturbation on the dynamics of the interactions.

Results We present NETGEM, a tractable model rooted in Markov dynamics, for analyzing temporal profiles of genetic expressions arising out of known protein interaction networks evolving with unknown dynamics. The model treats the interaction strengths as random variables which are modulated by suitable priors. This approach is necessitated by the extremely small sample size of the available observations. The model is amenable to a linear time algorithm for efficient inference. When applied to real data NETGEM was successful in identifying (i) temporal interactions and determining their strength, (ii) functional categories of the actively interacting partners and (iii) dynamics of interactions in perturbed networks.

Availability: The source code for NETGEM is available from http://www.sysbio.se/BioMet

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