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Inference of Topological Features of Gene Regulation Networks by Neural Nets

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Understanding the large-scale structures of gene regulation is fundamentally important in biology. Topological models such as exponential networks [1], scale-free networks [2], and small-world networks [3], have been used to describe topological features of various naturally occurring systems. Recent analysis of network properties of known biological networks have shown that they often display scale free features [4-5], but it is not yet clear whether these results apply to all biological networks. This work addresses the problem of inferring topological features of gene regulation networks from data that are likely to be available from current experimental methods, such as DNA microarrays. The challenge is that only limited information on actual biological pathways and their connectivity is available. To overcome these limitations and to expand the knowledge of biological network topology, we propose a novel method for network topology inference from microarray data. The proposed method uses observable features, including histograms of perturbation propagation, to train neural nets to predict features of the topology of the underlying gene regulation networks. A model based on the Boolean genetic network is used to provide theoretical grounds for the proposed inference method. Current results with simulated data are encouraging: A trained neural network has successfully classified class of topology as random (exponential) or scale-free with 90% accuracy [6]. In addition, we show neural nets can estimate the mean input connectivity parameters of networks with a small root mean squared error. The proposed method is expected to be more robust than previously proposed network connectivity inference methods that are often problematic with noisy microarray data. Furthermore, we show that the *perturbation data* required for the proposed method can be obtained without actual perturbation experiments such as knockout experiments that are not feasible in human framework.

References

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