Function constrains network architecture and dynamics: a case study on the yeast cell cycle Boolean network

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***Short Abstract* — We develop a general method to explore how the function performed by a biological network can constrain both its structural and dynamical network properties. This approach is orthogonal to prior studies which examine the functional consequences of a given structural feature, for example a scale free architecture. We illustrate the methods in an analysis of the yeast cell cycle cascade. This analysis uncovers strong constraints on the architecture of the cell cycle regulatory network as well as significant selection pressures on this network to maintain ordered and convergent dynamics, possibly at the expense of sacrificing robustness to structural perturbations.**

I. Introduction

There exists a large body of theoretical work exploring how the structure of a biological network constrains the range of functions, or types of dynamical behaviors, that it is capable of producing. The observation that many biological networks are scale free spurred a flurry of research into the dynamical consequences of the scale free structural feature [1–5]. A principal finding was that the scale-free architecture is more robust to random failures and dynamic fluctuations, and may be more evolvable.

The alternative question, that is, how the requirement of carrying out a specific function constrains the structural and more general dynamical properties of a network, remains relatively unexplored [6–8]. It is an important question because many biological functions are performed by relatively small network modules for which mean connectivity, or any kind of degree distribution, scale free or not, do not have a clear significance. A key example is the yeast cell cycle control network [9] that demonstrated a great deal of robustness of the cell cycle trajectory to perturbations of network structure despite the small network size. Is this robustness carefully selected for through evolution and encoded somehow in the topological structure of the cell cycle network, or does it arise for free, simply as a consequence of the functional constraint of having to produce the long cascade of gene expression that controls the cell cycle?

II. Results and Discussion

Using our analysis methods, we showed that positive feed-forward and negative feed back interactions are required to produce the cell cycle trajectory. We demonstrated that certain dynamical features, e.g. a large attractor state, high degree of convergence of trajectories, long transient times, and chaotic behavior on short time scales, arise purely as a consequence of performing the cell cycle function.

We also observed that the actual yeast cell cycle network is relatively less robust against structural perturbations but displays a higher degree of dynamical order on short time scales (robustness against noise) compared to an ensemble of networks that can produce the cell cycle trajectory. This suggests that there may be a tradeoff between ordered dynamics and structural robustness. Evolution may have favored a design that is ordered and less sensitive to fluctuations in the states of the nodes, by sacrificing robustness against perturbations to the network structure.

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