Form, Function, and Information Processing in Small Stochastic Biological Networks

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***Short Abstract* — We present an information-theoretic approach to quantitative comparison of signal processing in small networks of varying topology. Restricting ourselves to computational experiments using the experimental setup employed by Guet [1], we first quantify the ability of a network to transduce chemical information into genetic information (and the extent to which topology thwarts or enhances this transduction). We then investigate the extent to which similar (either parametrically or topologically) networks perform similar function. A key component of our analysis is framing the question in a way that does not assume which particular function a particular network is designed for, but rather allows this to be determined by optimal information processing.**

***Keywords* — Information theory, linear noise approximation, synthetic biology, systems biology**

I. Purpose

A topic of much discussion in the systems biology literature in the past half-decade has been the significance --- both statistical and biological --- of the topology of small biological networks. Most comparisons of the quality of such networks rely on some assumption of their preferred function or behavior. If one instead wishes to establish whether a particular network may support multiple behaviors, one must instead study the network using a function-independent measure. Employing an information-theoretic approach, we define such a measure and study the extent to which the topology and parameters of a network constrain its function or set of possible functions.

We find that all considered networks can exhibit surprisingly high fidelity (are able to transduce more than "on/off" information), despite the intrinsic noise imposed by the physics of small molecule copy numbers. These fidelities are well above the usual one-bit description employed by the majority of molecular biology literature. Topology of networks has minor effect on this fidelity, in a way that can be related (computationally and analytically) to the overall coherence of the regulation. All topologies are able to perform a variety of the possible functions, allowing us to quantify the extent to which similar networks (either in terms of parametric similarity or topological similarity) perform similar functions. In this way, the extent to which form dictates or even constrains function may be defined and quantified.

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II. Model and Methods

The experimental setup considered is that of Guet [1], in which small transcriptional regulatory networks are considered, such that each gene is (possibly auto-) regulated by only one transcription factor. The efficacy of these transcription factors is itself influenced by the presence of small molecules (e.g., in the experiment, aTc and IPTG). These chemical "inputs" (i.e., presence or absence of the small molecule) influence a genetic "output" (i.e., the steady state concentration of the "final" gene in the network). We consider networks in which either two or three small molecules may be introduced, or equivalently, in which either 2 or 3 bits of chemical information can be transduced into genetic information.

The dynamics are specified by standard Hill kinetics, with the additional feature that the effective abundance of the transcription factor is mollified by a scaling factor when the associated small molecule is present. The resulting deterministic dynamical systems yield fixed points that determine probability distributions (centered at these fixed points) by employing the linear noise approximation (as is well-studied in the systems biology literature [2]).

III. Form, Function, and Information Processing

We first show that such dynamics need not be binary, i.e., that even at small copy number, more than "on/off" communication may be employed. We then show the extent to which topology, copy number, and the relative reaction rates limit the information transmission. Finally we quantify the parametric and topological evolvability of these networks by measuring the extent to which similar parameter values and similar topologies can be related to similar functions. We relate the results to the oft-discussed "cross-talk dilemma" and illustrate how such analyses can predictively guide the design of future experiments in synthetic biology.

References

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