Robustness and modular design of the *Drosophila* segment polarity network

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***Short Abstract* — Robustness is compulsive for biological molecular networks and may cast effect on network topologies. We carried out an exhaustive computational analysis on network topologies in relation to a patterning function in *Drosophila* embryogenesis. We found that a small fraction of topologies emerges particularly robust for the required function. The topology adopted by *Drosophila* is a top ranking one among all topologies without direct self-regulation. Furthermore, we found that all robust topologies are modular.**

***Keywords* — Network, Function, Topology, Modularity.**

Biomolecular networks have to perform their functions robustly. A robust function may have preferences in the topological structures of the underlying network [1]. We can ask for a given function, how many distinct network topologies can perform the function and how many can do so robustly? What are the key features among these robust topologies—what are common and what are variable? How would nature pick among them? To address these problems, we carried out an exhaustive computational analysis on network topologies in relation to a patterning function in *Drosophila* embryogenesis.

The function studied here was chosen to be a well-defined patterning function in *Drosophila* embryogenesis, which is highly conserved among all insets, that of setting up a stable periodic pattern of gene expression that defines the sharp boundaries between parasegments (Figure 1E, F). The biochemical network responsible for the function is called segment polarity network (Figure 1A)[2]. This functional module has been proved to be robust [3][4]. We use ODE model to enumerate all the possible topologies for networks with only 3 nodes. We found that whereas the vast majority of topologies can either not perform the required function or only do so very fragilely, a small fraction of topologies emerges as particularly robust for the function. A tight relationship can be built between biology network and the simplified models (Figure 1A&B, C&D). The topology adopted by Drosophila, that of the segment polarity network, is a top ranking one among all topologies with no direct autoregulation (Figure 1D). Based on the simple model, we may "predict" missing links in previous model, slp represses mid represses wg and wg activates slp in Figure 1C, which is currently know in biology. Furthermore, we found that all robust topologies are modular—each being a combination of three kinds of modules. These modules can be traced back to three subfunctions of the patterning function, and their combinations provide a combinatorial variability for the robust topologies. Our results suggest that the requirement of functional robustness drastically reduces the choices of viable topology to a limited set of modular combinations among which nature optimizes its choice under evolutionary and other biological constraints.

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