How to Achive Perfect Adaptation

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Short Abstract —**Understanding design principles of certain biological function is an amazing task. Adaptation is our best candidate to study. First, we analyzed and enumerated topologies for gene regulatory process with three regulatory rules to find those adaptive ones. Second, we evolutionally searched adaptive topologies with more than three nodes for enzymatic reactions. We found two kinds of three-node topologies are adaptive and they partly differ from that of enzymatic ones; 15 four-node topologies are adaptive, and a coherent feed-forward loop coupled with a negative feedback loop emerged as a totally new one. Our study may provide a design table for adaptive circuits for different network size and biologoical processes.**

Keywords — **Design principle, Adaptation, Transcriptional regulation, Enzymatic reaction, Three node, Four node.**

I. INTRODUCTION

IN the quantitative era, with the huge accumulative experimental data. We need a simplified way to try to approach the underlying mechanism while every single perturbation may cause an inconvenient phenotype change of the complex biological networks. On one hand, a very exciting indication from previous studies really lightens the way [1]: *There should be a limited group of network motifs to execute certain functions*. On the other hand, small network is no doubt to achieve related function while its sufficiency to present complex biological system remains unclear due to the ignorance of many details and feature of the systems. So if we extend the small network to even one more node larger, will something new emerge? We chose adaptation as the best candidate function to study the network design principles because of its universality and clear mathematical definition.

II. TOPOLOGIES FOR ADAPTATIVE PROCESSES

First of all, despite the fact that enzymatic topologies for adaptation have been investigated systematically, the topologies for gene regulatory networks that are capable of adaptation are still unknown, due to the complexity of transcriptional regulations. For simplicity, we model transcription as a Hill function with three kinds of logics: AND logic(multiplied all the activation and repression terms); AND&Additive rule(taking he average effects of all the activation terms and multiplying the product of all repression terms); Competitive repression(the repressors merely decrease the effect of activators instead of blocking gene expression, and gene expression becomes weaker in the absence of repressors). From linear analysis and

simulation, we conclude that: 1) neither one- nor two-node (separate input and output nodes) topologies adapted perfectly; 2) three-node topologies that were capable of perfect adaptation fell into two classes, NFBLs(negative feedback loops) and IFFLs(incoherent feed-forward loops). However, some new skeletons emerged compared with enzymatic reactions, due to the consideration of complex regulatory rules and the degradation of gene products. Most important, all the NFBLs must have an auto-activation on buffer node B working in its linear region with Hill coefficient equals to 1. For the IFFLs, an inversed proportional mechanism breaks the necessity of proportional mechanism for enzymatic topologies and two new types of IFFLs are also feasible for perfect adaptation in gene regulatory networks.

Next, we evolutionally[2] searched enzymatic topologies with more than three nodes that can adapt. We found a mechanism that when the output node is catalyzed by enzymes which are proportional to each other in their steady states, the output node will be independent of input signal and then achieve perfect adaptation. We then explored the simplest proportional network motifs, and used the motifs as blocks to build networks with more nodes in which such motifs are coupled. Primarily, we started to build four-node networks which can be analytically handled. We found 15 four-node adaptive networks, and a totally new one emerged: A coherent feed-forward loop does not achieve adaptation by itself, but it is capable with the help of a negative feedback loop. This new one works as an "anti-spring" -firstly transmitting signal synchronously with input, while then giving an anti-response and make the coherent feed-forward loop capable of adaptation with the help of a negative feedback loop.

III. CONCLUSION

In this study, we systematically approached the design principles of adaptive networks involving in gene regulations and enzymatic reactions with different network size. Through this kind of study, we can help synthetic biologist build the functional tools they want and get closer to a dream that we may make a biological machine as electronic industry developed. Meanwhile, there still are questions afterward our study: How does God design a complex system with multifunctional modules? Follow these studies, we may get a clear clue about how nature designs.

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