Modulation of a genetic toggle switch by a downstream load

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Short Abstract — **In order to exploit synthetic biology's potential, we need to understand the effects of connecting network modules to downstream loads. We examined the behavior of a genetic toggle switch under various loading methods, studying the effects on the phase diagram, dynamic properties, and stochastic properties of the switch. We discovered a linear relationship between the rise- and decay-times and load and an exponential relationship between amount of inducer necessary to transition states and load. We used stochastic simulations to investigate the effect of load on noise-induced transitions between states, finding large differences in lifetime of the system in a given state depending on load.**

Keywords — **Synthetic biology, genetic toggle switch, retroactivity, modularity, stochastic simulations,**

I. Background

The properties of biochemical networks are affected by the interactions that the output of the network has with downstream elements, leading to the discovery that downstream components can change the dynamic and static properties of the upstream circuit without explicit feedback [1-3]. Understanding the properties of network modules connected in different ways to downstream components, i.e. a "load", is therefore necessary before we can reliably use these modules as parts of larger synthetic biology circuits. With this aim in mind, we studied the behavior of a simple genetic toggle switch [4] which has been used to build more complex synthetic biology networks [5].

II. Results

We applied a load to the toggle switch by allowing the two outputs of the toggle switch to reversibly bind to a downstream protein. This situation could arise, for example, when the toggle switch is connected to another network module. We simulated various loading methods, i.e. on either one or both of its outputs. We studied the effects on the phase diagram, the dynamic properties, and the stochastic properties of the switch.

A. Rise and Decay Time

We used deterministic simulations to calculate the rise-time and decay-time for transitioning into and out of a given repressor state. We find that there is a linear relationship between rise-time and load as well as between decay-time and load. The slope of this relationship increases when a load is applied to both outputs.

B. Inducer Required to Transition States

We used deterministic simulations to calculate the amount of inducer necessary to transition from a starting repressor state to the other repressor state. We find that there is an exponential relationship between the amount of inducer required to transition between states and the amount of load on the system. This relationship is independent of loading method.

C. Noise-Induced Switching

We lastly investigated the effect of a load on noise-induced transitions [6] between states using stochastic simulations. We found that the lifetime of the system in a given state follows an exponential distribution in the absence of a load. This distribution becomes significantly skewed in the presence of a load. In addition, there is a sharp increase in the average lifetime in the repressor state without the load when load is applied to one side; the load effectively stabilizing the switch.

III. Conclusion

The dynamic and stochastic properties of a simple genetic toggle switch change in the presence of a load. The changes are dependent upon amount of load and loading method (one or both outputs). Our simulations point out the necessity of incorporating the effects of a load when designing synthetic biology circuits.

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