Development and validation of a synthetic signaling system model

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Short Abstract —**Synthetic biology systems are becoming more complex, both in numbers of biological parts and in terms of the organism they are deployed in. As complexity increases, models of component interaction will play an increasingly important role in developing synthetic systems. We developed a predictive model of an existing synthetic signaling system and explored the parameter space with the goal of optimizing the response. The model suggested that increasing the ratio of input protein to transmission protein would impact sensitivity and signal-to-noise ratio. Experimental work has revealed unexpected variability in the dynamic range, leading us to re-evaluate our model**

***Keywords* — synthetic signaling system, model validation**

I. Background

SYNTHETIC biology strives to engineer systems using components that are modular (i.e., the individual parts can be easily interchanged) and orthogonal (i.e., independent of host interactions)[1]. As these systems become more complex, both in numbers of biological parts and in terms of the organism they are deployed in, the ability to model interactions between components will play an increasingly important role in the development of synthetic systems[2].

II. Abstract

As a Research Assistant/Graduate Student in June Medford's laboratory at Colorado State University, and in collaboration with the Prasad Lab, I am developing a working model of a synthetic signaling system and validating that model with experimental data in bacteria.

A. Synthetic Signaling System

The synthetic signaling system, developed by the Medford laboratory, relies on an "input," a ligand-binding protein that develops high affinity for the extracellular sensing domain chemotactic transmembrane protein[3]. This extracellular sensor domain is fused to an intracellular histidine kinase, resulting in a "transmission" component that moves the signal from the exterior to the interior of the cell. The signal takes the form of a high energy phosphate, which is transmitted to a relay and activation protein. This phosphorylated protein binds to a synthetic promoter, inducing expression[4].

The synthetic histidine kinase signaling system is modular, allowing us to change input, transmission, and response components in order to optimize the system or expand sensing capabilities.

B. Model Development

We used MATLAB SimBiology to build a model capable of predicting the behavior of the synthetic system in response to various inputs [5]. We then explored the parameter space and isolated the parameter which would have the greatest impact on the signaling system, the "input" protein. An increase in "input" protein while all other components were held steady was predicted to increase sensitivity and the signal-to-noise ratio of our signaling system.

C. Model Validation

By manipulating the expression of this protein with promoters of varying strengths, we can measure the response of the system over a range of "input" protein concentrations and thereby validate the model and the assumptions that underlie it.

III. Conclusion

Preliminary experimental data from bacteria suggest that increasing the amount of input protein may indeed have the predicted impact on the system. However, experimental work has also revealed unexpected variability in the dynamic range, leading us to re-evaluate our model.

A functional predictive model will solidify our understanding of the system and strengthen subsequent modeling efforts. Our experimental work used to engineer the synthetic system in bacteria can also be extended to plants due to evolutionary conservation of the histidine kinase signaling system.

References

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