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Article 2

1. Describe any validations the authors showed in the paper.

This paper introduces a model of a bi-stable genetic toggle switch as a potential regulatory component for gene regulatory circuits and tests their model by implementing it on E. coli plasmids. For validation, the authors constructed two classes of plasmids which are switched by different compounds, and for each class there were different variants to test for bi-stability.

They tested the bi-stability behavior to see how varying the concentration of the inductor would change the end concentration of the genes they encoded and compared it with theoretical curves in Figure 5a. The data from the control group was completely in range of the theoretical curve, but the toggle group behavior did not match with its theoretical curve. The theoretical curve doesn’t capture the bi-stable behavior that the authors intended, while the experimental data did.

This was the only comparison between their mathematical model and their experimental results.

1. How do these validations affect your level of certainty for any of the main conclusions of the paper?

The main conclusions from this paper are (1) confirmation of the feasibility of this toggle switch and (2) that it’s reasonable to use these models to design complex gene behaviors. From the data, the researchers showed a clear toggle switch system, so my level of certainty for their first conclusion is high. While they stated there was “reasonable agreement between the toggle theory and experiment,” I observed a large disparity between the theoretical behavior and the experimental data and therefore have low certainty that this modeling approach can be used to accurately represent complex gene behaviors.