Prototype Diverse Synthetic Biological Circuits in a Cell-Free Transcription-Translation System

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Synthetic biological circuits are the foundation for the ultimate goals of controlling cells and building artificial cells from the ground up. To get closer to these goals in a more efficient way, we utilize a cell-free transcription-translation system to help perfect biological circuits for the simplicity, freedom, and convenience that the system offers. In this work, we demonstrate three distinct aspects of biological circuits in a cell-free transcription-translation system: circuit dynamics, phosphorylation, and membrane proteins. We start with a simple feedforward circuit, which shows dynamic responses to the input. We first prototype the feedforward circuit in the cell-free system with the aid of mathematical modeling. Then, based on the knowledge learned from prototyping, we successfully implement the circuit in cells. Not only do we show that a circuit with dynamics can be prototyped in the cell-free system, but we also test a more complicated circuit involving a phosphorylation cycle. The phosphorylation-based insulator circuit is prototyped and then a model created for the circuit is shown to be identifiable in the cell-free system. To further expand the capability of the cell-free system, we demonstrate that biologically active membrane proteins can be generated in the cell-free system with engineering, suggesting that even biological circuits requiring membrane proteins can be prototyped in the system. These results help advance our knowledge of both biological circuits and the cell-free transcription-translation system, and bring us one step closer to our ultimate goals of implementing full control in synthetic cells.

Keywords: Synthetic biology, Biological circuits, Cell-free systems, Membrane proteins.

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Research interest: Our group is interested in using cell-free systems to assist the research in Synthetic Biology. We use a cell-free system to prototype biological parts and modules, with the goals of building and optimizing biological circuits and metabolic pathways. We are also exploring combining cell-free systems with protein engineering to generate more robust macromolecular machines.