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SYNTHETIC BIOLOGY

Simplifying design

Synthetic biological devices hold great potential for many biotechnological applications. However, the functional complexity of synthetic devices has been limited by the available design tools. An advance is presented in a paper that demonstrates a computer-aided approach for designing RNA-based devices with predictable functional properties in *Escherichia coli*.

Carothers *et al.* designed expression devices based on two naturally occurring control systems: ribozymes and aptazymes (aptazymes are ribozymes that are controlled by the binding of a ligand). A ribozyme or aptazyme can be engineered to be transcribed in the mRNA of a gene of interest, where it catalyses self-cleavage of the transcript and thus variably regulates expression. The design process used biochemical and biophysical modelling to take into account the many variables — such as rates of RNA folding or catalysis — that can alter the functional output of the device. Importantly, the authors showed that devices that achieved a wide range of expression levels could be obtained by tuning just a few of the design variables.

The authors tested the predicted output from their designed devices by using them to control the production of red fluorescent protein in *E. coli*; the predicted and observed expression levels were closely matched. They went on to show the use of the designed devices in controlling the metabolic flux of a chemical that is a precursor for bioactive compounds: namely, 2-*p*-aminophenylalanine.

These approaches for design and experimental testing could be extended to develop systems that control large numbers of genes, or they could be used to explore natural RNA activities.

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ORIGINAL RESEARCH PAPER Carothers, J. M. *et al.* Model-driven engineering of RNA devices to quantitatively program gene expression. *Science* **334**, 1716–1719 (2011)