Fluorescent biosensors light up high-throughput metabolic engineering

Genetically encoded fluorescent biosensors allow researchers to see how products form in real time in microorganisms, and to test billions of candidates at a time

Synthetic biologists are learning to turn microbes and unicellular organisms into highly productive factories by re-engineering their metabolism to produce valued commodities such as fine chemicals, therapeutics and biofuels. To speed up identification of the most efficient producers, researchers describe new approaches to this process and demonstrate how genetically encoded fluorescent biosensors can enable the generation and testing of billions of individual variants of a metabolic pathway in record time.

Biotechnologists that tinker with the metabolism of microorganisms to produce valued products look at the engineering process through the lens of the so-called 'design-build-test cycle.' The idea is that multiple iterations of this cycle ultimately allow the identification of combinations of genetic and metabolic elements that produce the highest levels of a desired drug or chemical. Key to the cycle's efficiency, however, is the ability to construct and test the largest number of variants possible; in the end, only a few of these variants will produce the product in industrially attractive amounts.

Bioengineers thoroughly understand how metabolic pathways work on the biochemical level and have a plethora of DNA sequences encoding variants of all of the necessary enzymes at their disposal. Deploying these sequences with the help of computational tools and regulating their expression with an ever-growing number of genetic elements, gives them access to an almost infinite pool of design possibilities. Similarly, revolutionary advances in technologies enabling DNA synthesis and manipulation have made the construction of billions of microorganisms, each containing a distinct design variant, a routine process.

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From prediction to reality: a history of the search for gravitational waves

- **1915 -** Albert Einstein publishes general theory of relativity, explains gravity as the warping of spacetime by mass or energy
- **1916 -** Einstein predicts massive objects whirling in certain ways will cause spacetime ripples—gravitational waves
- **1936 -** Einstein has second thoughts and argues in a manuscript that the waves don't exist—until reviewer points out a mistake
- **1962 -** Russian physicists M. E. Gertsenshtein and V. I. Pustovoit publish paper sketch optical method for detecting gravitational
- waves—to no notice
- **1969 -** Physicist Joseph Weber claims gravitational wave detection using massive aluminum cylinders—replication efforts fail
- **1972 -** Rainer Weiss of the Massachusetts