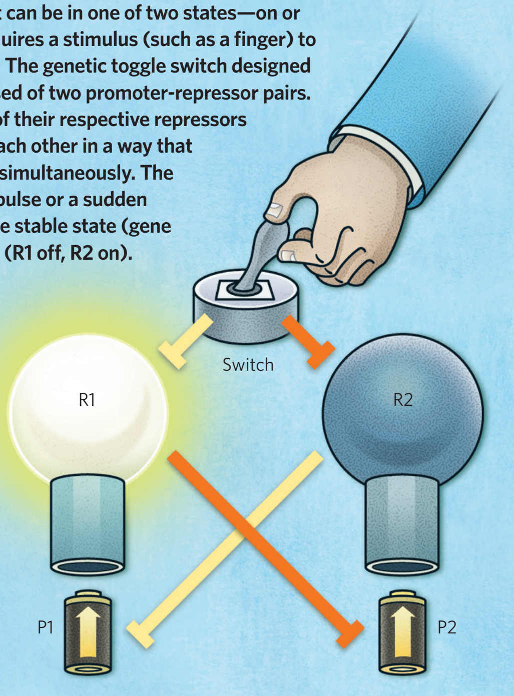
DESIGNING GENETIC CIRCUITS

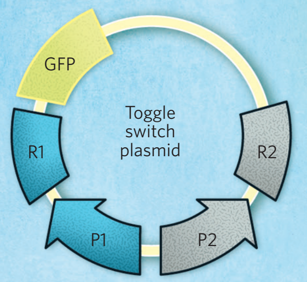
Near the turn of the millennium, James Collins and Stanislas Leibler independently undertook rather similar projects: design what would become synthetic biology's seminal genetic circuits. And they came up with strikingly similar action plans—use *E. coli* to pair promoters with repressors that control one another's behavior.

THE TOGGLE SWITCH

PETER AND MARIA HOEY FOR THE SCIENTIST, OCTOBER 2011

A toggle switch resembles a light switch. It can be in one of two states—on or off, in the case of the light switch—and requires a stimulus (such as a finger) to flip the system from one state to the other. The genetic toggle switch designed by James Collins and colleagues is composed of two promoter-repressor pairs. The promoters encourage the expression of their respective repressors by default, but the two repressors act on each other in a way that prevents them both from being expressed simultaneously. The addition of a stimulus, such as a chemical pulse or a sudden change in temperature, can toggle from one stable state (gene R1 on, gene R2 off) to its other stable state (R1 off, R2 on). And when R1 is linked to green fluorescent protein (GFP), the states can be visualized by the presence or absence of its characteristic green glow.





THE REPRESSILATOR

Stanislas Leibler and his colleagues designed a three-way oscillator that controls the cyclical expression of three repressor genes—R1, R2, and R3. Each repressor is linked to a promoter (P) that controls its expression and is inhibited by one of the other repressors. The result is a rock-paper-scissors relationship between the three and an unsynchronized oscillation of gene expression. R1 expression is suppressed by R2 (which suppresses R1's promoter P1); R2 expression is suppressed by R3; R3 expression is suppressed by R1. GFP is controlled by another copy of P1 located on a separate plasmid, such that GFP is expressed in parallel with R1, glowing in a periodic fashion.