PUZZLING**ADVENTURES**

Protein Chime

BY DENNIS E. SHASHA

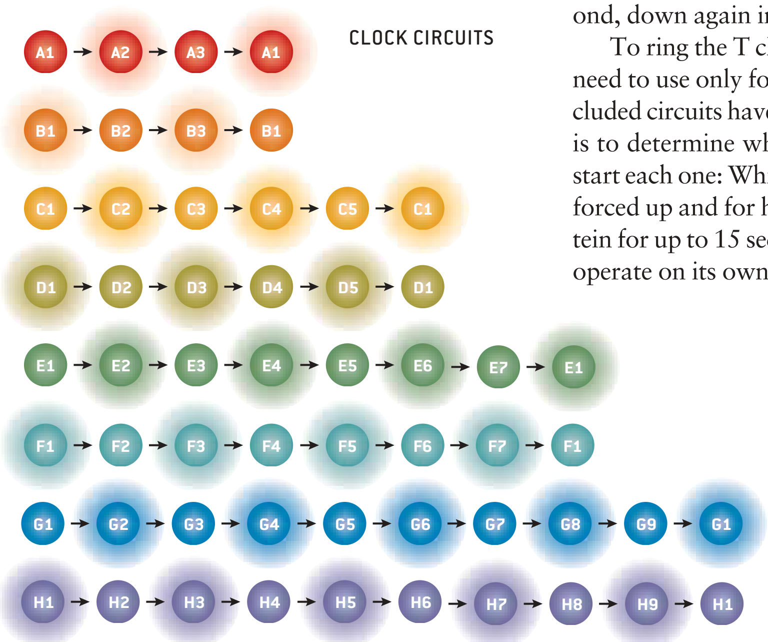
In the 1950s Jacques Monod and François Jacob of the Pasteur Institute in Paris showed that certain regulator proteins in *Escherichia coli* bacteria can repress the production of other proteins. Let's use the notation X → Y to mean that protein X represses protein Y. If X goes up (that is, the protein appears), then Y will go down (the protein disappears) after a short time (say, one second). If X goes down and no other repressor for Y is up, then Y will go up one second after X goes down.

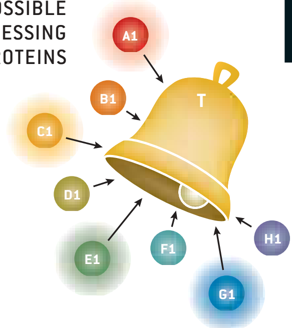
Now consider three proteins: A, B and C, such that A → B → C → A. If A goes up, B goes down one second later. After another second, C goes up, and after one more second A goes back down. Then the pattern continues: B up, C down, A up, B down, and so on. We call this a circuit of proteins: A, B and C periodically appear and disappear, acting like a biochemical clock. Such a clock was actually constructed a few years ago by Michael Elowitz, then a graduate student at Princeton University, and his adviser Stanislas Leibler.

The goal of this puzzle is to create a "protein chime" that will ring every 70 seconds. There are eight circuits, labeled A through H, each containing three, five, seven or nine proteins. No protein in any circuit has an effect on proteins in different circuits. But one protein in each circuit represses T, the special chiming protein that rings when it goes up. If any of these eight T-repressing proteins (labeled A1 through H1) goes up, T will go down one second later. And T will not go back up until one second after all eight proteins are down.

To start any of the circuits in this clock, you must force the production of one of the proteins in the circuit. For example, to start the C circuit, you can keep C4 forced up for five seconds. One second after the forcing begins, C5 goes down. In the succeeding seconds, C1 goes up, C2 goes down and C3 goes up. But C4 does not go down at the end of five seconds, because it is still being forced up. C3 does not push C4 down until one second after the forcing stops (that is, six seconds after the start). Then the cycle resumes without interruption: in the seventh second, C5 goes up, and in the eighth second C1 goes down. C1 goes up again in the 13th second, down again in the 18th, and so on.

To ring the T chime every 70 seconds, you will need to use only four of the eight circuits. (The excluded circuits have no effect on T.) Your challenge is to determine which circuits to use and how to start each one: Which protein in the circuit must be forced up and for how long? You may force a protein for up to 15 seconds; after that, the clock must operate on its own.





SARA CHEN

Answer to Last Month's Puzzle

If the advisers are labeled A_0 through A_8, the director should give tidbits to 25 foursomes determined by this protocol:

$A_7, A_x, A_{x+1}, A_{x+3}$

$A_8, A_x, A_{x+2}, A_{x+3}$

$A_x, A_{x+1}, A_{x+2}, A_{x+4}$

A_7, A_8, A_0, A_1

A_7, A_8, A_2, A_3

A_7, A_8, A_4, A_5

A_7, A_8, A_6, A_0

where x ranges from 0 to 6 and the + operation is modulo 7, which means 6 + 2 = 1. Once a tidbit produces a leak, the director determines which three-member subsets of the foursome cannot yet be exonerated. If more than one threesome remains suspect, he gives tidbits to all but one threesome. This strategy will identify the leakers directly or by elimination.

Web Solution

For a full explanation of last month's puzzle and a peek at the answer to this month's problem, visit www.sciam.com