Supporting Text

We present here the complete description of the networks shown in Fig. 3*C* and Fig. 5 as well as supplementary examples of networks that were created by our evolutionary procedure. Results of stochastic simulations of the switches of Fig. 3 *A* and *B* are also shown.

Examples of switches. As stated, the algorithm produced several bistable switches based on reciprocal inhibition. They provide working implementations of the idea sketched in Fig. 1. Two examples are shown in Figs. 6 and 7.

The switches of Fig. 3 *A* and *B* were obtained with a variety of imposed conditions. Figs. 8 and 9 provide kinetic constants obtained for imposed high concentrations of several hundred proteins. Several switches fundamentally based on the principles of Fig. 3 *A* and *B* but with more complex interactions were also produced. Fig. 10 presents one such "complicated" version.

Fig. 11 is a switch with three genes, but gene *b* on which selection was based is simply a "reporter" gene of an actual two-gene switch between *a* and *c*. The two-gene switch is based on the same mechanism as that of Fig. 3*B*.

Finally, Fig. 12 gives the complete description of the switch shown as Fig. 3*C*, which is really based on the interaction of three genes.

Simulations with stochastic dynamics. To gain insight into the noise resistance of the selected circuits, we simulated the switch networks of Fig. 3 *A* and *B* (also displayed in Figs. 8 and 9) with a stochastic algorithm (1). For parameters corresponding to high

concentration species with several hundred proteins (kinetic constants of Fig. 8), concentration fluctuations are clearly visible but the networks' switch function is not notably degraded, as shown in Fig. 13. For parameters corresponding to high concentration species with only a few 10s of proteins, the concentration fluctuations are stronger, but the networks still clearly perform as switches (Fig. 14). In these strong-fluctuation conditions, the switch of Fig. 3*A* displays spontaneous jumps between the two stable states, with a typical jump time of several hours. Such an event is shown in Fig. 14*A* after $\approx$ 400 min of free evolution. The switch of Fig. 3*B* displays much rarer spontaneous events in the same conditions (Fig. 14*B*). This difference does not appear to be an intrinsic feature of the two networks' topologies because, for other kinetic constants, the noise resistance of the switch in Fig. 3*A* is quite comparable to that of the switch in Fig. 3*B*.

Examples of oscillators. We provide here three examples of oscillating genetic circuits created by our evolutionary procedure. The first one (Fig. 15) is the complete description of the circuit of Fig. 5. Fig. 16 is another example that also has similarities to circadian oscillators. Fig. 17, on the contrary, is a biochemical oscillator with oscillations entirely at the protein level and no transcriptional regulation.

1. Gillepsie, D.T. (1977) *J. Phys. Chem.* **81**, 2340-2361.