Researchers Create DNA Logic Circuits That Work in Test Tubes

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Computers and liquids are not very compatible, as many a careless coffee-drinking laptop owner has discovered. But a new breakthrough by researchers at the California Institute of Technology could result in future logic circuits that literally work in a test tube--or even in the human body.

In the current issue of the journal *Science*, a Caltech group led by computer scientist Erik Winfree reports that they have created DNA logic circuits that work in salt water, similar to an intracellular environment. Such circuits could lead to a biochemical microcontroller, of sorts, for biological cells and other complex chemical systems. The lead author of the paper is Georg Seelig, a postdoctoral scholar in Winfree's lab.

"Digital logic and water usually don't mix, but these circuits work in water because they are based on chemistry, not electronics," explains Winfree, an associate professor of computer science and computation and neural systems who is also a recipient of a MacArthur genius grant.

Rather than encoding signals in high and low voltages, the circuits encode signals in high and low concentrations of short DNA molecules. The chemical logic gates that perform the information processing are also DNA molecules, with each gate a carefully folded complex of multiple short DNA strands.

When a gate encounters the right input molecules, it releases its output molecule. This output molecule in turn can help trigger a downstream gate--so the circuit operates like a cascade of dominoes in which each falling domino topples the next one.

However, unlike dominoes and electronic circuits, components of these DNA circuits have no fixed position and cannot be simply connected by a wire. Instead, the chemistry takes place in a well-mixed solution of molecules that bump into each other at random, relying on the specificity of the designed interactions to ensure that only the right signals trigger the right gates.

"We were able to construct gates to perform all the fundamental binary logic operations--AND, OR, and NOT," explains Seelig. "These are the building blocks for constructing arbitrarily complex logic circuits."

As a demonstration, the researchers created a series of circuits, the largest one taking six inputs processed by 12 gates in a cascade five layers deep. While this is not large by the standards of Silicon Valley, Winfree says that it demonstrates several design principles that could be important for scaling up biochemical circuits.

"Biochemical circuits have been built previously, both in test tubes and in cells," Winfree says. "But the novel thing about these circuits is that their function relies solely on the properties of DNA base-pairing. No biological enzymes are necessary for their operation.

"This allows us to use a systematic and modular approach to design their logic circuits, incorporating many of the features of digital electronics," Winfree says.

Other advantages of the approach are signal restoration for the production of correct output even when noise is introduced, and standardization of the chemical-circuit signals by the use of translator gates that can use naturally occurring biological molecules, such as microRNA, as inputs. This suggests that the DNA logic circuits could be used for detecting specific cellular abnormalities, such as a certain type of cancer in a tissue sample, or even in vivo.

"The idea is not to replace electronic computers for solving math problems," Winfree says. "Compared to modern electronic circuits, these are painstakingly slow and exceedingly simple. But they could be useful for the fast-growing discipline of synthetic biology, and could help enable a new generation of technologies for embedding 'intelligence' in chemical systems for biomedical applications and bionanotechnology."

The other authors of the paper are David Soloveichik and Dave Zhang, both Caltech grad students in computation and neural systems.

Source: Caltech

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