Heat-rechargeable design powers nanoscale molecular machines

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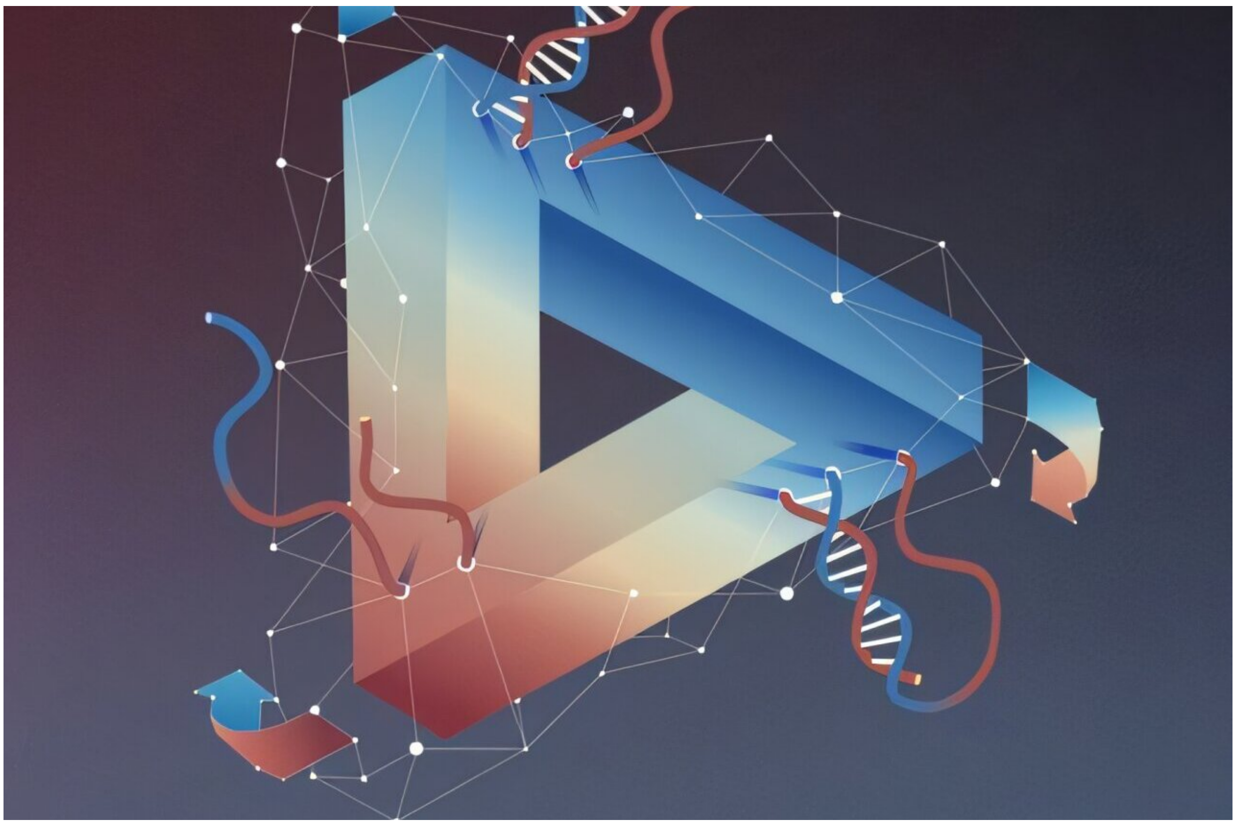

Artistic illustration of how heat recharges a DNA circuit. Credit: Olivier Wyart & Ailadi Cortelletti

Though it might seem like science fiction, scientists are working to build nanoscale molecular machines that can be designed for myriad applications, such as "smart" medicines and materials. But like all machines, these tiny devices need a source of power, the way electronic appliances use electricity or living cells use ATP (adenosine triphosphate, the universal biological energy source).

Researchers in the laboratory of Lulu Qian, Caltech professor of bioengineering, are developing nanoscale machines made out of synthetic DNA, taking advantage of DNA's unique chemical bonding properties to build circuits that can process signals much like miniature computers. Operating at billionth-of-a-meter scales, these molecular machines can be designed to form DNA robots that sort cargos or to function like a neural network that can learn to recognize handwritten numerical digits.

One major challenge, however, has remained: how to design and power them for multiple uses.

Now, Qian and former postdoctoral scholar Tianqi Song (now an assistant professor at the University of North Carolina Greensboro) have developed a method to power DNA circuits using heat. Their system resets itself when heated up, creating a reusable, rechargeable system that can be designed for diverse computations. A paper describing the research appears in the journal *Nature*.

"Unlike specialized fuels, heat is everywhere and easy to access," Qian says. "With the right design, it can recharge molecular machines again and again, letting them sustain activity and keep interacting with their environment. And unlike chemical batteries, this recharge leaves behind virtually no waste—only the remnants of the input signals themselves, which, in a natural environment, would simply be recycled over time."

The heat-recharging method builds on a phenomenon called a kinetic trap. Springs are a classic example of a kinetic trap—compressing a spring stores energy, and that energy is released when the spring pops open. In a similar way, the DNA molecules that make up the team's system are designed to bond together in such a way that heating them up stores energy within the molecular bonds themselves.

"Imagine two DNA strands that are meant to snap together, like puzzle pieces, but one of them is being held back by a third strand that slows the reaction down," Song says. "It's like a spring pressed down and held in place—the energy is there, waiting. The addition of a catalyst strand releases the block, causing the spring to suddenly let go and the DNA strands to quickly pair up, unleashing the stored energy to drive the system forward.

"When you heat up a test tube of DNA and then cool it down, the molecules don't always settle into their most stable arrangement. Instead—and especially when they have strong folded structures—the heating and cooling can reset them back into spring-loaded states, ready to release energy again."

Building on the two ideas—kinetic traps as energy stores and heat as a reset button—the team investigated whether heat could be used as a universal power source for complex molecular circuits. In their design, the circuits carry out their tasks at room temperature, spending the energy stored in kinetic traps, like molecular "springs." When their tasks are completed, the system can be recharged with a pulse of heat, resetting it so the system is ready for the next input.

The duo showed that this rechargeable method can be applied to power very different system behaviors; in this case, as a neural network and as a logic circuit. These two systems are archetypes of classical computing.

Importantly, the idea of reusability through kinetic traps isn't limited to heat.

"In principle, any energy source—light, salt, or acid gradients like those across cell membranes—could serve the same role as long as it can break weak bonds between molecules, letting them naturally fall back into their traps," Qian says. "With this kind of sustainable computation, we can begin to design molecular systems that don't just perform a task once but can show long-term behaviors more like those of living systems—such as learning and evolution."

"In the long run, such continuously running molecular machines —especially those with self-guided learning and evolving abilities—could 'live' inside everyday materials," she adds.

"Imagine a coating applied once to an airplane, constantly sensing stress and repairing cracks to keep passengers safe year after year. Or a pair of contact lenses you buy once, that rehydrate themselves and adjust to correct your vision no matter how it changes over time. Or even a smart drug you take once, that keeps learning to fight off new diseases for a lifetime. What now feels like mere imagination could become reality if others build on our proof-of-concept and carry the work forward in the coming decades."

More information: Tianqi Song et al, Heat-rechargeable computation in DNA logic circuits and neural networks, *Nature* (2025). DOI: 10.1038/s41586-025-09570-2

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