Robotics on the nanoscale

Nanoscale robots can be programmed to walk a DNA origami track.

Tiny, programmable robots: it sounds like something right out of science fiction. Yet scientists are beginning to engineer nanoscale machines that can manipulate the environment at the molecular level. One day, complex molecular assemblies may be made in nanofactories, and *in vivo* nanodevices that kill cancer cells or repair tissues may be a mainstay of medicine.

But first, a solid foundation of nanotechnology tools and methods must be developed, upon which these now fantastical applications can grow. Currently, DNA is the darling of a segment of the nanotechnology community owing to its well-defined specificity rules and the ease of working with it. The field has rapidly progressed as methods have been developed to create DNA origami (two- and three-dimensional folded DNA nanostructures), DNA walkers (mobile molecules powered by DNA hybridization) and various nanomechanical devices made from DNA. Two independent groups recently integrated these technologies to construct simple nanoscale robots.

A collaborative team led by Milan Stojanovic of Columbia University, Erik Winfree of the California Institute of Technology, Hao Yan of Arizona State University and Nils Walter of the University of Michigan, showed that a DNA walker can move along a programmed DNA origami track while following instructions to turn and stop by reading the landscape (Lund *et al.*, 2010). The walker consists of a streptavidin molecule with three deoxyribozyme, or catalytic DNA, legs, which catalyze strand shortening of a DNA substrate on the origami surface. After the leg dissociates from the product it looks for a fresh substrate; as such, the walker motors down the origami track, stopping when it binds to uncleavable DNA strands. The walker could take up to 50 steps, covering a distance of about 100 nanometers.

Nadrian Seeman of New York University and his team showed that a four-footed walker can move along an origami track as they add 'anchor' strands that join the walker's single-stranded DNA feet to the origami surface and 'fuel' strands that preferentially bind to the anchor strands, thus releasing

the feet (Gu *et al.*, 2010). Additionally, as the walker progresses, its three hands can pick up nanoparticle cargo from three different DNA machines flanking the track. "You can think of the walker as the chassis of a car running through an automobile assembly plant; it picks up nanoparticles in the same way that workers standing by the car would add a windshield wiper, a steering wheel, a radiator," explains Seeman. Depending on how the DNA machines are programmed, eight different products are possible.

One challenge both groups had to address was how to actually detect the movement of the walker; Stojanovic and colleagues achieved this with super-resolution fluorescence imaging and atomic force microscopy, and Seeman's team used atomic force microscopy to track the walker and transmission electron microscopy to verify assembly of the products. Both groups have immediate goals to extend the distances the DNA walkers can travel. In the future, Seeman hopes to scale up production of the assembly line and make it repeatable, so that it can be used to make useful products. Stojanovic is keen to investigate whether nanoscale robots can be programmed to interact with natural environments. However, "before we move to higher complexity," notes Stojanovic, "we have to improve the individual steps of assembly and how we observe it."

Another long-term goal is to even further reduce the scale on which these robots act. "It's hard to imagine anything more convenient [than DNA]," notes Seeman. But whereas the large size of DNA allows it to encrypt a lot of information, alternative chemistries will likely need to be developed to do work on the molecular scale.

What nanoscale robotics technology will be able to do in the future is limited only by researchers' imaginations. "The key question," sums up Stojanovic, "is how to learn how to program them to do things and see where we could really go."

Allison Doerr

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Gu, H. *et al.* A proximity-based programmable DNA nanoscale assembly line. *Nature* **465**, 202–205 (2010).

Lund, K. *et al.* Molecular robots guided by prescriptive landscapes. *Nature* **465**, 206–210 (2010).