

Scientists create the next generation of living robots

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Xenobots exhibit cooperative swarm activity, in this case working together to gather piles of tiny particles. Credit: Doug Blackiston, Tufts University

Last year, a team of biologists and computer scientists from Tufts University and the University of Vermont (UVM) created novel, tiny self-healing biological machines from frog cells called "Xenobots" that could move around, push a payload, and even exhibit collective behavior in the presence of a swarm of other Xenobots.

Get ready for Xenobots 2.0.

The same team has now created life forms that self-assemble a body from [single cells](#), do not require [muscle cells](#) to move, and even demonstrate the capability of recordable memory. The new generation Xenobots also move faster, navigate [different environments](#), and have longer lifespans than the first edition, and they still have the ability to work together in groups and heal themselves if damaged. The results of the new research were published today in *Science Robotics*

Compared to Xenobots 1.0, in which the millimeter-sized automatons were constructed in a "top down"

approach by manual placement of tissue and surgical shaping of frog skin and cardiac [cells](#) to produce motion, the next version of Xenobots takes a "bottom up" approach. The biologists at Tufts took stem cells from embryos of the African frog *Xenopus laevis* (hence the name "Xenobots") and allowed them to self-assemble and grow into spheroids, where some of the cells after a few days differentiated to produce cilia—tiny hair-like projections that move back and forth or rotate in a specific way. Instead of using manually sculpted cardiac cells whose natural rhythmic contractions allowed the original Xenobots to scuttle around, cilia give the new spheroidal bots "legs" to move them rapidly across a surface. In a frog, or human for that matter, cilia would normally be found on mucous surfaces, like in the lungs, to help push out pathogens and other foreign material. On the Xenobots, they are repurposed to provide rapid locomotion.

"We are witnessing the remarkable plasticity of cellular collectives, which build a rudimentary new 'body' that is quite distinct from their default—in this case, a frog—despite having a completely normal genome," said Michael Levin, Distinguished Professor of Biology and director of the Allen Discovery Center at Tufts University, and corresponding author of the study. "In a frog embryo, cells cooperate to create a tadpole. Here, removed from that context, we see that cells can repurpose their genetically encoded hardware, like cilia, for new functions such as locomotion. It is amazing that cells can spontaneously take on new roles and create new body plans and behaviors without long periods of evolutionary selection for those features."

"In a way, the Xenobots are constructed much like a traditional robot. Only we use cells and tissues rather than artificial components to build the shape and create predictable behavior." said senior scientist Doug Blackiston, who co-first authored the study with research technician Emma Lederer. "On

the biology end, this approach is helping us understand how cells communicate as they interact with one another during development, and how we might better control those interactions."

While the Tufts scientists created the physical organisms, scientists at UVM were busy running [computer simulations](#) that modeled different shapes of the Xenobots to see if they might exhibit different behaviors, both individually and in groups. Using the Deep Green supercomputer cluster at UVM's Vermont Advanced Computing Core, the team, led by [computer scientists](#) and robotics experts Josh Bongard and under hundreds of thousands of random environmental conditions using an evolutionary algorithm. These simulations were used to identify Xenobots most able to work together in swarms to gather large piles of debris in a field of particles.

"We know the task, but it's not at all obvious—for people—what a successful design should look like. That's where the supercomputer comes in and searches over the space of all possible Xenobot swarms to find the swarm that does the job best," says Bongard. "We want Xenobots to do useful work. Right now we're giving them simple tasks, but ultimately we're aiming for a new kind of living tool that could, for example, clean up microplastics in the ocean or contaminants in soil."

It turns out, the new Xenobots are much faster and better at tasks such as garbage collection than last year's model, working together in a swarm to sweep through a petri dish and gather larger piles of iron oxide particles. They can also cover large flat surfaces, or travel through narrow capillaries. These studies also suggest that the *in silico* simulations could in the future optimize additional features of biological bots for more complex behaviors. One important feature added in the Xenobot upgrade is the ability to record information.

Now with memory

A central feature of robotics is the ability to record memory and use that information to modify the robot's actions and behavior. With that in mind, the Tufts scientists engineered the Xenobots with a

read/write capability to record one bit of information, using a fluorescent reporter protein called EosFP, which normally glows green. However, when exposed to light at 390nm wavelength, the protein emits red light instead.

The cells of the frog embryos were injected with messenger RNA coding for the EosFP protein before stem cells were excised to create the Xenobots. The mature Xenobots now have a built-in fluorescent switch which can record exposure to blue light around 390nm.

The researchers tested the memory function by allowing 10 Xenobots to swim around a surface on which one spot is illuminated with a beam of 390nm light. After two hours, they found that three bots emitted red light. The rest remained their original green, effectively recording the "travel experience" of the bots.

This proof of principle of molecular memory could be extended in the future to detect and record not only light but also the presence of radioactive contamination, chemical pollutants, drugs, or a disease condition. Further engineering of the memory function could enable the recording of multiple stimuli (more bits of information) or allow the bots to release compounds or change behavior upon sensation of stimuli.

"When we bring in more capabilities to the bots, we can use the computer simulations to design them with more complex behaviors and the ability to carry out more elaborate tasks," said Bongard. "We could potentially design them not only to report conditions in their environment but also to modify and repair conditions in their environment."

Xenobot, heal thyself

"The biological materials we are using have many features we would like to someday implement in the bots—cells can act like sensors, motors for movement, communication and computation networks, and recording devices to store information," said Levin. "One thing the Xenobots and future versions of biological bots can do that their metal and plastic counterparts have difficulty doing is constructing their own body plan as the

cells grow and mature, and then repairing and restoring themselves if they become damaged. Healing is a natural feature of living organisms, and it is preserved in Xenobot biology."

The new Xenobots were remarkably adept at healing and would close the majority of a severe full-length laceration half their thickness within 5 minutes of the injury. All injured bots were able to ultimately heal the wound, restore their shape and continue their work as before.

Another advantage of a biological robot, Levin adds, is metabolism. Unlike metal and plastic robots, the cells in a biological robot can absorb and break down chemicals and work like tiny factories synthesizing and excreting chemicals and proteins. The whole field of synthetic biology—which has largely focused on reprogramming single celled organisms to produce useful molecules—can now be exploited in these multicellular creatures.

Like the original Xenobots, the upgraded bots can survive up to ten days on their embryonic energy stores and run their tasks without additional energy sources, but they can also carry on at full speed for many months if kept in a "soup" of nutrients.

What the scientists are really after

An engaging description of the biological bots and what we can learn from them is presented in a TED talk by Michael Levin (go.ted.com/michaellevin) (link will be live on March 31, 2021 2pm ET)

In his TED Talk, professor Levin describes not only the remarkable potential for tiny biological robots to carry out useful tasks in the environment or potentially in therapeutic applications, but he also points out what may be the most valuable benefit of this research—using the bots to understand how individual cells come together, communicate, and specialize to create a larger organism, as they do in nature to create a frog or human. It's a new model system that can provide a foundation for regenerative medicine.

Xenobots and their successors may also provide insight into how multicellular organisms arose from ancient single celled organisms, and the origins of

information processing, decision making and cognition in biological organisms.

Recognizing the tremendous future for this technology, Tufts University and the University of Vermont have established the Institute for Computer Designed Organisms (ICDO), to be formally launched in the coming months, which will pull together resources from each university and outside sources to create living robots with increasingly sophisticated capabilities.

More information: D. Blackiston et al., "A cellular platform for the development of synthetic living machines," *Science Robotics* (2021). robotics.sciencemag.org/lookup/doi/10.1126/scirobotics.abf1571

Provided by Tufts University

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