These Are the First Living Robots: Machines Made from Frog Stem Cells

Ladies and gentlemen, we have a new kind of life.

By Courtney Linder Jan 14, 2020

- Scientists from Tufts University, the University of Vermont, and the Wyss Institute at Harvard have developed tiny, living organisms that can be programmed. Called "xenobots," these robots were made with frog stem cells.
- The research, published in the scientific journal *Proceedings of the National Academy of Sciences*, is meant to aid development of soft robots that can repair themselves when damaged.
- Ultimately, the hope is these xenobots will be useful in cleaning up microplastics, digesting toxic materials, or even delivering drugs inside our bodies.

What happens when you cross stem cells from a frog heart and frog skin? Not much—that is, until you program those cells to move. In that

case, you've created a xenobot, a new type of organism that's part robot, part living thing.

And we've never seen anything like it before.

Researchers from Tufts University, the University of Vermont, and Harvard University have created the first xenobots from frog embryos after designing them with computer algorithms and physically shaping them with surgical precision. The skin-heart embryos are just one millimeter in size, but can accomplish some remarkable things for what they are, like physically squirming toward targets.

"These are novel living machines," Joshua Bongard, a computer scientist and robotics expert at the University of Vermont who co-led the new research, said in a press statement. "They're neither a

traditional robot nor a known species of animal. It's a new class of artifact: a living, programmable organism."

By studying these curious organisms, researchers hope to learn more about the mysterious world of cellular communication. Plus, these kinds of robo-organisms could possibly be the key to drug delivery in the body or greener environmental cleanup techniques.

"Most technologies are made from steel, concrete, chemicals, and plastics, which degrade over time and can produce harmful ecological and health side effects," the authors note in a research paper published in the scientific journal *Proceedings of the National Academy of Sciences*. "It would thus be useful to build technologies using self-renewing and biocompatible materials, of which the ideal candidates are living systems themselves."

Building Xenobots

Xenobots borrow their name from *Xenopus laevis,* the scientific name for the African clawed frog from which the researchers harvested the

stem cells. To create the little organisms, which scoot around a petri dish a bit like water bears—those tiny microorganisms that are pretty much impossible to kill—the researchers scraped living stem cells from frog embryos. These were separated into single cells and left to incubate.

They differentiated the stem cells into two different kinds: heart and skin cells. The heart cells are capable of expanding and contracting, which ultimately aids the xenobot in locomotion, and the skin cells provide structure. Next, using tiny forceps and an even smaller electrode, the scientists cut the cells and joined them together under a microscope in designs that were specified by a computer algorithm.

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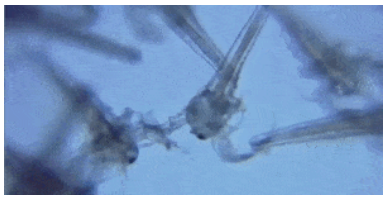

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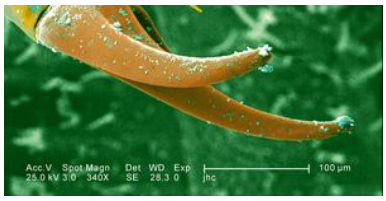

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Interestingly, the two different kinds of cells did merge together well and created xenobots that could explore their watery environment for days or weeks. When flipped like a turtle on its shell, though, they could no longer move.

Other tests showed whole groups of xenobots are capable of moving in circles and pushing small items to a central location all on their own, without intervention. Some were built with holes in the center to reduce drag and the researchers even tried using the hole as a pouch to let the xenobots carry objects. Bongard said it's a step in the right direction for computer-designed organisms that can intelligently deliver drugs in the body.

Evolutionary Algorithms

On the left, the anatomical blueprint for a computer-designed organism, discovered on a UVM supercomputer. On the right, the living organism, built entirely from frog skin (green) and heart muscle (red) cells. The background displays traces carved by a swarm of these new-to-nature organisms as they move through a field of particulate matter.

SAM KRIEGMAN, UVM

While these xenobots are capable of some spontaneous movement, they can't accomplish any coordinated efforts without the help of computers. Really, xenobots couldn't fundamentally exist without designs created through evolutionary algorithms.

Just as natural selection dictates which members of a species live and which die off—based on certain favorable or unfavorable attributes and ultimately influencing the species' characteristics—evolutionary algorithms can help find beneficial structures for the xenobots.

A team of computer scientists created a virtual world for the xenobots and then ran evolutionary algorithms to see which potential designs for the xenobots could help them move or accomplish some other goal. The algorithm looked for xenobots that performed well at those particular tasks while in a given configuration, and then bred those microorganisms with other xenobots that were considered "fit" enough to survive this simulated natural selection.

In the video above, for example, you can see a simulated version of the xenobot, which is capable of forward movement. The final organism takes on a similar shape to this design and is capable of (slowly) getting around. The red and green squares at the bottom of the structure are active cells, in this case the heart stem cells, while the blueish squares represent the passive skin stem cells.

DOUGLAS BLACKISTON

All of this design work was completed over the course of a few months on the Deep Green supercomputer cluster at the University of Vermont. After a few hundred runs of the evolutionary algorithm, the researchers filtered out the most promising designs. Then, biologists at Tufts University assembled the real xenobots in vitro.

What's the Controversy?

Anything dealing with stem cells is bound to meet at least *some* flack because detractors take issue with the entire premise of using stem cells, which are harvested from developing embryos.

That's compounded with other practical ethics questions, especially relating to safety and testing. For instance, should the organisms have protections similar to animals or humans when we experiment on them? Could we, ourselves, eventually require protection from the artificially produced creatures?

"When you're creating life, you don't have a good sense of what direction it's going to take," Nita Farahany, who studies the ethical ramifications of new technologies at Duke University and was not involved in the study, told *Smithsonian Magazine*. "Any time we try to harness life … [we should] recognize its potential to go really poorly."

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Michael Levin, a biophysicist and co-author of the study from Tufts University, said that fear of the unknown in this case is not reasonable:

> "When we start to mess around with complex systems that we

> don't understand, we're going to get unintended consequences," he said in a press statement. "If humanity is going to survive into the future, we need to better understand how complex properties, somehow, emerge from simple rules."

At its heart, the study is a "direct contribution to getting a handle on what people are afraid of, which is unintended consequences," Levin said.

Source: The University of Vermont

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