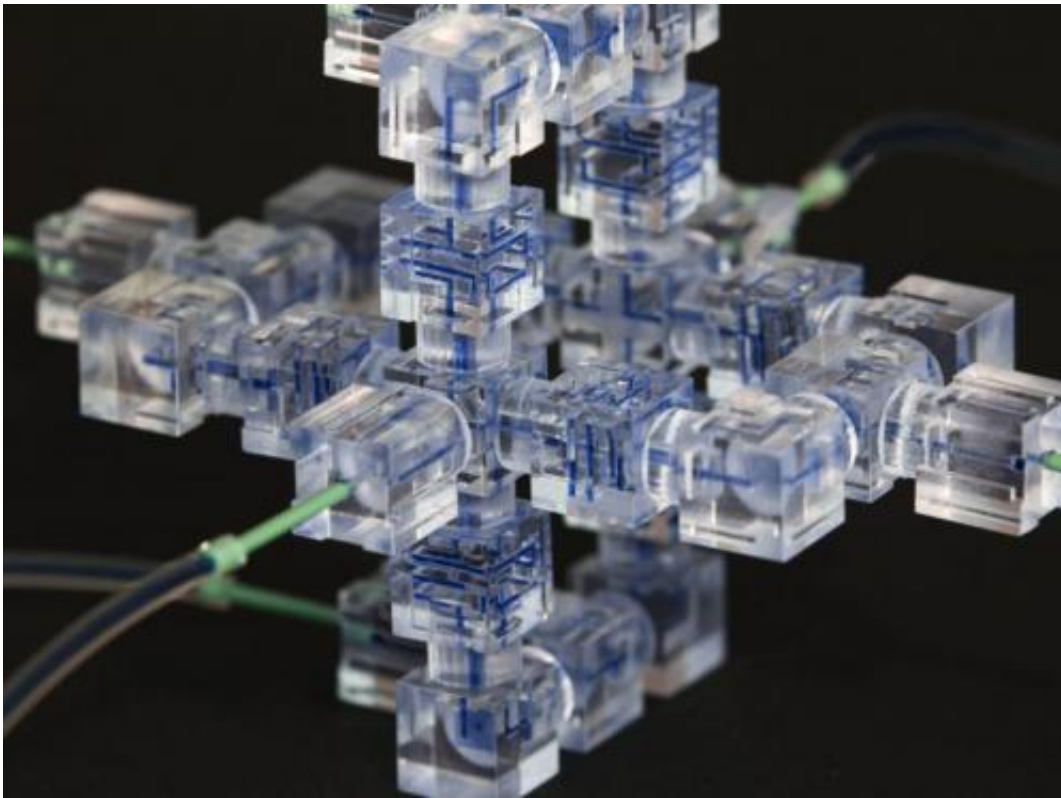


Lego-like modular components make building 3-D 'labs-on-a-chip' a snap

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Modular fluidic and instrumentation components developed by researchers at the University of Southern California Viterbi School of Engineering. Credit: USC Viterbi School of Engineering

Thanks to new LEGO-like components developed by researchers at the USC Viterbi School of Engineering, it is now possible to build a 3-D microfluidic system quickly and cheaply by simply snapping together

small modules by hand.

Microfluidic systems are used in many fields including engineering, chemistry and biotechnology to precisely manipulate small volumes of fluids for use in applications such as enzymatic or DNA analysis, pathogen detection, clinical diagnostic testing, and synthetic chemistry. Traditionally, microfluidic devices are built in a cleanroom on a two-dimensional surface using the same technology developed to produce integrated circuits for the electronics industry.

Though tiny, designing, assembling and testing a new microfluidics system can take a lot of time and money. Building a single device can often require multiple iterations, each of which can take up to two weeks and several thousand dollars to manufacture. And the more complex the system, the higher the number of iterations needed.

"You test your device and it never works the first time," said Krisna Bhargava, materials science graduate student at the USC Viterbi School of Engineering. "If you've grown up to be an engineer or scientist, you've probably been influenced by LEGO at some point in your childhood. I think every scientist has a secret fantasy that whatever they're building will be as simple to assemble."

Frustrated that reproducing a simple microfluidic circuit could cost him so much time and money, Bhargava set out simplify the construction process. First, he identified the primitive elements commonly used in microfluidic systems, much like how circuitry is broken down in electrical engineering. Basic microfluidic functions would be separated into standardized modular components, not an entirely revolutionary concept. But then, he abandoned the two-dimensional method of building [microfluidic devices](#) altogether.

"The founders of the microfluidics field took the same approach as the

semiconductor industry: to try to pack in as much integrated structure as possible into a single chip," explained Bhargava. "In electronics, this is important because a high density of transistors has many direct and indirect benefits for computation and signal processing. In microfluidics, our concerns are not with bits and symbolic representations, but rather with the way fluidics are routed, combined, mixed, and analyzed; there's no need to stick with continuing to integrate more and more complex devices."

Borrowing an approach from the electronics industry, which uses prototype boards to build circuits, Bhargava conceived of three-dimensional modular components that encapsulated the common elements of microfluidic systems, as well as a connector that could join the separate components together. Inspired by recent advancements in micron-scale 3D-printing, he and a USC Viterbi research team that included chemical engineering and materials science professor Noah Malmstadt and biomedical engineering graduate student Bryant Thompson, designed computer models for eight modular fluidic and instrumentation components (MFICs, pronounced "em-fix") that would each perform a simple operation. Examples are a "helix" component that can mix two fluid streams and a component that contains an integrated optical sensor for measuring the size of small droplets. The components constructed for this study are approximately 1 cm³, slightly smaller than a standard 6-sided die.

The team's development of these MFICs represents the first attempt to break a device into separate components that can be assembled, disassembled and re-assembled over and over.



Like Lego blocks, modular fluidic and instrumentation components developed by USC Viterbi researchers are easy to assemble, break apart, and re-assemble. Credit: USC Viterbi School of Engineering

"What we've built looks more like a hobby breadboard," said Malmstadt. "You can build a circuit on the cheap with your bare hands."

The team attributes much of the success in the fabrication stage to recent advancements in high-resolution 3-D printing.

"We got the parts back from our contract manufacturer and on the first try they worked out better than I could have dreamed. We were able to build a working microfluidic system that day, as simple as clicking LEGO® blocks together," said Bhargava.

Using the 3-D-printed MFICs, in a matter of hours the team was able to build and test a device that mixed fluids using a helix component and turned the mixture into droplets. Essentially a very long track packed into the same standardized module footprint, the helix component allows adjustments in flow resistance or can serve as an efficient mixer. In

[microfluidic systems](#), mixing is dominated by diffusion, and a complex helix can speed up the process by folding the fluid onto itself.

"Trying to control how things mix has always been a major issue in this field just due to the way that fluids flow at very small dimensions," explained Malmstadt. "People have come up with all sorts of ways to twist and turn the channels to try to improve the mixing. The fact that we can do it in three dimensions with this 3-D helix really simplifies things."

Such work lies at the heart of the convergence of science and engineering at USC, where researchers from both fields collaborate to create the tools that make scientific breakthroughs possible.

The team reports their recent invention in "Discrete Elements for 3-D Microfluidics," published in *Proceedings of the National Academy of Sciences (PNAS)* of the United States of America on September 22. In the paper, the researchers also described how off-the-shelf sensors or other integrated components can be easily incorporated into systems built from MFICs, and demonstrated how the MFICs can size droplets precisely, a useful function for drug delivery or studying microreactor chambers. In detecting droplet size, they found that a 30-cent component yielded results comparable to those from the traditional tool, a \$30,000-plus optical microscope.

The result is an extremely cheap, standardized, easy-to-use set of components that can quickly be assembled and re-assembled into a microfluidic system for a mere fraction of the time and cost it currently takes to produce a device to perform the same operation.

"You pull out everything you think is going to work, you stick it together and you test it," said Bhargava. "If it doesn't work, you pull part of it out, swap out some pieces and within a day you've probably come to a final design, and then you can seal the system together and make it

permanent. You have a massive productivity gain and a huge cost advantage."

For the past 20 years, microfluidics has been considered a boon for fields like biotechnology and engineering, but has yet to be standardized or universally adopted by the wider community of researchers and in industry. The technology, often dubbed "Lab-on-Chip", has the potential to accelerate the pace of development and provide the means for high-precision experiments to be carried out in low-resource settings. The USC Viterbi team's goal is to finally help that happen.

"MFICs will vastly increase the productivity of a single grad student, postdoc, or lab tech by enabling them to build their own instruments right in the lab and automate their workflow, saving time and money," said Malmstadt. "I think of it as a technological approach to the STEM shortage – make each researcher more powerful by enabling them to do their own automation without having to be an expert in microfabrication or having the capability to design complex integrated devices."

The team envisions an open community where designs can be shared via an open-source database. They have plans to develop more components and hope that other researchers will begin using MFICs for their own experiments as well as contribute to the development of new components and systems that will help speed advancements in the microfluidic research community.

"People have done great things with microfluidics technology, but these modular components require a lot less expertise to design and build a system," said Malmstadt. "A move toward standardization will mean more people will use it, and the more you increase the size of the community, the better the tools will become."

More information: Discrete elements for 3D microfluidics, *PNAS*,
www.pnas.org/cgi/doi/10.1073/pnas.1414764111

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