

**THIS PAGE:** Little and his colleagues have found that nature-based delivery schedules are better at prompting new vascular growth than the bulk administration of growth factors currently employed by docs. These endothelial cells have been treated with a regimen of growth factors on a schedule that mimics aspects of natural wound healing.

**OPPOSITE:** These “synthetic pathogens” (red spheres) act like Trojan horses. They not only deliver genetic material to immune cells but also trick the cells into believing that the engineered pathogen is dangerous, leading them to prompt an immune response.

IN THE NASCENT FIELD OF BIOMIMETICS,  
THE LAB TAKES INSPIRATION FROM NATURE  
IMAGES | LABORATORIES OF STEVEN LITTLE  
TEXT | JOE MIKSCH

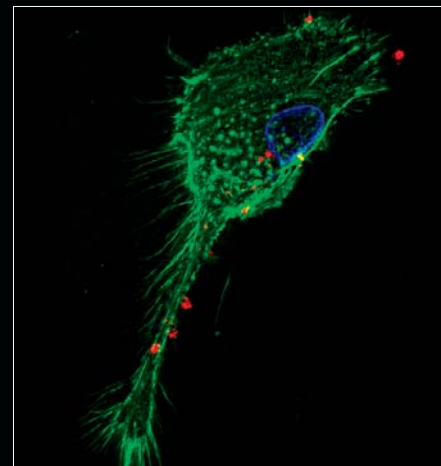
# WHEN MEDICINE IMITATES LIFE

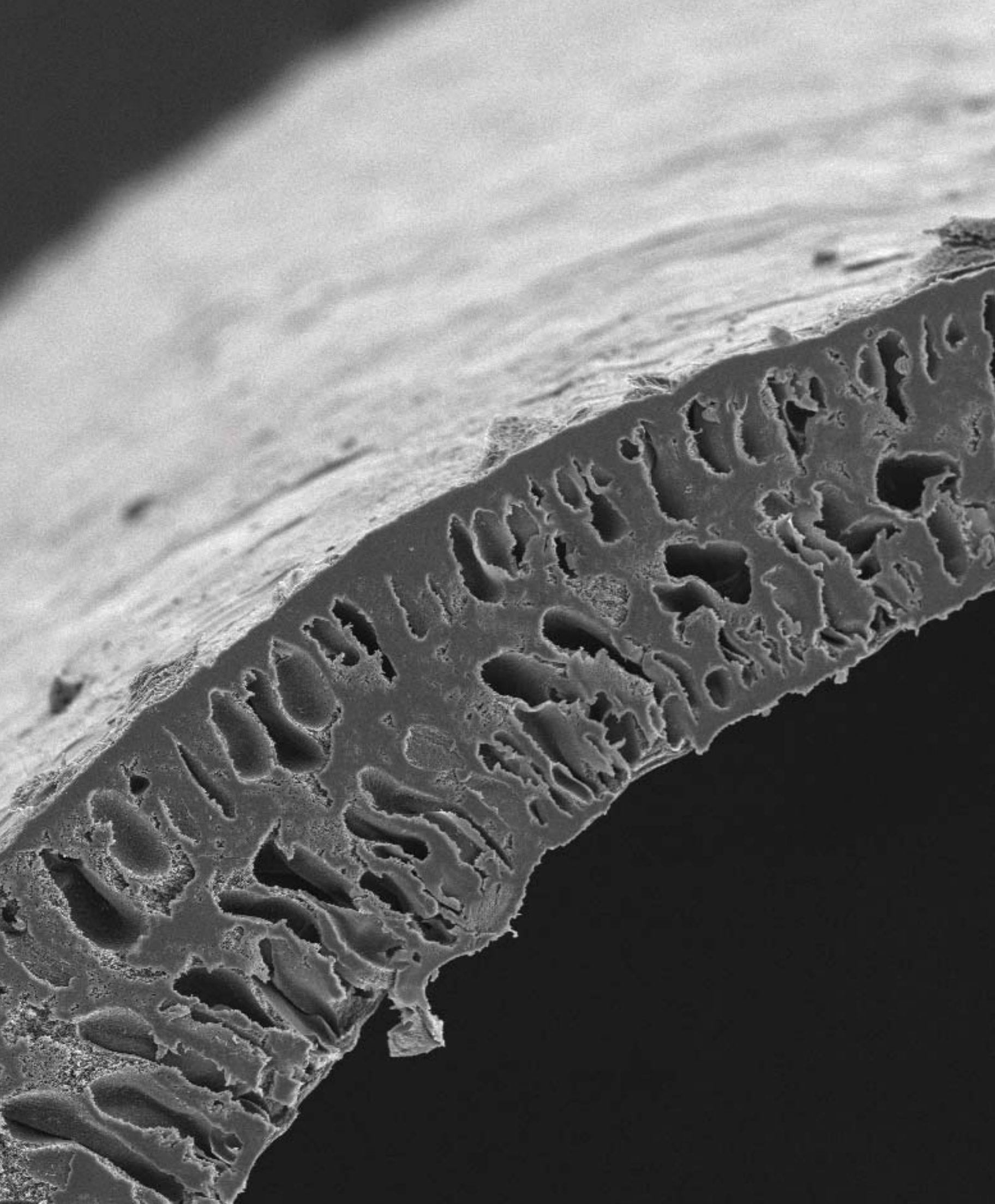
Steven Little, a PhD assistant professor of chemical engineering, bioengineering, and immunology at the University of Pittsburgh, is something of a puppeteer. He doesn't make wooden marionettes dance around a small stage like creatures of flesh and blood, yet he has managed to manipulate what's manmade so it behaves as though it's part of nature.

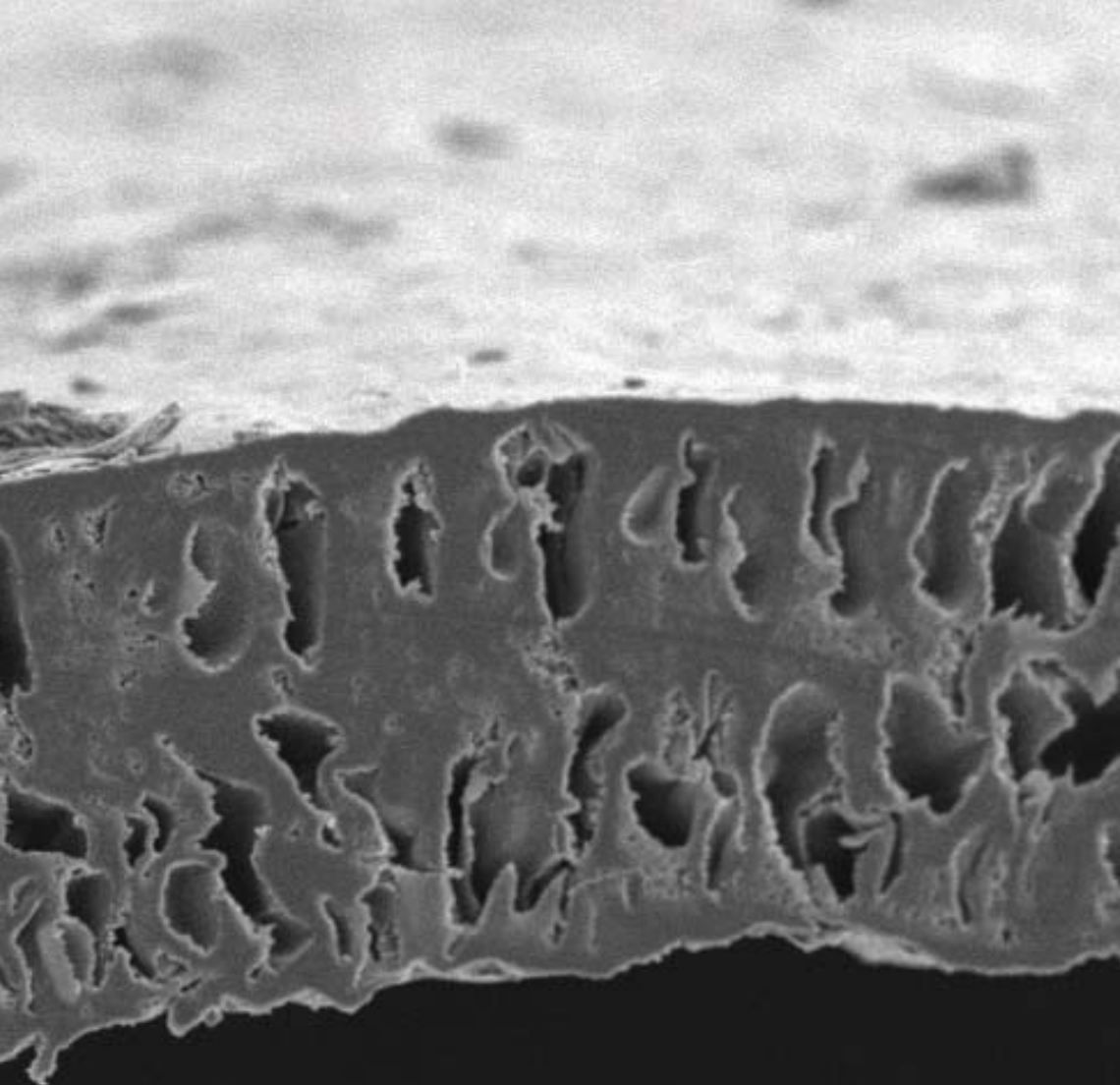
Little is a biomimetician.

Biomimetics, as the word suggests, is the science of making something synthetic act like something that's alive. Little's work represents the melding of myriad disciplines, from immunology to tissue engineering to basic biology. His lab seeks ways to make synthetic cells do the bidding of doctors.

Little and his colleagues have a lot of strings to pull. You have to know how nature works to imitate it successfully. And you have to have the engineering chops necessary to take the lessons nature gives you to create artificial entities that perform like—and maybe even better than—biological ones.

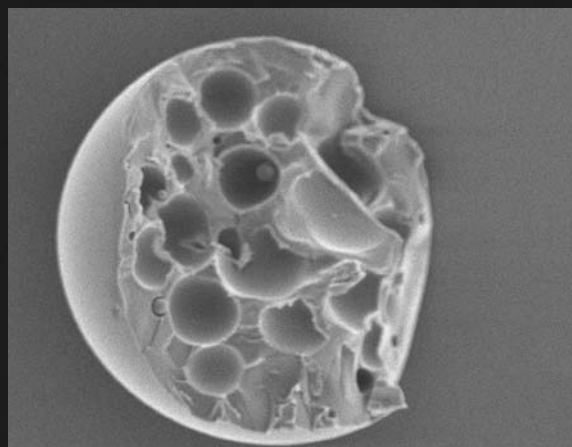




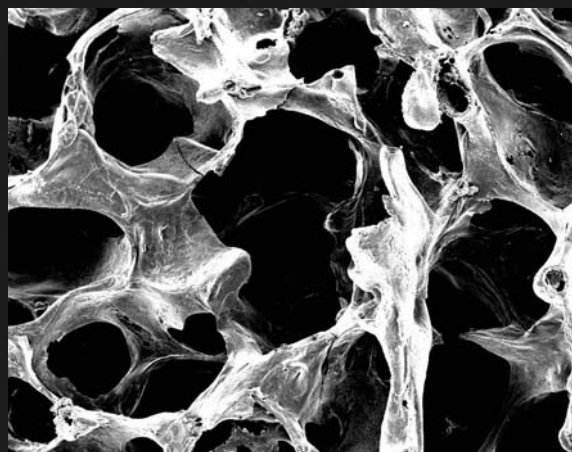


**ABOVE:** A cross section of tiny, porous, hollow fibers fashioned from various inert, man-made materials. Little's group is working toward making networks of these fibers to deliver nutrients, oxygen, and growth factors to wounds.

**RIGHT:** This particle was designed to deliver aqueous drugs, which don't always dissolve simultaneously with the polymer that delivers them. During fabrication Little's lab created "pockets" in the micron-size particles to encapsulate and release the drug. These particles were intentionally frozen at -320 degrees Fahrenheit and cracked open to reveal the interior pockets.



**LOWER RIGHT:** A scanning electron micrograph of a tissue-engineering scaffold made from biodegradable, synthetic polymers. Little's lab is screening massive libraries of materials to choose those that endow biological activity to the surface with the end goal of generating more expedient tissue growth.



Researchers in the Little labs want to accelerate wound healing by using synthetic vasculature to deliver growth factors. (They believe the key is to deliver the factors on a specific order and on a strict schedule.) When the job is done and the wound is healed, Little says, the synthetic system can be dissolved using a fluid containing enzymes.

Another project in the lab seeks to create artificial and biodegradable, yet bioactive, scaffolding to encourage tissue growth.

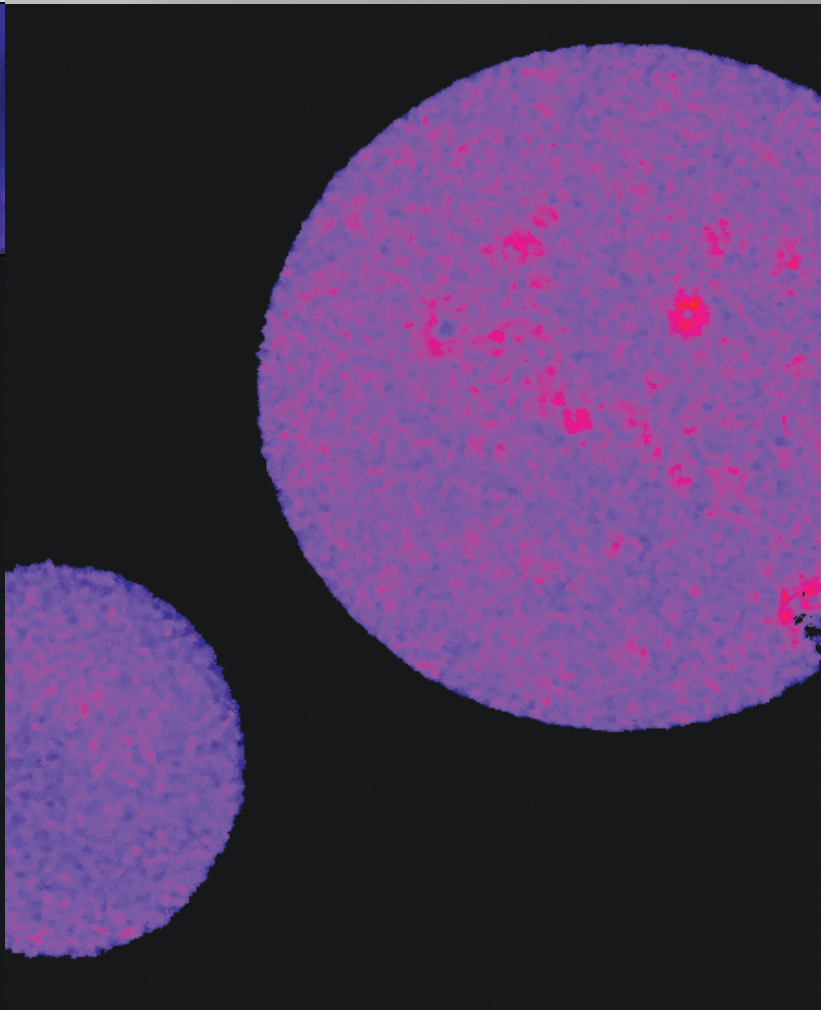
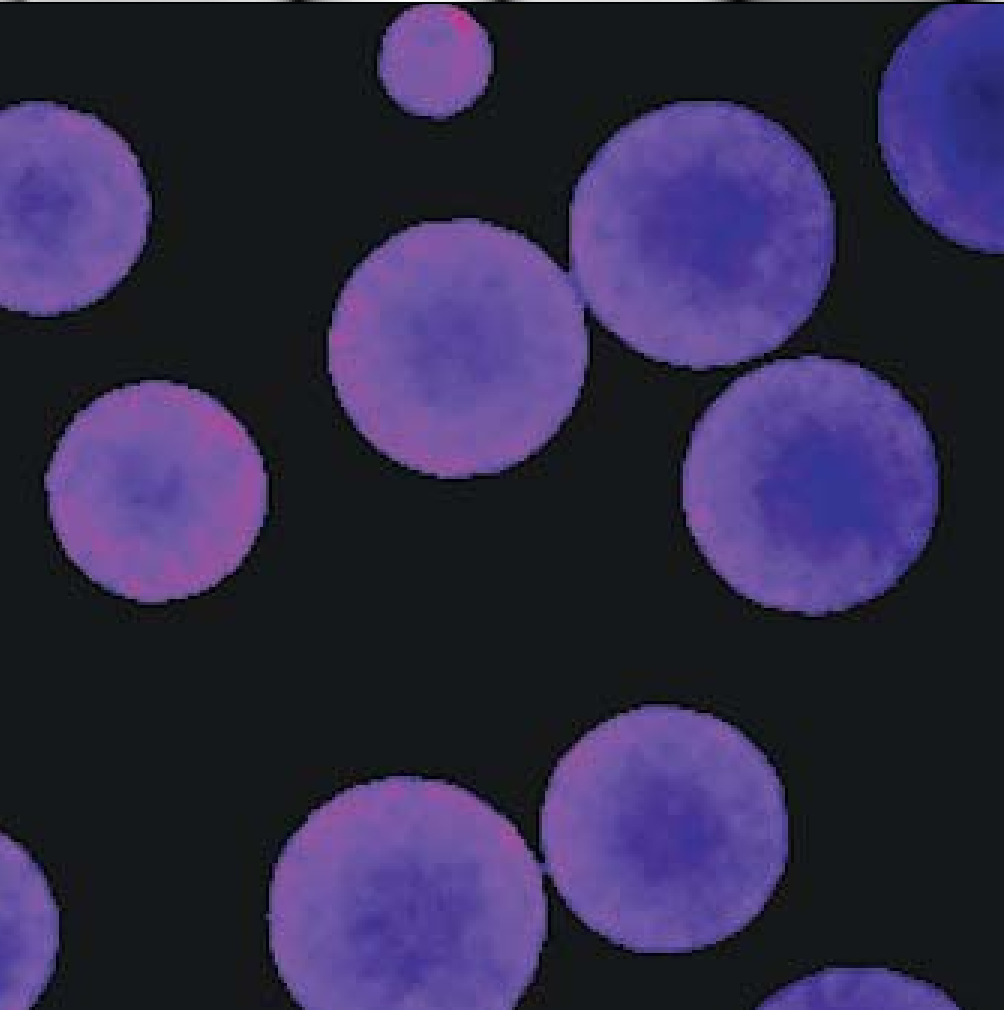
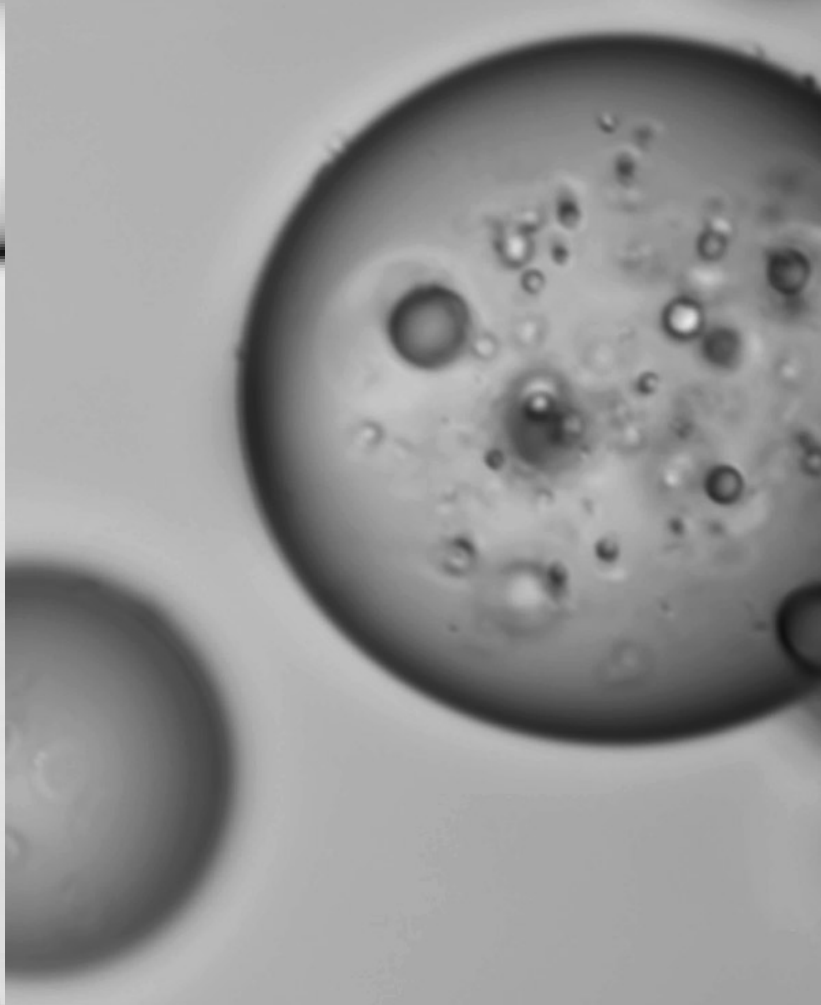
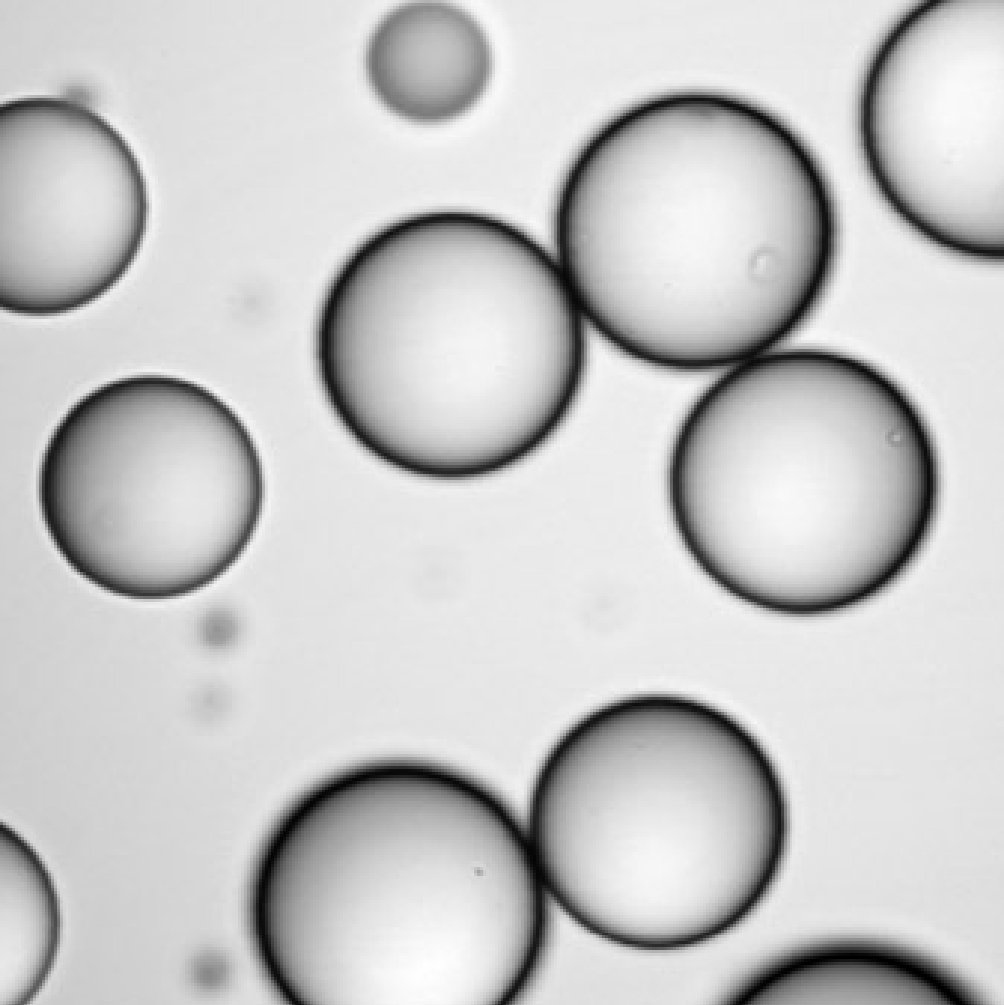
They've also used synthetic pathogens to facilitate delivery of genetic material to immune cells by tricking these cells into thinking they've met a dangerous invader.

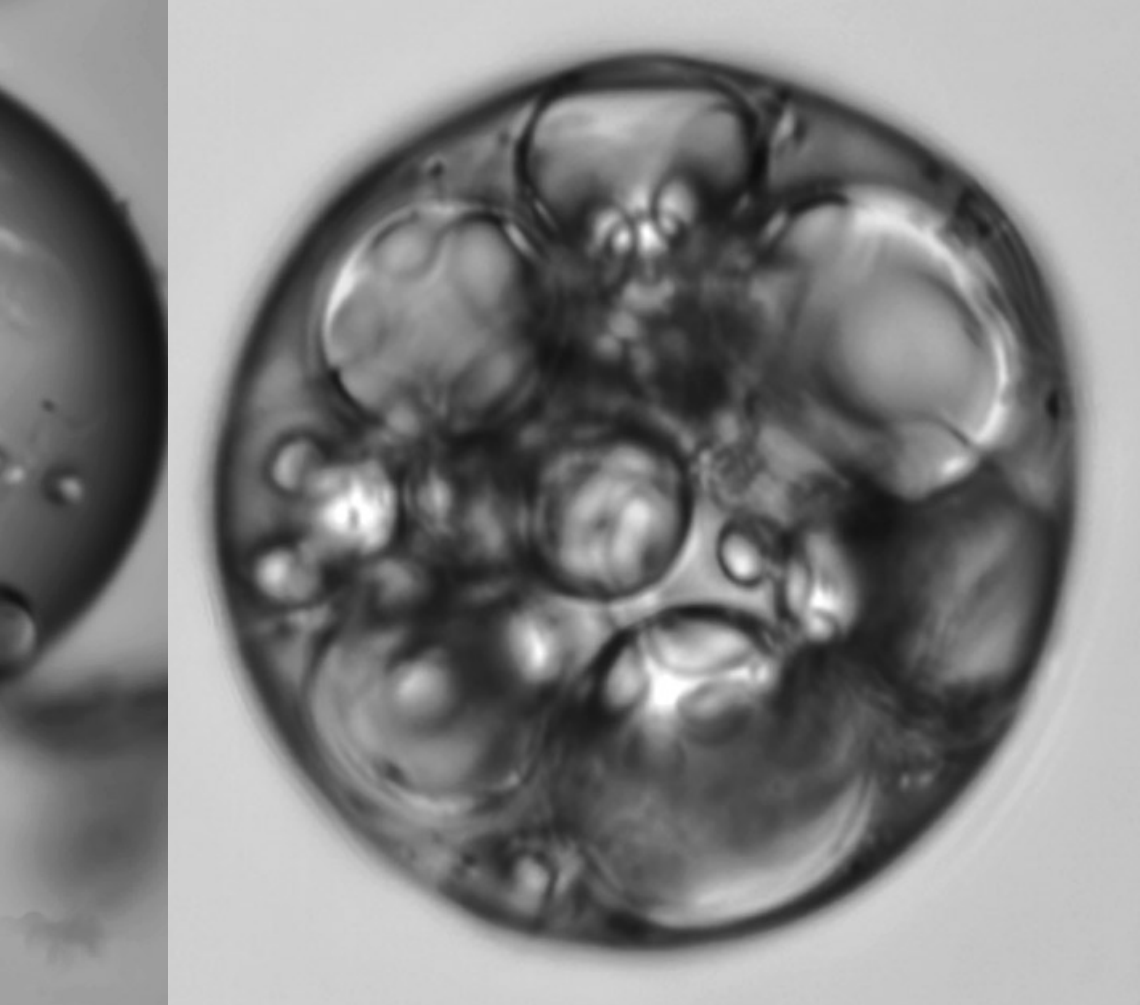
A significant portion of the Little lab's work relates to immunology. In 2007, the Massachusetts Institute of Technology-trained PhD nailed down a few grants to fund research into the development of a "smart" artificial dendritic cell. Not that our immune system's antigen presenters aren't MENSA-eligible in their own right—Little calls dendritic cells "almost sentient"—but he's been able to engineer a homogenous and essentially inexhaustible supply of antigen-presenting cells that can spur or limit an immune response more efficiently than their natural cousins.

The whys and wherefores remain a bit of a mystery, Little concedes, though it's clear that the order and manner in which dendritic cells—natural or engineered—send their chemical signals to T cells affect immune response.

"What I'm talking about is that you have one part of the process and you've got another part of the process. Depending on the way these are oriented or presented, you can get an entirely different immune response," says Little of the chemical signals cells use to communicate.

Researchers in his group are also working to find a way to more accurately target immunosuppressant agents, such as those used to help transplant patients fight off rejection. Immunosuppressant regimens can themselves be highly toxic, but Little thinks it's possible to engineer a drug-delivery particle that will present an immunosuppressant drug to dendritic cells only. Getting the drug directly to the dendritic cell rather than broadcasting it systemwide would allow for lower dosages, thereby reducing or eliminating toxic side effects.





In a somewhat related realm, Little and his collaborators are in the process of making drug delivery vehicles that can be custom-crafted to release a specific drug over a particular time course.

They also are investigating a strategy for summoning cells through the controlled release of chemokines. That is, instead of aiming a delivery vehicle at a cell, the group hopes to use the chemokines to call the targeted cell to a signaling source. Several biological entities use this approach to communicate or signal for help in healing wounds or fighting infection. In this instance, the chemokine may serve as more than a signal—it could potentially lead to a unique biological response. Little says that this approach exemplifies a basic biomimetics principle: Cells are smart enough to know that the context in which a signal is presented is part of the signal itself.

Little says he and his colleagues are at the beginning of what may become a new discipline. This excites him. “Biomimetics is tremendously new,” he says. “We are definitely pushing the limits of what chemical engineers do and what bioengineers do.

“That’s what makes me so excited about it,” he says. “It just looks at this stage to be limitless in what we might be able to accomplish.” ■

**FOR MORE INFORMATION:**  
[www.littlelab.pitt.edu](http://www.littlelab.pitt.edu)

**OPPOSITE:** Little’s group requires an extremely high level of control over the rates and phases of “drug” release from their delivery vehicles in order to simulate biological communication. In these images, Little’s lab has reinforced a hypothetical particle erosion mechanism that is used in mathematical models to predict release of drugs and to rationally design biomimetic delivery systems.

