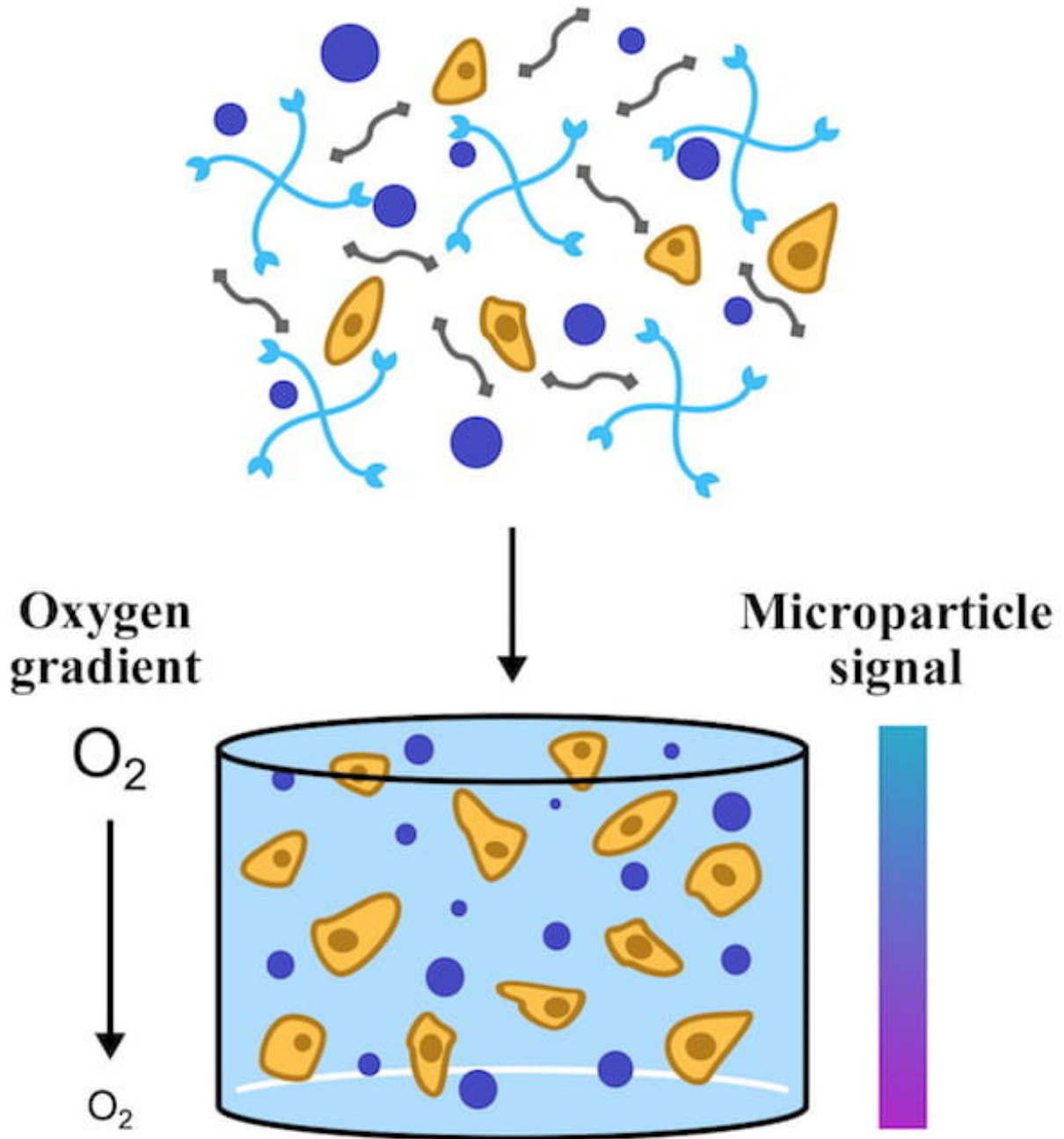


Scientists develop fluorescent sensors to track nutrients in hydrogel-based healing

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Hydrogel precursor with cells and microparticles



Rice University bioengineers developed fluorescent microparticles that can be suspended in hydrogel scaffolds seeded with live cells. The microparticles can be used to monitor for the presence of oxygen in hydrogel cultures that help injuries

heal. Credit: Reid Wilson

It's important to know one's new cells are getting nourishment. Rice University scientists are working on a way to tell for sure.

The Rice lab of bioengineer Jane Grande-Allen has invented soft microparticle sensors to monitor [oxygen](#) levels in hydrogels that serve as scaffolds for growing tissues.

Hydrogels being developed at Rice's Brown School of Engineering and elsewhere can be placed at the site of an injury. Seeded with [live cells](#), they encourage the growth of new muscle, cartilage or, perhaps someday, entire organs. Ideally, the hydrogel attracts [blood vessels](#) that infuse the material and bring nourishment to the cells.

Grande-Allen and her team designed their fluorescent particles to report on [oxygen levels](#) inside gels. Their work appears in the American Chemical Society journal *ACS Biomaterials Science and Engineering*.

"We've been collaborating with investigators in intestinal mechanobiology and wanted a straightforward way to tell what level of oxygen we had throughout our 3-D tissue cultures," Grande-Allen said. "Where we intend a specific level of oxygen, we want to be sure that's what the cells are getting.

"There are multiple ways of doing this," she said. "We can have computational models, but we'd have to make several assumptions about the way oxygen permeates the culture medium and 3-D scaffold material. A better way is to measure it directly, so that was our goal."

Lead author Reid Wilson, an M.D./Ph.D. student at Rice and Baylor

College of Medicine, built on the work of Rice alumnus Matthew Sapp and Rice graduate student Sergio Barrios to develop soft microparticles that incorporate an oxygen-triggered fluorescent molecule based on palladium and a reference fluorophore.

Wilson went through several iterations of dye combinations and concentrations to develop those microparticles. "The problem with using oxygen-responsive fluorophores in three-dimensional cultures is their signal isn't bright enough to measure reliably," he said. "So we loaded the microparticles with high concentrations of dye, which allowed more reproducible measurements of the oxygen concentration."

The particles can be suspended in hydrogel along with living cells, and tests showed they are not toxic to those cells. Signals from the fluorescent components can be read at their individual wavelengths, but their power lies in combining the response from both, which gives clinicians the ability to measure oxygen content as far as 2 millimeters into tissues.

"That's small, but oxygen diffusion limits are usually tiny," Grande-Allen said. "Some cells are quite close to a blood supply, with a high oxygen level brought in by blood cells with hemoglobin. But some bacteria in the microbiome are normally anaerobic and survive better without oxygen."

Grande-Allen said the particles aren't susceptible to photobleaching (fading) when illuminated at the proper wavelength, nor did they sink out of the hydrogel, as larger fluorescent particles were prone to do, even after a year in storage.

She noted that tissues like cartilage and certain types of diseased heart valves don't have vascular networks, yet their cells thrive. "I've always wondered how these [cells](#) get nourishment and what they need to survive," she said. "With oxygen-sensing microparticles and other

techniques we use in my lab to stretch living and engineered materials, we can start to work toward answering these questions."

More information: Reid Laurence Wilson et al. Monitoring oxygen levels within large, tissue-engineered constructs using porphyrin-hydrogel microparticles., *ACS Biomaterials Science & Engineering* (2019). [DOI: 10.1021/acsbomaterials.9b00257](https://doi.org/10.1021/acsbomaterials.9b00257)

Provided by Rice University

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