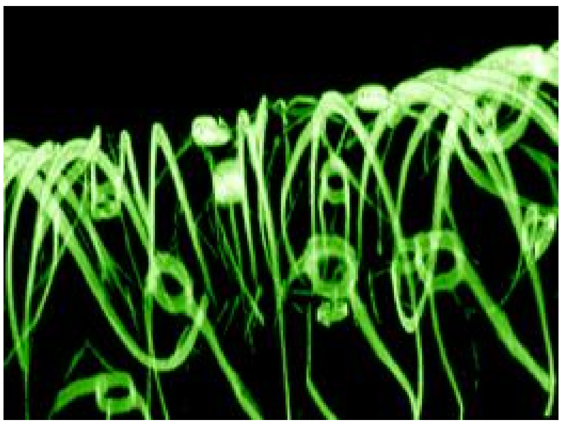
Merging bioengineering and electronics: Scientists grow artificial tissues with embedded nanoscale sensors

August 26 2012, by



A 3-D reconstructed confocal fluorescence micrograph of a tissue scaffold. Image: Charles M. Lieber and Daniel S. Kohane.

A multi-institutional research team has developed a method for embedding networks of biocompatible nanoscale wires within engineered tissues. These networks—which mark the first time that electronics and tissue have been truly merged in 3D—allow direct tissue sensing and potentially stimulation, a potential boon for development of engineered tissues that incorporate capabilities for monitoring and stimulation, and of devices for screening new drugs.

The researcher team—led by Daniel Kohane, MD, PhD, in the

Department of Anesthesia at Boston Children's Hospital; Charles M. Lieber, PhD, at Harvard University; and Robert Langer, ScD, at the Massachusetts Institute of Technology—reported their work online on August 26 in Nature Materials.

One of the major challenges in developing bioengineered tissues is creating systems to sense what is going on (e.g., chemically, electrically) within a tissue after it has been grown and/or implanted. Similarly, researchers have struggled to develop methods to directly stimulate engineered tissues and measure cellular reactions.

"In the body, the autonomic nervous system keeps track of pH, chemistry, oxygen and other factors, and triggers responses as needed," Kohane explained. "We need to be able to mimic the kind of intrinsic feedback loops the body has evolved in order to maintain fine control at the cellular and tissue level."

With the autonomic nervous system as inspiration, a postdoctoral fellow in the Kohane lab, Bozhi Tian, PhD, and his collaborators built mesh-like networks of nanoscale silicon wires—about 80 nm in diameter—shaped like flat planes or in a "cotton-candy"-like reticular conformation. The networks were porous enough to allow the team to seed them with cells and encourage those cells to grow in 3D cultures.

"Previous efforts to create bioengineered sensing networks have focused on 2D layouts, where culture cells grow on top of electronic components, or on conformal layouts where probes are placed on tissue surfaces," said Tian. "It is desirable to have an accurate picture of cellular behavior within the 3D structure of a tissue, and it is also important to have nanoscale probes to avoid disruption of either cellular or tissue architecture."

"The current methods we have for monitoring or interacting with living systems are limited," said Lieber. "We can use electrodes to measure activity in cells or tissue, but that damages them. With this technology, for the first time, we can work at the same scale as the unit of biological system without interrupting it. Ultimately, this is about merging tissue with electronics in a way that it becomes difficult to determine where the tissue ends and the electronics begin."

"Thus far, this is the closest we've come to incorporating into engineered tissues electronic components near the size of structures of the extracellular matrix that surrounds cells within tissues," Kohane added.

Using heart and nerve cells as their source material and a selection of biocompatible coatings, the team successfully engineered tissues containing embedded nanoscale networks without affecting the cells' viability or activity. Via the networks, the researchers could detect electrical signals generated by cells deep within the engineered tissues, as well as measure changes in those signals in response to cardio- or neurostimulating drugs.

Lastly, the team demonstrated that they could construct bioengineered blood vessels with embedded networks and use those networks to measure pH changes within and outside the vessels—as would be seen in response to inflammation, ischemia and other biochemical or cellular environments.

"This technology could turn some basic principles of bioengineering on their head," Kohane said. "Most of the time, for instance, your goal is to create scaffolds on which to grow tissues and then have those scaffolds degrade and dissolve away. Here, the scaffold stays, and actually plays an active role."

The team members see multiple future applications for this technology, from hybrid bioengineered "cyborg" tissues that sense changes within the body and trigger responses (e.g., drug release, electrical stimulation) from other implanted therapeutic or diagnostic devices, to development of "lab-on-a-chip" systems that would use engineered tissues for screening of drug libraries.

Provided by Children's Hospital Boston