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Sensing Cyborg Tissues Now Feasible

Scientists have developed a technique for constructing silicon nanowire tissue scaffolds that contain nanoscale electrodes capable of monitoring intra- and extracellular function within living biological tissues grown through them. The porous three-dimensional (3D) biocompatible scaffolds can be generated as a mesh or planar construct and manipulated into just about any shape required before seeding with living cells. Embedded in the framework are silicon nanowire field-effect transistor (FET) detectors that can monitor and detect changes in physicochemical parameters within tissues grown through the scaffold. Initial experiments demonstrated utility of the platform to monitor electrical responses in tissues grown from cardiac and neural cells, and also to monitor pH changes in synthetic blood vessels constructed from smooth muscle cells.

The Harvard University and Massachusetts Institute of Technology researchers claim the technology marks the first time that electronics and tissue engineering have been combined at the scale of the structures within the extracellular matrix surrounding cells, and without affecting cell viability or function. And while they say the technology could have numerous applications for sensing in tissues in vitro and potentially in vivo, one of the most obvious initial uses will be as a tool for studying how drug candidates affect different types of tissues grown in physiologically relevant three dimensions. Harvard's Daniel S. Kohane, M.D., Charles M. Lieber, Ph.D., Bozhi Tian, Ph.D., and colleagues report their work in *Nature Materials*, in a paper titled "Macroporous nanowire nanoelectronic scaffolds for synthetic tissues."

Scientists have to date struggled to develop a synthetic tissue system that can monitor cellular activity and physicochemical changes deep within a tissue in real time without damaging the cells themselves, the Harvard and MIT team states. "Previous efforts to create bioengineered sensing networks have focused on 2D layouts, where cultured cells grow on top of electronic components or on conformal layouts where probes are placed on tissue surfaces," Dr. Tian explains. In contrast, the new technique takes at its inspiration the ability of the autonomic nervous system to keep track of pH, chemistry, oxygen, and other factors within every tissue in the body.

The biocompatible nanowire electronic scaffolds (nanoES) designed to mimic this ability comprise three basic building blocks: semiconductor nanowires, polymer precursors, and the cells themselves. The nanowires are deposited into a polymer to generate the basic nanowire FET lattice, and the polymer is subsequently removed. The resulting nanowire FET devices are then lithographically patterned and integrated into free-standing macroporous scaffolds to generate the nanoES construct, and combined with synthetic or natural macroporous extracellular matrices to provide an overall structure that has electrical sensory function while retaining biocompatibility to enable tissue culture.

Initial experiments demonstrated that the nanoES were capable of supporting the 3D growth of heart and nerve cells seeded into them. The embedded sensors effectively detected electrical signals in the deepest regions of the resulting tissue, and measured changes in these signals in response to the administration of cardio- or neurostimulating drugs. The team subsequently used the nanoES to generate bioengineered blood vessels using smooth muscle cells, and measure pH changes both inside and outside the vessels.

"The nanoES are distinct from conventional 2D multielectrode arrays, carbon nanotube/nanofiber arrays, implantable microelectrodes, and flexible/stretchable electrodes in that the sensors are nanoscale semiconductors and, critically, that the sensor network is flexible, macroporous, and 3D," the authors write. "As a result, nanoES are suitable for 3D cell cultures that are known to resemble the structure, function, or physiology of living tissues ... Looking forward, there are several areas to develop. Cell interactions with nanoES could be tuned by modification of the nanoES with growth determinants. In addition, the elements in the nanoES could be expanded to incorporate nanoscale stimulators and stretchable designs to provide electrical and mechanical stimulation to enhance cell culture."