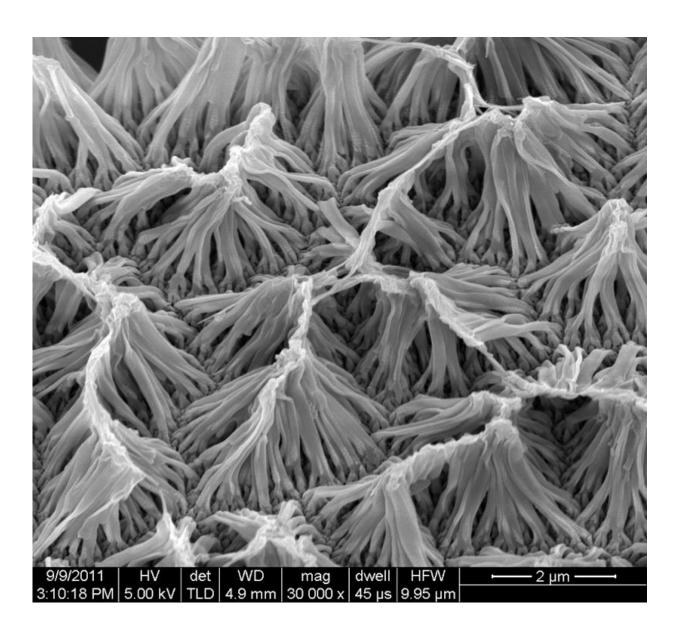


Nanowire implants offer remote-controlled drug delivery

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An image of a field of polypyrrole nanowires captured by a scanning electron microscope is shown. A team of Purdue University researchers developed a new



implantable drug-delivery system using the nanowires, which can be wirelessly controlled to release small amounts of a drug payload. Credit: Purdue University image/courtesy of Richard Borgens

A team of researchers has created a new implantable drug-delivery system using nanowires that can be wirelessly controlled.

The nanowires respond to an electromagnetic field generated by a separate device, which can be used to control the release of a preloaded drug. The system eliminates tubes and wires required by other implantable devices that can lead to infection and other complications, said team leader Richard Borgens, Purdue University's Mari Hulman George Professor of Applied Neuroscience and director of Purdue's Center for Paralysis Research.

"This tool allows us to apply drugs as needed directly to the site of injury, which could have broad medical applications," Borgens said.
"The technology is in the early stages of testing, but it is our hope that this could one day be used to deliver drugs directly to spinal cord injuries, ulcerations, deep bone injuries or tumors, and avoid the terrible side effects of systemic treatment with steroids or chemotherapy."

The team tested the drug-delivery system in mice with compression injuries to their spinal cords and administered the corticosteroid dexamethasone. The study measured a molecular marker of inflammation and scar formation in the central nervous system and found that it was reduced after one week of treatment. A paper detailing the results will be published in an upcoming issue of the *Journal of Controlled Release* and is currently available online.

The nanowires are made of polypyrrole, a conductive polymer material



that responds to <u>electromagnetic fields</u>. Wen Gao, a postdoctoral researcher in the Center for Paralysis Research who worked on the project with Borgens, grew the nanowires vertically over a thin gold base, like tiny fibers making up a piece of shag carpet hundreds of times smaller than a human cell. The nanowires can be loaded with a drug and, when the correct electromagnetic field is applied, the nanowires release small amounts of the payload. This process can be started and stopped at will, like flipping a switch, by using the corresponding electromagnetic field stimulating device, Borgens said.

The researchers captured and transported a patch of the nanowire carpet on water droplets that were used used to deliver it to the site of injury. The nanowire patches adhere to the site of injury through surface tension, Gao said.

The magnitude and wave form of the electromagnetic field must be tuned to obtain the optimum release of the drug, and the precise mechanisms that release the drug are not yet well understood, she said. The team is investigating the release process.

The electromagnetic field is likely affecting the interaction between the nanomaterial and the drug molecules, Borgens said.

"We think it is a combination of charge effects and the shape change of the polymer that allows it to store and release drugs," he said. "It is a reversible process. Once the electromagnetic field is removed, the polymer snaps back to the initial architecture and retains the remaining drug molecules."

For each different drug the team would need to find the corresponding optimal electromagnetic field for its release, Gao said.

This study builds on previous work by Borgens and Gao. Gao first had to



figure out how to grow polypyrrole in a long vertical architecture, which allows it to hold larger amounts of a drug and extends the potential treatment period. The team then demonstrated it could be manipulated to release dexamethasone on demand. A paper detailing the work, titled "Action at a Distance: Functional Drug Delivery Using Electromagnetic-Field-Responsive Polypyrrole Nanowires," was published in the journal *Langmuir*.

Other team members involved in the research include John Cirillo, who designed and constructed the electromagnetic field stimulating system; Youngnam Cho, a former faculty member at Purdue's Center for Paralysis Research; and Jianming Li, a research assistant professor at the center.

For the most recent study the team used mice that had been genetically modified such that the protein Glial Fibrillary Acidic Protein, or GFAP, is luminescent. GFAP is expressed in cells called astrocytes that gather in high numbers at central nervous system injuries. Astrocytes are a part of the inflammatory process and form a scar tissue, Borgens said.

A 1-2 millimeter patch of the nanowires doped with dexamethasone was placed onto spinal cord lesions that had been surgically exposed, Borgens said. The lesions were then closed and an electromagnetic field was applied for two hours a day for one week. By the end of the week the treated mice had a weaker GFAP signal than the control groups, which included mice that were not treated and those that received a nanowire patch but were not exposed to the electromagnetic field. In some cases, treated mice had no detectable GFAP signal.

Whether the reduction in astrocytes had any significant impact on <u>spinal</u> <u>cord</u> healing or functional outcomes was not studied. In addition, the concentration of drug maintained during treatment is not known because it is below the limits of systemic detection, Borgens said.



"This method allows a very, very small dose of a drug to effectively serve as a big dose right where you need it," Borgens said. "By the time the drug diffuses from the site out into the rest of the body it is in amounts that are undetectable in the usual tests to monitor the concentration of drugs in the bloodstream."

Polypyrrole is an inert and biocompatable material, but the team is working to create a biodegradeable form that would dissolve after the treatment period ended, he said.

The team also is trying to increase the depth at which the <u>drug delivery</u> <u>device</u> will work. The current system appears to be limited to a depth in tissue of less than 3 centimeters, Gao said.

More information: Remote-Controlled Eradication of Astrogliosis in Spinal Cord Injury via Electromagnetically-induced Dexamethasone Release from "Smart" Nanowires, *Journal of Controlled Release*, 2015.

Provided by Purdue University

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