NOVEL NEURAL PROBE HELPS TO UNLOCK MYSTERIES OF THE BRAIN

In April of 2013, President Obama announced the launch of the BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative, an ambitious grand challenge aimed at vastly increasing our understanding of the human brain. The goal of the Initiative, Obama said, is to unlock the mysteries of the brain, to improve our treatment of conditions like Alzheimer’s and autism and to deepen our understanding of how we think, learn and remember.

The BRAIN Initiative will provide funding of more than $3.5 billion over 12 years to accelerate the development and application of new technologies that will allow researchers to understand how individual brain cells and complex neural circuits interact at the speed of thought.

There’s a big gap between what we want to do in brain research and the technologies available to take us there, said Francis S. Collins, director of the National Institutes of Health (NIH), which sponsors a major part of the Initiative. The initial awards are focused on developing the tools and technologies needed to make the next leap in understanding the brain.

One of those initial NIH awards went to Jack Wolfe and Wei-Chuan Shih, both professors in the UH Cullen College of Engineering’s department of electrical and computer engineering. Their collaborator on the project is Gopathy Purushothaman at the Vanderbilt School of Medicine. Together, they aim to develop a novel brain probe for use in optogenetic studies of the brain. Their award totals $428,406 over two years.

Optogenetics, named the method of the year by the journal Nature Methods in 2010, is a transformative technology wherein a tiny volume of suspended virus particles is injected into a region of the brain associated with a specific behavior (for example, walking in a counterclockwise circle). The virus transfers a gene to the specific neurons responsible for the behavior, which causes the neurons to become sensitive to and excited by light.

Shining a light on the sensitized neurons will cause them to emit electrical pulses that, in turn, cause the animal
to walk in a counterclockwise circle.

Because the neurons respond to light extremely quickly, neuroscientists are able to track the link between brain activity and behavior at the speed of thought. The technique can be equally applied in the sensory systems, in learning, and even in creative thought. Optogenetics is also useful in understanding how the brain is disrupted by neurological and psychiatric disease.

The ultimate hope, said Wolfe, is that light stimulation of the brain’s neurons will one day be added to the current treatment options for brain disorders.

But the neural probes that are currently available for optogenetics studies have some drawbacks. For starters, they can’t probe very deep inside of the brain — only a few millimeters, in fact. This poses a problem when it comes to studying the brain, as many of its neural networks are located as deep as 50 millimeters.

Secondly, current probes are much larger in diameter than the probe being developed by Wolfe and Shih, which means they cause more damage when inserted into the brain.

By comparison, the probes being developed at the Cullen College are less than 60 microns in diameter, while commercially available probes measure between 125 to 500 microns in diameter. Wolfe and Shih’s probe is so fine, in fact, that it is smaller than a single strand of human hair. Their goal is to make the probe even smaller — about a third of the size of a human hair, or about 30 microns in diameter — by the end of this project.

At the core of Wolfe’s novel probe is a single strand of optical fiber. Using lithography, the researchers print sets of electrodes directly onto the fiber. These electrodes record and transmit information on brain activity resulting from light stimulation.

Even more impressive, they are able to print more than one set of electrodes on a single fiber at varying distances from one another. This will allow researchers to monitor neurons in different layers of the brain simultaneously with a single probe, a research technique that has not been previously available for deep brain probes. We will be able to create accurate, three-dimensional maps of the brain’s neural circuits for the first time ever, Wolfe said.

Unlike many probe prototypes in use today, the probe being developed by Wolfe’s team is compatible with high-throughput manufacturing at very low cost. That is to say, the new probe could be cheaply and reliably manufactured, making it an optimal option for use in research centers and clinics around the world.

The emphasis is on being able to make them very quickly and reliably, Wolfe said. A wide variety of tests will be performed to make sure they are reliable in all the ways they need to be.

This finer, stiffer and longer probe would be particularly helpful to researchers such as Purushothaman, whose primary research interest is mapping the neural networks involved in the brain’s vision system. Current probes can only reach a few millimeters into the brain, but critical structures, such as the thalamus, a switching center for visual signals, are located several centimeters inside of a primate’s brain.

As you can imagine, Purushothaman said, this is a very exciting development for myself and many other researchers who have been waiting for a probe that is long enough to reach deep into the brain.

The brain’s circuitry, even in a small piece of brain tissue, is incredibly complicated, Purushothaman said. There are thousands of neurons that are very specifically connected, so it’s like having a highly complex integrated circuit in a very compact space that is in three dimensions.?

This probe gives me the ability to understand how those neurons are connected and how they work together in the circuit, he added. That is a major benefit to my research, and that’s precisely the goal of the BRAIN Initiative — to decipher, in as much detail as possible, the brain circuitry.
Although this study is still in its early phases, all three of the researchers said there is a very high chance their probe will be tested in human clinical trials. ?Once we get this project done we will have a working product which can then move into the clinical arena,? Purushothaman said.