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Researcher creates neurons that light up as they fire

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In a scientific first that potentially could shed new light on how signals travel in the brain, how learning alters neural pathways, and might lead to speedier drug development, scientists at Harvard have created genetically-altered neurons that light up as they fire.

The work, led by John L. Loeb Associate Professor of the Natural Sciences Adam Cohen, and described in Nature Methods on Nov. 28, involved using a gene from a Dead Sea microorganism to produce a protein that, when exposed to the electrical signal in a neuron, fluoresces, allowing researchers to trace the propagation of signals through the cell.

"It's very exciting," Cohen said of the research. "In terms of basic biology, there are a number of things we can now do which we've never been able to do. We can see how these signals spread through the neuronal network. We can study the speed at which the signal spreads, and if it changes as the cells undergo changes. We may someday even be able to study how these signals move in living animals."

To create the light-up neurons, Cohen and his team infected brain cells that had been cultured in the lab with a genetically-altered virus that contained the protein-producing gene. Once infected, the cells began manufacturing the protein, allowing them to light up.

"The way a neuron works is it has a membrane around the whole cell, sort of like a wire and insulation, except in a neuron the membrane is an

active substance," Cohen said. "Normally, the inside of the cell is negatively-charged relative to the outside.

"When a neuron fires, the voltage reverses for a very short time, about 1/1,000th of a second," he continued. "This brief spike in voltage travels down the neuron and then activates other neurons downstream. Our protein is sitting in the membrane of the neurons, so as that pulse washes over the proteins, they light up, giving us an image of the neurons as they fire."

The research has the potential to revolutionize our understanding of how electrical signals move through the brain, as well as other tissues, Cohen said.

"Before, the best way to make a measurement of the electrical activity in a cell was to stick a little electrode into it and record the results on a volt meter," he said. "The issue, however, was that you were only measuring the voltage at one point, you weren't seeing a spatial map of how signals propagate. Now, we will be able to study how the signal spreads, whether it moves through all neurons at the same speed, and even how signals change if the cells are undergoing something akin to learning."

Another limitation of using electrodes, Cohen said, is that the process tends to kill the cells relatively quickly, making it impossible to study processes that take place over time. His new process, however, opens the door to studying the effects of growth and development on neurons, or to monitor how stem cells develop.

Being able to track the electrical pathways in cells also holds practical applications, Cohen said, particularly when it comes to the development of new drugs or other therapies.

"Many, many drugs target ion channels, which are important proteins in

governing the activity of the heart and brain," he said. "Right now, if you want to test a compound designed to activate or inactivate a particular ion channel, you have to culture the cell, test it with an electrode, then add the drug and see what happens. This is an extremely slow process – it typically takes an hour or two for each data point.

"Now that we can do it optically in the microscope, we can test the efficacy of a drug on a cell in a few seconds. Instead of testing one compound or ten compounds, we can try to test thousands or even hundreds of thousands. We can test different conditions, different mixtures – it will increase the throughput for testing new drugs."

The process may even open new research avenues for those studying genetic conditions ranging from depression to heart disease.

Using stem cells, researchers can culture cells in the lab that are genetically identical to a patient known to carry a genetic predisposition to a particular condition, then study how signals move through those cells.

Provided by Harvard University