New biochip helps study living cells, may speed drug development

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Purdue University researchers have developed a biochip that measures the electrical activities of cells and is capable of obtaining 60 times more data in just one reading than is possible with current technology.

In the near term, the biochip could speed scientific research, which could accelerate drug development for muscle and nerve disorders like epilepsy and help create more productive crop varieties.

"Instead of doing one experiment per day, as is often the case, this technology is automated and capable of performing hundreds of experiments in one day," said Marshall Porterfield, a professor of agricultural and biological engineering who leads the team developing the chip.

The device works by measuring the concentration of ions -- tiny charged particles -- as they enter and exit cells. The chip can record these concentrations in up to 16 living cells temporarily sealed within fluid-filled pores in the microchip. With four electrodes per cell, the chip delivers 64 simultaneous, continuous sources of data.

This additional data allows for a deeper understanding of cellular activity compared to current technology, which measures only one point outside one cell and cannot record simultaneously, Porterfield said. The chip also directly records ion concentrations without harming the cells, whereas present methods cannot directly detect specific ions, and cells being studied typically are destroyed in the process, he said. There are several advantages to retaining live cells, he said, such as being able to conduct additional tests or monitor them as they grow.

"The current technology being used in research labs is very slow and difficult," said Porterfield, who believes the new chip could help develop drugs for human disorders involving ion channel malfunction, such as epilepsy and chronic pain. About 15 percent of the drugs currently in development affect the activities of ion channels, he said, and their development is limited by the slower pace of current technology. The biochip would allow researchers to generate more data in a shorter time, thus speeding up the whole process of evaluating potential drugs and their different effects on ion channels.

Ion channels are particularly important in muscle and nerve cells, where they facilitate communication and the transfer of electrical signals from one cell to the next.

Within the 10-by-10 millimeter chip -- roughly the size of a dime -- cells are sealed inside 16 pyramidal pores, analyzed, and then can be removed intact. Since the technology does not kill the cells, it could be used to screen and identify different crop lines, Porterfield said.

"For example, let's say you were interested in developing corn varieties that need less fertilizer," he said. "If you had a library of genes that were associated with high nitrogen-use efficiency -- thus making the plant need less nitrogen fertilizer -- you could transform a group of maize cells with these genes and then screen each cell to determine the most efficient. Then you could raise the one that needed the least fertilizer, rather than putting a lot of different genes into hundreds of plants and waiting for them to grow, as is currently done."

In addition to the potential savings in time and money, Porterfield said the chip has allowed him to do research that would otherwise be impossible. He recently conducted a study on the "Vomit Comet," the nickname for a high-flying research plane used by NASA to briefly simulate zero gravity. The experiment analyzed gravity's effect on plant development, trying to solve the riddle of how a plant determines which way is "up."

"We conducted research with the chip while we were flying in parabolas over the Gulf of Mexico, going from two times Earth's gravity to zero gravity again and again," he said. "There is absolutely no way this experiment could have been done without this chip."

The current technology for analyzing cells' electrical activity, called "patch clamping," uses a tiny electrical probe viewed under a microscope. The technology garnered its inventors the Nobel Prize for Medicine and Physiology in 1991.

"It requires a lot of know-how and hand-eye coordination," Porterfield said of patch clamping.

The chip, on the other hand, is automated and could be mass-produced in the future. Such a readily available chip could record reams more data than patch-clamping, he said.

Ion channels and pumps establish a difference in electrical potential across a cell's membrane, which cells use to create energy and transfer electrical signals. By quickly allowing ions in and out, they are useful for rapid cellular changes, the kind which occur in muscles, neurons and the release of insulin from pancreatic cells.

The chip currently can detect individual levels of different ions. Porterfield believes that with some modifications, however, the chip will be able to measure multiple ions at once and perform even more advanced functions such as electrically stimulating a cell with one electrode while recording the reaction with the remaining three.

Because ion channels are a prominent feature of the nervous system and elsewhere, they are a popular target for drugs. For example, lidocaine and Novocain target sodium-channels. In nature, some of the most potent venoms and toxins work by blocking these channels, including the venom of certain snakes and strychnine.

Porterfield's chip is technically classified as a "cell electrophysiology lab-on-a-chip." The device is further described in an article in the journal *Sensors and Actuators*, published online this month and scheduled to appear in the print edition in November.

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