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'Chemisthode' to aid in study of biological processes

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Measuring an electrical current in an organism is pretty straightforward. All you need is an electrode, an amplifier and years of training. Measuring the flow of chemicals in cells or live tissue, however, is much more difficult because the molecules diffuse, mix with one another and interact with their surroundings.



Photo by Lloyd DeGrane

Graduate student Delai Chen adjusts the chemisthode, a new droplet-based, microfluidic device for studying stimulus-response dynamics in chemistry and biology. Chen brings the V-shaped device into contact with the tissue under study. A steady stream of stimulating chemicals is pumped into the device through tiny tubes on one end, and the resultant chemicals flow out through tiny tubes on the other end.

To help understand biological processes, University researchers have invented a new device, the "chemisthode," which makes it possible to stimulate, record and analyze molecular signals at high resolution—in terms of precisely when, where and in what sequence the signals occurred.

The chemisthode will help researchers study any surface that responds to chemical stimulation, including cells, tissue, biofilms and catalytic surfaces. It may also help neurologists, cardiologists and endocrinologists study and diagnose diseases, according to those who developed the device in the lab of Rustem Ismagilov, Professor in Chemistry. Researchers already have used it to measure how a single murine islet responds to glucose.

The developers have begun to apply for a patent on the new device, and their research is described in Tuesday, Nov. 4 edition of the *Proceedings of the National Academy of Science*.

"An analogue of the electrode, the chemisthode is a droplet-

based, microfluidic device that will provide exciting opportunities to study stimulus-response dynamics in chemistry and biology,” said Ismagilov, who conceived the device, coined its name and heads up the team that developed it.

Previous techniques for stimulating and measuring chemical reactions in organisms relied on laminar flow, which allows the chemicals in question to intermingle and disperse, making them hard to control and measure.

The new V-shaped device, on the other hand, traps the chemicals in water droplets and suspends the droplets in a fluorocarbon carrier fluid. This keeps the chemical-laden droplets intact, allowing a controlled stream of stimulating chemicals to enter on one end of the device and a steady stream of distinct resultant chemicals to be captured on the other. The chemical-laden droplets can be analyzed immediately or stored for future analysis. Furthermore, the droplets can be split up for parallel study by different techniques.



Rustem Ismagilov

“The inspiration for this work was the microelectrode, but the key to its success was encapsulating the chemicals in aqueous droplets so that the chemicals could be delivered to and picked up from the reactive site in a controllable, measurable fashion,” said Delai Chen, a graduate student in Chemistry and the University’s Institute for Biophysical Dynamics. Chen was one of the four lead authors of the *PNAS* research paper, along with University post-doctoral researchers Wenbin Du and Ying Liu, and graduate student Weishan Liu.

A year-and-a-half in the making, the chemisthode is compatible with traditional methods of culturing cells and tissues because—like the electrode—it can be used on any surface. The device is brought into contact with the surface of a cell or tissue under investigation. An array of tiny droplets containing chemical stimuli is then delivered to the sample. Chemical reactions occur, or molecules are released from the sample, as in the case of a hormone; the resultant chemical-laden droplets are carried away. All the while, the fluorocarbon carrier fluid remains in contact with the droplets and shields them from the wall of the device.

“The chemisthode offers a time-resolved, high-fidelity record of molecular stimulation and response dynamics,” Ismagilov said. “Our *PNAS* paper describes the physical principles that guide the operation of the chemisthode. It also implements the chemisthode to test the feasibility of each step and the compatibility of this platform with living cells.”

For now, the device “allows you to look very hard and precisely at living cells in a dish, but it has the potential to be used in whole organisms as well,” said Louis Philipson, Professor in Medicine and Pediatrics and a co-author on the paper. “The chemisthode offers real-time input-output analysis captured in excellent resolution. As such, it will facilitate research in a lot of areas and holds the potential for widespread applications in medicine.

“The development of this device is a wonderful example of the lack of walls at the University of Chicago,” Philipson added. “Here, physicians can interact with other scientists in unconventional ways and bring together different kinds of technology. The result is new ways of looking at things and new answers to old problems.”
