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New chemistry method uses 'test tubes' far smaller than the width of a hair

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Using a water droplet 1 trillion times smaller than a liter of club soda as a sort of nanoscale test tube, a University of Washington scientist is conducting chemical analysis and experimentation at unprecedented tiny scales.

The method captures a single cell, or even a small subcellular structure called an organelle, within a droplet. It then employs a powerful laser microscope to study the contents and examine chemical processes, and a laser beam is used to manipulate the cell or even just a few molecules, combining them with other molecules to form new substances.

This nanoscale "laboratory" is so minuscule that it covers just 1 percent of the width of a human hair, said **Daniel Chiu**, a UW associate chemistry professor who is developing the unique method.

"Anything you can do in the test tube we hope to be able to do in the droplet. We just don't need a lot of cells. We don't even need one cell, just a few molecules," **Chiu** said.

The new approach makes it easier to get a wide range of information about a cell. Researchers typically use microscopy to see how proteins move within a cell and collect spatial information, but that provides very little biochemical information, **Chiu** said. Likewise, they can use large amounts of material in a test tube to understand biochemical processes, but that doesn't provide the fine detail of microscopy.

"The cell is very small but it is very complex," **Chiu** said. "It has many hundreds of thousands of proteins. It is probably the ultimate nanomachine."



Daniel Chiu

Top image shows an arrow pointing to target as a water droplet forms in oil. Bottom image shows an organelle called a mitochondrion after it has been encapsulated in the water droplet.

The new method, employing a process called microfluidics, allows researchers to perform chemical analysis and to study structure and form at the same time.

The tiny droplet is contained in a microfluidic device, which is far too small to be seen with the naked eye and is mounted on a platform about the size of a dime so researchers can carry it from one place to another. The device has water in one channel and oil in an adjoining channel. The target -- a cell, an organelle or just a few molecules -- is placed at the interface between the oil and water using a laser beam, so the target is encapsulated as the water droplet is formed.

Once the droplet captures its target, it is held fast while researchers use lasers to manipulate it and

conduct analysis and experimentation.

"If you have 10 molecules that you're interested in, you can combine those with other molecules to make new molecules," **Chiu** said. "You can control their reactivity, move them and combine them if they are confined in a droplet. As soon as you put them in a test tube, they're diffused and you lose the ability to see them."

Chiu presented his work today during a session of the American Chemical Society's fall meeting in Washington, D.C.

The new method allows researchers to address specific biological questions that cannot be answered by testing in large quantities in the test tube, such as how organelles within a cell differ from each other, or how different proteins are expressed within the same cell, **Chiu** said.

"At this point it is still limited to fundamental biological studies," he said. "It provides finer, higher resolution than working with standard test tubes. There are things you cannot find out in bulk, and every cell and organelle is different."

Currently **Chiu** is focused on continuing development of the process, essentially creating a nanoscale test tube. But he believes the process holds great promise for future chemical and biological research.

"We're still trying to develop the process and to understand the chemistry at this small scale, which could be very different from chemistry at the macro scale," he said.

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For more information, contact Chiu at (206) 543-1655 or chiu@chem.washington.edu

During the conference, **Chiu** can be reached by calling UW News and Information, (206) 543-2580, or by leaving a message at Grand Hyatt Washington hotel, (202) 582-1234.

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