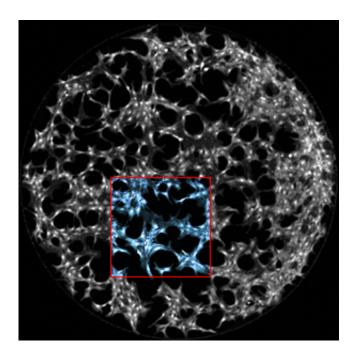


Eavesdropping on the body: New device tracks chemical signals within cells

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Microarray image overlaid with brightfield microscopy of fibroblasts probed using digital microfluidic immunocytochemistry in single cells. Credit: Alphonsus Ng/ U of T Engineering

Biomedical engineers at the University of Toronto have invented a new device that more quickly and accurately "listens in" on the chemical messages that tell our cells how to multiply. The tool improves our understanding of how cancerous growth begins, and could identify new targets for cancer medications.



Throughout the human body, certain signalling chemicals—known as hormones—tell various <u>cells</u> when to grow, divide and proliferate. However, not all cells respond to these signals in the same manner. In rare instances, the internal chemical response of a cell can cause unregulated cell growth, leading to cancer.

To look into the responses of different cells, the U of T team harnessed the emerging power of digital microfluidics, which involves shuttling tiny drops of water around on a series of small electrodes that looks like a miniature checkerboard. Published today in *Nature Communications*, the paper explains how they were able to increase the speed at which chemical changes can be detected by a factor of 100.

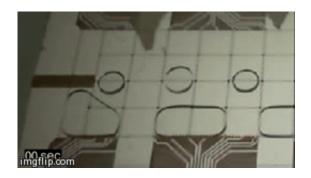
"By applying the right sequence of voltages, we can create electric fields that attract and move around droplets containing any chemical solution," says first author Alphonsus Ng who recently graduated with a PhD from the U of T Institute of Biomaterials and Biomedical Engineering (IBBME) and Donnelly Centre, and is now a post-doctoral fellow in the lab of Professor Aaron Wheeler.

Ng and his team's method allows the scientists to deliver a quick-fire sequence of chemicals to small groups of cells stuck to the surface of the board.

For example, the first drop might contain a hormone that tells cells to grow faster. Within seconds, this hormone sets off a chain reaction called a "phosphorylation cascade," modifying certain proteins within the cell in a specific sequence. To see these changes, scientists deliver a second drop containing formaldehyde, which freezes the all the proteins in place. They then deliver a third drop containing fluorescent antibodies that stick only to the proteins modified in the cascade. Looking at the antibodies in a microscope provides a snapshot of what has changed and what hasn't.



By building up a series of snapshots at different time intervals, scientists can see how the cascade progresses. "It's like a flipboard; each snapshot gives us a static image, but when you combine them all together, you can see movement or action," says Dean Chamberlain, a post-doctoral researcher at IBBME, the Donnelly Centre and the Department of Chemistry.



Passive dispensing of three successive 1.8-microliter droplets to a virtual microwell. Credit: Alphonsus Ng/ U of T Engineering

Using sequences of chemicals to measure how cells respond to a hormone is nothing new. But until now, scientists were limited by how fast they could add each chemical in the sequence. Using an eye-dropper or a pipette to drop solutions into petri dishes is inherently cumbersome. "Even with robots, you just can't pipette that fast," says Chamberlain. "In general, a two-minute time scale is considered pretty good." By contrast, the new microfluidic system can deliver drops only seconds apart

The team also made some interesting discoveries when they tested the technique on a type of <u>breast cancer cells</u>. "Roughly 10 per cent of the cells had a very rapid and strong response that we could detect up to five minutes before the rest of the population," says Chamberlain. The team speculates that these "rapid responders" may be involved in the early



stages of tumour generation, although more research is needed to confirm this.

While scientists have long suspected that some <u>cancer cells</u> respond to signals faster and more strongly than others, the new device offers a way to study such cells in unprecedented detail. "With the ability to probe these reactions with the same speed at which they occur, we're better equipped to figure out the internal wiring of the cell," says Ng. The team hopes to discover new cell types or proteins that could be targeted by drugs, eventually leading to new medicines to fight <u>cancer</u>.

Provided by University of Toronto

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