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## Disposable Chip Rapidly Detects Infectious Particles at the Point of Care: July 29, 2011

Is your coughing and sneezing caused by a common cold or potentially life-threatening swine flu?

Because different microbes (e.g., seasonal flu versus swine flu) cause many of the same symptoms, having the genetic information to identify a particular strain is critical in making an accurate diagnosis and eventually containing an outbreak. Current tests are not well suited for use at the point of care (the doctor's office or local clinic) because they require skilled laboratory personnel to perform the tests and it can take up to several days to get results. "In this country, for example, the current rapid flu tests are notoriously unreliable at the point of care," says postdoctoral fellow Scott Ferguson, University of California, Santa Barbara (UCSB). Rapid flu tests fail to detect the infection in up to 50 percent of cases and occasionally may be positive in people who do not have the flu. "Having a more sensitive detection method in the clinic would be extremely valuable," he adds.

To address these shortcomings, Ferguson is working with his research advisor, H. Tom Soh, Ruth Garland Professor at UCSB, and colleagues to design a system that integrates three laboratory processes on a single disposable chip. The system would accurately identify a microbe at the point of care, eliminating the time and expense of sending samples to a laboratory for identification by trained personnel.

### Purify, Amplify, Measure

Dubbed MIMED for Magnetic Integrated Microfluidic Electrochemical Detector, the device combines sample preparation (purification and genetic amplification) and electrochemical readout to detect



viruses directly from patient samples. In early testing, MIMED was able to detect as few as ten H1N1 influenza viruses spiked into samples swabbed from Ferguson's throat—an impressive feat given that detecting such small amounts of a microbe in a complex

The MIMED system is a universal point-of-care pathogen detection system. The 6x1 cm disposable chip integrates sample preparation and sequence-specific detection and can identify microbes in unprocessed biological, water, food, and forensic samples.

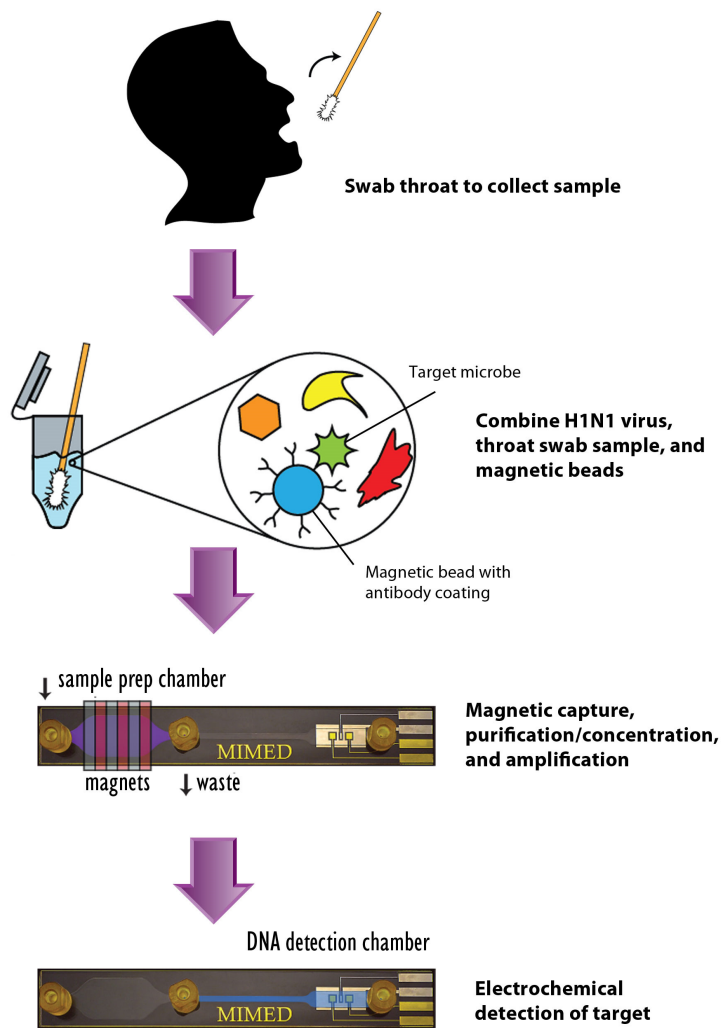
biological sample is like finding a four-leaf clover in a meadow.

Effective sample preparation is crucial for molecular detection. After dissolving the viral outer shell with a detergent to release the genetic material, researchers add antibody-coated magnetic beads to the throat swab sample and inject the mixture onto the chip. The antibodies capture the viral genetic material, and an external magnet holds the beads in one chamber of the chip while the researchers wash away target-degrading enzymes and other materials in the sample that interfere with the test. Concentrating the targets in this way enables detection of rare microbes in unprocessed biological samples. Next, the viral genetic material is amplified—replicated into many copies—and converted to single-stranded DNA (ssDNA) that can be detected using an electrochemical sensor.

The sensor generates an electrical signal when the target ssDNA binds to the matching ssDNA strand (probe) on the sensor. “The strength of the signal that we detect is correlated to the initial amount of viral particles,” explains Ferguson. MIMED can detect as few as 10 viral particles in a sample in about 4 hours; other molecular testing methods that can distinguish between viral strains take one or more days. The chip is 100 times more sensitive compared to other rapid tests for swine flu virus. “We’re trying to do extremely sensitive detection,” says Soh.

### A Chip for All Seasons

Ferguson and Soh conceived MIMED with a vision of universal application at the point of care. The device is capable of detecting pathogens in a variety of complex biological samples, such as blood, urine, or saliva. The system also could be adapted to detect a broad range of microbe concentrations. As long as the genetic code is known, the ssDNA probe can be designed to detect any microbe. And, using multiple sensors, the chip could simultaneously detect several different microbes in the same sample. In cases where a patient displays symptoms common to



To test MIMED's performance, researchers spike H1N1 (swine flu) virus into throat swab samples, add magnetic beads coated with anti-H1N1 antibodies, and drop the mix onto the chip. The antibodies capture the viral genetic material, and an external magnet holds the

multiple diseases, this single test could determine the actual cause of the disease. Beyond the clinic, rapid and accurate

beads in the sample prep chamber while the waste is washed away, effectively purifying and concentrating the target. The viral genetic material is subsequently amplified and converted to single-stranded DNA. Sequence-specific electrochemical detection takes place in the detection chamber. The MIMED device is 100 times more sensitive than other rapid tests for swine flu virus.

detection also could be very useful in food and water safety monitoring, forensics, and environmental monitoring.

Down the road, the researchers expect that the MIMED chip would be accompanied by an instrument that would integrate pumps, heaters, tubing, and other elements of the system. The chip itself may cost less than a dollar to manufacture. "The disposable chip would go into an instrument, much like an inkjet printer; it will handle all the sample prep, and there doesn't need to be any human involvement," says Ferguson.

Soh remarks that much more work needs to be done before the technology will be ready for use in the clinic. The lab is currently working on alternative, robust capture agents to replace antibodies, so that they can be used at the point of care without refrigeration. The Soh research team is also very interested in measuring the amount of pathogen in a sample in real time, an approach that could inform more effective courses of treatment.

Soh is already thinking of ways to apply this technology to in vivo detection of targets that cannot be amplified, such as proteins. He is particularly interested in proteins that signal presence or progression of disease, such as prostate-specific antigen for prostate cancer, platelet-derived growth factor-BB for cancer growth, and various microbial proteins for infectious disease. According to Soh, "This work has shown what can be done with genetically amplifiable targets, but targets that don't carry amplifiable information are by definition harder." He adds that his team needs to think of innovative ways to detect low levels of the target pathogen directly in raw, complex samples.

This work is supported by the National Institute of Biomedical Imaging and Bioengineering and the Institute of Collaborative Biotechnologies, Army Research Office.

### References

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H. Tom Soh



Scott Ferguson

Last reviewed on: 08/01/2011

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