Progress on detecting glucose levels in saliva

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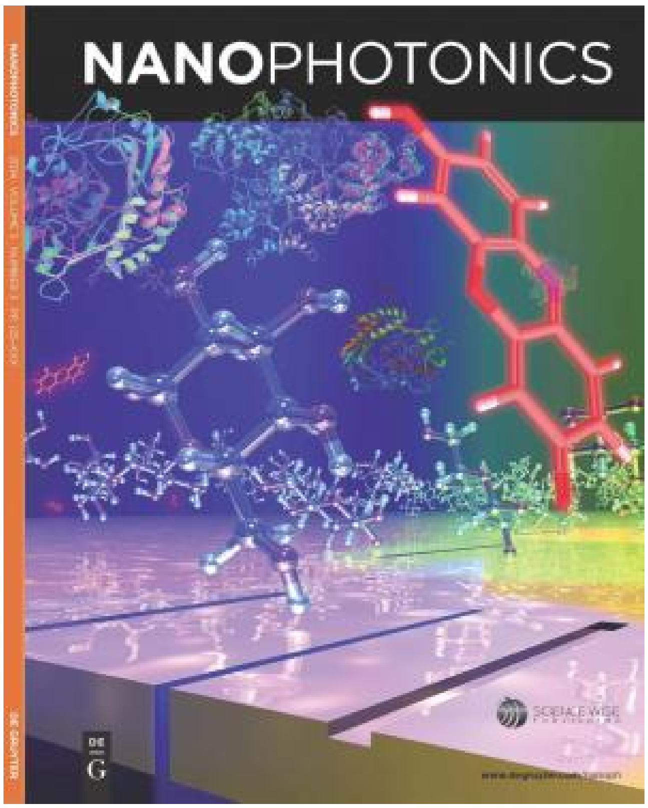

A plasmonic interferometer can detect glucose molecules in water. Detection of glucose in a complex fluid is more challenging. Controlling the distance between grooves and using dye chemistry on glucose molecules allows researchers to measure glucose levels despite the 1 percent of saliva that is not water.

Researchers from Brown University have developed a new biochip sensor that can selectively measure concentrations of glucose in a complex solution similar to human saliva. The advance is an important step toward a device that would enable people with diabetes to test their glucose levels without drawing blood.

The new chip makes use of a series of specific chemical reactions combined with plasmonic interferometry, a means of detecting chemical signature of compounds using light. The device is sensitive enough to detect differences in glucose concentrations that amount to just a few thousand molecules in the sampled volume.

"We have demonstrated the sensitivity needed to measure glucose concentrations typical in saliva, which are typically 100 times lower than in blood," said Domenico Pacifici, assistant professor of engineering at Brown, who led the research. "Now we are able to do this with extremely high specificity, which means that we can differentiate glucose from the background components of saliva."

The new research is described in the cover article of the June issue of the journal *Nanophotonics*.

The biochip is made from a one-inch-square piece of quartz coated with a thin layer of silver. Etched in the silver are thousands of nanoscale interferometers—tiny slits with a groove on each side. The grooves measure 200 nanometers wide, and the slit is 100 nanometers wide—about 1,000 times thinner than a human hair. When light is shined on the chip, the grooves cause a wave of free electrons in the silver—a surface plasmon polariton—to propagate toward the slit. Those waves interfere with light that passes through the slit. Sensitive detectors then measure the patterns of interference generated by the grooves and slits.

When a liquid is deposited on the chip, the light and the surface plasmon waves propagate through that liquid before they interfere with each other. That alters the interference patterns picked up by the detectors, depending on the chemical makeup of the liquid. By adjusting the distance between the grooves and the center slit, the interferometers can be calibrated to detect the signature of specific compounds or molecules, with high sensitivity in extremely small sample volumes.

In a paper published in 2012, the Brown team showed that interferometers on a biochip could be used to detect glucose in water. However, selectively detecting glucose in a complex solution like human saliva was another matter.

"Saliva is about 99 percent water, but it's the 1 percent that's not water that presents problems," Pacifici said. "There are enzymes, salts, and other components that may affect the response of the sensor. With this paper we solved the problem of specificity of our sensing scheme."

They did that by using dye chemistry to create a trackable marker for glucose. The researchers added microfluidic channels to the chip to introduce two enzymes that react with glucose in a very specific way. The first enzyme, glucose oxidase, reacts with glucose to form a molecule of hydrogen peroxide. This molecule then reacts with the second enzyme, horseradish peroxidase, to generate a molecule called resorufin, which can absorb and emit red light, thus coloring the solution. The researchers could then tune the interferometers to look for the red resorufin molecules.

"The reaction happens in a one-to-one fashion: A molecule of glucose generates one molecule of resorufin," Pacifici said. "So we can count the number of resorufin molecules in the solution, and infer the number of glucose molecules that were originally present in solution."

The team tested its combination of dye chemistry and plasmonic interferometry by looking for glucose in artificial saliva, a mixture of water, salts and enzymes that resembles the real human saliva. They found that they could detect resorufin in real time with great accuracy and specificity. They were able to detect changes in glucose concentration of 0.1 micromoles per liter—10 times the sensitivity that can be achieved by interferometers alone.

The next step in the work, Pacifici says, is to start testing the method in real human saliva. Ultimately, the researchers hope they can develop a small, self-contained device that could give diabetics a noninvasive way to monitor their glucose levels.

There are other potential applications as well.

"We are now calibrating this device for insulin," Pacifici said, "but in principle we could properly modify this plasmonic cuvette sensor for detection of any molecule of interest."

It could be used to detect toxins in air or water or used in the lab to monitor chemical reactions as they occur at the sensor surface in real time, Pacifici said.

More information: Paper: www.degruyter.com/view/j/nanop … nanoph-2013-0057.xml

Provided by Brown University

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