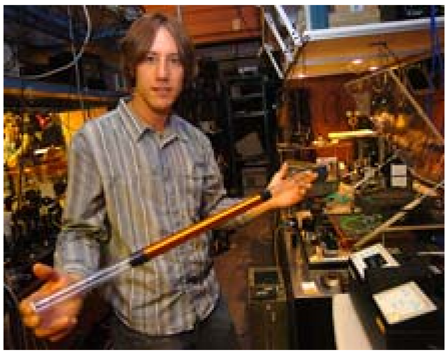
AN MIT ENTERPRISE
TECHNOLOGY
REVIEW

March 14, 2008

New Breath-Based Diagnostic

An innovative technique for detecting different biomarkers could result in a precise, easy-to-use diagnostic tool.

By Katherine Bourzac



Telltale breath: Michael Thorpe, a graduate student at the University of Colorado, Boulder, holds part of a machine that uses optical techniques to analyze traces of chemicals on the breath. Inside the tube is a system of mirrors that exposes a subject's breath to laser light. Light is absorbed by the breath according to its chemical composition.

Credit: Jun Ye, JILA

People with cancer, asthma, and many other diseases carry trace amounts of distinctive biomarkers in their breath. Detecting these markers could allow doctors to diagnose such diseases in their early stages, noninvasively, and before symptoms arise. Existing techniques for analyzing the breath's chemical composition have limitations. Simple, relatively inexpensive methods can be imprecise; conversely, highly precise devices are complicated and expensive. Now, researchers at the University of Colorado, Boulder, and the National Institute of Standards and Technology are developing a sensitive optical technique for real-time breath analysis that may overcome some of these hurdles.

The new breath analyzer, developed by Jun Ye, a physics professor at the University of Colorado, uses a kind of laser light called an "optical frequency comb" to identify about a thousand compounds in a few seconds. Ye's system works by measuring how the breath absorbs light. The subject breathes into a tube that contains a laser, a system of mirrors, and a photodetector. The laser emits rapid pulses of light in frequencies ranging from infrared to visible. The light's frequency changes as it encounters compounds in the breath. The system analyses these changes determine which compounds are present.

The lungs have an intimate relationship with the blood: as a result, many volatile compounds from all over the body can be found in the breath. The best evidence of this comes from studies of lung and breast cancer and tuberculosis, says Michael Phillips, a medical doctor and CEO of Menssana Research, a company developing diagnostic breath tests. Currently, the Food and Drug Administration approves only two breath-analysis diagnostics. One uses nitric oxide levels to diagnose asthma; another, marketed by Menssana, analyzes hydrocarbon levels to predict a patient's likelihood of rejecting a heart transplant.

"For chemical analysis, optical techniques in general are the best you can get," says Margaret Ryan, principle investigator on the electronic nose project at NASA's Jet Propulsion Laboratory. But Ryan says since the sensitive optical breath analyzer has not been through clinical trials, it's not clear yet whether it will be better than existing techniques.

There are different approaches to detecting compounds on the breath, each of which has limitations, says Peter Mazzone, an oncologist at the Cleveland Clinic who's developing a breath test for lung cancer. Mass spectrometry, for example, uses sophisticated chemical analysis techniques to determine exactly what chemicals are in a breath sample, and at what concentrations. But this kind of approach can't be performed in a doctor's office: the equipment is expensive bulky, and requires specialists to operate. Moreover, mass spectrometry requires a concentration step. Before it can be analyzed, the breath must first be concentrated on a trap. This slows the process and, says Mazzone, may influence the results. "When breath chemicals have to be concentrated on some medium, then taken off the trap for analysis," something might be getting lost in the process, says Mazzone.

Other approaches are nonspecific. While such approaches tend to be cheaper and easier to use, Mazzone notes that they "don't tell concentrations or exactly what's there." Mazzone is currently developing his own nonspecific approach, which uses an array of dye spots that change color on contact with the breath. Certain color patterns are associated with certain diseases, but these color changes aren't traced back to the presence of particular chemicals on the breath.

Mazzone says Ye's optical system is a "step forward" towards developing a machine that can perform a detailed analysis using equipment that could be operated by a general practioner in their office. So far, says Ye, he's only used the optical frequency comb to identify simple molecules made up of moderate numbers of atoms. For example, the comb can detect nitric oxide, carbon monoxide, and pentane, all of which have been associated with asthma. More work is needed before the device can be used to identify what Ye calls "giant biomolecules." The light absorption signatures of these molecules will be more complex, but detecting them may expand the range of diseases that can be diagnosed with Ye's system, he says.

BioOptics WORLD
Advances in lasers, optics, and imaging for the life sciences
March 2008

Frequency-comb spectroscopy detects disease via breath analysis

A team of scientists at JILA, a joint institute of the National Institute of Standards and Technology (NIST; Boulder, CO) and the University of Colorado at Boulder, has found that cavity-enhanced direct optical-frequency-comb spectroscopy may one day allow doctors to screen people for certain diseases simply by sampling their breath. According to Jun Ye, who led the research, optical-comb spectroscopy is powerful enough to sort through all the molecules in human breath but is also sensitive enough to find rare molecules that may be markers of specific diseases. Just as bad breath may indicate dental problems, excess methylamine can be used to detect liver and kidney disease, ammonia on the breath may be a sign of renal failure, elevated acetone levels in the breath can indicate diabetes, and nitric oxide levels can be used to diagnose asthma. When many breath molecules are detected simultaneously, highly reliable and disease-specific information can be collected.

In the experiments performed by Ye and his colleagues, optical-frequency-comb spectroscopy was used to analyze the breath of several student volunteers. The researchers showed that they could detect trace signatures of gasses like ammonia, carbon monoxide, and methane on the students' breath. In one of these measurements, they detected carbon monoxide in a student smoker and found that it was five times higher when compared to a nonsmoking student.