

IIT-B: Sniffing out lung cancer, explosives

Clinical applications for early-stage detection will become possible once validated on humans

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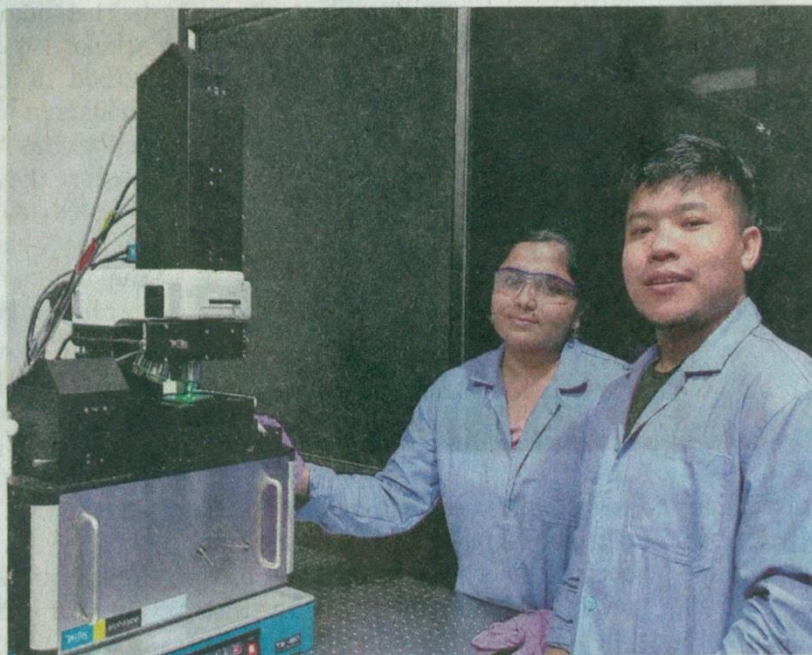
Researchers at the Indian Institute of Technology (IIT) Bombay have set the stage to possibly sniff out in about a minute early-stage lung cancer from exhaled breath. A two-member team led by Chandramouli Subramaniam from the institute's Department of Chemistry has developed a platform that detects volatile organic compounds such as benzene, acetone, benzaldehyde and ethanol in a gas phase at single molecular levels. These organic compounds in exhaled breath are clinically established biomarkers for early stage lung cancer. The same platform can also be used to monitor air-pollution levels or detect explosives like TNT (trinitrotoluene).

The volatile compounds have been detected using lab samples and clinical applications for detecting early-stage lung cancer will become possible once validated on human subjects. The results were published in the journal *ACS Sustainable Chemistry and Engineering*.

Raman scattering

Since Raman scattering is an inherently weak phenomenon, the researchers turned to surface-enhanced Raman scattering to dramatically increase the sensitivity of the platform such that it detects molecules at extremely low concentrations using a small amount of sample. "In our studies, we were able to reliably achieve sensitivities to the level of tens of molecules," he says.

"We put the molecule of interest on a gold or silver nanoparticle and then record the Raman spectrum. When we shine light [laser] on the sample [molecule plus the nanoparticle], the Raman spec-



We were able to detect the analyte even when only few molecules of it were present, says Maku Moronshing (right)

trum of the molecule gets enhanced," says Prof. Subramaniam. "The intensity enhancement of Raman spectrum happens predominantly through the interaction of localised electromagnetic field on the nanoparticles surface with the vibrational modes of the molecule."

The Raman spectrum intensity increases tremendously – 10,000 million times – and this allows the detection of molecules at very low concentration.

Scientists across the world have so far been unsuccessful in applying surface-enhanced Raman scattering to reliably detect molecules in gas or vapour phase.

In the case of molecules present in liquid phase, the addition of the liquid to nanoparticles allows the molecules to get adsorbed on the nanoparticle. Once adsorbed, the Raman spectrum gets enhanced. But capturing the molecule and adsorbing it on the nanoparticle has proven to be difficult when the

molecule is in a gas phase.

"This is what we have solved using out technique," he says. The challenge was overcome by designing nanoparticles that behave as a cage to capture the molecule from the gas phase.

When liquid containing the nanoparticles is subjected to a thermal gradient (one end is kept hot while the other is cold) the nanoparticles tend to migrate from the hot end to the cold one. As a result, the concentration of nanoparticles at the cold end increases. When the concentration of nanoparticles at the cold end increases they self-assemble to form the cage. The cage then traps the molecule, whether it is in a liquid or gas state. "Once the molecule gets trapped, the Raman spectrum gets enhanced as the cage is made of nanoparticles," explains Prof. Subramaniam.

"Since we don't use any chemical or lithography to bring the nanoparticles together, there is mini-

mal interference to the signal. So we were able to detect the analyte [chemical substance of interest] even when only few molecules of it were present," says Maku Moronshing from IIT Bombay and first author of the paper.

Validation of platform

Since testing the technique on human subjects for early-stage lung cancer detection is riddled with ethical and clinical challenges, the researchers looked at low-hanging fruit. This platform is particularly suited for the detection of plastic explosives such as TNT and RDX.

To detect the presence of explosives, air sample containing the molecules is forced into water that contains nanoparticle cages; the molecules get trapped in the cages. The presence of molecules is detected by shining laser and measuring the Raman spectrum. The entire process of sample collection and signal acquisitions takes about 2-3 minutes.

"As each molecule has a characteristic signature, the presence of the molecule in the sample tested can be ascertained by looking for specific signatures," Prof. Subramaniam. "Unlike in the case of early-stage lung cancer, validation for explosives and air-quality monitoring will be easy as no ethical clearances are required."

The researchers are now looking at incorporating data analytics into the platform to make the system to read the signatures automatically. And they are also trying to reduce the size of the platform to make it portable. "We are talking to companies to build miniaturised Raman spectrometers so that this detection technique can be truly portable and field-deployable," he says