nature news

Published online 24 October 2007 | Nature | doi:10.1038/news.2007.193

News

Small-scale technique hits the big time

Mini-explosions under a cell sample could help to identify disease.

Katharine Sanderson (/news/author/Katharine+Sanderson/index.html)

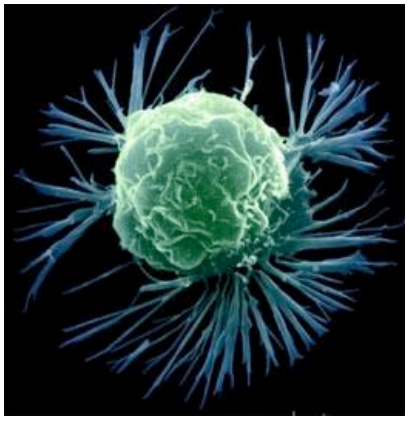
An explosive chemical technique can now be used to identify individual molecules in biological samples, down to the single-cell level.

Researchers hope the procedure could be used in clinics a few years from now to screen blood or urine for metabolites — the final products of biological processes — that can be used to diagnose disease.

"The vast majority of small molecules in humans are unknown," says Gary Siuzdak at the Scripps Center for Mass Spectrometry, La Jolla, California. "People don't appreciate this." But his technique could change that: "The potential for diagnosing and understanding disease is really wonderful," he says.

The mass-spectrometry technique developed by Siuzdak and colleagues, known as nanostructure-initiator mass spectrometry (NIMS), is reported in *Nature* [1](#B1) this week.

The process relies on a slab of silicon etched with nanometre-sized holes filled with 'initiator' molecules. The sample sits on top of this layer. The uneven surface is then hit with an ionising beam, or a laser, at which point the molecules trapped in the nanoholes heat up until they explode outwards into the sample. This pushes molecules off the sample surface as gaseous ions, which can be detected and identified by the mass spectrometer.



Mass spectrometry on single cells could tell if they are cancerous or diseased.

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Strong but gentle

The technique offers a number of advantages over others, Siuzdak says. Although the exploding initiator molecules are "pretty forceful", in some ways they are relatively gentle: because the sample is ionised by exploding particles — rather than being directly hit with an ion beam or a laser — surface molecules are released whole rather than being shattered into fragments.

And because the sample doesn't need to be mixed with anything, it is easier to identify the molecules coming from it. Metabolites can be tricky to detect using techniques where the sample is dissolved and mixed with a matrix material before it can be analysed, since the metabolites often look similar to the matrix.

Matrix-based systems also don't let the user work out exactly where in a sample a certain molecule has come from. NIMS does.

This is a real advantage, says Renato Zenobi, a mass spectrometry expert at the Swiss Federal Institute of Technology in Zurich. “In any imaging technique, spatial resolution is important,” he says. For example, with NIMS you could potentially tell whether a drug being tested in an animal made it into the intended cell, or if it got stuck in the cell walls.

Siuzdak has used NIMS to detect the metabolites present in a single cancer cell. The spatial resolution of the technique meant that he was able to distinguish cancerous and normal cells in his sample, he says.

The full applications of the technique have not yet been fleshed out. But Siuzdak's team is dedicated to seeing what it can do: even to the extent of testing it on themselves. "I walked into the lab one day and literally saw [my postdoc] with a needle in his hand," says Siuzdak.

References

1. Northen, T. R. *et al. Nature* **449**, 1033-1036 (2007). | **Article** (http://www.nature.com/doifinder/10.1038/nature06195) |

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How easier is the separation of initiator molecules may be from the sample, once on getting exploded ? what might be the composition of the initiator molecule ? Can this technique be used in finding out any other clinical disorders ?

Posted by: **Nirmal Kumar** | 25 Oct, 2007

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