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Ionization

# New Mass Spec Technique Method eliminates need for sample preparation

Celia Arnaud

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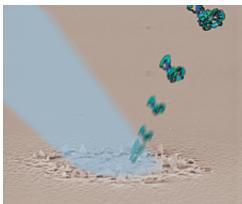
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MASS SPECTROMETRISTS at Scripps Research Institute report a new desorption/ionization method for mass spectrometry that is particularly suited for small-molecule metabolomic analysis and MS imaging (*Nature* 2007, 449, 1003). NIMS, or nanostructured initiator MS, uses surface activator molecules to initiate the desorption and ionization of sample molecules. In contrast, the current workhorse method, matrix-assisted laser desorption ionization (MALDI), uses a molecular matrix, and secondary ion MS

<sup>\*</sup> Macromedia Flash Player 8 is required to view videos. Videos Courtesy of Scripps Center for Mass Spectrometry

#### (SIMS) uses high-energy ions.



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Zap In NIMS, irradiation with a laser or ion beam vaporizes initiator molecules trapped in surface pores, thereby triggering desorption/ionization of sample molecules on top.

Key to NIMS are initiator molecules trapped in the pores of a porous nanostructured surface. Perfluorinated polymers make the best initiator molecules, forming a fluorous phase into which analyte molecules don't dissolve, according to <u>Gary Siuzdak</u>, an associate professor of molecular biology and director of the Center for Mass Spectrometry at Scripps.

In NIMS, the sample is placed on top of the prepared surface. Heating the surface with an irradiation source such as a laser or ion beam vaporizes the trapped initiator molecules. As they break through the surface, they force sample molecules into the gas phase as well. "We like to think of the prepared surface as a rug that's essentially being pulled out from underneath the analyte," Siuzdak says.

The Scripps team has analyzed a wide range of samples with NIMS, including blood, urine, and tissue sections, says <a href="Trent R. Northen">Trent R. Northen</a>, a research associate at the center. Northen is excited about the prospects for clinical analysis. "You don't need to do any sample preparation," he says. "Basically, you can just put a drop of blood on a chip and analyze it."

NIMS works better for small molecules such as metabolites than for proteins, although it can ionize proteins as well, Siuzdak says. In this respect, NIMS is complementary to MALDI, which works better for proteins than for small molecules. Laser-based NIMS is sensitive enough that it can analyze attomole (10<sup>-18</sup>) amounts of sample routinely and has even detected specific molecules in the yoctomole (10<sup>-24</sup>) range, he adds.

A key question is whether the method will turn out to be easy to use by others. "If it is a robust approach in other laboratories, it will be quickly adapted by many groups when the appropriate nanostructured surfaces become available," says <u>Jonathan V. Sweedler</u>, a chemist at the University of Illinois, Urbana-Champaign, who uses MALDI imaging for single-cell analysis. "We certainly will explore its use for our single-cell and small-volume measurements."

<u>Nicholas Winograd</u>, a chemist at Pennsylvania State University who is a leader in SIMS imaging, comments that NIMS's nanopore format is a creative way to achieve the molecular specificity of MALDI with the resolution of SIMS. "It will be fascinating to see what new applications emerge," he says.

Siuzdak and coworkers have focused on laser-based NIMS because they have the necessary equipment in their own lab. They eagerly anticipate that other users will identify other combinations of nanostructured surfaces and initiators in addition to those they've already developed. To help that process, they've made videos explaining how to make the surfaces.

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