Exploding cells, one by one

WASHINGTON – Blowing up cells really isn't anything new. It's done in laser surgery, for example, to tissues in cells. But a new mass spectrometry method now can create explosions on a one-by-one basis without wrecking a cell's chemical properties.

Akos Vertes, a professor of chemistry, biochemistry and molecular biology at The George Washington University in Washington, and graduate student Bindesh Shrestha are conducting studies in which they examine individual cells under various conditions, including how a plant cell reacts to drought conditions or an animal cell to the lack of nutrients. In the study, as reported September 2009 in the journal *Analytical Chemistry*, the researchers explore the metabolic variations among different types of cells.

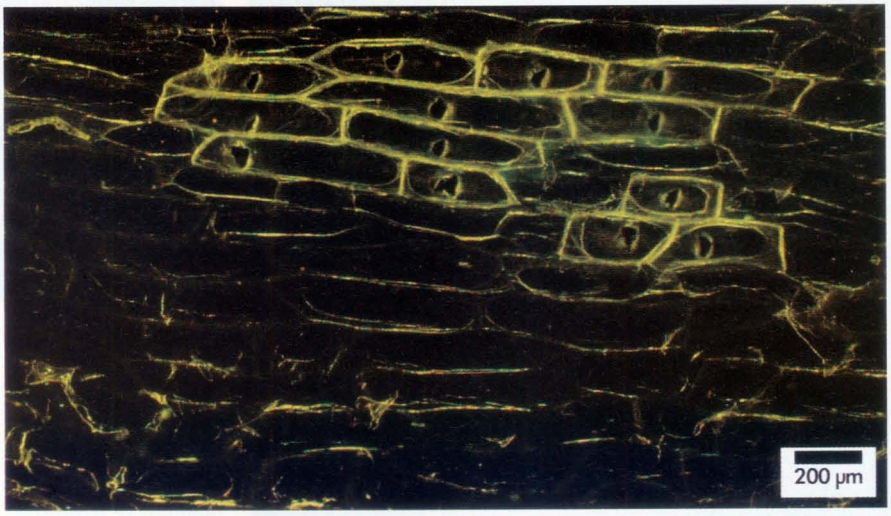
Vertes, also founder and co-director of the university's W.M. Keck Institute for Proteomics Technology and Applications, noted that "most studies like these use fluorescence tagging of a particular molecule, but the diversity of metabolites and compounds in cells, in my view, calls for mass spectrometry."

Because a major consideration was the ability to study functioning cells in as close to in vivo condition as possible, they combined mass spectrometry with atmospheric pressure sampling. The group developed a laser ablation method that uses electrospray ionization to change the generated plume.

The laser radiation was produced by an Opolette, a diode-pumped Nd:YAG laser-driven optical parametric oscillator from Opotek Inc. of Carlsbad, Calif., operating at 2.94 µm, with a repetition rate of 100 Hz and a 5-ns pulse width. The laser light was sent to the target through a GeO_2-based optical fiber (450-µm core diameter) from Infrared Fiber Systems of Silver Spring, Md.

In the past, researchers avoided using the atmospheric pressure technique because 99.9 percent of the ablated material is neutral, Vertes said. But when the electrospray ionization is added, the ablated material is converted into ions that can be analyzed by mass spectrometry.

One challenge was in leaving the chemical properties intact within the cell. By using the laser ablation tool in the mid-IR range (2.94 µm), energy is directed into the water molecules and not into the other molecules in the cell. The laser pulse is only 5 ns, which also is very efficient, Vertes noted.



Shown is cell-by-cell ablation of epidermal cells from a garden onion (*Allium cepa*). Each ablation was used to generate a mass spectrum reflecting the metabolic profile of the individual cell.

Another challenge was in targeting individual cells. Using mid-IR optics, even corrected for spherical aberration, one cannot focus better than 70 to 100 µm in spot diameter, Vertes said. To go below that size, the researchers used a special optical fiber that works in the mid-IR region, then applied an etching technique to the tip of the GeO_2-based glass fiber.

"What we ended up with was a commercial mass spectrometry system with a slightly modified front end," Vertes said.

The group is continuing its work with an eye toward imaging biological cells in a more natural, three-dimensional grid structure. Usually, tissue is analyzed by mass spectrometry spot by spot on a grid. The problem, Vertes said, is that it forces a rectangular grid over nature, and "nature has its own grid structure." To image cells in two or three dimensions, the researchers are taking an optical image to see where the cells are, then designing a pattern for the laser ablation that better follows the cell distribution.

In this way, he explained, they are reconstructing a "biologically more meaningful image."

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