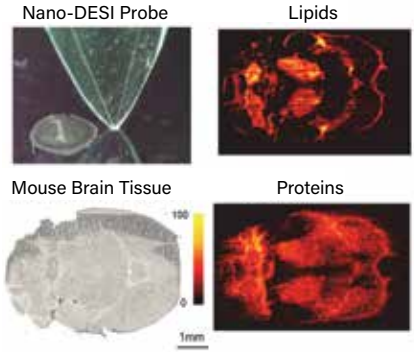
Enhanced Chemical Imaging with Nano-DESI Mass Spectrometry

Mass spectrometry imaging (MSI) provides researchers with the ability to answer questions about the chemical composition of features observed through microscopy and about the distribution of otherwise invisible molecules within a sample. For example, MSI can provide information about some molecules produced by biological systems in response to environmental factors, inflammation, or toxic substances, which are often difficult to observe using conventional imaging modalities.

The technique is rapidly gaining favor among researchers studying drug metabolism and pharmacokinetics, where tissue sections can be imaged to highlight the distribution of drugs, metabolites, lipids, and other compounds of interest. In addition, researchers in agriscience, energy, and other fields are beginning to explore the technique as a tool for understanding bioprocesses important in their fields.

The National Science Foundation (NSF) Center for Bioanalytical Metrology (CBM) is working to enhance the utility of an important new chemical imaging technique called nanospray desorption electrospray ionization (nano-DESI) MSI, developed by Purdue Univ.'s Julia Laskin. Nano-DESI is an ambient ionization technique that does not require sample pretreatment and enables sensitive imaging with a high spatial resolution of ~10 μm.



▲ This figure shows part of the nano-DESI probe near a tissue sample during an imaging experiment and selected images of lipids and proteins in mouse brain tissue.

CBM consists of three university sites and 13 corporate members that collaboratively investigate new approaches for addressing the key measurement science needs of industry. Working through CBM, the Laskin group has improved the spatial resolution and sensitivity of nano-DESI and expanded its ability to detect a wider range of compounds of interest.

Nano-DESI utilizes a specially designed probe with a flowing solvent that makes a liquid contact on the sample. Molecules are extracted from the sample into the liquid bridge, gently ionized to generate ions of intact species, and analyzed using a mass spectrometer. A standard is added to the solvent to obtain quantitative results, which addresses one of the limitations of MSI techniques. Furthermore, no special sample preparation is required, which simplifies the experimental methodology and increases the rate at which the samples are analyzed. Precision design of this contact probe has enabled molecular imaging of individual cells in tissues. Improvements in sensitivity by a factor of 10–100 have been achieved by tailoring the composition of the extraction solvent and designing new data acquisition strategies in collaboration with CBM member Agilent Technologies.

"The nano-DESI technique has a potential to be a real game-changer for researchers in the pharmaceutical industry," notes AbbVie's David Wagner, one of the industry scientists collaborating on the project. "Julia and her team have a great opportunity to determine the distribution of drugs and metabolites within tissues with a high sensitivity and low ion suppression effect, potentially providing more data for informed decisions."

"The technique is also being embraced by researchers at Corteva Agriscience and Exxon Mobil," notes CBM director Paul Bohn. "This is a great example of a successful CBM research project that delivers value across a very diverse group of industry members."

Laskin and her team have developed a host of innovations to improve spatial resolution, sensitivity, and detectability, and have recently reported the ability to directly image proteoforms using nano-DESI MSI. "Mapping the spatial distribution of different variants of the same protein that are excellent reporters of the state of cells in biological systems has been an important unmet need in chemical imaging for some time," notes Laskin.

The new capabilities of nano-DESI MSI used in this project promise to shed light on many unanswered questions related to metabolic processes in biological systems and their response to environmental conditions, drug treatment, and other factors.

"CBM projects provide students with unique networking opportunities with industry project team members. One of the most valuable outcomes of these interactions is that students apply skills and techniques they develop in other projects in the lab to a completely different set of scientific problems than what they experience in academic research," says Laskin. "The fast-paced, interactive, and deliverable-driven environment of these projects helps them prepare for future careers and provides insights into research in industry." CEP

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