

New frontiers in structural mass spectrometry: Unraveling dynamic metabolomics

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Systems-wide analyses typically necessitate multi-dimensional datasets, which is often times challenging to obtain. In many contemporary strategies, concentrating on only one or a handful of molecular targets limits the utility of the information for diagnostic and predictive purposes. Guided by the paradigm of systems biology, we have developed structural mass spectrometry technologies for the characterization of complex biological systems in for temporal and spatial dimensions. In parallel with these strategies, we have also developed new bioinformatics/biostatistical workflows to allow experiments to begin in an untargeted coarse grain hypothesis and funnel into increasingly targeted fine grain information.

Metabolomics dynamics studies are performed through the integration of microfluidic cell trapping devices fluidly coupled with the structural mass spectrometer. Cells are trapped and kept viable by constant perfusion of cell culture media. By introducing a chemical perturbation to the media, the exometabolome is constantly readout in near real-time. Cell cycle experiments can be performed by perturbation and relaxation to the new cell state. By combining multiple cell trapping devices, paracrine signaling events can be examined with exquisite detail. Metabolomic mapping experiments are performed by integrating spatially-resolved MALDI ionization with structural mass spectrometry. In this technique, broad-scale metabolomics is performed where relative abundance is recorded at every spatial location and map reconstructions for every metabolite measured are made. The report will describe advances made in both temporal and spatial metabolomics for cell culture and intact tissue in areas ranging from cancer biology and parasitology to drug discovery and pathogen exposure.

Biography

John A McLean is an Assistant Professor in the Department of Chemistry at Vanderbilt University and a faculty fellow in the Institute of Chemical Biology and Institute of Integrative Biosystems Research and Education. His recent awards include an Excellence in Teaching Award from the student members of the American Chemical Society, a Defense Threat Reduction Agency Research Award, an American Society for Mass Spectrometry Research Award, a Spectroscopy Society of Pittsburgh Award, an R&D 100 Award, and the Bunsen-Kirchhoff Prize from the GDCh. He has published over 60 manuscripts in the peer-reviewed literature, 8 book chapters, and 15 patents.

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