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Editorial overview: Recent innovations in the metabolomics revolution

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Metabolism involves a complex set of chemical processes that allow organisms to transform nutrients into energy, reducing power, and the diverse range of cellular building blocks necessary for life. Although metabolism has been intensively studied for more than a century, the technology for understanding metabolic phenomena from a comprehensive, network-level perspective has only been available for a short time. The metabolomics approach – the analysis of all observable metabolites in complex biological samples – has rapidly advanced with the introduction of high-resolution mass spectrometry, sophisticated chromatography, multidimensional nuclear magnetic resonance spectroscopy, clever isotope labeling strategies, and powerful software. These technological developments have dominated the field over the last two decades and have laid the foundation for the recent explosion in demand for metabolomics. In this special edition of *Current Opinion in Biotechnology*, we have invited a selection of both well established and emerging leaders of the metabolomics field to describe the current state-of-the-art as well as their visions for the future of metabolomics. These authors represent a cross-section of researchers who are driving the modern renaissance of metabolism research through technical innovation and biological creativity.

Mass spectrometry

Mass spectrometry (MS) has become the most widely used analytical platform in metabolomics because of its high sensitivity, excellent dynamic range, and ability to analyze a wide range of molecules. Although metabolomics studies strive to analyze theoretically *all* metabolites, capturing molecules with vastly different chemical properties is impossible using traditional chromatography. In this special issue, Burgess and Haggarty discuss recent innovations in liquid and gas chromatography that are taking metabolomics a step closer to global coverage of the metabolome. They highlight the benefits of placing two separation columns in series, column switching, and various approaches to two-dimensional chromatography mass spectrometry (2D LC–MS) that capture a much broader range of compounds than is currently possible. Recent developments in supercritical fluid chromatography – a technique that has yet to reach its full potential in metabolomics – are also discussed in this review.

Another technology that may dramatically increase metabolome coverage is capillary electrophoresis (CE). CE is an exciting alternative to more traditional liquid and gas chromatography. It has unrivaled separation efficiency and the ability to cope with low sample volumes. Unfortunately, hyphenating CE with mass spectrometry has proven to be a major technical challenge.

Ian Lewis is an Assistant Professor and Alberta Innovates—Health Solutions (AIHS) Translational Health Chair in the Department of Biological Sciences at the University of Calgary. The Lewis laboratory specializes in harnessing metabolomics technology to understand the role metabolism plays in infectious diseases. The goal of this research is to develop new diagnostic methods to identify high risk patients and novel antimicrobial therapies to control infections.

Ramautar et al. describe recent innovations in interfacing CE to MS using a novel sheathless porous tip interface. These innovations are playing a critical role in improving the performance and practicality of CE-MS and may eventually bring this transformative technology to the forefront of metabolomics.

Another emerging frontier of metabolomics is MS-based tissue imaging, a challenging application of metabolomics with a tremendous scientific potential. Borchers et al. are pioneering new approaches in matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS), including new types of matrices and new ways to deposit them. These technical advances have made it possible to study a wider range of proteins, peptides, lipids, drug molecules, and metabolites than what was previously possible.

Lipidomics, the comprehensive characterization of the lipid component of biological systems, is a rapidly expanding sub-discipline of metabolomics. As Tumanov and Kamphorst argue, the widespread characterization of lipids as homogenous apolar molecules belies their true structural diversity. They describe a practical combination of extraction and separation procedures that dramatically improves the scope and chemical diversity of molecules that can be captured in lipidomic analyses, and describe some of the powerful new applications of this emerging approach.

Nuclear magnetic resonance spectroscopy

Nuclear magnetic resonance (NMR) spectroscopy played a pivotal role in the early development of metabolomics and continues to provide an essential orthogonal analytical approach to MS. NMR's outstanding quantitative performance, ability to detect any organic molecule in solution within its sensitivity limit, and the ability to unambiguously characterize novel compounds *de novo* ensures that NMR will retain an important place in field. However, the increasing popularity of MS-based approaches has encouraged the leaders of the NMR-based metabolomics community to critically evaluate the evolving role of NMR. The future vision, as articulated by seven preeminent North American NMR spectroscopists – John L Markley, Rafael Brüschweiler, Arthur S Edison, Hamid R Eghbalnia, Robert Powers, Daniel Raftery, and David S Wishart – is an exciting contribution to this special issue. In addition to this long-term vision, this special issue includes several focused contributions from the frontiers of NMR-based technology. Giraudeau et al. describe several recent breakthroughs in multidimensional NMR techniques, high sensitivity analyses, and high-throughput approaches that collectively represent the future for NMR-based studies. Likewise, Brüschweiler and Bingol introduce a powerful suite of computational, chemical, and analytical techniques that dramatically improve the scope of NMR-based approaches and extend the number of molecules that can be robustly identified in a single assay.

Computation/bioinformatics

Ongoing technical innovations in metabolomics are driving a continual increase in the size and complexity of metabolomics datasets. Analyzing these data and preserving a usable record of each study is a significant challenge. Commercial software tools, such as those distributed by instrument manufactures, have been unable to keep pace with the rapid advances in the field. Consequently, a worldwide network of academic groups has been driving the development of software packages, data standards, and open source databases for metabolomics.