

A. Daniel Jones

Professor, Department of Biochemistry & Molecular Biology and Department of Chemistry and Director, RTSF Mass Spectrometry Core
Michigan State University, East Lansing, MI 48824

Title:

High-throughput LC/MS approaches to large-scale analyses of metabolic phenotypes

Abstract:

The textbook view of how metabolism is regulated is incomplete and often based upon faulty assumptions about gene and protein functions. Reliable predictions of metabolic regulation will require a more complete cataloguing of metabolites, functional characterization of metabolic enzymes, and assessment of the dynamic behavior of metabolic networks. Though mass spectrometry has been used for decades to profile metabolites, high-throughput approaches capable of large-scale analyses of multiple biological replicates, treatments, time points, and genetic variants are recent developments that can address these needs but leave room for improvement. Several approaches will be presented that represent efforts to propel LC/MS technologies to detect, identify, and quantify metabolites in crude biological extracts. Specific examples include a 6-minute LC/MS/MS method for quantifying amino acids and related metabolites, LC/TOF MS using fast fused-core HPLC columns and multiplexed collision induced dissociation for metabolite annotation and functional genomics, and sorting of unknown metabolites according to relative mass defect information. Examples will be discussed regarding how these approaches have accelerated forward- and reverse-genetics approaches to understanding gene functions. The performance of these LC/MS and data processing methods will be discussed in the context of attempts to define the maximum number of metabolites that can be measured per minute of instrument time.