

## Quantitative and Ultra-sensitive High Throughput Proteomics

*Richard D. Smith*

Environmental Molecular Sciences Laboratory and Biological Sciences Division,  
Pacific Northwest National Laboratory, Richland, WA 99352

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Technological advances are enabling proteomics measurements that are increasingly effective, comprehensive and of higher throughput. The challenges associated with proteomics measurements include identifying and quantitating large sets of proteins where components of interest may have relative abundances that span more than six orders of magnitude, vary broadly in chemical and physical properties, have transient and low levels of modifications, and are subject to endogenous proteolytic processing. The utility of proteomics data depends significantly on the quality of the data, both the confidence of protein identifications as well as its quantitative value.

This presentation will describe advanced nanoscale separations and mass spectrometry (MS) instrumentation for making comprehensive, quantitative, and high throughput proteomic measurements. The use of stable isotope labels and/or relative MS peak intensities of these peptide markers provides the basis for quantitation. The approach developed involves two primary modes of operation: (1) the identification of peptide markers for proteins that are then used in conjunction with higher throughput high accuracy mass spectrometric measurements (i.e. without the need for tandem MS), and (2) the use of the same higher throughput measurements followed by data-directed tandem MS measurements to identify specific components of interest (e.g. potential biomarkers).

While the initial applications focused on microbial systems, work over the last several years has included studies of mammalian systems. As an example, the initial characterization of the human blood plasma proteome has provided confident identification peptide markers for several thousand proteins. The presentation will highlight the importance of high quality separations and MS measurements, and the informatics challenges associated with the massive data production rates.