Multi-dimensional Portable Mass Spectrometry for Biological Detection

Ethan McBride 1, Zachary Sasiene 1, William Hlavacek 2, Nileena Velappan 1, Erick LeBrun 1, Nathan Patterson 3, Martin Dufresne 3, Melissa Farrow 3, Jeremy Norris 4, Richard Caprioli 3, Trevor Glaros 1
1 Biochemistry and Biotechnology Group, Bioscience Division, Los Alamos National Laboratory, Los Alamos, NM 87545, USA.
2 Theoretical Biology and Biophysics, Theoretical Division, Los Alamos National Laboratory, Los Alamos, NM 87545, USA
3 Mass Spectrometry Research Center, Vanderbilt University, Nashville, TN 37240
4 Bruker Corporation, Billerica, MA 01821

Over the last two decades, there has been an explosion of new rapid detection and diagnostic assays which can be used in the field or at the bedside. Most of these technologies are antibody-based and thus issues with false positives & negatives are common and there is need for prior knowledge regarding the causative organism. Modern genomic technologies like PCR have addressed specificity but are costly to develop and validate, require a significant amount of sample preparation, must be performed in a brick-and-mortar laboratory, and can result in false negatives via genetic engineering or naturally acquired mutations. Mass spectrometry (MS) technologies have best-in-class sensitivity and specificity for detecting pathogens in clinical settings utilizing an approach known as mass fingerprinting. In the clinic, mass fingerprinting is achieved by extracting protein from clinical samples, digesting it into peptides, and acquiring of a parent mass scan (MS1) on a high-resolution mass spectrometer to yield a unique 'fingerprint'. Manufacturers have not designed these FDA-approved instrument platforms to operate outside of a laboratory, which would enable widespread deployment to the front lines or in point-of-care settings. As a direct result, like sequencing technologies, diagnostic mass spectrometry technologies are also limited to centralized, brick-and-mortar laboratories operated by highly trained staff. Utilizing resources contained within Los Alamos National Laboratory's Mass Spectrometry Center for Integrated -Omics (MSCIO), we will develop a robust, field portable, analytical platform for detecting biological pathogens at the molecular level, which pose a threat to the health of the Warfighter and the public. This platform will combine innovative methods of data acquisition with supervised machine learning to increase the performance of commercially available, low-cost mass spectrometers for the classification of bacteria. These innovations will significantly advance field- and clinic-ready capabilities to accurately identify pathogens compared to the current paradigm that relies heavily on centralized laboratory testing.