Robust CE-MS methods for metabolomics: achieving greater throughput, lower costs and better data comparability

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Abstract:

Capillary electrophoresis-mass spectrometry (CE-MS) is widely perceived as a promising microscale separation platform that ultimately lacks robustness for large-scale metabolomic studies due to migration time variations and conditions that are difficult to reproduce in other laboratories or comparable with previously validated methods. Much of these problems stem from inadequate method validation during assay development, the lack of standardized operating conditions and quality assurance protocols and poor support by vendors in terms of training with software tools that are customized to the unique separation principles of CE relative to LC methods. Recent efforts in our laboratory towards enhancing sample throughput, data fidelity and quality assurance will first be discussed as a way to accelerate biomarker discovery in metabolomics using multiplexed CE-MS technology as applied to population health and precision medicine. For instance, aminolysis of the outer polyimide coating of the fused-silica capillary and incidental capillary fractures when using alkaline ammonia-based buffers will be first discussed as a simple way to improve method robustness for anionic metabolite profiling under negative ion mode conditions that has long been associated with poor reliability.

Also, temporal signal pattern recognition using multiplexed separations coupled to high resolution, accurate MS will be presented as a novel strategy for high throughput screening, unambiguous identification and reliable quantification of biomarkers associated with in-born errors of metabolism in asymptomatic neonates from a dried blood spot, such as galactosemia.

An inter-method comparison of validated isotope-dilution flow injection analysis-tandem MS derived from an accredited clinical laboratory with CE-MS results will be evaluated in terms of screening performance for unambiguous confirmatory testing of a diverse array of presumptive/screen-positive diseases. The development of faster, less expensive yet more reliable CE-MS methods that provide quality assurance is critical to biomarker discovery in metabolomics, as well as quantitative biomarker measurements in clinical medicine that is ideally suited to the analysis of volume-restricted and bio-banked specimens.

Short Biography:

Philip is a Professor in bio-analytical chemistry at the Department of Chemistry and Chemical Biology at McMaster University (Hamilton, Canada), and he is a Cystic Fibrosis Canada Researcher. He is also an affiliate member of the Metabolomics Innovation Centre (TMIC) – Canada's national laboratory for metabolomics analytical services and technology development while also serving as a founding member of the North American Metabolomics Chapter. Philip's research contributions include the design of novel analytical strategies to quantify and identify metabolites in biological samples, as well as characterization of their interactions with protein for drug discovery. Philip is a leading proponent of metabolomics research and major innovator in capillary electrophoresis-mass spectrometry-based technology development. His multidisciplinary research program involves both fundamental studies and clinically relevant applications of metabolite profiling relevant to advancing clinical diagnostics, personalized health and population health with a focus on chronic disease prevention. Philip's research contributions have been recognized by several prestigious provincial, national and international awards of merit from Cystic Fibrosis Canada (2015), American Chemical Society (2010), Japan Society for Promotion of Science (2009), Petro-Canada Young Investigator Award (2007) and Premier's Research Excellence Award (2004-2010).