Proteomics aims to comprehensively identify and quantify proteins in a biological system, including protein expression, localization, interaction, post-translational modifications (PTMs) and turn over. It routinely employs reversed-phase liquid chromatography (RPLC)-electrospray ionization (ESI)-tandem mass spectrometry (MS/MS) for protein identification. Capillary zone electrophoresis (CZE)-ESI-MS/MS has also attracted great attentions for proteomics due to its advantageous features. First, CZE-MS and RPLC-MS can produce complementary identifications and the combination of these two techniques can improve proteomic scale, and especially enhance protein isoform identifications. Second, CZE can produce much better intact protein separation than RPLC. Third, CZE-MS can yield higher sensitivity than RPLC-MS. Fourth, CZE can separate proteins in their native conditions (close to pH 7), and CZE-native MS is invaluable for native proteomics.

Our research focuses on development of new techniques for exploring CZE-MS for high-resolution, ultrasensitive and native proteomics, and also applications of the new techniques for answering important questions in developmental biology and cancer.

(I) Couple multi-dimensional LC and/or electrophoresis-based protein pre-fractionation with CZE-MS/MS to improve the resolution of protein isoform separation and identification. The long-term goal is to generate a complete protein isoform database for human cells. We also collaborate with biologists to apply our proteomic techniques for understanding embryo early development using Zebrafish and fruit fly as model systems.

(II) Couple magnetic beads and monolithic materials-based immobilized enzymes with CZE-MS for highly efficient digestion and ultrasensitive detection of proteins from single cells. Single cell proteomics is invaluable for understanding cellular heterogeneity, and is particularly useful for the fields of stem cell biology, neuroscience and developmental biology. This work focuses on understanding how a particular cell (blastomere) develops into the final cell type or organ during embryo development. The long-term goal is to approach deep proteomics on individual cancer cells, which can provide new insights on cancer heterogeneity and cancer therapies.

(III) Develop a microdialysis interface using a hollow fiber membrane for highly efficient and rapid removal of detergents and salts from native proteins. We will couple the interface with CZE-MS for online native protein cleanup, separation and native mass spectrometry detection. The long-term goal is to apply this system for native proteomics, which aims to achieve large-scale analysis of protein complexes in native conditions.

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**Selected Publications**


