Single Cell Analysis Using Microfluidics Coupled to Ultrasensitive Mass Spectrometry

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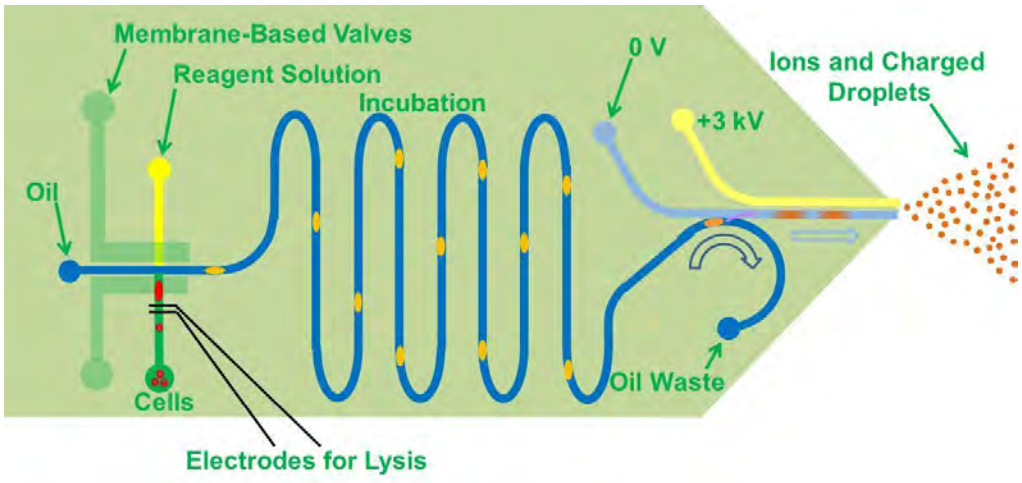
Proteomics and metabolomics measurements in their present form require large populations of cells and thus average over and obscure important heterogeneity that is present even in clonal populations cultivated under highly controlled conditions. For “real world” samples, this means that important but rare events go undetected, and the effects of stochastic expression and the microenvironment are blurred. The objective of this proposal is to combine microfluidic sample preparation and separations with the ultrasensitive mass spectrometry (MS) capability located in the EMSL to extend proteomic and metabolomic analyses to the level of single eukaryotic cells. At present, the most established option is flow cytometry, which is best suited to labeling cell surface markers in suspension cells and is limited to analytes having an available immunofluorescent tag. In contrast, MS provides for information-rich analyses in which chemical species can be unambiguously identified due to its high mass measurement accuracy and resolution. MS is also broad-band or multiplexed in that large numbers of analytes, including proteins, peptides and metabolites can be detected simultaneously without the need for chemical labeling. We will combine our expertise in the fields of microfluidics, chemical separations and ultrasensitive mass spectrometry to isolate, prepare and analyze individual eukaryotic cells. We will use cultured mammalian cells for our initial tests, but the platform will be adaptable to a wide range of biological systems.


Membrane-Based Valves
Reagent Solution
Incubation
0 V
Ions and Charged Droplets
+3 kV
Oil
Cells
Oil Waste
Electrodes for Lysis