220. Pan-omics: Development of a Universal Next Generation Pan-omics Measurement Pipeline

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Project Goals: An aim of the Pan-omics Program at PNNL is to develop and apply advanced mass spectrometry (MS)-based platforms and bioinformatics approaches for 'pan-omics' measurements that will greatly accelerate the understanding of biological systems important to the U.S. Department of Energy and its Genomic Science Program. In this context, we are developing a new ion mobility separations (IMS) technology that can provide dramatically increased throughput and resolution to facilitate faster and better measurements. The approach uses novel Structures for Lossless Ion Manipulations (SLIM) to provide fast separations that exceed the resolving power of liquid chromatography and provide the basis for either large increases in throughput (e.g. 100-fold) or depth of 'ome coverage (i.e. completeness). The new SLIM IMS-MS platform will be applicable to all MS- based pan-omics measurements, can be interfaced to essentially any MS platform, and will provide a basis for future massively parallel MS arrays.

Our general approach for next generation pan-omics measurements includes a coherent universal pipeline involving the fractionation of biological samples prior to a new SLIM IMS-MS analysis platform (Figure 1). This pipeline uses a "one pot" approach to isolate proteomes, metabolomes, and lipidomes from the same parent sample, followed by fractionation of each sub-sample, e.g. using chromatographic separations. The degree of fractionation will depend on the desired depth of the measurements, as well as the capabilities of the new IMS-MS platform. Initially, we plan to prepare ~50 to 100 fractions for each sample, but larger numbers will be practical if deeper coverage is necessary. The analysis of each fraction will require only seconds, as compared to approximately one hour today. Because of the robust nature of these steps and their ready automation, sample processing needs for our initial applications will be readily addressable based on the use of conventional LC approaches and the developing SLIM IMS technology in conjunction with existing MS platforms. However, future advanced multiplexed and highly parallel MS platforms will also be enabled by these approaches and will provide the potential for measurement throughput that is even greater, and indeed comparable to that achieved with the fastest genomic technologies.

The new IMS-MS platform will employ a radically new approach to achieve ultra-fast mobility separations based upon SLIM. SLIM technology (Figure 2) has conceptual similarities with integrated electronic circuits, but instead of moving electrons, we use electric fields to create pathways, switches, etc for manipulating ions in the gas phase. SLIM enables sequences of ion separations, transfers, and trapping in the space between two surfaces positioned ~4 mm apart. We have developed key components that provide for lossless linear ion transport, ion transport around a corner (i.e. a 90-degree bend), ion switches (to direct ions to one of two paths), ion elevators (for transporting ions between different levels of multilevel SLIM devices), and ion traps (for trapping, accumulation, and reaction of ions). The capabilities are being initially used to enable long path length, high resolution IMS, as well as necessary ancillary capabilities such as extended ion trapping and accumulation necessary to achieve practical and high dynamic range MS-based measurements. The planned developments will facilitate understanding of biological systems and simultaneously enable more effective extraction of new knowledge and insights.
Figure 1. Overall Pan-omics pipeline being developed.

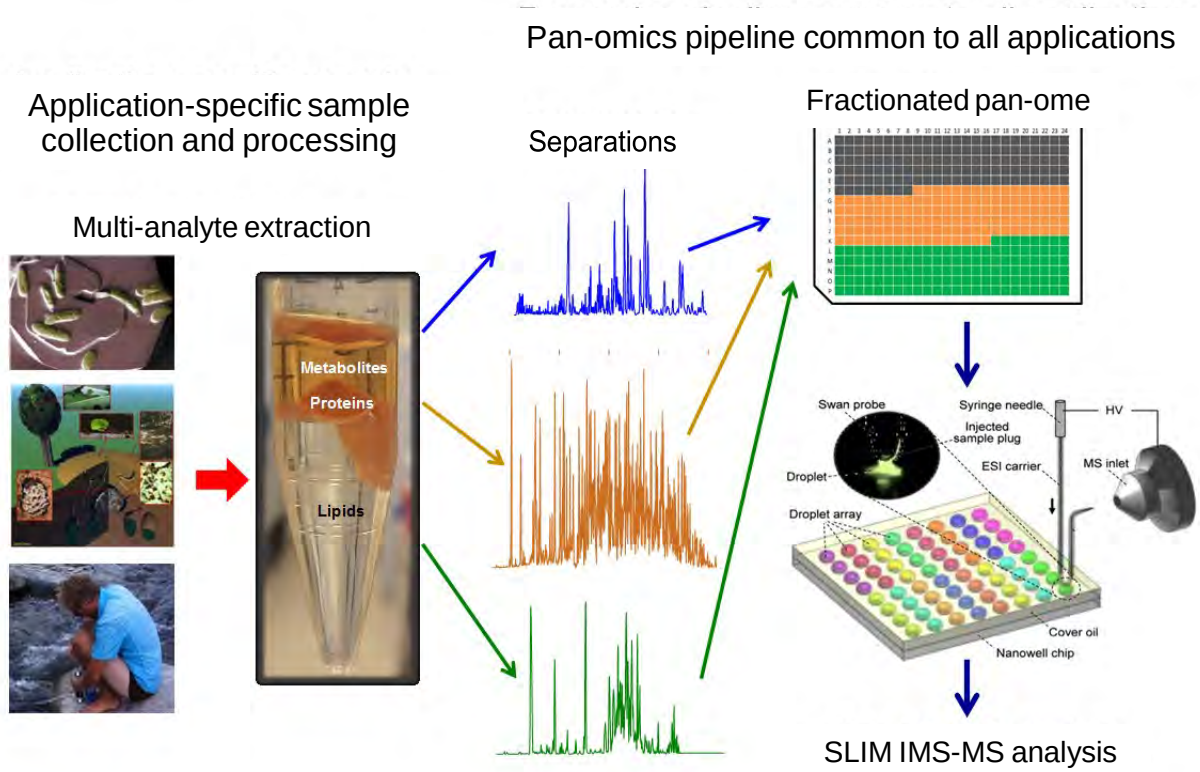
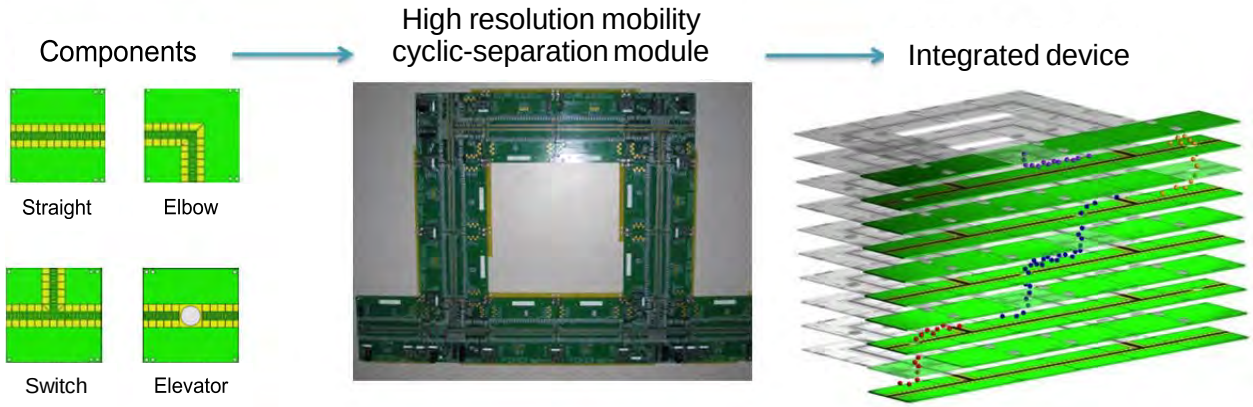
Figure 2. The new SLIM technology separations platform being developed is constructed using printed circuit board (PCB) technologies and involves the use of new approaches for fast gas phase ion mobility separations that replace on-line LC separations.