MANIPULATING NANOLITER SAMPLES IN SEGMENTED FLOWS FOR HIGH-THROUGHPUT SEPARATIONS AND ANALYSIS

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Interfacing microscale separations to post-column reaction or detection systems has typically been complicated by the low volumes and desire to prevent extra-column band broadening. Similarly, interface to automated sampling systems, such as autosamplers or on-line injection schemes, is limited by the small volumes required. Often miniaturized vials or injection valves are used which require much more sample than required by the separation column. Furthermore, such systems limit the speed of analysis. We have explored the use of multiphase flow wherein sample is formed into a series of plugs or droplets separated by gas or immiscible liquid as a way to manipulate samples in microfluidic and microscale analytical systems. Methods for formation and manipulation of such plugs on the nanoliter scale have been developed and are increasing in sophistication so that it is now possible to perform many common laboratory functions such as sampling from and reagent addition to plugs in microfluidic systems. We have developed systems that allow droplets to be used for injection onto capillary electrophoresis and chromatography columns. The resulting systems can have extremely high throughput because of limited time required for rinsing between samples. We have also explored fraction collection by segmenting column effluent into droplets. In this way, complicated sample treatment and off-line interface to detectors such as mass spectrometry can be performed. Splitting droplets allows collected fractions to be stored and re-analyzed at a later time. This allows, for example, samples to be collected and then analyzed by multiple mass spectrometers. It also enables stopped flow (also known as “peak parking”) electrospray ionization-mass spectrometry analysis. The injection and fraction collection systems have applications for “separations-based sensing”, high-throughput screening and analysis, process analytical technology, multi-dimensional analysis, and metabolomics. In this talk we describe the formation and manipulation of segmented flows,