

Microfabricated Fluidic Devices for Protein and Peptide Mapping

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Miniaturized chemical instruments, “Lab-on-a-Chip” technologies, are being developed for rapid, comprehensive analysis of cellular proteins, as an alternative to the slow and labor-intensive 2D gel methods currently used for protein mapping. The microfabricated devices integrate on a single structure, elements that enable multidimensional separations of protein or peptide mixtures and on-chip labeling for fluorescence detection of rapidly migrating analyte bands. Moreover, the longer-term goal is to incorporate chemical and biochemical processing procedures and electrospray capability into the microfabricated devices. It is anticipated that these devices will exhibit many advantages including small size, inexpensive fabrication, high speed, low volume materials consumption, high throughput, and automated operation. These attributes are also attractive for eventually addressing the ability to perform protein mapping studies on individual cells under high throughput conditions. First generation devices, combining open channel electrochromatography or micellar electrokinetic chromatography with open channel electrophoresis, have been demonstrated for the analysis of proteins and tryptic digests. We have also demonstrated a microchip device that accomplishes field gradient focusing of proteins, a method for concentrating and separating proteins. Field gradient focusing is similar to isoelectric focusing but concentrates materials in a charged state rather than at their isoelectric point, thus reducing precipitation problems. Proteins and peptides have been concentrated nearly 1000 times by this process while also providing modest chemical separation. We are exploring the use of field gradient focusing as a front-end processor for feeding the two-dimensional separation devices discussed above. The status of our efforts to demonstrate an integrated protein processor will be provided.

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