

A Decade of Progress in Microscale Electrical Field-Flow Fractionation

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Microscale field flow fractionation (FFF) has shown significant progress since it was first reported in early 1997 [1]. The first electrical FFF systems were lucky to function for more than a few days and generated only minimal levels of retention and separation, while current systems now easily function for years and can generate multicomponent separations [2]. A variety of microscale FFF systems have now been reported, including multiple versions of normal electrical FFF (EIFFF), cyclical electrical FFF (using oscillating fields), dielectrophoretic FFF, thermal FFF, acoustic FFF, a combined thermal-electric FFF channel, and flow FFF. The first nanoscale electrical FFF systems have recently been reported. Microscale EIFFF systems have been used to analyze and separate nanoparticles, DNA, proteins, cells, viruses, liposomes, large polymers, and other materials. EIFFF clearly improves upon system miniaturization due to the reduction in sample and carrier volumes, analysis times and more notably an increase in the separation resolution with a reduction in analysis times. Other advantages of miniaturized FFF include: parallel processing with multiple separation channels, batch fabrication with reduced costs, high quality manufacturing, and potentially disposable systems. Additionally, the possibility of on-chip sample injection, detection and signal processing favors the microfabrication of FFF systems.

Instead of applying an electrical field parallel to the flow of carrier as in electrophoresis, FFF applies the electrical field perpendicular to the flow and employs differential electrophoretic mobilities and diffusion rates to separate particles, as shown in Fig.1.

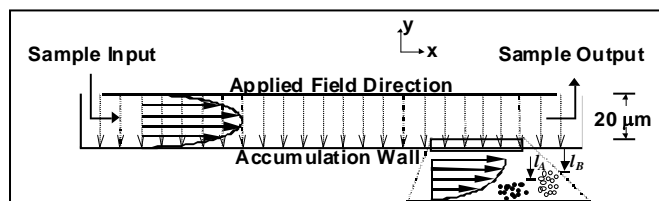


Figure 1. Schematic diagram of FFF. The particle clouds depicted by closed circles and open circles in inset figure are sample A with average thickness l_A and sample B with average thickness l_B . B will move faster through the channel than A since $l_B > l_A$.

However, separation in FFF is achieved at voltages three orders of magnitude lower than those used in electrophoresis, a major advantage. Retention in EIFFF is determined by the ratio between diffusion and electrophoretic transport ($D/\mu E$). Since EIFFF is an elution method, all eluted samples can be collected for later analysis. Thus, EFFF is ideal for sample preparation in lab-on-a-chip devices, for use in nanoparticle characterization, and for use with an orthogonal analysis system.

Although electrical FFF is a powerful method, it is limited by the polarization layer formed at the electrodes when a DC field is applied. This polarization or double layer reduces the electric field in the channel to less than 3% of the applied field value and the separation efficiency suffers accordingly. However, this problem can be countered by applying an alternating or cyclical electrical field, which does not allow the build up of a double layer. Thus, cyclical electrical FFF (CyEIFFF) was developed to take advantage of these miniaturized systems [3].

CyEIFFF has shown significant promise using electrical fields to separate nanoparticles and colloids. In CyEIFFF, the direction of the applied field is rapidly switched (~ 1 -20 Hz) and particles oscillate near one wall or travel between the two walls of the channel. CyEIFFF retains particles based on electrophoretic mobility alone and is not particle size dependent. Voltages as low as 0.25 V can retain particles easily.

CyEIFFF can also be tuned to maximize resolution by adjusting voltage and frequency of the applied field. Nanoparticles, viruses, and liposomes have all been characterized using CyEIFFF.

Pioneering work on microscale dielectrophoretic FFF (DEP-FFF) was done by Gascoyne's group with applications in cancer research and cell separations [4,5]. These systems are technically DEP-Gravitational FFF systems in which dielectrophoretic (DEP) fields are used to drive particles away from the wall and gravitational forces drive the same particles towards the wall. Thus a balance between these competing fields determines the average particle location in the channel and the elution time.

Researchers have recently demonstrated nanoscale EIFFF using channels that "apply" the electric field naturally. In other words, the native charge on the typical surface of a nanoscale capillary drives particles to or away from the wall, just as in normal FFF. Both pressure driven flow and electroosmotic flow can be used, since at the nanoscale, electroosmotic flow profiles begin to approach those for pressure driven flow. Sep-arations of particles in 40 nm channels based on charge have been demonstrated [6] and the theory and models derived [7].

Even with work in this area progressing well, there is still significant work remaining to make EIFFF a standard process in scientific and research circles. More information on microscale FFF can be found at www.mems.utah.edu/Project_Pages/FFF.htm

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