Chapter 12
Microscale Field-Flow Fractionation: Theory and Practice

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1. Introduction

The last decade has seen exponential growth in the development of lab-on-a-chip or micro-total-analysis system (µ-TAS) components to create better, faster, and cheaper chemical and biological analysis platforms [1]. Lab-on-a-chip type analysis systems typically include a separation-based sample preparation unit to achieve this objective or to prepare the sample for further interrogation using orthogonal techniques. Researchers have employed a host of sample preparation techniques based on electrophoresis [2, 3], ultrasound [4, 5], flow [6, 7], mechanical ratchets [8, 9], electrophoresis [10, 11], packed bed systems [12], membranes [13] magnetics [14, 15], temperature [16], optics [17], dielectrophoresis [18, 19], and so forth. Microscale field-flow fractionation (FFF) techniques have been an integral part of these efforts. Most of these techniques are simply miniaturized versions of conventional macroscale units with the rationale being that the reduction in physical size of the instrument results in smaller sample volumes and faster analysis times. While, many of these systems work well when miniaturized, this approach proves inadequate for systems that do not scale well. FFF, at least for many subtypes, has been shown to scale very well and FFF meets many of the design challenges for a successful separation module in a µ-TAS including (a) ease of manufacturing, (b) low power, (c) wide range of sample type and size, (d) integration to fluidic
components, and (e) material compatibility. Thus, FFF is potentially an important solution to many problems in microfluidic system design.

Field-flow fractionation clearly improves when miniaturized due to the reduction in sample and carrier volumes, analysis times, and more notably an increase in the separation resolution (at least for the electrical and thermal subtypes). Other advantages of miniaturized FFF can include the following: 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.

Several demonstrations of the effectiveness of FFF systems on the microscale have been made and will be reviewed in the work. Techniques that are often lumped in with FFF include split flow thin cell (SPLITT) fractionation and hydrodynamic chromatography. These related techniques have also been miniaturized and will be discussed later in this work.

![Sample Input and Output](image)

**Fig. 1.** FFF operational principle with two parallel plate type channel walls, laminar flow profile with transverse field direction and location of particle clouds near accumulation wall. The particle clouds depicted by closed circles and open circles in inset figure are particle cloud A with average thickness \(l_A\), and particle cloud B with average thickness \(l_B\), respectively

### 2. Background and Theory

FFF is a versatile separation technique that relies on the dual effect of the flow behavior and field distribution in a thin, open channel. FFF channels typically consist of a thin spacer enclosed by two parallel plates, modified to impart the external field as shown in Fig. 1. Flow in the channel is laminar resulting in a parabolic fluid velocity profile with differential velocity zones across the height of the channel. The versatility of FFF stems from the numerous types of fields and operating modes that can be employed to separate a wide range of sample types. Researchers over the years have developed different types of FFF systems differentiated primarily by the