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Optimization and characterization of a microscale thermal field-flow fractionation system

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ABSTRACT

A thorough investigation of the design considerations for microscale thermal field-flow fractionation and characterization of a 25 μm thin microscale thermal field-flow fractionation system is reported. A 4–50 times volume reduction from mesoscale and macroscale systems warrants customized design and operational conditions for microscale separation systems. Theoretical calculations are done to illustrate the importance of the increased dispersion due to extra-column tubing, off-chip detection and sample injection volume with reduced channel dimensions. An optimized microscale thermal field-flow fractionation (ThFFF) channel is fabricated using rapid and cost effective manufacturing and assembly processes. Specifically, improvements in material selection and arrangement are implemented to achieve higher particle retentions. The new instrument arrangement includes high conductivity silicon as the cold wall and a thin polymer layer with low thermal conductivity as the hot wall which results in high temperature gradients (~10^6 °C/m) across the microchannel and subsequently high retention. Single particle retention separations are carried out with polystyrene nanoparticle samples in an aqueous carrier to characterize the device and demonstrate the improvements.

1. Introduction

In the last few years, microscale field-flow fractionation (FFF) based techniques have generated substantial interest from researchers, as indicated by an increase in the number of publications in this field [1–3]. A wide range of FFF subtypes with different geometric dimensions that range from microscale to mesoscale have been reported [4–8]. Typically, microscale systems have channel heights of the order of 10–50 μm and channel volumes less than 10 μL.

With miniaturization, both operating conditions and system integration approaches should be carefully chosen in order to obtain high resolution separations [1]. Microscale FFF systems require careful packaging and interconnections with the minimum possible pre-column and post-column volumes, including minimal detector volumes with on-chip detection as the preferred option [1,4,9]. In addition, operating conditions such as carrier flowrate should be optimized so as not to increase band dispersion and early peaks due to inadequate sample relaxation. Thus, a number of design and operational issues need to be considered while optimizing a microscale field-flow fractionation system, which is the focus of this paper (exemplified by characterization of thermal FFF).

Lately, great progress in the development of mesoscale thermal systems has been reported by Janča [10]. They reported typical channel thicknesses of 100–250 μm and utilization of the same fabrication methods utilized since the 1960s to fabricate ThFFF macroscale systems [11]. By using a 23 μm thin and 96 mm long channel with a 1 μL sample injected, using an injection loop with no results, the authors concluded that smaller microscale systems will only produce poor retention and resolution [12]. The main problem with such an arrangement is that the sample volume is more than 12% of the total channel volume and with an injection time of 1 min, the sample occupies a large volume in the channel with the potential for considerable band broadening, even if the sample is fully relaxed. With relatively high flowrates (6 mL/h) for a typical microsystem and use of off-chip detectors, the result is poor resolution, entirely due to improper operating conditions. In comparison to macroscale systems, the sample volume and sample concentration in a microsystem present a bigger challenge for proper operation. In FFF, a relaxed sample is concentrated as a very thin layer near the accumulation wall. Even a low concentration sample stream becomes focused to the point that it becomes a compact layer. Then the sample stream washes over the compact

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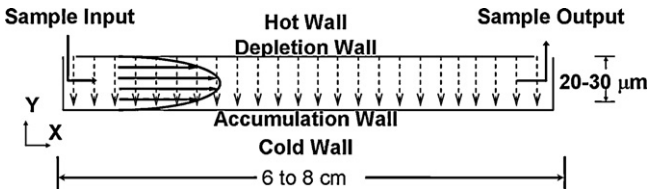

Fig. 1. Diagram of a FFF system operation showing the input and output ports, application of the thermal field, the parabolic flow profile, and relative channel dimensions. The thermal FFF system employs a temperature gradient to induce the separation with a fluid channel encompassed by hot and cold walls.

sample leading to early elution. If the sample volume is high, a significant portion of the sample will be excluded from the compact layer typical in FFF and increased secondary effects arise, such as particle–particle and wall repulsion effects, causing increased peak-broadening, reduced retention, and more importantly, poor repeatability [13]. The high sample volume may have resulted in the poor resolution for 23 μm microscale ThFFF [12]. In microsystems, this effect seems to be more pronounced when compared to macroscale systems due to the much smaller particle cloud to channel thickness ratios [9]. Our experience with FFF microsystems has shown that 0.1–0.2 μL injection volumes provide reasonable results [1,14]. This paper reports the operating conditions for ThFFF system that results in powerful retention of nanoparticles.

Another important design aspect related to miniaturization is minimization of the instrumental plate height [14]. In particular, post-column tubing and detector volumes need to be as small as possible, as was shown by the difference in obtainable resolution by an electrical FFF microsystem employing off-chip and on-chip detectors [4,14]. Similar results should be expected for other FFF systems employing other types of fields such as thermal FFF. The variation of the plate height contribution with scaling to indicate important design and operating considerations for microscale FFF systems is discussed here.

Recently Janča group has reported excellent results using a thermal FFF system at mesoscale that was build using methods reported in 1960s by Giddings group [16–18]. Our paper reports a microscale thermal FFF system with an improved design [18] when compared to systems used in earlier communications [6,12,19]. This microscale thermal FFF system was fabricated without the use of extensive microfabrication techniques [2].

Thermal FFF utilizes a temperature gradient perpendicular to the flow direction to induce retention (Fig. 1) [1]. A major consideration when designing a microscale ThFFF system is the choice of channel wall materials and their geometric arrangement due to the high heat fluxes involved with μ-ThFFF. The high heat fluxes inherently require the system to be provided with an efficient heat exchanger on the cold wall side to maintain the required temperature gradient (~10^6 °C/m) across the thin microchannel. Otherwise, the result will be a low temperature drop and poor retention [6]. Ideally, the walls of the channel should be made of a material with high thermal conductivity for efficient heat transfer and uniform heat distribution, but a good insulation layer is required to prevent heat loss from the hot wall. To address this design challenge, the thermal microsystem reported here uses a hot wall made of thin plastic (high heat capacity) and silicon with high thermal conductivity. It should be noted that a system with copper walls will require much smaller heater power and coolant flow rates to achieve the required temperature drop as compared to a plastic hot wall with the same geometrical dimensions. Reduced hot wall thickness reduces the power required to as low as 10–15 W, thus justifying the design change for a given temperature drop.

In this paper, we report a μ-thermal FFF system fabricated using rapid prototyping techniques [2]. A knife plotter was used to pattern microchannels from a tape with adhesive applied on both sides and bonded to the plastic and silicon substrate to create a composite μ-thermal system. The plastic substrate was machined to create corrugation with only a thin layer of material remaining, into which a thin film heater is placed. The power required to heat the hot side of the channel and the time to reach a steady state temperature are reduced due to a substantial reduction in the thermal mass of the substrate, which results in a reduced load on the heat exchanger that is maintaining the cold wall temperature at a constant value. The newly designed microsystem was employed to characterize the particle retention in an aqueous environment using a thermal field.

2. Theory

The goal of any separation system optimization effort is to maximize the separation efficiency (reduce plate height) and resolution or fractionating power. The total plate height can be depicted as the summation of several contributing factors such as non-equilibrium effects, H_n, instrumental effects, H_i, polydispersity, H_p and the contribution due to diffusion, H_D [20] as given by

$$H = H_n + H_i + H_p + H_D. \quad (1)$$

The non-equilibrium part of the plate height is given by

$$H_n = \frac{\chi(\lambda) w^2 \langle v \rangle}{D}. \quad (2)$$

where w is the channel height, $\langle v \rangle$ is the average velocity and D is the particle diffusion coefficient. The details on the function $\chi(\lambda)$ and other plate height related factors are detailed elsewhere [15,23].

Other plate heights that need to be considered during the optimization efforts of microscale systems are related to the sample volume, sample relaxation and extra-column tubing and detector volumes [23].

The plate height contribution due to the sample volume injection is given by

$$H_s = \frac{v_{inj}^2}{12(b/w)^2 w^2 L}. \quad (3)$$

where v_{inj} is the volume of the sample injected, and b and L are the channel width and length respectively [23].

The plate height contribution, H_r, due to the sample relaxation is given by

$$H_r = \frac{17}{140}\frac{h_0^2}{L}. \quad (4)$$

where h_0 is the span of the fully relaxed sample along the channel length and can be related to the retention parameter, λ and flow velocity by [23]

$$h_0 = \frac{w}{\lambda}\frac{\langle v \rangle}{D}. \quad (5)$$

The main band broadening related contributions due to the off-chip detector are related to the volume of the detector, V'_c [23]

$$H = \frac{1}{L}\left(\frac{V'_2}{bw}\right)^2. \quad (6)$$

and length of the extra-column tubing, L_t,

$$y = \frac{L_t \dot{V} L \pi r_t^4}{48 D V_r'^2 H}, \quad (7)$$

where V'_r is the retention volume, y is the plate height factor, $\dot{V}$ is the volumetric flowrate and r_t is the radius of the extra-column tubing [23].

While the plate height contributions represented through Eqs. (2)–(4) have been reported for FFF and general chromatography,