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Surfactant addition and alternating current electrophoretic oscillation during size fractionation of nanoparticles in channels with two or three different height segments

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ABSTRACT

An array of parallel planar nanochannels containing two or three segments with varying inner heights was fabricated and used for size fractionation of inorganic and biological nanoparticles. A liquid suspension of the particles was simply drawn through the nanochannels via capillary action. Using fluorescently labeled 30 nm polyacrylonitrile beads, different trapping behaviors were compared using nanochannels with 200–45 nm and 208–54–30 nm height segments. Addition of sodium dodecyl sulfate (SDS) surfactant to the liquid suspension and application of an AC electric field were shown to aid in the prevention of channel clogging. After initial particle trapping at the segment interfaces, significant particle redistribution occurred when applying a sinusoidal 8 V peak-to-peak oscillating voltage with a frequency of 150 Hz and DC offset of 4 V. Using the 208–54–30 nm channels, 30 nm hepatitis B virus (HBV) capsids were divided into three fractions. When the AC electric field was applied to this trapped sample, all of the virus particles passed through the interfaces and accumulated at the channel ends.

1. Introduction

Nanofluidic devices are structures having at least one dimension in the submicron range, which is of the same order of magnitude as the sizes of biological macromolecules such as proteins and DNA. As a result, separations (especially size-based) are important applications for nanofluidics [1–4]. Well-defined nano device structures fabricated via micromachining have greatly reduced sample consumption and enabled separations in a parallel fashion, promising faster analysis, and better resolution and reproducibility [5–7] compared to traditionally used size characterization tools. Using dynamic light scattering (DLS) [8], accurate measurements become extremely difficult for samples containing a broad particle size distribution, large aggregates, or contaminants. Conventional electron microscopy techniques, such as transmission electron microscopy (TEM) [9], allow the direct visualization of nanoparticles, including their sizes, shapes and degrees of aggregation. However, TEM must be operated under vacuum conditions. Also, sample preparation for TEM is time-consuming, and usually leads to sample alteration during drying. Size separation techniques based on chromatography and field flow fractionation (FFF) provide good resolution and are sensitive and non-destructive. However, size exclusion chromatography (SEC) [10,11] is limited by sample loss caused by nonspecific sample-column interactions and narrow size separation range, depending on the pore size distribution of the SEC column. Hydrodynamic chromatography (HDC) overcomes most nonspecific interactions by using nonporous beads for column packing. It also allows a wider size separation range from 5 to 1200 nm [12]. However, similar to DLS, HDC suffers from poor resolution.

FFF separates macromolecules and particles based on the interaction between analytes and a particular applied field. FFF can be used to fractionate particles ranging from 1 nm to 1 μm. However, FFF utilizes complex devices and requires skilled operators to obtain reproducible and reliable data [13].

For purification and separation, polymer gels and membranes with various pore sizes have been extensively used as molecular sieve matrices. Unfortunately, the microscopic structures of these systems are inherently random, which hinders both theoretical and experimental studies aimed at improving separations. Microfluidic systems for biomolecule size separation have generally adopted the same random nanoporous sieving materials [14,15,2] and, hence, the same limitations.

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In contrast, carefully designed regular micro/nanostructures via micro/nanofabrication provide unique capability in biomolecule analysis by improving control over the molecular sieving process. Microfiltration, a separation technique based on size, has been applied in sample preparation to reduce the complexity of the original sample. Different designs and sizes of filters, such as arrays of posts [16], tortuous channels [17], comb-shaped filters [18] and weir-filters [19], have been fabricated and utilized for efficient isolation of human blood cells from whole blood. Size fractionation is not only useful for purification, but provides valuable information concerning sample size distribution. Tremendous effort has been dedicated to accomplishing this goal. Huang et al. [20] reported a microfluidic particle separation device that made use of laminar flow through a periodic array of micrometer-scale obstacles. A mixture of 0.8, 0.9 and 1.0 μm microspheres was separated in 40 s with a resolution of approximately 10 nm. Huh et al. [21] described a microfluidic sorting system for size profiling using a combination of gravity and hydrodynamic flow, and demonstrated the sorting of different-sized polystyrene beads and perfluorocarbon liquid droplets. Yamada and Seki [22] proposed a new hydrodynamic filtration method for concentrating and classifying particles in microfluidic devices, where a particle suspension was repeatedly introduced into the microchannel and the particles were aligned and collected according to size through side channels.

The regular molecular sieving systems discussed above have proven effective for separation of cells and microspheres, however, their applicability to smaller molecules or particles are questionable. In a move to significantly smaller size scale (10–100 nm), we have developed a new size characterization method using nanofluidic devices, where particles are size-fractionated by simply flowing a liquid suspension of the particles through an array of parallel planar nanochannels via capillary action [23]. By varying the inner channel heights, large particles become trapped when they arrive at an interface where the channel steps from a deeper to a shallower segment. Therefore, size separation is accomplished within minutes on a single chip.

In this study, we utilized two- and three-segment nanofluidic chips for size fractionation of synthetic spherical nanometer particles. Two issues related to the application of nanochannels were resolved. First, we developed a new external micro-reservoir to accommodate microliter-sized samples, which allowed proper delivery of liquid into the nanochannels. Also, in an effort to eliminate jamming or clogging, we investigated the effects of surfactants and an applied oscillating electric potential, which helped to prevent particle agglomeration. Our nanofluidic systems are capable of fast particle separation, and they offer advantages of small size and low cost.

2. Generation of liquid flow

The operation of our nanosieving devices is simple, since liquid flow and particle trapping are based on capillary action and liquid carrier evaporation from the outlet ends of the channels. The Young–Laplace equation can be used to describe the capillary pressure difference across the interface between air and water:

$$\Delta p = \gamma \left(\frac{1}{R_1} + \frac{1}{R_2} \right) \tag{1}$$

where γ represents the surface tension of water, and R_1 and R_2 are the principal radii. In the case of a planar nanochannel, where the channel height, h, is much smaller than the channel width, this equation can be converted to

$$\Delta p = 2\gamma \cos \frac{\theta}{h} \tag{2}$$

where θ is the contact angle of water on the channel walls. The surface tension of water is 0.0728 N/m at 25 °C [24]. Assuming a water contact angle of 60° [25], the capillary pressure ranges from 7.28 to 72.8 bar for channel depths from 100 to 10 nm [26]. Such a high pressure ensures fast liquid filling of the nanochannels. For instance, theoretically, it would only take ~1 s for a single nanochannel (1 mm long × 100 nm deep) to fill with liquid. From the Hagen–Poiseuille equation, the volumetric flow rate, Q, in a straight nanochannel is given by

$$Q = \Delta P \times \left(\frac{D_r^2 \omega d}{32 \mu L} \right) = \frac{\Delta P}{R_h} \tag{3}$$

where ΔP is the capillary pressure drop across the channel, L is the length of the channel, ω is the width of the channel, d is the depth of the channel, μ is the viscosity of the liquid, D_r is the hydraulic diameter of the channel, and R_h is the hydraulic resistance of the channel [22]. For a rectangular nanochannel:

$$D_r = \frac{2\omega d}{\omega + d} \tag{4}$$

For our nanosieving devices, each single nanochannel was approximately 1 mm long and 15 μm wide. Assuming that the channel was 100 nm tall and that the viscosity of the bead suspension was the same as water (8.9×10^{-4} Pa s), then the hydraulic resistance in a single nanochannel was approximately 4.75×10^{20} Pa s m^{-3} and the volumetric flow rate was approximately 1.5×10^{-12} L s^{-1}. In practice, the force that moved the particles in the channels was a combination of capillary action and evaporation from the channel ends. In a trapping experiment performed in a two-segment chip, it was typical to see the rate of increase in fluorescence intensity decrease with time regardless of the channel dimensions, signaling the end of capillary action and the beginning of evaporation-dominated flow through the channels [23].

3. Experimental

3.1. Nanofluidic device fabrication

This work utilized two-segment channels with 200 nm and 45 nm high segments connected in series (1 mm and 0.2 mm long, respectively) and three-segment channels with 208 nm, 54 nm, and 30 nm high segments connected in series (0.8 mm, 0.2 mm and 0.2 mm long, respectively). The fabrication process for the two-segment chips was described in previous work [23]. Similar procedures were used to prepare three-segment chips, which began with depositing approximately 250 nm of silicon dioxide on a silicon substrate via plasma-enhanced chemical vapor deposition (PECVD). A 30 nm layer of aluminum was then deposited using a thermal evaporator to form the short segments. Photoresist (PR) AZ nLOF 2020 (AZ Electronic Materials, Branchburg, NJ, USA) was spun on, patterned and developed, exposing an area where a second layer of aluminum was deposited to form the 54 nm tall segments. The PR was then lifted off using N-methylpyrrolidone (NMP) and heated to 95 °C, leaving two aluminum covered areas of different heights. The photolithography step using AZ nLOF 2020, metal deposition and NMP lift-off was again repeated, defining three distinct segment heights of 30–54–208 nm. AZ 3330 PR (AZ Electronic Materials, Branchburg, NJ, USA) was spun on and patterned to define the aluminum core lines. The exposed aluminum was removed using a commercial aluminum etchant (Transene, Danvers, MA, USA) heated to 50 °C, and the PR was rinsed off with acetone and 2-propanol. The aluminum channel core heights were verified with atomic force microscopy (AFM). Then, a capping layer of approximately 5 μm silicon dioxide was deposited using PECVD.