ON-CHIP ASSEMBLY OF POLYELECTROLYTE CAPSULES ON MAGNETIC TEMPLATES

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ABSTRACT

We have developed microfluidic devices for the continuous flow coating of magnetic templates (droplets/cells) with polyelectrolytes towards rapid layer-by-layer (LbL) assembly of drug delivery capsules. Magnetic ferrofluid droplets and magnetically functionalized yeast cells were deflected across a reaction chamber through reagent and washing streams to achieve fast layer deposition (<10 s).

KEYWORDS: Magnetic droplets, Droplet deflection, Layer-by-layer assembly, Polyelectrolyte

INTRODUCTION

Polymer multilayer capsules (PMLCs) have attracted much attention in areas as wide ranging as drug delivery, catalysis and synthetic chemistry. Conventionally, PMLCs are fabricated by a layer-by-layer (LbL) technique involving the deposition of *ca.* ten layers onto a template, which is then dissolved to yield a hollow capsule. This process requires multiple incubation and washing steps with processing times of around 40 min per layer (fig. 1a). Recently, microfluidic LbL approaches have been utilized for achieving fast and automated deposition of materials using somewhat complex micropillar designs to guide droplet templates [1, 2]. Magnetic templates, e.g. droplets, particles or cells, offer an elegant alternative, enabling convenient manipulation via magnetic fields to afford simple chip designs and setups (fig. 1b). Previously, we have demonstrated the coating of negatively-charged magnetic yeast cells with fluorescently labeled, positively-charged polyelectrolyte, poly(allylamine hydrochloride) (PAH) [3]. However, employing conventional PAH and PSS (poly(sodium 4-styrenesulfonate)) polyelectrolytes for droplet templates proved challenging, with droplets found to be unstable. Here, we report the deposition of negatively-charged poly(acrylic acid) (PAA) onto magnetic droplets and yeast cells coated with the surface active polymer, poly(vinylpyrrolidone) (PVP).

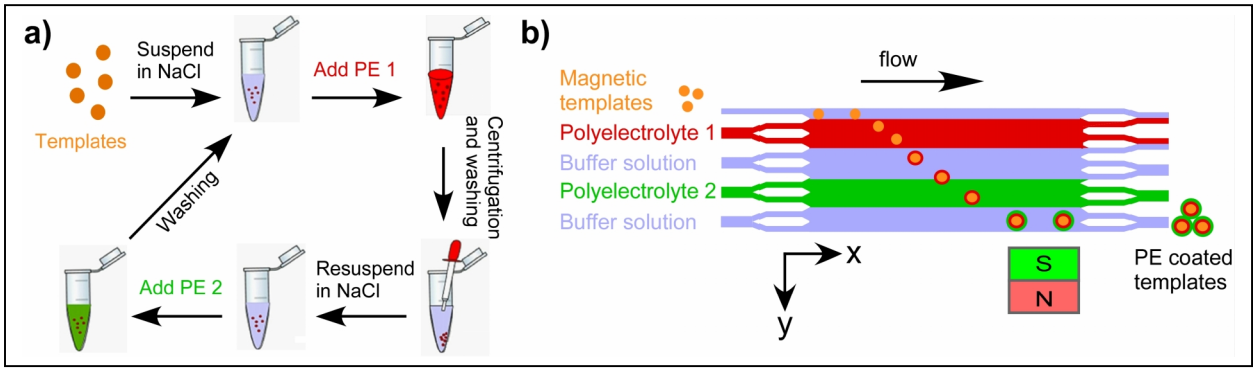

Figure 1: (a) Conventional LbL deposition of polyelectrolytes (PE) using tubes and centrifugation. (b) Concept of continuous flow layer deposition on magnetic templates in a microfluidic device.

EXPERIMENTAL

Experiments with magnetic droplets were conducted in a two layer glass chip (fig. 2a). The top layer featured a flow focusing network for droplet generation and was etched to a depth of 20 µm to allow generation of small droplets. The bottom layer was etched to a depth of 100 µm and featured all of the remaining inlet channels for introducing parallel laminar streams of reagents and buffers, as well as outlet channels and a reaction chamber of 8 mm length and 4.1 mm width. The chip was mounted into a chip holder and interfaced to a syringe pump with capillaries and Tygon tubing (fig. 2b).

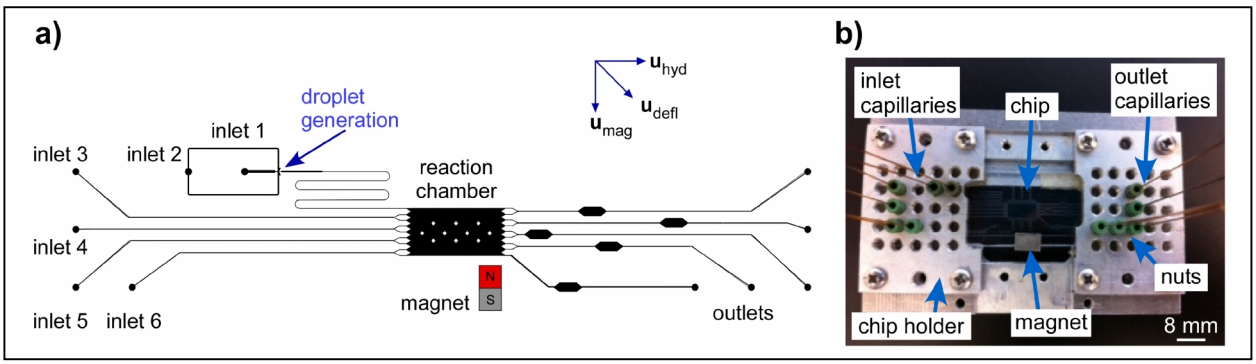

Figure 2: (a) Chip design for droplet generation via flow focusing and deflection through a reaction chamber. The droplet generation region was etched to a depth of 20 µm in one glass layer, and the remainder of the design was etched to 100 µm in a second glass layer. (b) Photograph of the setup showing the glass chip in its holder with inlet and outlet capillaries, and a permanent magnet.

Magnetic droplets were prepared from an oil-based ferrofluid (FF) (EMG901, Ferrotec) pumped through inlet 1 and an aqueous continuous phase (CP) pumped through inlet 2. The CP was a 20 mM sodium acetate buffer (pH 4) with 10 mg mL^{-1} PVP and 0.05% Tween 20. Sodium acetate buffer (pH 4, with 0.05 % Tween 20) was also pumped through inlets 3-6. For the deposition of a polyelectrolyte layer, a solution of negatively-charged, fluorescent poly(acrylic acid)-Rhodamine 123 (PAA-Rhod123) (10 mg mL^{-1} in buffer) was pumped through inlet 4 to generate a laminar reagent stream between the buffer streams. Droplets were deflected across the width of the reaction chamber by an external neodymium-iron-boron (NdFeB) magnet.

Magnetic yeast cells were prepared as detailed in [3], and featured an outer layer of PVP. The yeast cells were pumped into a reaction chamber and deflected through a stream of PAA-Rhod123.

RESULTS AND DISCUSSION

An example of droplet generation and deflection is shown in fig. 3. The ferrofluid was pumped at a flow rate of 1 µL h^{-1} and the CP at 100 µL h^{-1}, while the flow rate for inlets 3-6 was set at 200 µL h^{-1} each. Droplets formed at the 20 µm deep flow focusing junction and adopted a spherical shape when entering the 100 µm deep main channel. The droplets were 59 µm in diameter at the flow rates stated above. Varying the CP flow rate between 50 and 500 µL h^{-1} allowed for droplet size variation between 71 µm and 46 µm. Droplets were deflected across the chamber via a 2 x 2 x 5 mm^3 magnet (fig. 3b), generating forces of around 320 pN on the magnetic droplets. Droplets were also deflected through alternating streams of inks to visualize the crossing of multiple streams (fig. 3c).

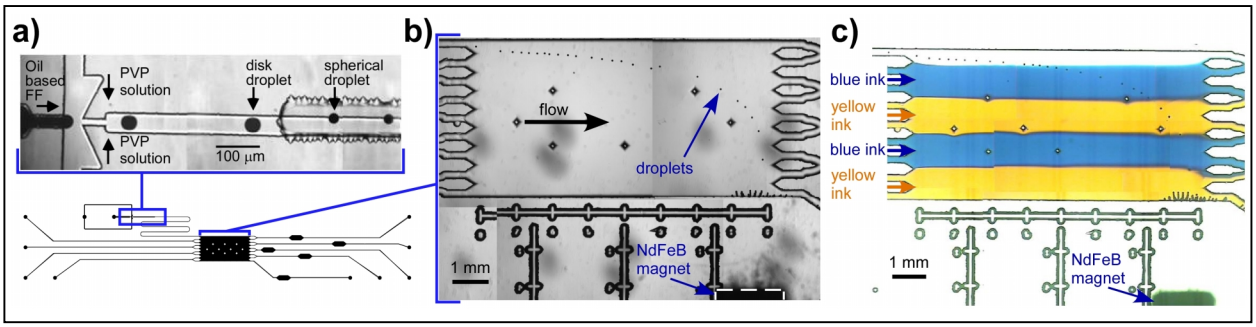

Figure 3: (a) Two-layered device for generation of small, spherical FF droplets. (b) Deflection of droplets across chamber (flow in chamber 1.2 mm s^{-1}, magnetic force 320 pN). (c) Deflection of droplets through multiple laminar flow streams of aqueous inks.

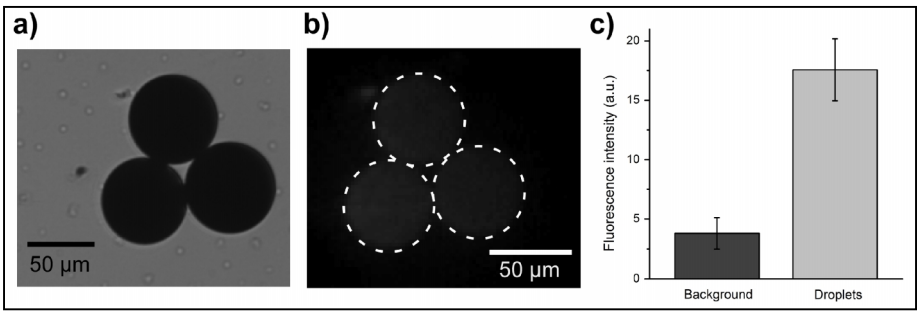

Figure 4: PVP-coated ferrofluid droplets after passing through the PAA-Rhod123 stream: (a) microscope photograph, (b) fluorescence image, (c) fluorescence increase against background.

The feasibility of deflecting droplets across a polyelectrolyte (PAA) stream for layer deposition was also demonstrated (fig. 4). By introducing negatively-charged PAA-Rhod123 into inlet 4, the ferrofluid droplets were coated as they passed through the stream, with excess material washed away by subsequent buffer streams. The measured increase in fluorescence demonstrated the rapid coating of droplets (<2 s), showing promise for LbL deposition in continuous flow.

Magnetic yeast cells (PVP-coated) were also tested as templates by deflecting them through a stream of negatively-charged PAA-Rhod123. The chip design featured a deflection chamber with five inlets/outlets (fig. 5a). Flow rates were 10 µL h^{-1} in each inlet. The measured increase in fluorescence showed the cells were coated with PAA-Rhod123 (fig. 5b/c), demonstrating fast (<10 s) deposition that will be beneficial to LbL microcapsule production.

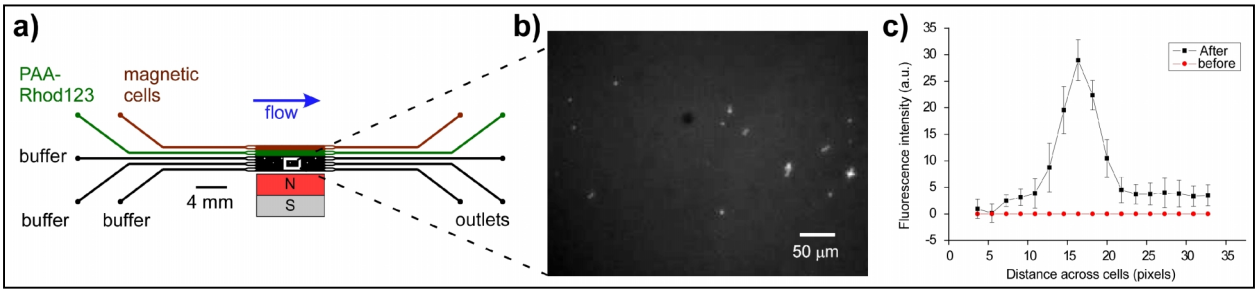

Figure 5: Deflection of PVP-coated magnetic yeast cells through negatively-charged PAA-Rhod123. (a) Schematic of chip design and flow streams. (b) Photograph of fluorescent yeast cells after leaving the PAA-Rhod123 stream. (c) Plot of fluorescence intensity across the cells before and after passing through the PAA-Rhod123 stream. Cells exhibited no fluorescence prior to the reagent stream.

CONCLUSION

In summary, magnetic templates (droplets and cells) were successfully manipulated and deflected across a microfluidic chamber, allowing deposition of a polyelectrolyte layer and subsequent washing in less than 30 s. Further layers can be deposited by incorporating additional reagent streams.

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