Letter

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Rapid patterning of PDMS microfluidic device wettability using syringe-vacuum-induced segmented flow in non-planar geometry

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Abstract: We present a simple and rapid method to spatially pattern the surface wetting properties of PDMS microfluidic devices by Layer-by-Layer (LbL) deposition of polyelectrolytes using syringe-vacuum-induced segmented flow in non-planar geometry. Our

technique offers selective surface modification in microfluidic chips with multiple flow-focusing junctions, enabling production of monodisperse double- and triple- emulsion drops.

Drop-based microfluidic devices generate and manipulate discrete drops through precise control of immiscible multi-phase flows inside microchannels.[1] A widely used material for microfluidic devices is poly(dimethylsiloxane)(PDMS) due to the simple and reproducible device fabrication procedures via soft-lithography and the possibility of integrating large number of drop makers within a small area, leading to great potential to mass produce these devices.[2-5] Moreover, PDMS is optically transparent, non-toxic, biologically inert and permeable to gases, adding significant value in many applications.[6, 7] Despite all these advantages, the inherent hydrophobic nature of PDMS often limits the types of these emulsion drops that can be formed.[8] For example, to form stable oil-in-water (O/W) emulsions, the microchannel surface needs to be modified to be hydrophilic to assure an effective wetting of the channel surface by the continuous aqueous phase. Furthermore, to form multiple emulsions, or drops within drops, using multiple flow junctions in microfluidic devices, the surface wettability needs to be spatially patterned to have subsequent continuous fluids favorably wet the microchannel; this allows the inner drops to be formed in one part of the device and the outer drops in another part.

 Several modification methods have been developed to spatially control the surface wettability in microfluidic devices to produce these multiple emulsions.[9-17] One approach involves selective surface functionalization of microchannels via thermal- or photo-polymerization.[18, 19] However, this approach requires specialized equipment such as sophisticated optics and a powerful UV-light source, complicated flow control, and in some cases, precise alignment of the optical pattern. Alternatively, channel-guided plasma oxidation has been proposed to spatially tune the surface wettability in microfluidic device.[20] This approach allows surface modification without

introducing any liquids into the device, eliminating the complicated flow control that is often tedious, labor intensive, and prone to failure. However, this surface treatment is not permanent and leads to temporarily hydrophilic regions in the PDMS device that regain their original surface properties over time.[8] A more robust method is the Layer-by-Layer (LbL) deposition of positively and negatively charged polymers onto the surface which has been successfully used to modify the wettability in PDMS microchannels.[21] Huck *et al.* have suggested automated LbL assembly to alter the PDMS surface hydrophilicity by utilizing sequential injection of positively- and negatively- charged polyelectrolyte solutions.[22] While this technique is a rapid and low cost approach, it still requires complicated flow control which makes selective surface modification challenging in more complex channel designs with multiple flow-focusing junctions.

In this communication, we describe a simple and rapid method to spatially pattern the surface wetting properties of flow-focusing microfluidic devices by Layer-by-Layer (LbL) deposition of polyelectrolytes. We use syringe-vacuum-induced air-water segmented flow to deposit polyelectrolytes and modify the surfaces of PDMS microchannels to make them hydrophilic; this is achieved by pulling the syringe by hand, without the use of any specialized equipment. The devices have a non-planar geometry, which enables a facile control of the fluid flow within the device to spatially modify the surface wettability and to reliably produce monodisperse double- and triple- emulsion drops in PDMS microfluidic devices.

We prepare a PDMS microfluidic device with non-planar geometry using soft-lithography to make two complementary molds, one for the top part of the non-planar junction and a second for the bottom part.[23] Each of the molds consists of two or three photo-resist layers depending on the number of flow focusing junctions required, as shown in Supporting Information Figure S1-2. These molds with different channel depths are fabricated via multi-step lithography in which

additional photo-resist layers are applied between UV exposures and are aligned with the prior layers using a mask aligner. After replication of the molds with PDMS, two replicas are bonded together by using the Lock-and-Key align marks[23] (one is positive, the other is negative) in each mold after oxygen plasma treatment followed by dry baking at 65°C overnight, resulting in a microfluidic device with 3D non-planar geometry.
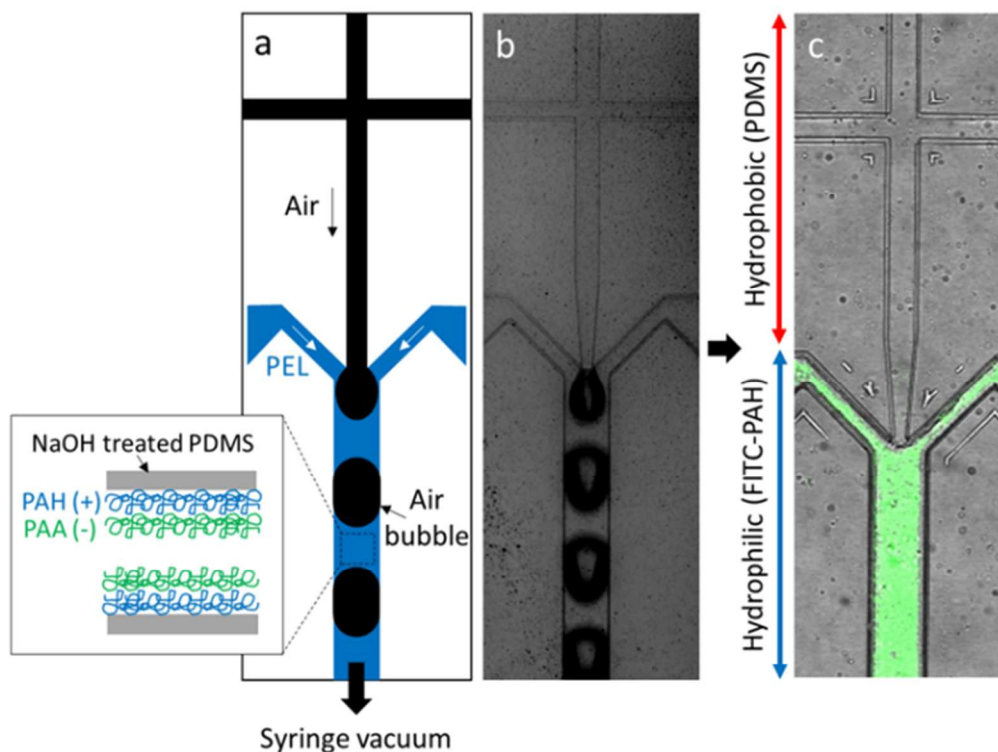
Figure 1. (a) Schematic of the Layer-by-Layer (LbL) deposition of polyelectrolytes (PEL) in the continuous microchannel using syringe-vacuum-induced segmented flow. (b) Air bubbles are continuously generated through the microchannels for the dispersed phase as negative pressure is applied to the collection port. (c) Fluorescence micrograph of the PEL-deposited microfluidic device showing excellent spatial control in surface modification.

To spatially pattern the surface wetting properties of the microfluidic device, we first pre-treat the PDMS with sodium hydroxide (1M NaOH) for 10 min. This promotes the formation of ionizable functional groups on the PDMS surface[24] in a much milder condition than oxygen plasma treatment which often results in activation and subsequent wetting of the coating fluids in undesired regions within the microfluidic device. Then, we Layer-by-Layer (LbL) deposit

polyelectrolytes (PEL) and modify the surfaces of the desired PDMS microchannels to make them hydrophilic. To implement the surface wettability patterning via sequential injection of PEL solutions with opposite charges, we insert a pipet tip into the injection port for the outer phase and connect a syringe to the collection port to apply negative pressure, leaving the other injection ports open to air, as shown in Supporting Information S3. By pulling the syringe, we generate a syringe-vacuum-induced air-PEL segmented flow through the microchannel for the continuous phase, depositing only in the region in contact with the PEL solution. While PEL is selectively deposited in this region, air bubbles are continuously generated through the open ports as negative pressure is applied to the collection port. This prevents the PEL solution from entering into the channels for the dispersed phases. The non-planar geometry of the microfluidic device, in which the channel for the disperse phase is positioned in the center both vertically and horizontally with respect to the continuous channel, also contributes to increasing the flow resistance into this channel, therefore decreasing the likely of back flow into the channel, as shown in Figure 1a-b and Supporting Information Figure S4.

 To LbL deposit polyelectrolytes, two oppositely charged PEL solutions, poly(allylamine hydrochloride)(PAH) for the polycation (+) and poly(acrylic acid)(PAA) for the polyanion (-), are sequentially injected into the port for the outer phase with rinsing steps in between. In a traditional LbL assembly process, two complementary polymers constitute a single bilayer and deposition of more bilayers typically results in more uniform coverage of the target surface. We measure the advancing contact angle of 2.5% PVA solution before and after the chemical modification of PDMS to confirm that more bilayers of PAH/PAA result in a decrease in the contact angle and thus more uniform surface coverage, as shown in Supporting Information Figure S5. However, to achieve rapid surface modification, we deposit a single bilayer of

polyelectrolytes; by comparing the drop formation with a single bilayer and 3 bilayers of PAH/PAA, we find that a single bilayer is sufficient. PEL solutions are each treated for 5 min, followed by a rinsing with de-ionized water for 1 min. The concentration of the PEL solutions used was 1 mg/mL and the pH of the PAH and PAA solutions were 7.5 and 3.5, respectively. The deposition of PAA in the microchannel makes the coated surface hydrophilic due to its high polarity.[25] We observe that a PAH/PAA polyelectrolyte coating allows consistent production of emulsion drops even two months after the surface modification, confirming that the hydrophilic layer is long lasting. We note that these coatings have also been reported to be stable under operation with organic solvents including troublesome aprotic solvents of industrial importance such as isopropyl alcohol (IPA), acetonitrile (ACN), tetrahydrofuran (THF), and *N,N*-dimethylformamide (DMF).[26]

To validate the spatial control of the surface modification, we use fluorescent dye-labeled polyelectrolyte, poly(fluorescein isothiocyanate allylamine hydrochloride) (FITC-PAH) and monitor the fluorescence signal of the PEL-deposited microfluidic device with confocal microscopy; indeed, fluorescence signal is only observed in the collection channel, confirming that this method provides excellent spatial control in surface modification as shown in the fluorescence images of Figure 1c.

The ability to spatially pattern the surface wetting properties of PDMS microfluidic devices in a simple, rapid, and robust manner offers new opportunities for reliable production of multiple emulsion drops. To produce water-in-oil-in-water (W/O/W) double emulsion drops, a single microfluidic device with both hydrophobic and hydrophilic regions is required; one part needs to be hydrophobic for stable water-in-oil emulsion drops formation while the other part needs to be hydrophilic for oil-in-water emulsion drops.
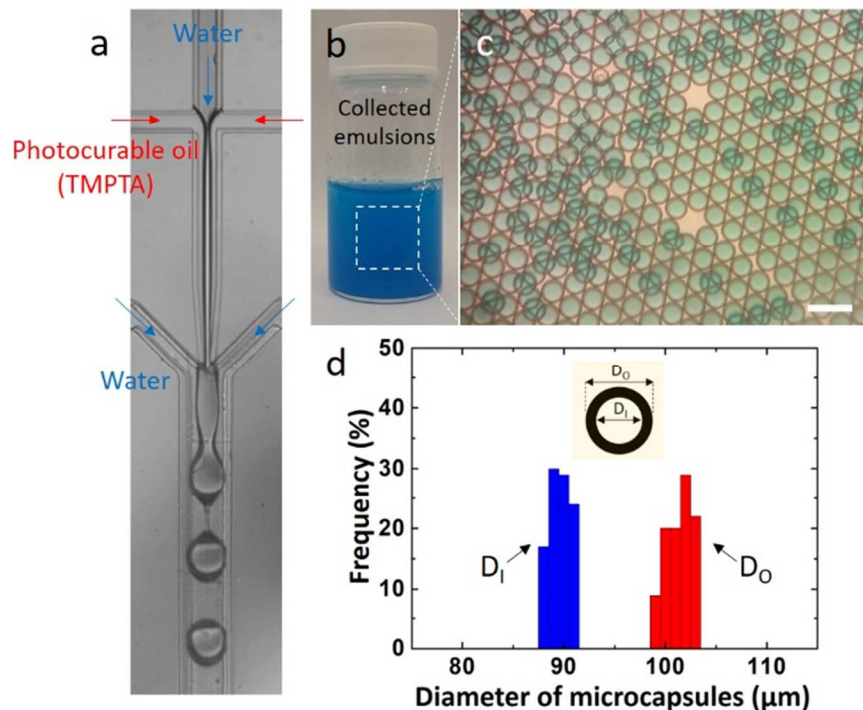
Figure 2. (a) Micrograph of a spatially patterned microfluidic device producing water-in-photocurable oil-in-water (W_1/O/W_2) double emulsion drops, where Q_{w1}=500 µL/hr, Q_O=500 µL/hr, and Q_{w2}=2000 µL/hr (b) Photograph of the sample collected after 6 hrs of operation. (c) Micrograph of the collected double emulsion drops confirming that they are formed properly. Scale bars represent 200 µm. (d) Size distributions of the double emulsion drops.

To test our surface modification method for producing double emulsion drops, we chose water-in-photocurable oil-in-water (W/O/W) double emulsion drops as our model system. We use 2.5% aqueous solution of poly(vinyl alcohol)(PVA) as the inner aqueous phase, trimethylolpropane triacrylate (TMPTA) as the middle oil phase, and 2.5% PVA solution as the continuous aqueous phase. The inner aqueous phase and the photocurable oil phase are introduced into two separate injection ports and are co-flown through the first flow-focusing junction where the microchannel is not treated and is thus hydrophobic. This water-in-oil stream then breaks up into drops by the shearing of the continuous aqueous phase at the second flow-focusing junction in which the microchannel surface is hydrophilically modified with PEL. This abrupt change in surface wettability enables production of stable W/O/W double emulsion drops, as shown in Figure 2a.

While the non-planar geometry of the microfluidic device forms W/O/W double emulsion drops even when the surface is non-treated, in this case, the flow rate of the continuous phase needs to be sufficiently large to prevent the hydrophobic oil phase from wetting the channel surface.[23] Moreover, when wetting of the dispersed phase does occur, it is often irreversible and requires excessive washing of the device to function again, as shown in Supporting Information Figure S6. Furthermore, this minimum required flow rate of the continuous phase substantially limits the range of operation both in terms of tuning the overall size of the emulsion drops as well as operation of the device in dripping mode, which is often preferred due to enhanced monodispersity.[27] By utilizing our method to spatially pattern the surface wetting properties of PDMS microfluidic devices, we obtain consistent production of double emulsion drops for 6 hrs, indicating that this method is robust, as shown in Figure 2b. To measure the inner and outer diameter of the drops produced, we perform image analysis on multiple images obtained with optical microscopy. We analyze at least 100 drops to determine the average value of the inner and outer diameter. The resulting double emulsion drops are highly uniform (CV = 1.5%), as shown in Figure 2c and Figure 2d.
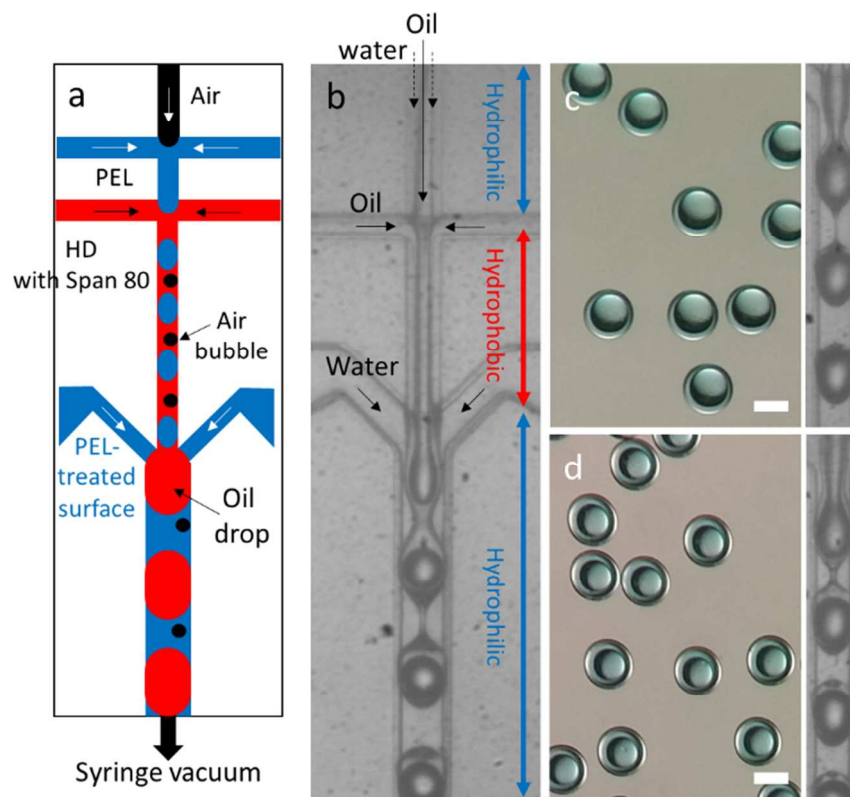
Figure 3. (a) Schematic showing the selective modification of surface wettability in a microfluidic device with three flow-focusing junctions. (b) Micrograph showing the production of O/W/O/W triple emulsion drops in surface patterned PDMS microfluidic device. These emulsions are produced at Q_{O1}=1000 µL/hr, Q_{W1}=500 µL/hr, Q_{O2}=1000 µL/hr, and Q_{w2}=5000 µL/hr. (c-d) Micrographs showing the triple emulsion drops formed at different volumetric flow rates. By tuning the flow rates, triple emulsion drops with a thin intermediate water layer can be produced. Scale bars represent 100 µm.

The simple and robust nature of this method also provides a route to selectively modify the surface wettability in complex channel designs even with additional flow-focusing junctions, allowing production of higher order emulsion drops such as triple emulsion drops. To validate this, we prepare a non-planar microfluidic device with three flow-focusing junctions for the production of $O_1/W_1/O_2/W_2$ triple emulsion drops. The detailed dimensions of the device can be found in the Supporting Information Figure S2. We spatially pattern the surface wetting properties of the microfluidic device in two-steps. In the first step, we modify the microchannel for the continuous aqueous phase (W_2) to be hydrophilic via LbL deposition of polyelectrolytes, as shown in Figure 1a. After the PEL layer deposition in the continuous microchannel, we load

hexadecane with 2% Span 80 into the pipet tip connected to the injection port for the second oil phase (O_2), and sequentially load PEL solutions, comprising of two oppositely charged polyelectrolytes, into the pipet tips connected to the first aqueous phase (W_1); the injection port for the innermost oil phase (O_1) is left open to air. By pulling the syringe and thus applying negative pressure, hexadecane with 2% Span 80 enters into the microchannel for the second oil phase (O_2) while PEL solutions containing air bubbles are sequentially introduced through the channel for the first aqueous phase (W_1). The high affinity of hexadecane with PDMS[28] and the presence of Span 80 in the hexadecane results in PEL solution to break up into drops while being fully surrounded by the hexadecane phase. This allows selective modification of the microchannel for the first aqueous phase to be hydrophilic, while the microchannel for the second oil phase (O_2) retains its hydrophobicity, as schematically shown in Figure 3a. Similar to the double emulsion device, a non-planar geometry is used wherever abrupt changes in surface wettability from hydrophobic to hydrophilic are required, as shown in the Supporting Information Figure S2.

To test our surface modification method for producing $O_1/W_1/O_2/W_2$ triple emulsion drops, we use hexadecane as the innermost oil phase (O_1), 2.5% PVA solution as the inner aqueous phase (W_1), TMPTA as the second oil phase (O_2), and 2.5% PVA solution as the continuous aqueous phase (W_2). We obtain consistent production of these triple emulsion drops for 6 hrs, confirming that our method enables precisely controllable patterning of surface wettability in PDMS microfluidic devices with multiple flow-focusing junctions, as shown in Figure 3b. Moreover, by controlling the volumetric flow rates, we produce triple emulsion drops with a thin intermediate water layer, as shown in Figure 3c and d; this unique structure offers great opportunity for highly efficient encapsulation of small actives.

We demonstrate a facile route to spatially pattern surface wettability in PDMS microfluidic device using syringe vacuum guided flow. Compared to other approaches that often require complicated flow control, our method utilizes simple syringe vacuum and non-planar geometry to guide the coating fluids and to controllably deposit them in the desired regions, allowing patterning of surface wettability in a robust and precisely controlled manner. Moreover, this approach enables selective surface modification even in complex channel designs with multiple flow-focusing junctions, allowing production of double emulsion drops as well as higher order multiple emulsion drops.

The simplicity and the robustness of our method offer the possibility of patterning the surface wettability in a large number of devices simultaneously which is of practical importance for parallelization of these microfluidic devices. Moreover, with the guidelines provided in this work, microfluidic devices can be designed to produce other types of emulsion drops such as O/W/O double emulsion drops and W/O/W/O triple emulsion drops. We also anticipate that the surface modification method could be extended for patterning biological functions through functionalization with DNA, protein, or cells in desired regions within the microfluidic devices for biosensor applications.

ASSOCIATED CONTENT

Supporting Information. Schematics of non-planar microfluidic devices, photograph showing the experimental setup, schematics showing the detailed procedures, advancing contact angles of 2.5% PVA solution on untreated and treated PDMS and micrographs showing the production

emulsion drops are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript. ‡These authors contributed equally.

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Synopsis TOC:

Spatial Surface Patterning in Microchannels via Syringe-vacuum-Induced Flow

Production of Multiple Emulsions