Water-in-Ferrofluid Digital Microfluidic System for Single Cell Isolation and Transport

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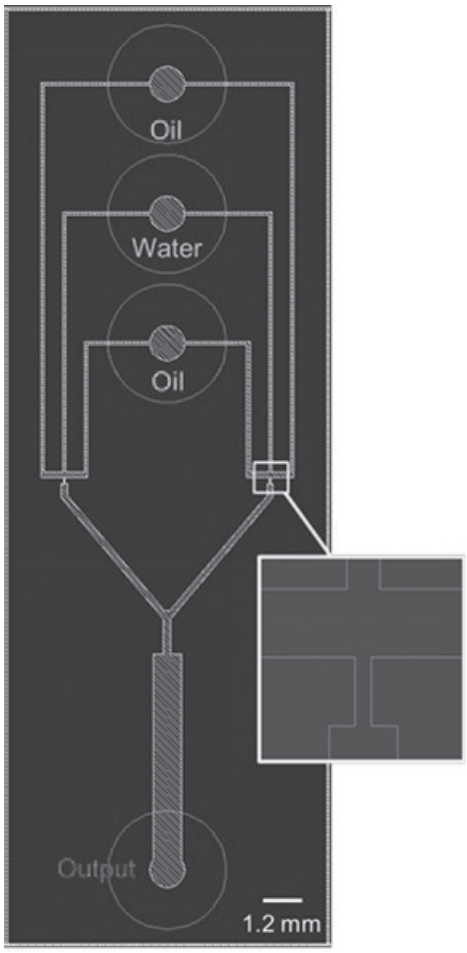

Figure 1: The layout of our microfluidic chip. The enlarged area is where the two liquids merge and emulsions are generated.

Introduction:

The isolation and study of circulating tumor cells (CTCs) is of great interest to researchers and clinicians in the medical field [1]. Current approaches involve labeling the cells, which negatively affects their viability [2]. We envision a label-free microfluidic device capable of isolating and transporting single cells while preserving the viability of the cells. Cells will be encapsulated by aqueous emulsions in an oil-based ferrofluid microfluidic system. A magnetic field will be generated in the system by an electrode array embedded in the device; this will transport the emulsions in a process called negative magnetophoresis.

Our project focused on the design and fabrication of a microfluidic channel to be used in the study, optimization of water-in-ferrofluid emulsions, and the stabilization and characterization of the emulsions generated.

Design, Fabrication, and Experimental Setup:

A microfluidic system was designed to create and study emulsions of water in oil and of water in ferrofluid. As shown in Figure 1, our system had two emulsion generators with width as a design parameter; ranging from 40, 60, 80, to 100 μm. There were two input ports for oil and one input port for water. The channels symmetrically merged to form two emulsion generators, which then met and rejoined into an outlet channel. Symmetry was used to allow for the study of both emulsion generation and convergence.

A standard multi-step photolithography process was employed to fabricate the chips (see Figure 2). We chose SU-8 50 to form the channel walls and bottom as it is hydrophobic and does not swell in the presence of a hydrocarbon-based oil. The base layer was a quartz wafer, which allowed for imaging from both sides. Good adhesion in bonding the glass cover slip to the top SU-8 layer was difficult with a two-part epoxy. We ultimately used a double-sided cleanroom Kapton® tape as the bonding layer and achieved good adhesion (see Figure 3). Ports were attached on top of the cover slip using a standard two-part biocompatible epoxy, and tubing connected the ports to a computer-operated LabSmith pump/valve system.

Emulsion Generation:

By changing the width of the emulsion generators on our chips, we successfully modulated the size of emulsions. We fabricated chips of generator width 60, 80, and 100 μm and found that the emulsions generated by the 40 μm channels were significantly smaller in diameter than those generated by the 60, 80, and 100 μm channels. This held true regardless of

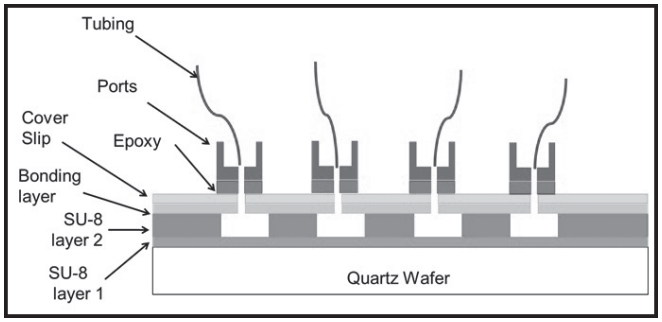

Figure 2: A side view of the multi-step fabrication process. SU-8 and the bonding-layer material were chosen for being hydrophobic and for not swelling in the presence of a hydrocarbon-based oil. Width, a design parameter of SU-8 layer 2, is set to 50, 80, or 100 µm.

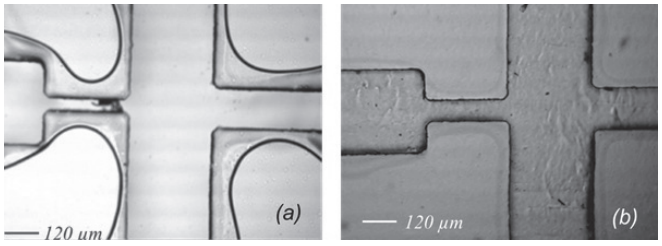

Figure 3: (a) Poor adhesion by epoxy. (b) Good adhesion by double-sided Kapton tape.

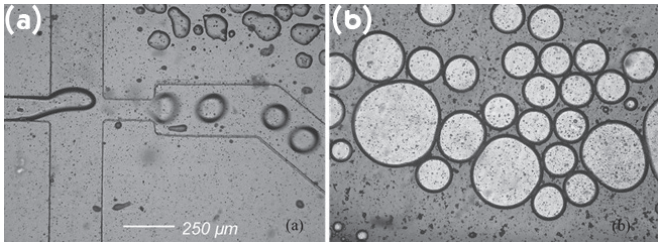

Figure 4: (a) Generation of water-in-mineral oil emulsions, stabilized with a surfactant. (b) Water-in-ferrofluid emulsions coalesce without a surfactant.

the flow rate. We also saw that an increase in the oil flow rate led to a decrease in the emulsion diameter. Figure 4 shows emulsions generated on our chips.

The size and shape of emulsions can be controlled by altering the flow rates of the components [3]. We modulated droplet size by varying the oil flow rate (Qo), the water flow rate (Qw), and the ratio of the water to oil flow rates (Qw/Qo). We found a non-linear relationship between the emulsion diameter versus the oil flow rate when plotting different Qw/Qo values. We analyzed Qw/Ao values of 1/2, 1/4, 1/20, and 1/100 and found all to have a similar non-linear trend. Further data points are needed to fully explain this phenomenon.

We used mineral oil in testing and characterizing the emulsions as it has similar chemical properties to the hydrocarbon-based ferrofluid while being more economical. A surfactant, 1% Span 80, was added to the oil phase to stabilize the emulsions. Without the surfactant, we saw droplets coalesce and Ostwald ripening occur [4].

Water-in-ferrofluid emulsions were generated using our chip. As expected, we found them to be unstable without a surfactant.

Conclusions and Future Work:

In this work, a microfluidic device was designed and fabricated to study and optimize water-in-oil emulsions. We controlled the size of the emulsions by varying the channel size and input flow rates, and we stabilized the emulsions with a surfactant. We then were able to create water-in-ferrofluid emulsions. The results of these studies will be used in the creation of a label-free microfluidic device capable of isolating and transporting CTCs on a single-cell basis. This second-generation device will be used to further study water-in-ferrofluid emulsions. Cells will be introduced to the system. Magnetic actuation will be used to study the negative magnetophoresis process. Ultimately, a device will be created with the ability to isolate and transfer CTCs.

Acknowledgements:

This work was accomplished with help from P.I. Professor Roger T. Howe, mentor José I. Padovani, the Howe research group, Stanford University REU program director Dr. Michael Deal, Stanford Nanofabrication Facility (SNF) staff, and fellow Stanford REU students. Funding for this work was graciously provided by the National Science Foundation (NSF), the National Nanotechnology Infrastructure Network Research Experience for Undergraduates (NNIN REU) Program, and the Center for Integrated Systems (CIS) at Stanford University.

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