Microfluidic System Incorporating Layer-By-Layer Nanofabricated Capsules

M. Prevot¹,², A. L. Cordeiro², G. B. Sukhorukov³, Y. Lvov¹, R. S. Besser³ and H. Möhwald²
¹Institute for Micromanufacturing, Louisiana Tech University; ²Max Planck Institute Colloids and Interfaces, ³Stevens Institute of Technology

ABSTRACT

A microfluidic system was designed, fabricated and implemented to study the behavior of polyelectrolyte capsules flowing in microscale channels. The silicon component of the system contains microchannels that leads into constrictions, which were fabricated using lithography techniques. Polyelectrolyte microcapsules were also fabricated with well-known layer-by-layer assembly technique, on a spherical template. Once the template was removed, the resulting hollow capsules were introduced into the system. The behavior of the capsules at the constrictions was visualized and the properties of the capsules were investigated. Capsules recovered from the system appear to have undergone a plastic deformation.

Keywords: Microcapsules, Silicon micromachining, Mechanical properties.

1. INTRODUCTION

The revolution in microfabrication and nanofabrication has led to the development of new materials and structures inconceivable just a few decades ago, with micro-electro-mechanical-systems (MEMS) an example of this revolution. Advances in nanotechnology have made it possible to integrate nanoscale and microscale functions within individual systems.

Today the use of lithography and bulk micromachining are well-accepted forms of silicon microfabrication (1). Likewise the layer-by-layer (LBL) (2) self-assembly process is also accepted as a way to linearly build up thin films from nanoscale building blocks. By merging these technologies, we combine the advantages of both for high-performance microscale devices.

Recently there has been much progress in fabricating well-defined micro- and nanocapsules with designed physical and chemical surface properties. These capsules possess great application potential as microcontainers, - reactors and delivery vehicles. They can be manufactured from polymers (3,4,5), proteins (6,7) or inorganic particles (8,9), and thus their mechanical properties can be tuned over a broad range (10,11,12). However, little is know about the mechanical properties, and essentially nothing is known about the behavior in flow. This, understanding on the other hand is required for many delivery applications, and therefore experiments in microfluidic channels are needed. In addition, it has been shown that these capsules respond to stimuli, and one may envisage them as active components like valves or pumps in microfluidic devices.

2. FABRICATION

2.1 Silicon Flow Chamber

The silicon chamber was made to simulate a blood vessel reducing into a capillary. Since 5µm cores are readily available, and capsules that are larger than 5µm have problems during core dissolution; the constriction was designed to have a size of 5 µm. The silicon device used in this project was made from a (100) silicon wafer. The flow chamber consists of a via (a hole through the wafer) to allow liquid to flow into the device, inlets, outlets, and the constriction

* Gleb@mpikg-golm.mpg.de; Am Mühlenberg 1, 14476 Golm, phone +49 331-567-9429; fax +49 331-567-9202
geometry. Each fluidic device contains 10 microchannels, which are shown in Figure 1. The fluidized capsules flow through the via into the device and into the inlet area. After entering the inlet, the microcapsules will flow into the constriction where deformation can be observed. After passing through the constriction the capsule will go through the outlet and another via. The effluent is collected for further imaging.

![Figure 1: Layout of the silicon chip.](image)

The flow chamber was fabricated using lithography-based process and dry etching methods. The fabrication process starts with a double-side polished silicon wafer with the natural layer of silicon dioxide removed from both sides. The wafer was cleaned and baked; photoresist was applied uniformly on the wafer through spin coating. The pattern was exposed using a UV lamp and developed leaving the desired structure in the photoresist. The structure served as a mask during the etching process, which was done using Inductively Coupled Plasma (ICP). Due to the restriction of the size of the via, the ICP was chosen to eliminate the crystallographic effects that occur during wet etching processes (13). To ensure complete penetration of the via, the lithography step was done on the backside of the wafer aligned to the topside. After the etching process the wafer was cut, separating the individual chips. To complete the assembly of the chip, a piece of Pyrex glass that is cut to match the dimensions of the silicon chip is anodically bonded to the chip. The anodic bonding process is accomplished by applying a negative voltage to the glass and a positive to the silicon. The voltage across the glass–silicon system used in the project was 750V. This process was done at a temperature of 450°C for 45 minutes (14). This whole process is demonstrated in Figure 2.
The device was analyzed with Scanning Electron Microscopy (SEM). The SEM revealed that the geometry was larger than the desired 5µm constriction. This larger constriction was on average 10µm and is likely a result of lithographic and etch process variations. The etching process was later found to display across-the-wafer non-uniformity, and size dependent rates (15). In order to circumvent this problem, cores of larger diameter corresponding to the new constriction size were chosen as the starting substrate for microcapsule fabrication.

2.2 Capsule preparation
Depositing a material with the layer-by-layer assembly method is a process of alternately dipping the substrate in oppositely charged solutions. This procedure can be employed to deposit everything from magnetic particles to proteins. Both of the solutions used were aqueous, however, one solution is a polycation and the other a polyanion (16). The first few layers of the self-assembly are considered to comprise a precursor layer and provide a uniform, well-defined starting surface on which the remaining polymer layers are deposited. The mechanism of deposition for the polymers is electrostatic attraction, van der Waal forces, and capillary forces (17). The main force that enables the assembly in this project is the ionic attraction between the oppositely charged entities (18).

In preparing capsules silica particles (purchased from G. Kisker GbR) with an average size of 20µm were used as the template. Polyethylene imine (PEI) MW 70,000 (purchased from Polysciences Inc) in Milli-Q water was first deposited on the silica particle to yield a good coverage. The remaining layers were polystyrene sulphonate (PSS) MW 70,000 and polyallylamine hydrochloride (PAH) MW 70,000 that was labeled with rhodamine. The PSS and PAH were purchased from Sigma-Aldrich. PSS and PAH layers were assembled in the presence of 0.5M NaCl. In each successive layer the polymer was added and was agitated for 20 minutes. After the deposition time the solution was centrifuged, leaving the coated particles in the bottom. The supernatant was removed and the capsules were washed with Mill-Q water. After ten layers were deposited in this manner the silica core was removed by drop-by-drop addition of the coated silica particles into 2mM Hydrofluoric acid. This is demonstrated in Figure 3.
Figure 3: Preparation of capsules. Steps A, B, C, and D represent assembly of polymer layers. Step E is the removal of the core. Step F represents the completed capsule.

3. SETUP AND EXPERIMENTAL WORK

3.1 Setup
An injection system was built to easily introduce the assembled capsules into the fabricated microfluidic device. The injection system is composed of the microfluidic device, a syringe filled with the capsules, a stainless steel block to facilitate the flow from the syringe to the microfluidic device, a syringe pump, and a glass bottle to retain the effluent from the system. The components of the setup are shown in Figure 4.

The microcapsule suspension was introduced into the microchip using a syringe pump (kdScientific Inc.; New Hope, Pennsylvania, USA). The images of the behavior of the capsules at the constrictions were captured using a CCD camera (TVCCD-460COL, Monacor, Bremen, Germany) set on an AX70 Provis Olympus microscope (Olympus Optical Co GmbH., Berlin, Germany). The proper filter settings for rhodamine excitation and emission were used in order to visualize the capsules in fluorescence. The images were grabbed by an online PC and later analyzed. The capsules that were recovered were retained and further analyzed.
3.2 Experimental Procedure
The capsules were injected into the channels and visualized there. First we pumped 4.0 ml of water to eliminate large air/liquid interfaces, and to clean the chip. The microscope and camera were focused on the constriction area of the device. Then a diluted solution of the prepared capsules (discussed in section 2.2) was injected at a rate of 3.0 ml/hr. After observing the capsules at 3.0 ml/hr the flow rate was increased to 6.0 ml/hr to see the behavior of the capsules under higher pressure. All pictures were taken in fluorescence mode.

4. RESULTS AND DISCUSSION
The capsules were observed entering the channels and in the constriction. An image of a single capsule was not obtained due to problems with the video capturing equipment. In some of the channels clogging was observed, where at some point a capsule that could not go through blocked the constriction. The remaining capsules in the solution accumulated behind the blockage. After the channel was filled the pressure on the channel compacted the capsules. This is shown in Figure 5 in a time series of frames taken out of the video. It can be seen that the constriction gets brighter in the frames. This is due to the increase fluorescent signal as the capsules are compressed into the constriction.
Figure 5: Frames in sequence taken from video. Pictures are shown at a 0.8 second interval. Arrow shows same capsule moving through the channel.

In channels further away from the center of flow blocking and clogging were also observed; however, there were a few capsules that passed through the constriction. An example of this is shown in Figure 6.

Figure 6: Channel at the edge of the chip demonstrating capsule that flowed through.

The capsules that passed through were collected and analyzed with confocal fluorescence microscopy. The micrographs were obtained using a Leica TCS NT confocal scanning system (Leica, Germany). A 100x oil-immersion objective was used. The standard filter settings for Rhodamine excitation and emission were used. Capsules before and after passage through the constriction and observation in this manner are shown in Figure 7. All the recovered capsules, that were observed by confocal microscopy were deformed or were broken. The concentration of the effluent was much lower than that of the original solution and contained no aggregation of capsules.
5. CONCLUSIONS AND OUTLOOK

In this work we have shown that the movement of micron-sized hollow capsules through microfluidic channels of silicon dimensions can be observed. One detects an accumulation at the constrictions and plastic deformation after passing through them. Optimizing the video observation system will enable imaging individual capsules and their deformation in situ. We also anticipate that varying the mechanical properties and adhesion by preparation and external stimuli will yield a richness of behavior in the channels. This work should be considered a starting point on one hand to understand capsule mechanism and on the other hand to serve application perspectives like drug delivery, through biological filters, or construction of integrated microfluidic devices.

REFERENCES


