Facile fabrication of microfluidic systems using electron beam lithography

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We present two fast and generic methods for the fabrication of polymeric microfluidic systems using electron beam lithography: one that employs spatially varying electron-beam energy to expose to different depths a negative electron-beam resist, and another that employs a spatially varying electron-beam dose to differentially expose a bi-layer resist structure. Using these methods, we demonstrate the fabrication of various microfluidic unit structures such as microchannels of a range of geometries and also other more complex structures such as a synthetic gel and a chaotic mixer. These are made without using any separate bonding or sacrificial layer patterning and etching steps. The schemes are inherently simple and scalable, afford high resolution without compromising on speed and allow post CMOS fabrication of microfluidics. We expect them to prove very useful for the rapid prototyping of complete integrated micro/nanofluidic systems with sense and control electronics fabricated by upstream processes.

Introduction

Microfluidic systems are finding extensive use in diverse application areas ranging from IC thermal management systems[1] to micro total analytical systems (μTAS)[2] to biomedical microsystems where their applications range from implantable drug delivery devices and lab-on-chip systems to neural prosthetics.[3,4] This increased popularity is driven by the synergy of advantages accrued from smaller dimensions, increased sensitivity and resolution, the potential for proximal incorporation of sensing and actuation mechanisms and circuitry, and the possibility of batch fabricating complex systems at relatively low costs.

At their crux, most microfluidic systems need unit structures for transport, actuation and sensing that have either embedded or suspended movable structures. These are inherently 3-D structures and most approaches to construct them using standard planar microfabrication processes tend to involve many complex steps like the patterning and etching of sacrificial layers to release parts or bonding to seal the structures.[5] Also, the properties of traditional materials like silicon and glass impose performance limits in many applications.

This has spurred the development of progressively simpler fabrication schemes many of which use soft polymeric materials. Recent replication based approaches such as soft lithography, *in-situ* construction techniques, and micro-molding[5,6] do away with many of the complexities and cost of fabrication.

Direct fabrication approaches using ion-beams,[7] gray-scale photolithography with anti-reflective coatings[8] and scanned UV laser beams[9] have been demonstrated for making embedded channels in SU-8 and PMMA. Also, some self-supporting structures have been demonstrated in SU-8 with electron beam lithography.[10] Conceptually these techniques aim at differentially exposing regions of a single resist layer. In this work we demonstrate the versatility of the electron-beam energy and dose variation approach for facile single-step fabrication of polymeric microfluidic elements ranging from simple covered channels to complex multi-level microstructures that lend themselves to immediate use in biological and chemical applications. This is a direct CAD-to-structure method and hence simple and inexpensive yet versatile enough to fabricate complete microfluidic systems—thus very well suited for rapid concept demonstration. Moreover it allows post-CMOS downstream fabrication of microfluidics on a substrate with integrated sense and control electronics thus enabling the development of integrated lab-on-chip systems.

Principle

We have exploited specific features of electron absorption profiles in resists to design our fabrication process and hence begin with a brief outline of the underlying theory.

Electron beam lithography depends on the deposition of energy from accelerated electrons into the resist film on the substrate. The interaction of electrons with the polymeric resist material determines the deposited energy profile and resulting molecular weight and solubility change and finally, geometries of structures created in the resist after development. It is hypothesized that in the resist, electrons lose energy in inelastic collisions, while they also undergo elastic collisions that change their trajectories thus expanding the region of exposure.[11] Various theoretical and empirical models[12] have been proposed to quantify these processes.

While detailed numerical simulations are the only way to make accurate predictions, a widely accepted analytical model that closely matches most observations suggests that electron beam penetration into a solid target can be described by a

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characteristic depth of penetration or range R (in μm) which is given by:[13]

$$R = \frac{0.1E^{1.5}}{\rho} \quad (1)$$

where, E is the incident electron energy (in keV) and ρ is the target material density (in g cm^{-3}). Also, the increase in effective diameter D in nanometres of an electron beam due to forward scattering is given empirically by the formula:[11]

$$D = 0.9\left[\frac{R}{E}\right]^{1.5} \quad (2)$$

where R is the resist thickness in nanometres.

With this background, we now describe in detail the two schemes for fabricating microfluidic structures.

Varying energy process

Eqn (1) predicts a definite depth of exposure at a given electron beam energy. Consequently, if we can modulate the incident beam energies at different locations on a resist layer, we can vary the exact depth of resist exposure at those points. Further, if the chosen resist material undergoes cross-linking on electron beam exposure (which renders it less soluble to a developer), it is possible to retain self-supporting hanging structures in regions where the beam energy is not sufficient to penetrate the resist layer completely. This forms the basis of the varying energy process illustrated in Fig. 1a.

It is worthwhile to note that the existence of a step exposure profile is unique to interaction of energetic charged particles with matter as the exposure depth is close to the penetration depth of the incident beam. Light absorption on the contrary results in a continuously decreasing intensity and hence exposure profile.

We have chosen SU-8 as the material for this process. It is an epoxy based resist sensitive to UV as well as electron beam exposure. It is suited for obtaining thick, chemically and thermally stable images[14] and is transparent and flexible (Young's modulus = 4.5 GPa),[15] thus finding wide application as structural material in MEMS, microfluidics and micro-optics applications. These properties, and the fact that it has a low electron beam dose threshold (~1 μC cm^{-2}), which enables fast writing of even relatively large structures at a high turnover rate, made it the optimum choice for negative resist for this process.

Varying dose process

If a spatially varying electron beam dose is given to a resist bi-layer with a fast (*i.e.* low charge dose threshold) negative resist on top of a slower positive resist, it is possible to obtain capped channels in regions where the charge dosage exceeds the threshold for the lower resist layer. This is the basis of the varying dose process illustrated in Fig. 1b. This process is particularly suited for short, high resolution structures such as nano-channels and in-plane nanopores, especially since there are no issues of beam alignment here as both exposures can be potentially imparted in a single step by varying beam dwell times.

We have chosen SU-8 and PMMA as the negative and positive resist materials respectively. PMMA with a dose threshold of ~100 μC cm^{-2} is a high-resolution electron-beam resist which also has been used commonly as a structural material for microfluidic channels made using other methods.[16] We exploit the wide difference in charge dose thresholds of these two materials for this process to obtain embedded structures with PMMA walls and SU-8 capping membranes.

Experimental

Varying energy process

We started with a thermally oxidized silicon substrate (oxide thickness ~200 nm) on which SU-8 2015 (Microchem Corp., MA, USA) was spin-coated at 3000 rpm to obtain a 15 μm

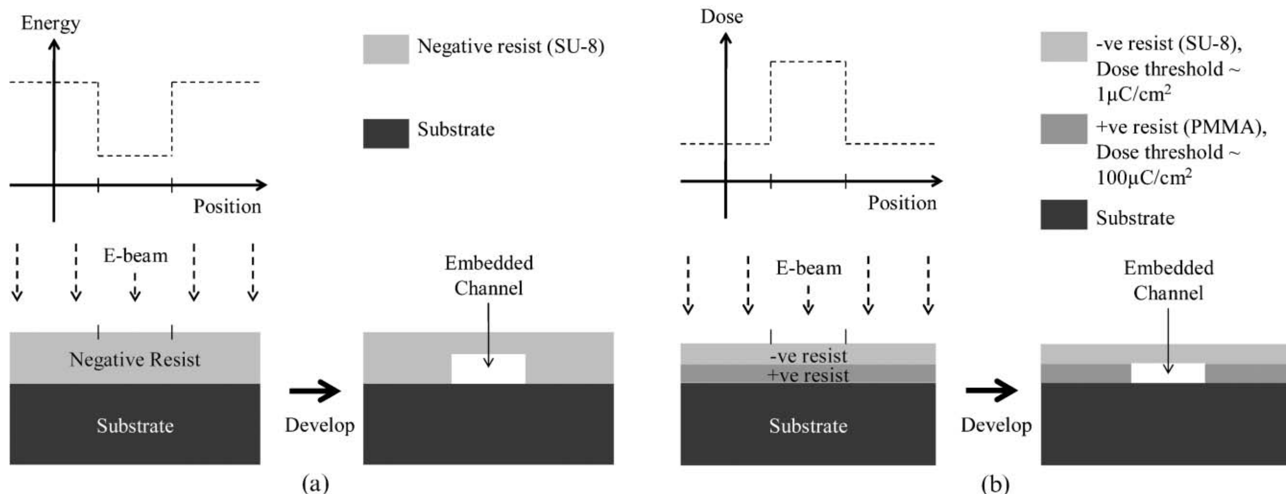

Fig. 1 (a) Varying Energy Process: The negative resist layer is first exposed to a high energy electron beam in the regions where the channel banks are required, and subsequently to a low energy electron beam in the intervening regions where only the channel capping membrane is required. Resist development yields a capped channel. (b) Varying Dose Process: A high threshold positive and low threshold negative resist bi-layer structure is exposed to a spatially varying electron beam dose: in the regions with low dose exposure only the upper layer is affected, while in the high dose exposure regions the lower layer too gets affected. Development yields a capped channel.

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layer of the resist. This was then soft-baked on a hot-plate for 10 min at 70 °C followed by 5 min at 90 °C to remove the solvent without causing thermal stress in the resist film.

The structure to be fabricated was visualized as a stack of multiple layers and patterns were designed for each layer using a GDSII/DXF compatible drafting software package. A Raith Elphy Plus nanolithography system attached to a JEOL JSM 6400 SEM was then used to perform the electron beam exposure on the resist using the designed patterns aligned in the same coordinate system, at different accelerating voltages. A registration mark on the substrate was used to compensate for misalignment, if any, due to stage movement between exposures. The energies and doses used for various structures are detailed along with the results in the next section.

After exposure, the substrate was given a post-exposure bake cycle identical to the soft-bake mentioned above and developed in Nano™ (Microchem Corp., MA, USA). The duration of development depended on the size and aspect ratio of the embedded structures and has been documented for various structures presented below. Finally the sample was rinsed in isopropanol and blow dried.

Varying dose process

The substrate was prepared as in the last section and PMMA (Nano™950 PMMA A11, Microchem Corp., MA, USA) was spin-coated at 3000 rpm to obtain a 2 μm layer. This was baked at 170 °C for 5 min to remove the solvent and then SU-8 2002 was spun on top at 3000 rpm to obtain a 2 μm layer. This was then soft-baked as described in the last section.

The structure is visualized as a stack of two layers and patterns are prepared. First, the SU-8 layer was exposed at a low accelerating voltage and dose. This was then developed for 1 min as above leaving out the IPA rinse. Then, using a registration mark on the substrate or the SU-8 layer itself, the PMMA was exposed at a higher voltage and dose and developed in 1 : 1 :: MIBK : IPA with some agitation till the embedded structures opened up.

Note that, to prevent alignment issues the two exposure steps can be combined into one exposure with varying beam-dwell times. However, in this case wherever high dosage is used to expose PMMA, the upper SU-8 also will get exposed and this could result in the formation of overhanging flap-like structures at peripheries, for example, at the openings of channels.

Results and discussion

Varying energy process

To begin with, we need a calibration of electron beam penetration depth into SU-8 *vs.* accelerating voltage. This was studied by fabricating anchored, flopped membranes with the anchor written at 35 kV to ensure complete penetration, while the membrane was written at different voltages. The thickness of these membranes was then measured using a Dektak II A Profilometer. The schematic of the calibration technique used and the calibration curve obtained are shown in Fig. 2. The experimental curve is in good agreement with the general form of the theoretical estimate given by eqn (1) above.

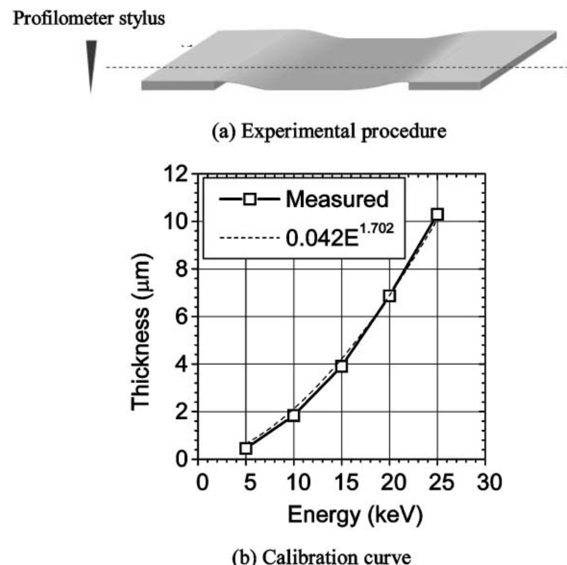

Fig. 2 (a) Schematic of the calibration technique for determining membrane thicknesses: A profilometer tip is scanned over a flopped, anchored membrane to get its thickness. (b) Measured electron beam penetration depth in SU-8 2015 *versus* electron beam energy used for exposure and a fitted power law.

This enables a choice of energy parameters for various structures.

The most basic structure needed in all microfluidic systems is a covered microchannel. We have tested the efficacy of our method in making this by fabricating microchannels of various sizes. Fig. 3 has representative micrographs showing clearly the channel opening, walls and membrane cover. Here the channel banks were written at 35 kV and the capping membrane at 10 kV both to a dose of 3 μC cm^{-2}. This results in a 2 μm thick membrane and hence a 13 μm × 50 μm effective channel cross-section. Due to beam spreading, the channel is expected to be slightly narrower at the bottom than the top though. Development took 10–15 min for the 200 μm long channel imaged here. Various lengths of channels up to 3 mm were made. The development of such large aspect ratio channels often required 2–3 h. Cross-linked SU-8 is not visibly affected even after 2 days in the developer. So this development time can be made very large if need be, such as for long channels with very fine cross-sections.

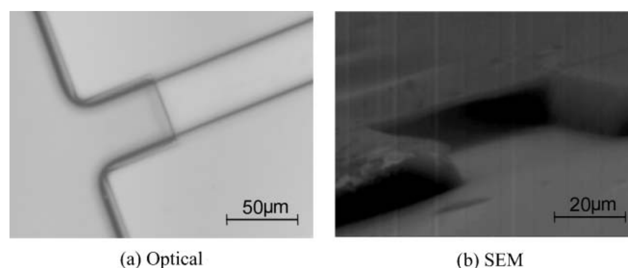

Fig. 3 (a) An end of a microchannel made using the varying energy process showing the banks and the capping membrane. (b) A view of the entrance to the microchannel tilted to show clearly the membrane cover.

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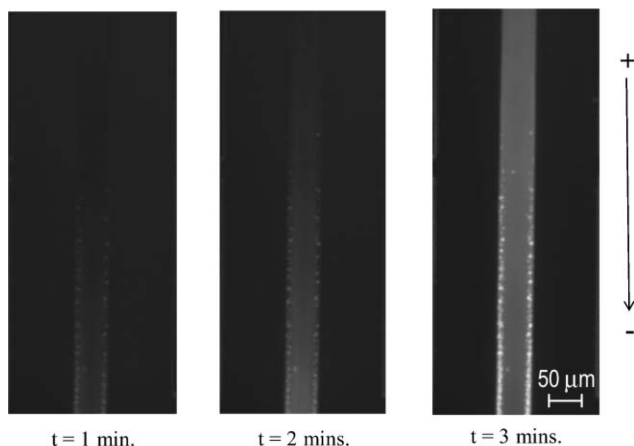

Fig. 4 Fluorescence micrographs of a suspension of SYBR Green I tagged DNA molecules moving due to an electric field ($\sim$10 V cm^{-1} in the direction of the arrow) a microchannel filled with buffer.

We have also tested these channels for usability in practical microfluidics applications. Aqueous solutions readily filled the channels by capillary action. We think that it was the underlying oxide that aided this filling up as SU-8 is known to be hydrophobic (contact angle $\sim$70–80°). However SU-8 microchannels can also be made hydrophilic by exposure to agents that reduce the epoxy bonds at the surface to generate –OH groups[17] or by modifying the polymer itself.[18]

The ready use of these channels for biological applications is demonstrated by the fluorescence micrographs of DNA electrophoresis shown in Fig. 4. Here we used DNA (ϕX174 Hae III Digest—Bangalore Genei, India) tagged with SYBR Green I (Molecular Probes, OR, USA), suspended in 1X TAE buffer (SRL, Bombay, India). Note that the motion of the DNA is towards the positive electrode implying that electroosmosis is not significant for this choice of channel materials, *viz*. SU-8 walls and ceiling, and a SiO_2 base. While this itself can be advantageous in many applications, we think that these properties can be tailored by altering the SU-8 surface as mentioned above.

An integrated system with sensing electrodes inside a channel is shown in Fig. 5. This highlights the ease of integration and alignment of embedded electrodes in this scheme. In this case, channel fabrication steps were begun with coating resist on top of the patterned Cr–Au electrodes and an

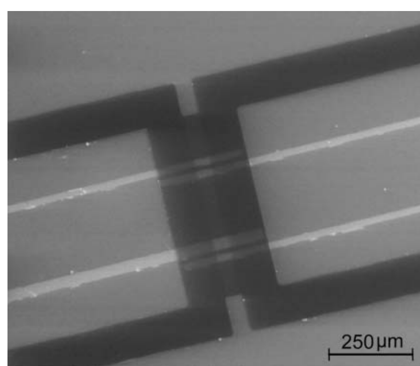

Fig. 5 A capped microchannel made on top of gold electrodes.

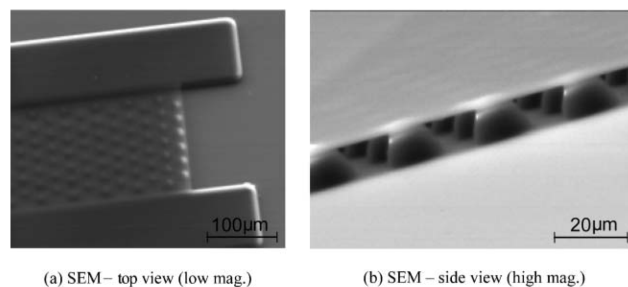

Fig. 6 (a) A microchannel with micro-pillars inside. Pillars and walls were written at 35 kV and the capping membrane at 10 kV. (b) Zoomed-in view of the rows of micro-pillars inside the microchannel tilted at an angle.

alignment mark in the metal layer was used to align the electron beam exposure. This can be compared with the cumbersome and error-prone manual alignment needed in many replication based methods.

While the above are basic structures, the versatility and true power of this approach is the great ease with which complex multilevel structures can be fabricated. For example it is possible to fabricate in a single electron beam run, synthetic gels for electrophoresis, as proposed by Volkmuth *et al.*,[19] where the channels contain embedded micro-pillars to sieve bio-molecules. Fig. 6 shows such a structure where the channel walls and pillars were written at 35 kV and the membrane was written at 5 kV. The magnified view clearly shows the effect of beam spreading described earlier.

An even more complex structure is the chaotic micro-mixer with in-channel hanging bas-relief structures proposed by Stroock *et al.*[20] The corrugated roof structure induces a chaotic flow that enhances fluid mixing. This too can now be fabricated easily (as shown in Fig. 7) in a single electron beam run with the walls, roof corrugations and the membrane written at 35 kV, 20 kV and 10 kV, respectively. In fact much more complex 3-D roof corrugation patterns can be made simply with this method.

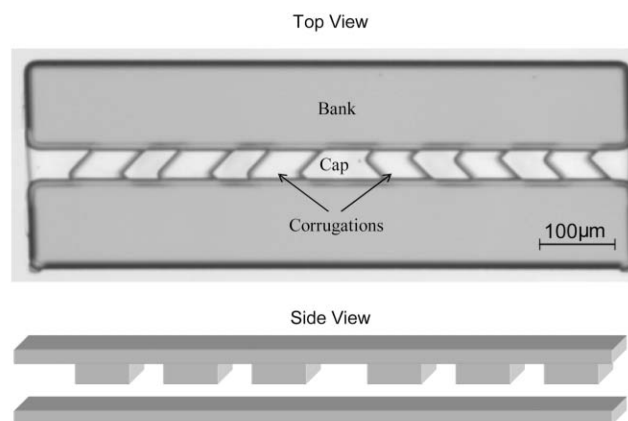

Fig. 7 Optical micrograph of a chaotic micromixer showing the three levels (channel banks, capping membrane and corrugations on the channel roof) in the structure (an aligned cartoon cross-sectional view is provided to better appreciate the three levels).

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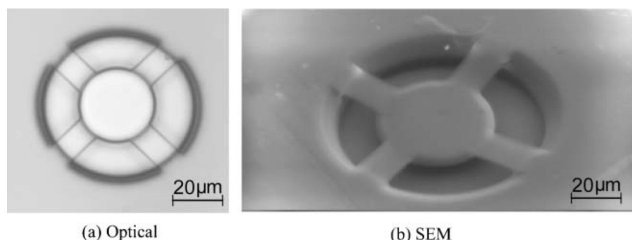

Fig. 8 (a) Optical micrograph of a structure with a seismic mass supported by four beams attached to an anchoring region. (b) Zoomed SEM micrograph of the above structure tilted at an angle to show hanging mass and beams clearly.

To show the possibility of extending this technique to fabricating movable elements as those needed in valves and pumps and other MEMS unit structures such as beams and cantilevers, we have also fabricated a structure with a diaphragm supported by beams as shown in Fig. 8. This could be used for making accelerometers, or a diaphragm for a non-return valve or pump. The flexibility and mechanical durability of SU-8 would aid in the design and use of such structures. Also the mechanical properties of the material could possibly be tuned by varying the charge dose in different parts of the same structure as this changes the degree of cross-linking of the polymer, thus creating the possibility of designing novel mechanical structures.

Varying dose process

We have used this scheme to fabricate microchannels of various widths as shown in Fig. 9, with banks made of 2 μm thick PMMA 950K and a capping membrane of 2 μm thick SU-8.

The membrane was first written at 10 kV and 3 μC cm^{-2} and developed and then the channels were written at 30 kV and 300 μC cm^{-2}.

Due to the high resolutions supported by PMMA, this scheme is ideal for making channels an order of dimension lower than the varying energy method. Here we have, as a proof of concept, fabricated channels with cross-sections ~4–12 μm × 2 μm. However use of higher beam energies and thinner resist layers should enable the fabrication of nanofluidic systems using this technique.

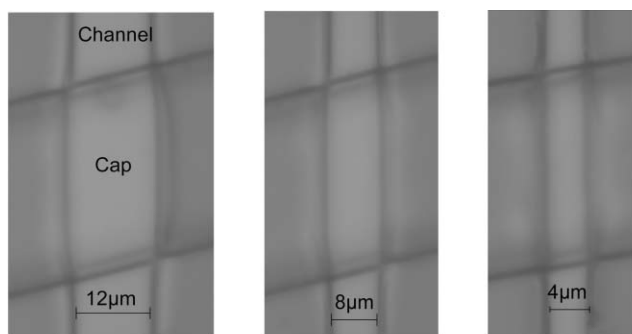

Fig. 9 Microchannels of various widths fabricated using the dose variation method. Here the cap is made of SU-8 while the channel banks are in PMMA.

Design considerations

In both of the above techniques, geometries of structures that can be fabricated must obey certain design rules dictated by theoretical and practical considerations.

A practical limit on the length of microchannels is placed by the development time. This is expected to rise as the square of the channel length, since the inlet and outlet would be the only openings accessible to the developer for removal of the unpolymerised resist. In the varying energy method, the absolute insolubility of crosslinked SU-8 in the developer would in principle permit as large development times as needed without damage to features. The maximum writing field of the e-beam exposure system imposes another practical constraint on the maximum size of structures. In our case, this is 3.2 mm. Beyond this one needs to stitch multiple write-areas needing either alignment features or a laser-guided sample stage.

The limit on the minimum feature size *viz.* channel width is imposed by the lateral beam spread which, as quantified by eqn (2), depends on the total depth of the resist and the beam energy being used. With the 35 kV maximum acceleration voltage that we have available in our laboratory SEM based e-beam exposure system and the 15 μm resist thickness used, this is expected to be about 8 microns. This lateral spread would be ~200 nm for a 2 μm thick resist and an acceleration voltage of 100 kV used in most dedicated electron beam lithography systems permitting the fabrication of nanofluidic elements.

The throughput of both techniques is good enough for practical use. In the variable energy method, for the beam current of 50 pA used, the longest channels patterned (3 mm × 50 μm with 50 μm wide walls) took about 6 min to write. In the variable dose method the channels shown took 3 min in all to pattern. There is to some extent, a trade-off between throughput and resolution in both schemes since for larger dimensions higher beam currents can be used. Also, a dedicated system with shaped beam and vector write capabilities would be about hundred times faster. In general it can be said that these methods are more suited for short, high resolution or high complexity features rather than long geometries.

Robust connections to the outside world are a very important practical concern in most microfluidic fabrication technologies which is the case with the methods reported here. The plumbing methods described and referred to in a recent review article[21] are compatible with our fabrication methods too.

Conclusions

To summarize, we have proposed and demonstrated two simple, direct CAD-to-structure processes for the fabrication of 3-D polymeric structures in general and microfluidic unit structures and systems in particular. The first method, consisting of the variation of electron beam energy during the exposure of a negative resist-cum-structural material was demonstrated by fabricating microchannels, a synthetic gel, a chaotic mixer and suspended structures in SU-8. The second method where we use the variation of charge dose on a resist bi-layer was used to fabricate microchannels using PMMA and SU-8. While the first method is well suited for making complex structures with characteristic dimensions above a few microns

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(*i.e.* most microfluidic systems), the second method is easily extensible to the fabrication of nanofluidic elements. The processes are compatible with post CMOS fabrication that would permit downstream integration of microfluidic elements with sense and control electronics in CMOS. Both the materials used have been popular choices for a variety of other microsystems and we think that these generic methods can be used for the facile fabrication of complete integrated microsystems with electrical, optical, mechanical and fluidic sensing and actuating elements especially for biological and chemical applications.

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