Manipulation of 10 – 40 µm Diameter Cells Using a Thermally Actuated Microgripper

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ABSTRACT

This work presents the successful fabrication of a thermally actuated U-shaped microgripper that has been specially designed to enable low voltage operation for bidirectional in plane deflection. The microgripper tips are carefully designed to match the biological species being manipulated, which has been demonstrated by the successful manipulation of 10 – 40 µm diameter particles used to simulate biological cells.

INTRODUCTION

Most eukaryotic plant and animal cells have diameters within the 10-100 µm and 10-30 µm range respectively. Our previously reported thermally actuated microgripper device described tip spacing's around 150 µm [1]. This needed to be greatly reduced to enable a larger range in size and shape of cells to be manipulated.

Thermally actuated microgrippers are based on the asymmetric expansion of a beam composed of materials with different coefficients of expansion (C-shaped) [2] or asymmetric heating and expansion of materially homogeneous structures, where actuators with different cross sections are connected either in a U- or V-shape configuration [3,4]. With resistive heating the different geometries cause a temperature difference, resulting in the 'thin hot' arm expanding more than the 'thick cold' arm, causing in-plane deflection. While many papers describe one of the actuator arms as cold, in practice they are cooler than the hot arm, meaning that in order to achieve the necessary temperature differences to give a discernable deflection, the absolute temperatures are often quite high.

The thermally actuated microgripper reported here has significant advantages over many alternative manipulators. The device is operated using thermal actuation via a hot/cold arm principle, but in this case the cold arm has no actuator encapsulated within it [1]. The tips are maintained at ambient temperature due to the dimensions of the device and the use of an insulating structural material, which ensures compatibility with biological material. The microgripper can be designed to close from open (Figure 1(a)), open from closed (Figure 1(b)) or with bidirectional movement.
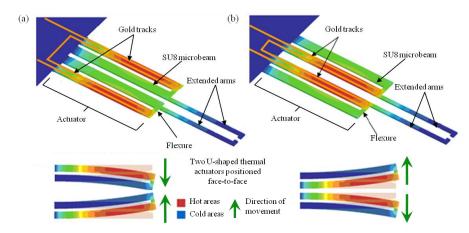
Figure 1 – Schematic of the thermal actuation of a microgripper designed to be (a) close from open and (b) open from closed.

A main benefit of the microgripper design is that the pressure exerted on the manipulated object as it is maneuvered is much lower due to the large surface area of the object being in contact with the microgripper tip. This has been demonstrated via manipulation of mouse oocytes; where it was possible to move a cell through an air-liquid interface without causing it to deform, a process which is unreliable with vacuum pipettes [5].

To maintain a low pressure exerted on the manipulated object as it is maneuvered the shape of the tips are tailored, at the mask design stage, to the item being manipulated so that a large surface area of the object is in contact with the microgripper tip. A few examples are shown in Figure 2. With a large range of available tip sizes and shapes made to best suit the species of interest, the microgripper is a very competitive micromanipulation tool and will enable studies to be conducted in a wide range of biological fields.
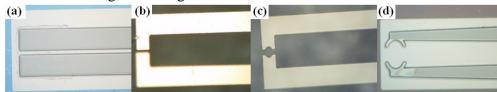

Figure 2 – Tip designs of (a) 30 µm gap, flat tips; (b) 10 µm gap, square tips; (c) 40 µm gap, recessed curve tips; (d) 100 µm gap, curved tips

The main building material used in the microgripper fabrication is SU8 (Figure 3); a multi-branched epoxy resin that has advantages over other Microelectromechanical Systems (MEMS) compatible polymers, such as good mechanical properties and biocompatibility. The epoxide rings are cross linked during the SU8 process stage, forming very chemically resistant structures.
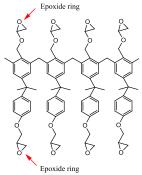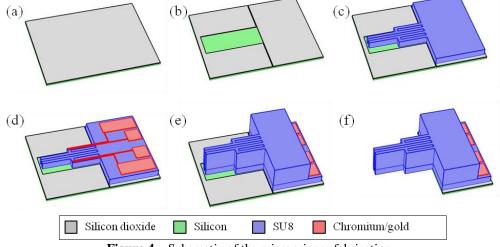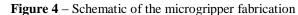

Figure 3 – Chemical structure of the SU8 resin indicating the epoxide rings.

The main challenges in miniaturizing the device were in the adhesion between the layers and the feature definition, both of which are related to the thin film stress of each individual layer deposited during fabrication. It was also important to maintain good vertical sidewall profiles, which is increasingly challenging as the aspect ratio becomes greater (i.e. the feature line width is smaller than the layer thickness). With careful consideration of the processing parameters of SU8 it is possible to fabricate high aspect ratio structures, making it a good choice of material for miniaturization.

FABRICATION

The microgrippers were fabricated via the following method (Figure 4).

Figure 4 – Schematic of the microgripper fabrication

Initially, a thin oxide was thermally grown onto the silicon wafer **(a)**. This was patterned and the exposed silicon oxide was etched in buffered HF **(b)**. The oxide thickness is sufficiently thin such that the effects of the stress on the system can be ignored. A 2 μm layer of SU8-2002 was patterned to give the microgripper structure **(c)**. In SU8 processing the soft bake parameters contribute up to 50% of the internal stress of the film, followed by 30, 15 and 5% for the exposure dose, post exposure bake (PEB) and development respectively [6]. Molecular mobility after baking has a serious impact on the thin film stress within the device. If the SU8 polymers are unable to flow, the layer shrinks to a greater extent upon cross linking, increasing the level of tensile stress which causes cantilever bending, as well as adhesion failure when the SU8-substrate adhesion is poor. The next processing step involved 30 nm of chromium and 100 nm gold being e-beam evaporated and patterned into the design of the actuation tracks **(d)**. These metal films are sufficiently thin so that their effects on the stress on the system can also be ignored. A 60 μm layer of SU8-2025 was then patterned to encapsulate the metal **(e)**. The viscous SU8 solutions (used to achieve thick layers) are notoriously difficult to evenly spin and often result in an edge bead profile. They can also cause an uneven coating on previously patterned wafers due to existing underlying step heights. Furthermore, centrifugal forces applied to the wafer during spinning cause tensile stress within the SU8 layer which, if not relaxed, cause significant cantilever bending at the tip release stage. In the final stage of fabrication the exposed silicon was etched (3T XeF_2 and 3T N_2 cycled every 60 s for 3 hours), releasing the microgripper tips **(f)**.

A 10 min rest period was introduced after the spin and before the baking stage when processing SU8. This allowed the polymer to relax and flow to back fill any potential air pockets caused by spinning over step heights, and to level the film thickness, reducing edges beading effects. A temperature ramp profile was also introduced to replace the generally used 2-step process, as ramping the temperature caused a gradual change which evaporated the solvent much more slowly, maintaining a more uniform bake (helping to reduce the tensile stress gradient). A slow cool down period was also included, which helped to reduce the chance of adhesion failure due to fast layer shrinkage.

The orientation of the wafer during development of PMMA affects the ease of production of high aspect ratio structures with good feature definition [7]. Given the similarities in the chemistry between PMMA curing and development and that of SU8, some of these procedures were applied to the device fabrication, with successful results. The non cross linked material absorbs the solvent and forms a gel like matrix. This has a higher density than the surrounding solvent, so when the wafer is inverted, the gel is cleanly removed leaving behind well resolved features.

Figure 5 shows the improved effect of implementing these improvements to the fabrication of SU8 on the cantilever bending resulting from thin film stress.
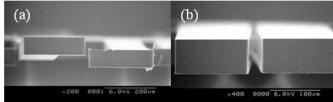

Figure 5 – Effect of thin film stress on cantilever bending with the (a) original and (b) improved fabrication process.

The exposure dose is proportional to the rate of polymerization of the epoxide rings in SU8 (i.e. cross linking) [8]. So with doses over that sufficient to saturate the layer, the dimensions of the device can be controlled by affecting the kinetics of the cationic polymerization occurring during the curing stage.

The inclusion of the 360 nm Omega Optical mask aligner filter results in the sidewall profiles being near vertical for the range of exposure doses and dimensions used in the microgripper fabrication. For proof of concept, Figure 6 shows SEM images of the near vertical sidewall profiles of the microgripper tips at different exposure doses with the gap distance reducing as the exposure dose increases.
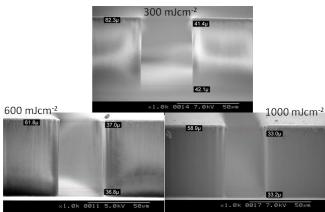

Figure 6 – SEM images of the sidewall profiles (dark field mask dimensions of 42 μm) at various exposures.

The implementation of the thin film stress processing improvements and fine tuning of the device dimensions by altering the exposure dose appropriately has resulted in the successful fabrication of microgripper devices with tip distances down to 10 µm (Figure 7).
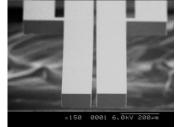

Figure 7 – SEM image of the microgripper device with a tip distance of 10 µm.

Operation of miniaturized devices

For ease of connection and maneuvering the microgrippers were mounted on printed circuit boards (PCBs). This is shown in Figure 8. The PCBs were fixed to an x,y,z macro manipulator to allow the user to easily position the microgripper close to an object.
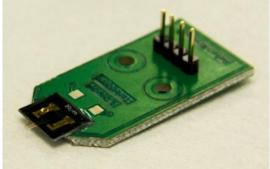

Figure 8 – Image of the microgripper on the PCB

A video capturing the successful manipulation of a 30 µm particle, used to simulate manipulation of biological cells, was taken using the microgripper with a 30 µm tip distance. Figure 9 shows stills of the capture and release of this particle.
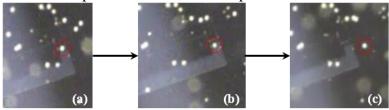

Figure 9 – Stills from the video of a 30 µm particle being manipulated by a microgripper. [(a) Capture of the particle; (b) Release of particle; and (c) Retraction of the microgrippers.]

Current work is focused on including a gold electrode down the extended arm of the microgripper structure protruding from the tip of the device. This allows the microgripper to be used as the working electrode in an electrochemical set up, enabling development of the microgripper into an ion sensor for use in cell sensing. This is done by modifying the protruding gold electrode. The results from preliminary work can be found in [9, 10].

CONCLUSIONS

Previously it has been shown that this device; operated via a U- shaped thermal actuation hot/cold arm process, realizes working temperatures considerably lower than other thermally activated microgrippers. The tips are maintained at ambient temperature due to the dimensions of the device, ensuring compatibility with biological material. A fabrication route has been developed to miniaturize the device that takes great care in controlling thin layer stress, which is particularly problematic due to significant cantilever bending occurring after release. The dimensions of the SU8 layer can be resolved to a high degree of accuracy by controlling the chemistry occurring within the layer simply by adjusting the processing parameters. Specifically the irradiating dose proportionately affects the dark field line width, allowing features of any size down to 10 μm to be resolved. The tip shapes of the microgripper device are tailored, at the mask design stage, to the item under study which enables a large range of biological species to be manipulated. This makes the microgripper a very competitive micromanipulation tool and will enable studies to be conducted in a wide range of biological fields.

ACKNOWLEDGMENTS

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