POLYMER MEMS-BASED MICROGRIPPER FOR SINGLE CELL MANIPULATION

Nikolas Chronis and Luke P. Lee

Berkeley Sensor and Actuator Center, Department of Bioengineering
University of California at Berkeley, California 94720, USA

ABSTRACT

We present the development of a polymer MEMS-based microgripper that can operate in physiological ionic solurtions. The electrothermally activated polymer gripper consists of two 'hot and cold arm' actuators placed antisymmetrically next to each other. The polymer microgripper is fabricated in a standard two-mask surface micromachining process. The high thermal expansion coefficient of the polymer (SU-8) allows the activation of the microgripper with small temperature elevations (20-40 ^{O}C) at low voltages (1-2 Volts). The developed polymer microgripper can be used for the manipulation of single cells and other biological species in solution with minimal undesired interactions.

1. INTRODUCTION

The development of miniaturized tools for manipulating biological samples in ionic solutions has become a great technological challenge for the future of the rapidly growing area of genomics and proteomics. Polymer MEMS-based microgrippers that are activated in physiological ionic environments can be used for single cell manipulation and positioning, cell separation, as well as for minimally invasive surgery and various endoscopic operations.

Most of the previously developed microgrippers [1,2,3] cannot be activated in physiological solutions because the actuation mechanism is not compatible with liquid operation. Electrostatic actuators cannot be stimulated in electrolytic media. Thermal actuators operate at extremely high temperatures, and SMA actuators consume high power resulting in high applied voltages (bubble formation by electrolysis occurs at ~2 Volts in water). Piezoelectric actuators produce small displacements requiring multilayer actuators or amplification mechanisms and high voltages. Electroactive polymer actuators based on ionic absorption and swelling [4] can operate in aqueous solutions, but they have a slow response time, limited actuation control, and possibly alter the chemical properties of the biological sample under investigation.

Taking advantage of the structural rigidity and the ability to define high aspect ratio structures on SU-8 films, we present the development of an electrothermally activated SU-8 microgripper that can operate in both liquid and dry environment. Due to the large thermal expansion coefficient of SU-8, the microgripper can be activated inside physiological solutions with small temperatures changes. We report initial experimental results on the static performance of the microgripper and demonstrate the successful manipulation of a single HeLa cell *in vitro*.

2. MICROGRIPPER DESIGN

Our microgripper design was inspired by the well-established 'hot and cold arm' actuator design [5]. The 'hot and cold arm' actuator is composed of two arms of different widths that are joined at their free ends to form a U shape. The higher ohmic resistance in the narrower 'hot' arm results in greater heating and expansion than the wider 'cold' arm. Thus, the tip of the actuator can move laterally in an arching motion towards the 'cold' arm side.

The SU-8 microgripper consists of two 'hot and cold arm' actuators placed anti-symmetrically next to each other (figure 1). Thermal expansion of the SU-8 is achieved through resistive heating of a thin Cr/Au layer attached selectively at the bottom of the suspended polymer structure. The bimorph SU-8/gold structure is extremely stiff in the vertical direction and thus moves in plane rather than out of plane when is activated (the SU-8 layer is 100 times thicker than the Cr/Au layer). The two SU-8 gripper arms extend 450 microns away from the actuators forming a circular cell holder.

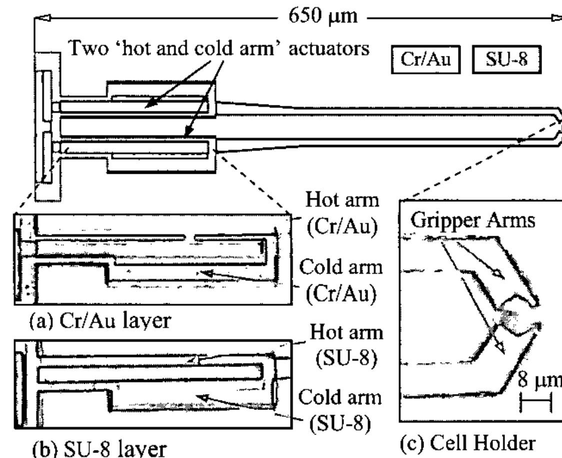

Figure 1: Schematic diagram and close ups of the SU-8 microgripper. A Cr/Au ohmic resistor (a) patterned on the bottom of the SU-8 structure (b) activates the two gripper arms of the cell holder (c).

3. FABRICATION PROCESS

The polymer-based microgripper is fabricated using standard surface micromachining techniques in a two-mask process (figure 2).

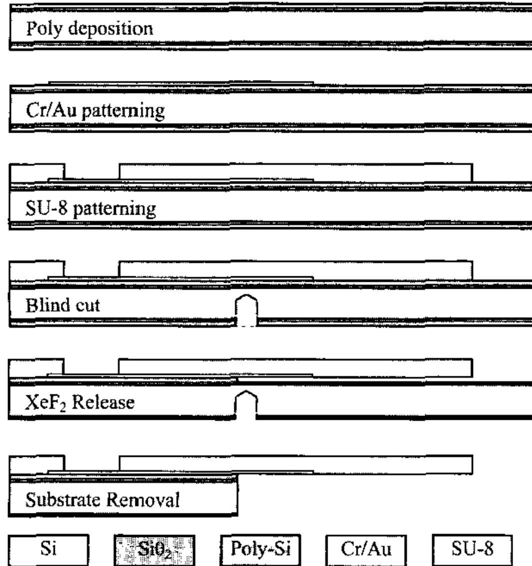

Figure 2: The two-mask fabrication process. Polysilicon is used as sacrificial layer.

A 0.3 microns thick layer of silicon dioxide is thermally grown on a bare silicon wafer followed by LPCVD deposition of 0.7 microns thick undoped polysilicon layer. The silicon dioxide layer provides thermal and electrical isolation while the polysilicon layer is used as the sacrificial layer. The metal heating elements and pads of the microgripper are subsequently defined by lift-off. The metal elements consist of a 10 nm/300 nm thick electron-beam evaporated chrome/gold film. A 20 microns thick SU-8-10 layer is then spun on the wafer and photolithographically patterned to form the structural layer. The structures are hard baked on a hot plate at 120°C for 15min and finally dry etch-released in xenon difluoride. Xenon difluoride has excellent selectivity to SU-8, produces gas products and thus eliminating stiction problems. The released microgripper is hard baked for a second time at 120°C for 15 min to complete the crosslinking of SU-8. To avoid the creation of additional out of plane residual stress due to SU-8 polymerization, the released structures are held flat with a glass slides placed on top of them. A blind cut can be made on the backside of the wafer prior to release to selectively remove the silicon substrate if overhanging structures are desired. The blind cut induces imperfection in the silicon crystal, facilitating the accurate manual breaking that is followed. The released overhanging SU-8 microgripper is shown in figure 3.

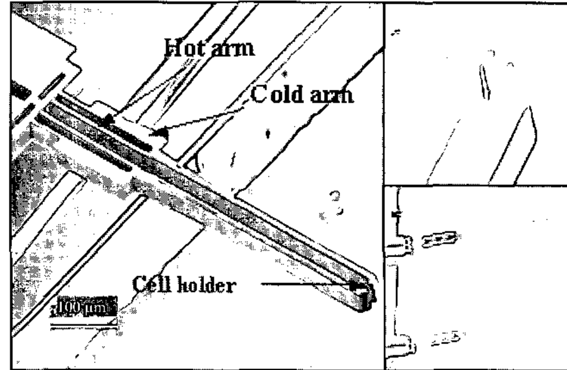

Figure 3: SEM micrographs of the SU-8 microgripper (the scale bars in the upper and lower right micrographs correspond to 10 microns and 100 microns respectively).

4. EXPERIMENTAL RESULTS

In order to determine the mechanical performance, we activated our microgripper using DC driving voltages and measured under a light microscope the corresponding displacement response. Of special interest was to identify the dependence between applied voltage and displacement when operation takes place in physiological media, since our microgripper is intended to work in such environments. High voltages and strong electric fields can cause electrolysis, electroosmotic flow and irreversible cell damaging. The need for low driving voltages becomes therefore a critical factor for biocompatible operation.

Figure 4 shows the displacement response when a DC voltage is applied in air and D-PBS (Dulbecco's phosphate buffered solution) environment.

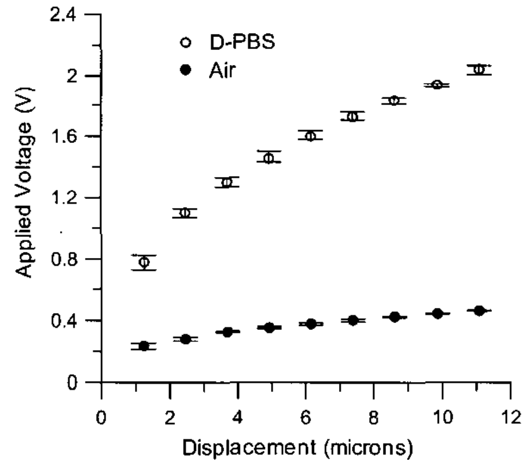

Figure 4: Applied DC voltage versus displacement. Operation in liquid (D-PBS) requires higher voltages than air.

The displacement corresponds to the total change in distance between the two gripper arms when both actuators are activated, starting from an initial separation of 7 microns.

Operation in PBS solution requires higher voltages than operation in air due to the higher convection-conduction coefficients encountered in liquids. Grasping a 10-micron diameter cell in D-PBS requires only 1.2 Volts (3 microns of displacement from rest). For the full range of displacements, no bubble formation was observed, confirming that minimum electrolysis was taken place. Alternatively, high frequency AC voltages can also be applied if electrolysis needs to be completely avoided. The error bars correspond to four sets of measurements. They are within 5% of the average value, hardly distinguishable and thus indicating great repeatability of the microgripper performance.

The average increase in temperature of the microgripper actuator was estimated from the change in resistance of the Cr/Au resistors:

$$\Delta T_{net} = \frac{R(T_{net}) - R(T_0)}{R(T_0)} \frac{1}{\alpha_{Cr/Au}}$$

where a value of 3.36 was used for the average temperature coefficient resistance $\alpha_{Cr/Au}$ of the Cr/Au film. The resistance of the microgripper had an average value of $R(T_0)=39\ \Omega$ at room temperature ($T_0=25°C$). Typical resistance changes for the full range of motion were less than 16% for operation in D-PBS, resulting average temperature increases less than 45°C (figure 5).

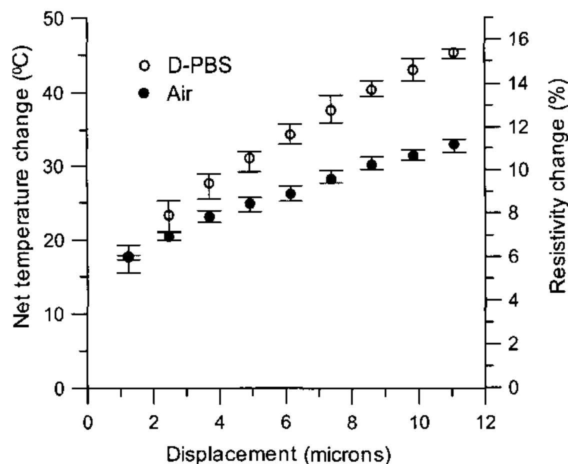

Figure 5: Net temperature increase versus displacement. Immersed in D-PBS, the gripper opens 10 microns at 40°C temperature change.

Unexpectedly, for the same amount of displacement higher average temperatures were measured for operation in D-PBS. We suspect that SU-8 absorbs water molecules that cause a reduction in the value of the coefficient of thermal expansion. Although the maximum temperature increase of the actuator is higher than the measured net temperature increase, the temperature of the tip of the cell holder is expected to be near room temperature due to the high convection coefficients of liquids.

5. Manipulation Of Single Cells In Solution

The ability of our microgripper to manipulate single cells *in vitro* was experimentally verified using the setup shown in figure 6. We photolithographically defined a chessboard on a gold film that was previously deposited on a silicon chip. The gold chessboard had 8 microns square patterns equally spaced (see figure 7). The silicon chip was mounted on a XYZ micromanipulator that allowed us to move the chessboard towards the gripper. During the experiment the microgripper was held fixed on the chuck of a probe station and powered by a DC power supply (Agilent 3130). The cells used in the experiment were HeLa cells, cultured in Dubelco's Modified Edge Medium.

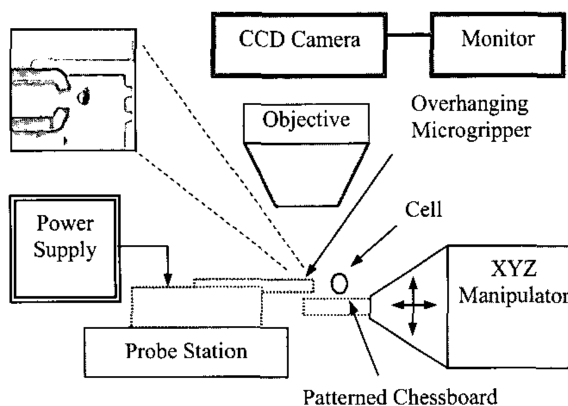

Figure 6: Schematic drawing of the experimental setup. An external micromanipulator is used to position the cell in front of the microgripper.

Figure 7 shows the successful gripping and position of a single cell on the third column of the chessboard. The cell is initially tens of microns away from the chessboard and the gripper is in its initial closed position (7a). The gripper is subsequently activated and the chessboard containing the cell approaches the open gripper (7b). The gripper closes, gripping the cell (7c). The silicon chip then starts moving so the cell is aligned to the third row of the gold chessboard. (7d). The gripper finally opens, releasing the cell and the chessboard returns to its initial position (7e, 7f).

6. Conlusions

The development of an electrothermally activated SU-8 microgripper is described. The polymer microgripper, consisting of two mirror-image 'hot and old arm' actuators can be inexpensively fabricated in a standard two-mask

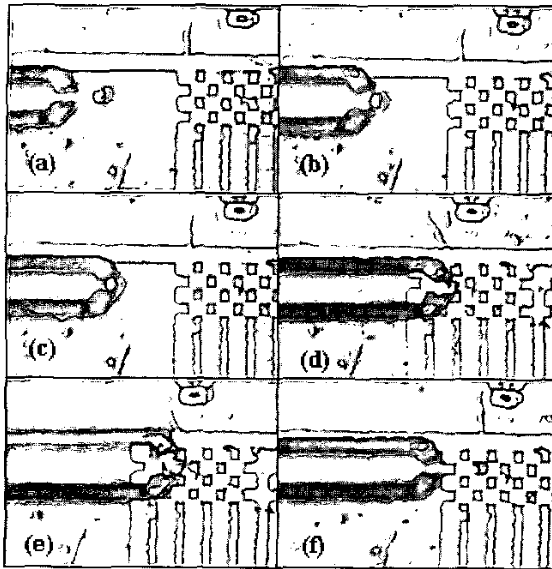

Figure 7: Manipulating a single HeLa cell in vitro: (a) initial position, (b) the gripper opens and approaches the cell, (c) the gripper grasps the cell, (d) the cell is aligned on the chessboard, (e) the gripper opens and drops the cell, (f) the gripper returns to its original position.

surface micromachining process. The high thermal expansion coefficient of SU-8 makes possible the operation of the microgripper with small temperature elevations at low voltages. Such feature makes possible the activation of the microgripper inside ionic or non-ionic aqueous media. Our microgripper can potentially be used in any type of biological assay where the manipulation of a single cell is needed.

ACKNOWLEDGMENTS

This work is fully supported by DARPA under the BioFlips program. We also acknowledge Jarett Diamond for his help with the HeLa cells.

REFERENCES

[1] C.J. Kim, A. Pisano, R.S. Muller, "Silicon Processed Overhanging Microgripper", *J. Microelectromech. Syst.*, vol. 1 (1), pp.31-36, 1992.

[2] C. G. Keller, R.T. Howe, "Hexsil tweezers for teleoperated micro-assembly", *Proc. MEMS 1997*, pp. 72-77, 1997.

[3] S. Butefisch, G. Pokar, S. Buttgenbach, J. Hesselbach," A new SMA actuated minaiature gripper", 7th *International Conference on new actuators*, pp. 334-337, Bremem, 2000.

[4] W.H Jager, O. Inganas, I. Lundstrom, "Microrobots for Micrometer-Size objects in Aqueous media: Potential Tools for Single Cell Manipulation", *Science*, vol. 288, pp. 2335-2338, 2000.

[5] J.Comtois, V.Bright, M. Phillips, "Thermal micro-actuators for surface micromachining processes", *Proc SPIE: Micromachined Devices and Components*, vol. 2642, pp. 10-21, 1995.