Wafer Level Fabrication of an Integrated Microdispenser with Electrical Impedance Detection for Single-cell Printing

Azmi Yusof*, Kiril Kalkandjiev*, Jonas Schöndube, Roland Zengerle and Peter Koltay
Laboratory for MEMS Applications, Department of Microsystems Engineering, IMTEK
University of Freiburg, Germany.
Equally contributed to this work

1 Introduction

Non-contact dispensing technologies have several attractive features such as the capability to deliver diverse classes of materials and the ability to confine the material into as small as picoliter sized droplets. This motivates technologist to adapt it to many applications. In cell biology for example, several promising results have been reported to deliver viable cells using modified home and office inkjet printers as well as other dispensing devices. Besides printing cells and cellular compounds for generating three-dimensional tissue structures or arraying cells for high throughput screening, recent work has demonstrated the capability to adapt on-demand dispensers to print and seed single cells on substrate surfaces for downstream single cell analysis [1]. In recent work, we presented a microfluidic dispenser chip to isolate individual micro particles from suspension and to deposited them on a substrate by non-contact micro dispensing [2] , [3]. In order to efficiently deposit individual particles as well as for advanced applications in cell biology, we present here the improvement of the micro dispenser device by integration of an impedance based single particle detection system into the dispenser chip.

2 Electrical impedance detection

The electrical impedance detection of single particles requires at least one pair of electrodes embedded in the microchannel oriented perpendicular to the flow of the suspended particles. The excitation signal applied on one of the electrodes generates the electric field within the detection volume. The impedance change due to perturbation of dielectric properties of the detection volume can be measured using a measuring device connected to the other side of the electrode. Two most commonly used electrode arrangement embedded in the micro channel are shown in fig. 1. The co-planar electrode arrangement (fig. 1b) generates an in-homogenous electric field whereby its magnitude increases close to the electrode's surface. On the other hand, parallel facing electrodes (fig. 1a) produce a virtually homogenous electric field within the detection volume, and the detection signal is less sensitive to the particle position in the micro channel.

However, embedding parallel facing electrode pairs into a micro device that features several integrated elements is challenging as far as fabrication is concerned, due to the planar topology created by most MEMS processing technologies. To address this

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shortcoming, we present a low-temperature full-wafer fabrication of an integrated micro dispenser featuring parallel facing electrodes using a combination of Silicon, TMMF dry photopolymer and Pyrex.

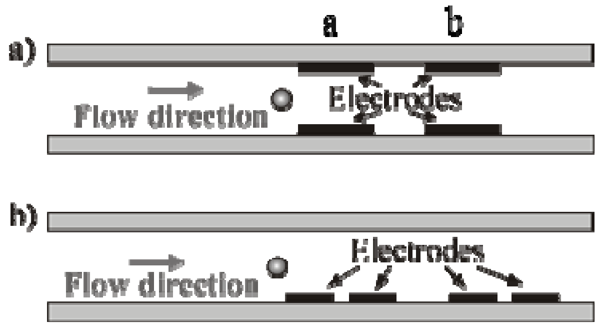

Fig. 1: Schematic of commonly used electrodes arrangements for electrical impedance detection of single cells. (a) Parallel facing electrodes. (b) co-planar electrodes.

3 Fabrication

The fabrication process steps for the Pyrex wafer were divided into two parts: The first step was to pattern the platinum electrodes by evaporation and fabrication of the hydraulic access holes by deep HF etching following our previous work [4]. The subsequent fabrication steps are depicted in Fig. 2a: A metal layer with a thickness of 100 nm was sputtered on silicon and patterned by lift-off to form the electrodes. TMMF with a thickness of 55 µm was applied onto the Pyrex wafer using hot roll lamination (60 °C, 1 m/min, 0.1 MPa). Cross-linking was initiated using contact i-line exposure through a printed mask with an exposure dose of 150 mJ/cm^2. After exposure, the Pyrex wafer was placed onto a hotplate for 2 minutes at 70 °C resulting in a partial cross-linking of the TMMF. Development was performed by immersion in propylene glycol monomethyl ether acetate (PGMEA, SU-8 developer) and followed by rinsing with isopropyl alcohol (IPA), deionised water and spin drying. The parallel facing electrode configuration was realized by the subsequent bonding of the glass/TMMF stack to the silicon wafer (90 °C, 60 N/cm^2, 50 minutes). Finally, dicing was performed to separate the chips and to open the dispensing nozzle.

4 Results

Fig. 2b shows the Pyrex wafer with microelectrodes and TMMF microchannels. At that time, the TMMF was not completely cured in order to be able to operate as a patterned adhesive. Fig. 2c shows a diced chip after bonding. A detailed view of the electrodes facing each other on opposite sides of the same channel and a cross-section of the wafer stack defining the nozzle are shown in Fig. 3a and Fig. 3c respectively. Tightness of the assembly was proven by filling the microchannels with water.

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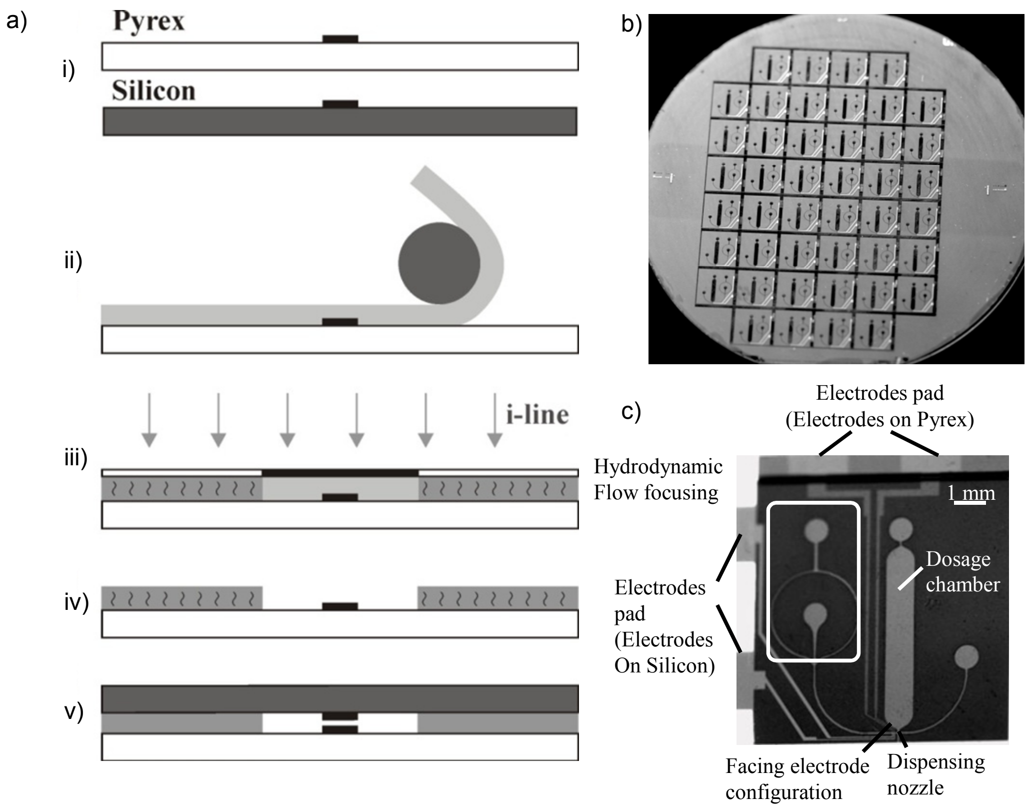

Fig. 2: (a) Fabrication process steps: (i) Electrode patterning, (ii) TMMF lamination, (iii) I-line exposure and (iv) Development, (v) Glass to silicon bonding. (b) photograph of the glass/TMMF stack prior to bonding. (c) Microdispenser with integrated microchannels, impedance sensor and micro dispenser.

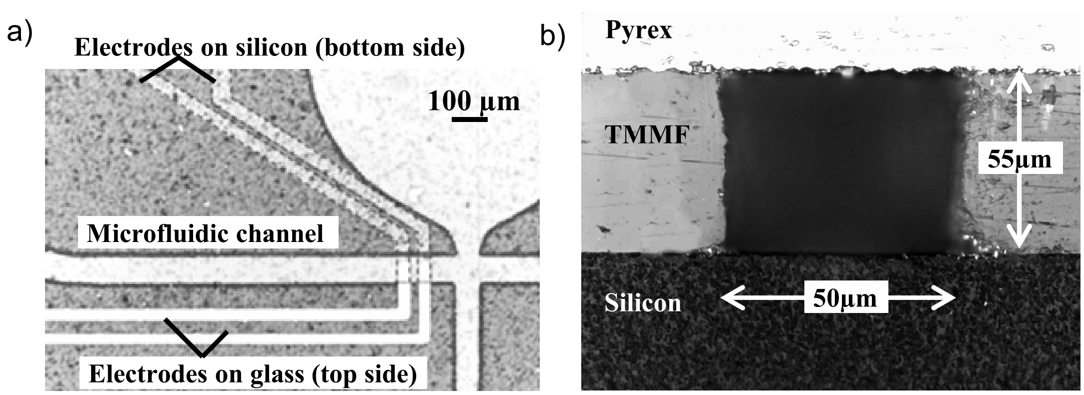

Fig.3: (a) Sectional view at the integrated electrodes. (b) Cross section of the dispensing nozzle having dimension of 50 µm X 55 µm.

The dispenser was assembled on a similar set-up like presented previously [2]. The electrical read-out to the sensor signal was performed using an impedance analyzer

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(Zurich Instruments, Switzerland) with a common excitation voltage connected to the bottom electrodes (electrodes on silicon) (fig. 4a). The measurement signals from the chip (electrodes on Pyrex) were first amplified via current amplifier (Zurich Instruments, Switzerland) and later analyzed by the impedance analyzer using a customized graphical user interfaced (GUI). The excitation signal was set at 1 Vpp and at frequency 550 Hz. Polystyrene bead suspension was prepared by dilution into PBS at a concentration of approximately 1 x 10^5 particles/ml and loaded into the chip.

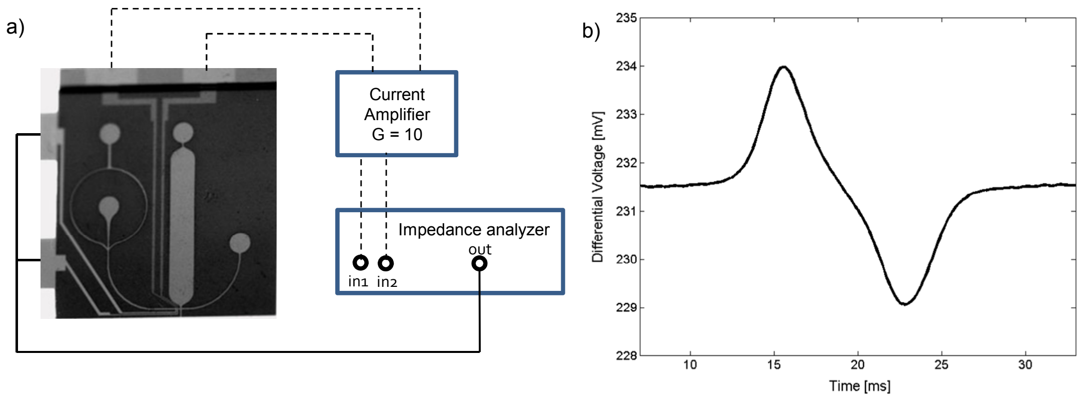

Fig. 4: (a) Electrical interfacing for impedance detection of single particle. (a) Transient differential impedance signal for single polystyrene beads (10µm dia.) flowing through the facing electrode pairs.

The differential impedance signal as a single polystyrene bead flows through both electrodes pairs is shown in fig. 4b. The positive peak represents the signal as the bead flows through the first set of electrode, while the negative peak represents the signal as the bead flows past the second electrode pair.

Conclusion

We have demonstrated the fabrication of a micro dispenser featuring integrated parallel facing electrodes using a low-temperature full-wafer bonding process based on TMMF as bonding layer. The measured signals for single polystyrene beads demonstrate the functionality of the sensor system. In the future, the possibilities to perform single cell printing and sorting with this system will be evaluated.

Reference

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