Silicon based microfluidic device with integrated electrodes for the assessment of cellular stiffness

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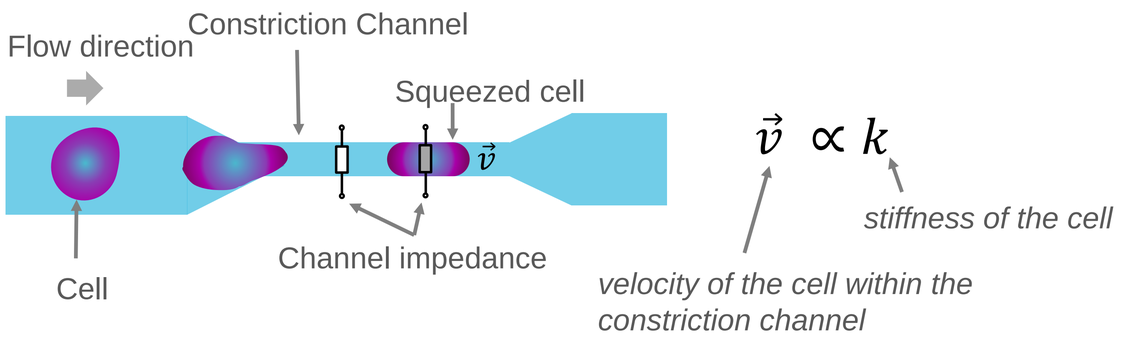
Introduction

Several diseases such as atherosclerosis, malaria and cancer are known to alter the stiffness of a cell. Chemotherapy to treat cancers are also known to alter the stiffness of a cell. Therefore, measuring cellular stiffness can be used to detect the stage of the disease or to measure the effectiveness of a treatment. Here a novel method to measure cellular stiffness is presented and fabricated using only standard IC based technology making the fabrication process scalable. Preliminary electrical measurement results are also presented.

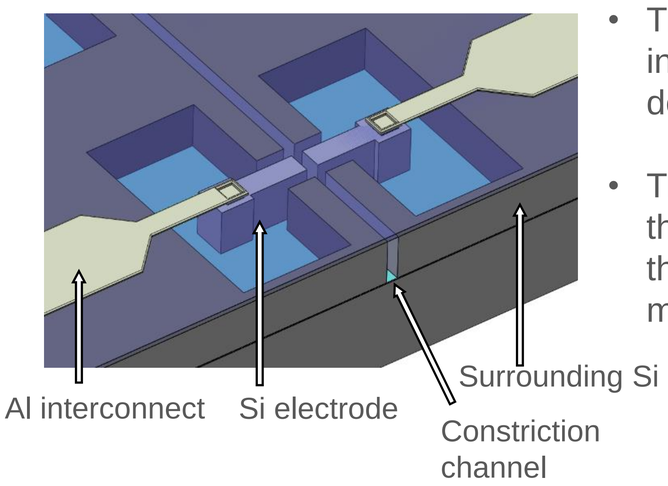
Measurement Principle



1. Cells are squeezed into a constriction channel
2. The cell changes the channel impedance between a pair of electrodes.
3. The change in impedance is detected at two different location and the velocity is measured

Fabrication Method

- Si electrode concept



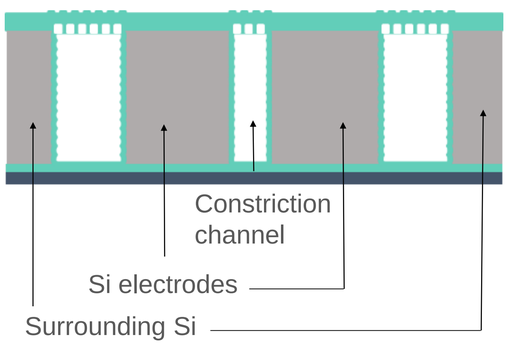
- The Si electrodes are fabricated inside the highly boron doped device layer of an SOI wafer.
- The Si electrode is isolated from the surrounding Si by the void, the BOX layer and sealing SiO_2 membrane.

- Process flow chart

(a)PECVD SiO_2 patterned with channel design

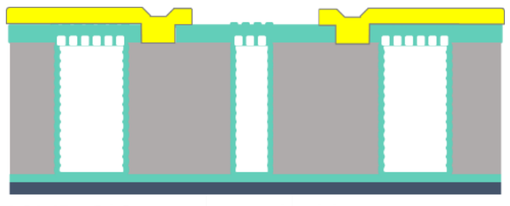
(b) DRIE

(c) PECVD SiO_2 (Sealing Channel)

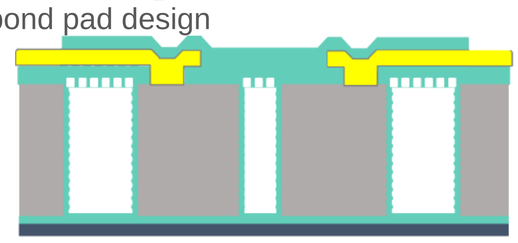


(d) Etch contact hole opening

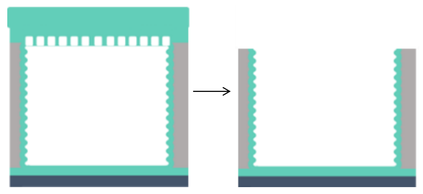
(e) Pattern Aluminium



(f) PECVD SiO_2 patterned with bond pad design

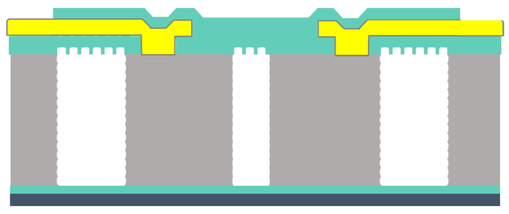


*(g) Etch open Inlet/Outlet



* different location on the wafer

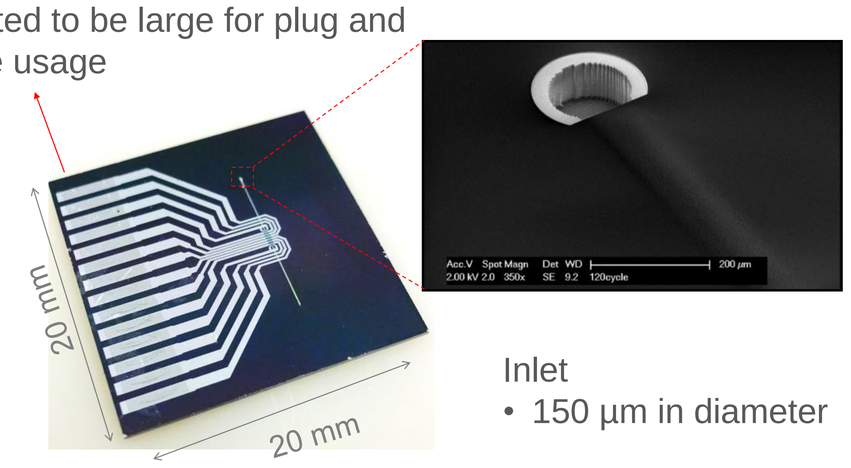
(h) Vapor HF to remove SiO_2 on inner walls



Fabrication Result

- Celllular stiffness measurement chip

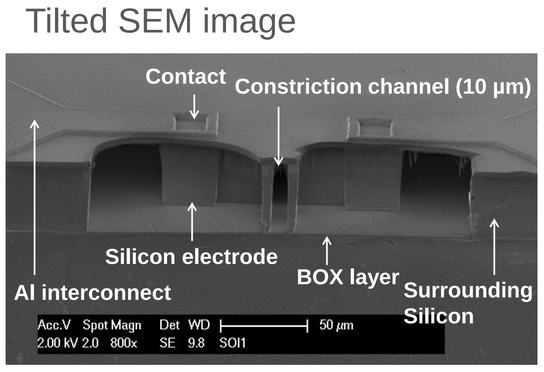
Bond pad
- Fabricated to be large for plug and play like usage



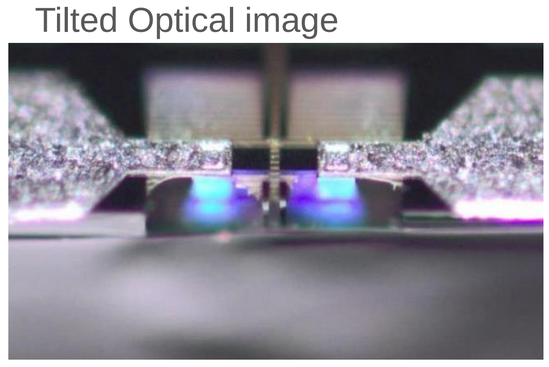
Inlet
- 150 µm in diameter

- Cross section image

Tilted SEM image

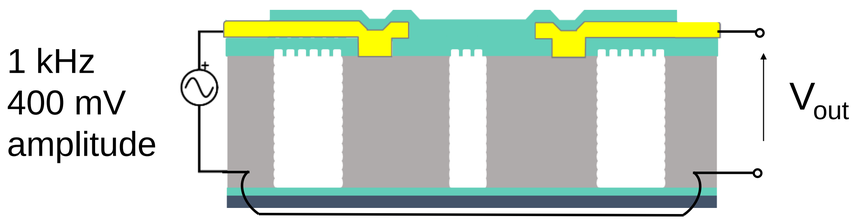


Tilted Optical image



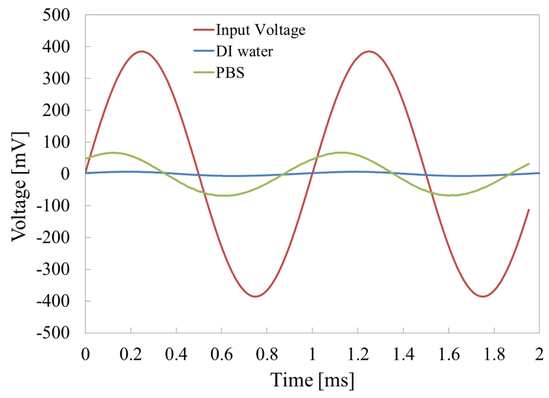
Electrical Measurement

- Measurement Setup



PBS or DI water was constantly injected into the channel while Vout was measured.

- Measurement Result



PBS is conductive while DI water is non-conductive. This was clearly measured because the output was measurable only when PBS was inside the channel

Conclusion

- Cellular stiffness measurement chip was fabricated with a scalable technology (= **Standard IC based fabrication technology**)
- The difference of PBS and DI water was **successfully detected**