細胞通過センサを有した集積化マイクロピペットによる単一細胞回収

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新発想：MEMS技術とプーラーを組み合わせてピペット機能に革新を起こす！

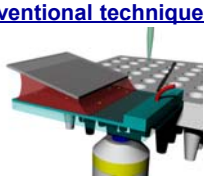
Background

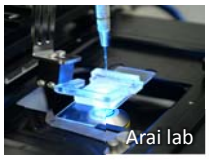
Single-cell analysis

- ✓High-precision cancer diagnosis
- ✓Clarification of Generation, differentiation
- ✓Evaluation of rare cell

Resent researches found that cell mass is hetero.
So, single-cell analysis is the more resent and highly regarded.
⇒Single-cell isolation/dispensing system is necessary.

Conventional technique





- ・Cell dispensing success rate is not perfect.
- ・It is serious problem in the case of rare-cell.

One of the reason…

✓Over sucking of cell.

Purpose

For the high precision cell-dispensing

- ○ Fabricate new pipette that has single-cell sensor.
- ○ Combine sensor and flow control

High-Functionalization of micropipette.

+ Cell-passage sensor | Isolator | Gripper | Pump | Valve | Electrode | Sorter | Force sensor | etc…

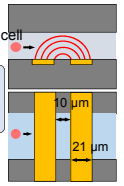
Glass capillary + Sensor = Integrated micropipette

- ✓ Aspirate a cell from tip of the pipette.
- ✓ Detect the cell by sensor.
- ✓ Stop the pump.
- ✓ Eject the cell to the well.

Design

Capacitance sensor

- ✓ High precision, high responsibility
- ✓ Can be designed in μm order
- ✓ Discriminate cell from bubble



Capacitance between two electrodes

$$C=\frac{Q}{2V_0}=\frac{2\varepsilon_0\varepsilon_r l}{\pi}\ln\left[\left(1+\frac{w}{a}\right)+\sqrt{\left(1+\frac{w}{a}\right)^2-1}\right]$$

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ε_0: electric constant
ε_r: dielectric constant of cell
w: width of electrode
a: distance of two electrodes

Effective width of electrode

$$\frac{w_{eff}}{2a}=\sqrt{1+\left(\frac{d}{a}\right)^2}-1$$

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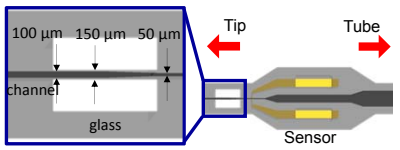
w_{eff}: effective width of electrodes
d: depth of channel

Tip of micro-capillary

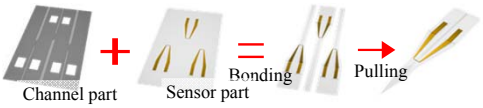
- ✓ To reduce dead volume (volume from tip to sensor)
- ✓ Narrow channel
- ✓ Small distance between tip and sensor

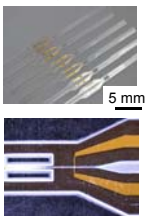


Toughness + Thinness

Fabrication

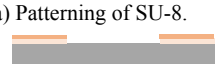
We fabricated integrated micropipette from two glass substrate.





Channel part

(a) Patterning of SU-8.



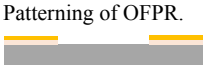
(b) Sandblast.

(c) Patterning of filmresist.

(d) Sandblast.

Sensor part

(e) Patterning of OFPR.



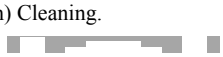
(f) Wet etching by HF.

(g) Sputtering Cr/Au.

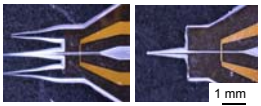
(h) Patterning of Cr/Au.

Bonding, Cutting, Pulling

(h) Cleaning.



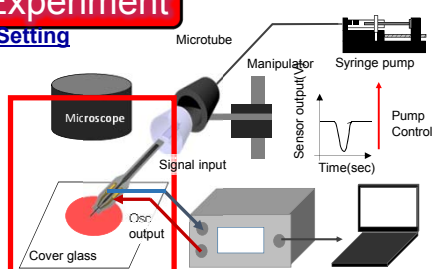
(i) Bonding, Cutting, Pulling

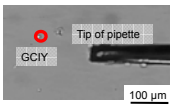


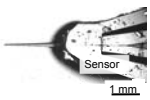
Fabricated micropipette

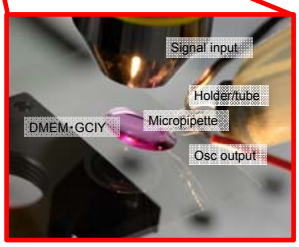
Experiment

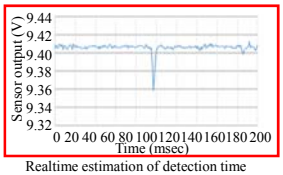
Setting











Realtime estimation of detection time

Conclusion

- ・We succeeded in fabricating glass capillary that havesensor for passage detection of cell.
- ・In experiment, we succeeded in sucking and detecting cell.

Reference

□ Kazuya Tashiro, et al, “Single cell picking by integrated micropipette having sensor for passage detection of cell”, 3P2I06, P254,Robomech2014

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