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MEMS-Electronics Integration: A Smart Temperature Sensor for an Organ-on-a-chip Platform

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1. Introduction

Incubators in cell cultures are used to grow and maintain cells under optimal temperature alongside with other key variables. As enzymatic activity and protein synthesis proceed optimally at 37 °C, a temperature rise can cause protein denaturation, whereas a drop can slow down catalysis and polypeptide initiation [1].

Inside the incubator, measurements nowadays are gauged via the temperature of the heating element which is not exactly the same of the cells. Apart from that, time spent outside the incubator can greatly impact cell health. In fact, out-of-incubator temperature and its evolution is an unknown variable to researchers. For a non-incubator temperature monitoring, besides a more accurate temperature measurement of the cell culture, *in situ* temperature sensing is of paramount importance. This also enables growth optimization of the cultured cells. To the authors' best knowledge, no fully integrated *in situ* temperature sensing for organ-on-a-chip (OOC) exists to date and this is the first time such integration is being reported using a custom-designed circuit fabricated on the same silicon substrate of the OOC.

Moreover, the simple, robust and flexible IC technology used for the sensor fabrication grants a very cost-effective integrated solution in virtue of the reduced cost per wafer along with the large silicon area available in the platform.

2. Methods

The temperature sensor circuit outputs a square-like waveform conveying a proportional to absolute temperature frequency information that can be post-processed with a microcontroller unit. Simulations of the circuit were run in Spectre from Cadence.

The fabrication used a "MEMS-last" process to avoid potential PDMS and other material contamination. A planar BiCMOS IC technology that requires only 7 masks steps is used to fabricate three main devices in the circuit: NPN, nMOS and pMOS transistors. The start material is a double-polished p-type silicon wafer. Mask 1 is used to define the n-well and the collector area of the NPN transistor, while masks 2 and 3 define, respectively, the n/p-type diffusion areas for the CMOS and the emitter/base area for

the bipolar device. Contact openings are wet etched after the patterning of mask 4, while mask 5 is used to pattern the interconnect and gate material via deposition of AlSi (1%). Masks 6 and 7 are used to open vias and deposit the second layer of metal. This last step is also used to deposit the first metal layer of the OOC module. The process follows with the SiO₂ deposition using PECVD on the front and back of the wafer. The SiO₂ layer on the back is patterned by dry etching to define the membrane area. Then, PDMS is spun onto the front of the wafer and cured for 30 min at 90 °C. Finally, the membrane is released removing the Si and the SiO₂ layers from underneath the membrane using DRIE and buffered hydrofluoric acid, respectively. The envisioned result of this process is shown in Figure 1.

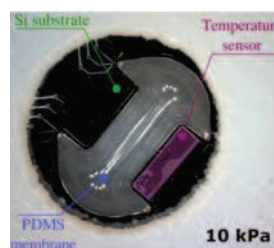


Figure 1: Envisioned MEMS-electronics integration of the smart temperature sensor and the OOC showing the PDMS membrane air-inflated at 10 kPa [2].

3. Results

Simulation results of the circuit reveal a responsivity of 4766 ppm/°C ranging from 30 °C to 44 °C, with a frequency conversion of 1.25 kHz/°C and jitter of 600 ps. Total power consumption is about 75 mW at 15 V of power supply.

Measurements and more detailed pictures of the OOC platform with the integrated sensor will be presented in the conference.

4. Discussion & Conclusion

The *in situ* temperature sensor presented here will allow a more accurate measurement than methods in use nowadays and, for the first time, out-of-incubator temperature monitoring using a simple, robust and very cost-effective IC solution.

References

- [1] Neutelings et al., "Effects of mild cold shock (25 °C) followed by warming up at 37 °C on the cellular stress response", *PLoS ONE*, vol. 8, p. e69687, 2013.
- [2] Gaio et al., "Cytostretch, an Organ-on-Chip Platform", *Micromachines*, vol.8, p. 120, 2016