Monolithic Integration of an In-situ Smart Sensor in a Silicon-based Organ-on-a-chip Platform for Monitoring the Temperature of Stem Cell Culture

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Monolithic Integration of an In-situ Smart Sensor in a Silicon-based Organ-on-a-chip Platform for Monitoring the Temperature of Stem Cell Culture

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This research reports on the design and co-fabrication of a time-mode signal-processing *in situ* temperature sensor customized for the Cytostrech, an organ-on-a-chip (OOC) device. The circuit was fabricated using an in-house integrated circuit technology (BiCMOS7) that requires only seven lithographic steps to fabricate npn and MOS devices, and is compatible with MEMS fabrication process. The technology was optimized to find the best trade-off between the the currrent gain (β_F) of the BJT and the current driving capacity of the MOS devices. The proposed circuit is developed to provide the first out-of-incubator real-time temperature monitoring of cell cultures on an OOC platform in a monolithic fabrication. The importance of this temperature monitorization stems from the fact that the temperature plays a pivotal role in the cell culture. As enzymatic activity and protein synthesis proceed optimally at 37.5 °C, a temperature rise can cause protein denaturation, whereas a drop in temperature can slow down catalysis and polypeptide initiation. The temperature setpoint of the incubator is controlled according to the temperature of its sensing element, which is not always the same what the cell culture is experiencing. On the other end, the cumulative effects of time spent outside the incubator can add up and greatly impact cell health. In fact, out-of-incubator temperature and its change over time are unknown variables to clinicians and researchers, while a considerable number of cell culture losses are attributed to this reason.
The system consists of two main blocks: a proportional to absolute temperature (PTAT) current generator (comprising of npn bipolar transistors to sense the temperature information) and a current-controlled relaxation oscillator.
Measurement results on wafer reveal a temperature measurement resolution of less than ±0.2 °C (3σ) and a maximum nonlinearity error of less than 0.3% across a temperature range from 25 °C to 100 °C.

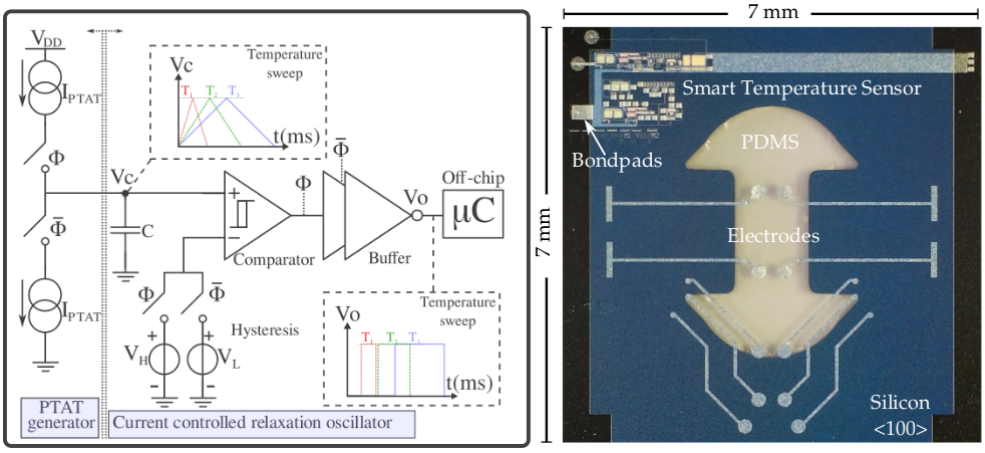

Figure 1: ***Left side:*** *System-level design detailing the main blocks: a PTAT generator and a current-controlled relaxation oscillator.* ***Right side:****The result of the MEMS-electronics co-fabricationusing the in-house EKL technology. A sheet of white paperwas placed beneath the chip to illustrate better the PDMS membrane area.*