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CMOS-BASED CAPACITANCE MEASUREMENTS FOR CELL ADHESION SENSING APPLIED IN EVALUATING THE CYTOTOXICITY OF NANOMATERIALS

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Scientific Context and Objectives

- Nanoscale materials compared to bulk may be harmful to health.
- EU banned cosmetics with animal tested ingredients → New, additional, ethical methods are needed to evaluate biological effects of nanomaterials.
- Here we introduce the IC chip designed for charge-based capacitance measurements for sensing cell adhesion to the substrate surface to evaluate the cytotoxicity of nanomaterials.
- Adherent cells normally spread out on the surface, but stressed cells "ball up" and finally detach as they die; this change in attachment can be sensed via a change in capacitance.



Figure 1. Fully differential rail-to-rail capacitance measurement circuit, a sensor block diagram .

S. B. Prakash, P. Abshire, "A Fully Differential Rail-to-Rail CMOS Capcitance Sensor With Floating-Gate Trimming for Mismatch Compensation", *IEEE Transaction on Circuits and Systems-I: Regular Papers*, 56 (2009) 975-986.

S. B. Prakash, P. Abshire, M. Urdaneta and E. Smela, "A CMOS capacitance sensor for cell adhesion characterization" 2005 IEEE International Symposium on Circuits and Systems (ISCAS) Vols 1-6, Conference Proceedings, Pages: 3495-3498 DOI:10.1109/ISCAS.2005.1465382

RESULTS

- The IC chips consisted of capacitance sensors arrays and readout circuitry.
 - The arrays were subdivided into four different sections for calibration, planar sensors, and two different types of interdigitated sensors.
- The capacitance sensors were fully differential to increase dynamic range and suppress noise.
- Adherent kidney cells of *Cercopithecus aethiops* were cultivated on the surface of the chip and exposed to TiO₂ nanowires earlier report as cytotoxic^{*)}.



Figure 2. Layout of the IC chip with capacitance sensor arrays and readout circuitry.



Figure 3. Microscope image of viable adherent kidney cells of *Cercopithecus aethiops* on the surface of the IC chip.



Figure 4. FESEM image of TiO₂ nanowires.

 *) A. Magrez. L. Horváth, R, Smajda, V. Slicio, N. Pasquier, L Forró, B. Schwaller, "Cellular Toxicity of TiO₂-based Nanofilaments", ACS Nano 3 (2009) 2274-2280.

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CONCLUSIONS and Future Activities

- Preliminary results indicate that for the interdigitated sensors the optimal sensor layout closely matches the cell size in terms of finger width and spacing.
- At the moment we are gathering reference data with commercial cytotoxicity kit^{**} to verify and interpret the capacitance signal and cell behaviour from the chip reflecting the cell viability after exposure to nanomaterials.
- This work in done in close collaboration with
 - University of Maryland: Ph.D. Student Timir Datta, Dr. Someshekar Prakash (currently working for Intel Corporation), Prof. Elisabeth Smela, Assoc. Prof. Pamela Abshire
 - Linköping University: Research Engineer Peter Möller, Prof. Anita Lloyd-Spetz
 - University of Oulu: Dr. Antti Hassinen, Dr. Sakari Kellokumpu, FiDiPro Anita Lloyd-Spetz



**)LIVE/DEAD®Viability/Cytotoxicity Kit from Life Technologies

Figure 5. Viable COS-7 cells on the left (green) and dead cells on the right (red) stained with LIVE/DEAD® Viability/Cytotoxicity Kit.

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