Guest Editorial
Special Issue on Advances and Open Challenges for Integrated Circuits Detecting Bio Molecules

DESPITE the continuing convergence of microelectronics with biomedicine, important technical challenges still constrain the deployment of integrated circuits in micro-analytical devices, operating both *in vivo* and *in vitro*. This Special Issue focuses on multidisciplinary advances which address open challenges for CMOS technology-based solutions. In particular, two critical aspects need to be solved. From the standpoint of electronic circuit design, the trade-offs between resolution (noise), area (cost), and power dissipation need to be carefully optimized. These tradeoffs, while familiar, are crucial for endowing portable, wearable, and implantable devices with high sensitivity. Some applications prioritize ultra low noise, such as single-biomolecule detection using nanopore sensors. In other spaces, power dissipation and die area are clearly major constraints when thousands of sensing channels are integrated on a single chip, as in the case of image sensors and electrophysiology arrays interfacing with live tissue.

Secondly, from a system-level point of view, reliable and scalable solutions are required for packaging CMOS chips to be used in contact with liquid samples. Fabrication approaches need to be found for creating chip-to-liquid interfaces (micro-to-macro scale), which are feasible both for small-scale academic prototypes and for high-volume manufacturing. Other perennial challenges include post-silicon fabrication of high performance transducers and electrodes. Finally, the different avenues for monolithic or hybrid integration of multichannel and low-noise analog front-ends with digital back-ends for data processing and wireless communication circuitry pose important technical design challenges.

This issue is composed of four papers whose applications range from optical fluorescence detection of biomolecules, to electrochemical detection of dopamine releases from cells, to high-resolution non-faradaic imaging of cells and nanoparticles.

In the paper "Integrated optoelectronics device for detection of fluorescent molecules" by *Lovecchio et al.*, a CMOS-compatible solution for the realization of a thin-film interferometric filter for fluorescent detection is presented. The filter bandwidth is $\sim$120 $\mathrm{nm_{FWHM}}$ at 580 nm, matched to the emission of a ruthenium complex used as DNA intercalator. It is coupled to a hydrogenated amorphous silicon photodetector (with 110 mA/W responsivity) and operated with a simple off-chip LED. It enables detection of 0.6 ng of DNA with a limit of detection of $\sim$0.4 ng, comparable to state-of-the-art laboratory machines.

Label-free on-chip single-cell amperometric recording of exocytotic release across 1024 simultaneous sites is demonstrated in the paper entitled "Single-cell recording of vesicle release from human neuroblastoma cells using 1024-ch monolithic CMOS bioelectronics" by *White et al.* Low noise (622 $\mathrm{fA_{RMS}}$ at 20 kS/s) is achieved in combination with a space-saving op-amp sharing solution. Gold is deposited using a post-processing approach, creating a square flat electrode (15 μm side) as the base of a cell trap patterned in SU-8.

Electrophysiology is complemented by impedance spectroscopy for morphological information as described in "Impedance spectroscopy and electrophysiological imaging of cells with a high-density CMOS microelectrode array system" by *Viswam et al.* An on-chip waveform generator and 32 lock-in demodulators enable 1 Hz to 1 MHz impedance spectroscopy, multiplexed across 59,760 sites, with a dynamic range of 102 dB and 420 μW power dissipation per channel including $\Sigma\Delta$ A/D conversion.

Dielectric imaging of nanoparticles over an array of 65,536 gold disks (90-nm radius) by means of capacitance detection (5 aF resolution measured up to 70 MHz) is reported along with calibration challenges in "A CMOS pixelated nanocapacitor biosensor platform for high-frequency impedance spectroscopy and imaging" by *Widdershoven et al.*

Together, these four papers highlight the range and power of CMOS integration, as well as important practical challenges for optimizing both electrical and physical parameters in micro-analytical biosensing platforms.

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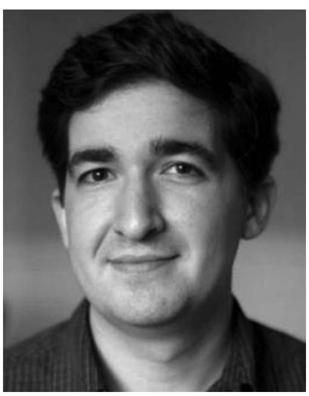

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Dr. Yoo received the Korean National Medal for his contribution to Korean DRAM Industry in 2011, the Electronic Industrial Association of Korea Award for his contribution to DRAM technology the 1994, the Hynix Development Award in 1995, the Korea Semiconductor Industry Association Award in 2002, the Best Research of KAIST Award in 2007, the Design Award of 2001 ASP-DAC, the Outstanding Design Awards of 2005, 2006, 2007, 2010, 2011 A-SSCC, and the Korean Scientist of the Month Award (Dec. 2010). He is a member of the executive committee of Symposium on VLSI, and A-SSCC. He was the TPC chair of the A-SSCC 2008, a Guest Editor for the IEEE JOURNAL OF SOLID-STATE CIRCUITS and the IEEE TRANSACTIONS ON BIOMEDICAL CIRCUITS AND SYSTEMS. He was the TPC Chair of International Symposium on Wearable Computer 2010, IEEE Distinguished Lecturer(2010–2011), Far East Chair of ISSCC (2010–2011), and currently ISSCC Technology Direction Sub-committee Chair, and an Associate Editor of the IEEE TRANSACTIONS ON CIRCUITS AND SYSTEMS—II: EXPRESS BRIEFS.