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**Bio/Nano/CMOS interfaces for Ultrasensitive Memristive Biosensors**

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In this Distinguished Lecture, the very best worldwide ever-reported electrochemical biosensors based on a memristive effect and aptamers or antibodies are presented. These novel sensing devices are developed to propose a completely new approach in the co-design of Bio/Nano/CMOS interfaces for cancer diagnostics. In this research, affinity-based techniques are presented for the detection of the prostate specific antigen (PSA) and the Vascular Endothelial Growth Factor (VEGF). The hysteretic properties of memristive silicon nanowires functionalized with proper biomolecules provide a label-free and ultrasensitive bio-detection technique. In order to develop full systems for diagnostics, the integration with CMOS frontend, in one side of the interface, and microfluidics, in the other side, is required too. Therefore, this lecture also discusses novel circuit approaches for an automated and quick characterization of arrays of memristive biosensors. One memristive parameter, the width of the voltage gap, is directly proportional to the target molecules concentration. Thus, CMOS readouts acquiring such width, meanwhile sorting-out faulty devices, i.e. non- conducting nanowires in the array, are presented together with analog-to-digital conversion for the acquired voltage gap. A prototype of these circuits is shown as an example of design in 0.35µm CMOS technology. The integration of the CMOS readout with the nanoscale sensors and a microfluidic platform is a must for the design of robust biosensing-systems for quick data acquisition in cancer diagnostics. Therefore, the development of an improved chip-platform for cancer diagnostics based on nanofabricated Memristive Biosensors integrated, for the first time, with a microfluidic structure is also presented in this lecture by also addressing critical issues, e.g., the problems related to long connections between the Memristive Biosensors and the CMOS frontend.

**Bio/Nano/CMOS interfaces for Remote Monitoring of Human Metabolism**

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Integrated electrochemical Nano-Bio-Sensors for diagnosis and/or treatment of patients with specific physiological conditions (e.g., heart, cardiovascular, cancer diseases) or convalescents is a key factor to provide better, more rationale, effective and ultimately low-cost health care also at home. The ultimate goal of improved health care on those subjects is the extension of the patients’ autonomy, the possibility for auto-monitoring, the improvement of their comfort levels and their integration into everyday life. Some systems for on-line monitoring are available in the market. They use wearable devices (accelerometers, heartbeat monitoring system, etc.). However, all these systems do not measure the human metabolism at molecular level (metabolites). The only available real-time, implantable/wearable systems for metabolic control are limited to glucose monitoring and used only for diabetic patients. However, electrochemical sensors may address so many other molecules, which have crucial relevance in human metabolism in chronic patients. So far, there are no available integrated nano-bio-systems for multi-metabolites, real-time, remote monitoring of the human metabolism. Thus, the aim of this tutorial is to present innovative concepts for multi-panel, highly integrated, fully implantable, remotely powered and real-time monitoring systems for human metabolism at molecular level. The considered metabolic molecules will be glucose, lactate, glutamate, ATP, and anticancer drugs as well as anti-inflammatory ones. In case of drugs, the specificity of electrochemical sensors is improved at system level. The proposed nanotechnology will be based on carbon nanotubes to improve the sensors performance. To pursue their detection, innovative VLSI solutions are discussed including the system remote powering. The new approach is demonstrated by showing Systems-In-Package with embedded System-On-Chip that integrate: (i) a sensors array for data acquisition; (ii) remote power and/or data transmission; (iii) nano-sensors; CMOS IC design; (iv) multi-panel metabolites detection. Systems applications are shown in the field of implantable devices with in-vivo experiments too by including packaging issues and monitoring in intensive care units.