

Emerging CMOS Bio-Sensors: A Paradigm Shift

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Short Communication

Recently, the state-of-the-art, first single-use Complementary-Metal-Oxide-Semiconductor (CMOS) based DNA sequencing device [1], featuring millions of *pH* sensors has greatly demonstrated the advantage of using standard CMOS technologies in life science applications.

It is well-established fact that the CMOS foundries, with several trillion dollars investment, are efficient mass-production platforms that lowered the cost of microelectronic devices, low enough to make most of consumer electronic products affordable to the end-users. As to their scale of integration, today's foundry processes have reached the threshold of 15 nm and hence they allow for the making of highly dense systems featuring millions of active elements such as Ion-Selective-Field-Effect-Transistors FET (ISFET). On other words, CMOS technology by offering the advantages of distinct costs and highly integrated sensors and circuits, experiences a paradigm shift toward life science application.

Nevertheless, despite the great advances achieved in developing a variety of CMOS based biosensors using magnetic [2], capacitive [3] or other electrochemical [4] techniques, little progress has been made by industrial researchers in bringing viably marketable devices to the level of mass production for various of bio-sensing applications.

The main obstacles facing CMOS designers for commercializing their bio-sensing devices are bio-interface-related. Indeed, CMOS should not directly come into contact with analytes (e.g., mRNA, Cells and Proteins) and when contact takes place; such devices are deemed to be single-use only due to the contamination of CMOS chip by biological sample and the uncertainty and instability of microelectronic characteristics when the fluids impinge on them. And *vice-versa*, residues from synthesis and fabrication phases may affect biological samples in an adverse manner, adsorption-driven concentration changes being the least troublesome; however it causes inter-devices variability of measurement outcomes.

In order to overcome these obstacles, the implementation of contact-free CMOS biosensor is a key solution to address this unmet challenge. For instance, a Radio-Frequency (RF) CMOS chip can be designed to detect magnetic resonance signal generated from a miniaturized Nuclear Magnetic Resonance (NMR) system without a direct contact with the biological sample [5]. Among a few efforts made, based on remote magnetic sensing, researchers from Harvard University deployed developed landmark hybrid microfluidic/CMOS chips for NMR relaxometry and manipulation purposes [6,7]. However, in these applications, the microfluidic chips were bonded on CMOS chip permanently and CMOS chip was a single-use device (Figure1).

Novel contact free microfluidic devices incorporated with reusable CMOS biosensors is the main objective of CMOS biosensors particularly for point-of-care diagnostics applications whose potential market is predicted to reach \$23 billion by the year 2023. The search for such a contact-free hybrid microfluidic/CMOS techniques is an essential step to take in view of developing novel affordable devices, so that, the cost of each experiment will be solely dictated by the fabrication fees of the microfluidic part rather than the whole hybrid system.

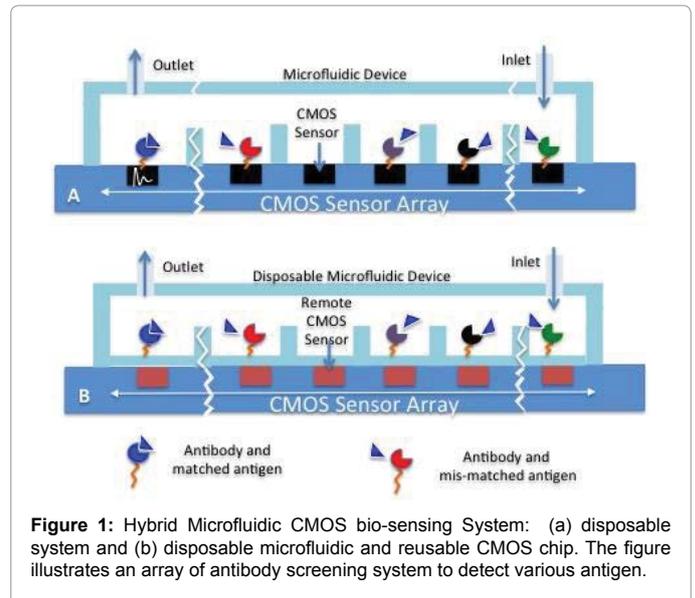


Figure 1: Hybrid Microfluidic CMOS bio-sensing System: (a) disposable system and (b) disposable microfluidic and reusable CMOS chip. The figure illustrates an array of antibody screening system to detect various antigen.

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