Highly-sensitive CMOS capacitive biosensors towards detection of single bacterial cell in electrolyte solutions

Keywords : Biological sensors; CMOS circuits; Modelling; Simulation; Measurements.

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For centuries, bacterial cells have been one of the major causes of human diseases, and are still responsible for several millions of deaths every year. Rapid detection and identification of pathogens in clinical, food or water samples is an important prerequisite step to establish a diagnosis and prevent the disease propagation. This work investigated how capacitive biosensors can be used for rapid, selective and sensitive pathogen detection in various biological buffers. Their integration with microfluidics, electrokinetics and CMOS technology is provided towards miniaturized and affordable lab-on-chips for point-of-care diagnosis tools.

The first part of the work studied the capacitive transduction, based on Al/Al2O3 interdigitated microelectrodes (IDEs). Real-time detection of Staphylococcus epidermidis in low-conductive solutions is experimentally shown, and explained by a comprehensive analytical model of the transducer. An innovative selectivity principle using lytic enzymes is then presented and shown to selectively detect of S. epidermidis among Enterococcus faecium cells in synthetic urine. Thanks to numerical simulations using Poisson-Nernst-Planck equations, the capacitive biosensor parameters are eventually optimized towards the maximal sensitivity.

The second part of the work investigated the use of electrokinetic effects to attract bacterial cells on the surface of capacitive biosensors. By using an annular-ring macroelectrode encompassing the IDEs, short and long-range trapping of S. epidermidis were observed and attributed to contactless dielectrophoresis and electrothermal flow, respectively. At 63 MHz precisely, a resonance effect related to device connectors was found to dramatically increase the trapping of S. epidermidis lowering the detection limit by two orders of magnitude. Analytical models and numerical simulations are provided to explain the observed phenomena.

The 3rd part of the work focused on the design of two analog circuits to interface on-chip capacitive biosensors in a 0.25-μm CMOS technology. The first is a capacitance-to-frequency converter working up to 575 MHz which demonstrates sensitivity to bacterial cells in high-conductive solutions. The second is a 16 $\times$ 16 capacitive biosensor array featuring micrometer-sized pixels to lower the absolute number of detectable bacteria to ca. 7. The innovative pixel architecture uses a capacitance-to-voltage converter followed by a gain stage to boost the sensitivity.

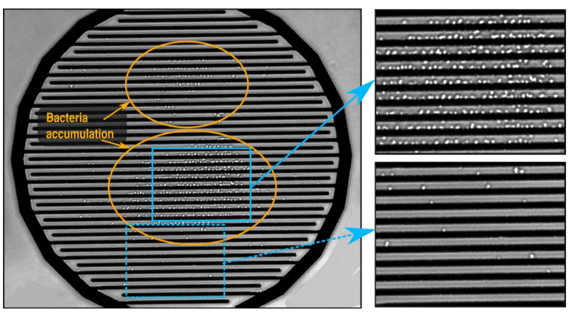

Figure 1: Concentration of bacterial cells on the capacitive sensor thanks to AC-electrosmosis.

In conclusion, capacitive biosensors towards bacteria detection

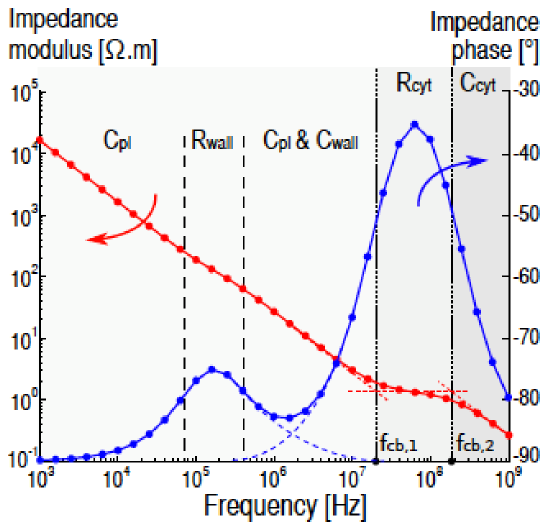

Figure 2: Bode diagrams of the bacterial complex impedance including cell wall, plasma membrane and cytoplasm components.

have extensively been studied in this work, first starting from the transduction principles and then integrating them into advanced electrokinetic and electronic systems. The innovations provided in this work offer interesting perspectives for the next generations of capacitive biosensors targeting point-of-care diagnosis of bacterial cells.

References

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