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Noise as data: why 2^{16} electrodes matter

Mohammad Saghafi,[a] Suryasnata Tripathy,[a] and Serge G. Lemay[a]

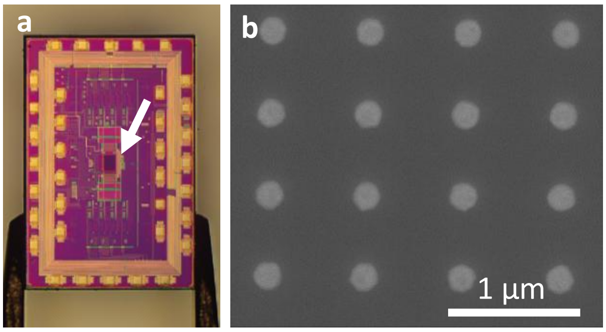
[a] *Faculty of Science and Technology, University of Twente, PO Box 217, 7500 AE Enschede, The Netherlands*
Email / Courriel de l'auteur présentant: s.g.lemay@utwente.nl

Single-entity electrochemistry methods represent the ultimate limit in mass sensitivity to an analyte. The fact that the detectors are themselves miniaturized however greatly limits their ability to work at very low concentrations due to mass transport and/or kinetic limitations. One way to circumvent these hurdles is to develop parallelized assays in which massive numbers of single-entity assays are conducted in parallel (1). Here we explore this approach by performing impedance measurements at nanoelectrodes. Our platform, implemented using commercial CMOS semiconductors technology, consists of arrays of 2^{16} separately addressable electrodes that can be operated at frequencies up to 70 MHz. For objects larger than its pitch (~1 µm), the array is reminiscent of a CMOS imager and permits obtaining spatial impedance maps of synthetic and biological entities (2). For nanoscale analytes, on the other hand, the response takes the form of stochastic, discrete changes in impedance (3).

I will present recent results from our lab in which we have applied this methodology to biological systems of increasing complexity, including:

1. Direct detection of single SARS-CoV-2 virus particles.
2. DNA detection via a toehold-mediated strand replacement mechanism.
3. Imaging of giant unilamellar vesicles and, more interestingly, their contents, through high-frequency impedance measurements.
4. The monitoring in real time of the formation of supported lipid bilayers from the fusion of individual lipid vesicles. This illustrates well the nature of stochastic processes: the nanoscale vesicles impinge upon the array at random times and locations as individual 'raindrops', yet ultimately form a static and spatially uniform bilayer.

This work is a collaboration with NXP Semiconductors.



Nanocapacitor array for high-frequency impedance measurements. *(a) CMOS chip (2×3 mm²) held with tweezers. The arrow points to the array of 65,536 electrodes. (b) Zoom on 16 electrodes. The circuity used to read out the signals from each electrode lies buried below the surface of the chip.*

References

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