ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

Self-Calibrating Multiplex Electrochemical Lab on Chip for Cell Culturing and High-Resolution Imaging

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Technology: silicon chips fabrication. Anodic Bonding and Dicing of the silicon wafer/glass cover into individual chips.

Figure S1. (A) Schematic images showing the anodic bonding between the wafer glass (containing the microfluidic cover) and the silicon chip (containing the electrodes) performed by applying temperature and electric field. Etched thickness of 0.35 mm. Bottom thickness of 0.15 mm. (B) Image of the individual chip after the dicing step of the bonded glass cover/silicon chip.

Technology: silicon chips fabrication. Bonding of the fluidic tubes and Encapsulation of the chip.



Figure S2. (A) Image of the bonding between the fluidic tubes and the rear fluid output of the silicon chip. (B) 3-D schematic view of the chip encapsulated in a PCB. (C) Image detailing the wire-bonding between the electrical pads of the chip and the electrical pads of the PCB.

Ag/AgCl pseudo-reference: profilometry.



Figure S3. Result of the profilometry performed on the pseudo-reference electrode, once Ag and AgCl were deposited. As can be seen, the thickness of both layers is around 4 μ m, which fits with the theoretical calculations, since for the formation of the 1.3 μ m AgCl layer, part of the 4 μ m of Ag has been consumed

Glucose biosensor. Enzymatic process for the glucose determination and Electrosynthesis of the PPy/ferrocyanide and the PPy/GOX membranes.



Figure S4. (A) Scheme of the bi-enzymatic reactions associated to the glucose detection. (B) Scheme of steps involved in the electrosynthesis of the glucose biosensor: (i) Thin-film gold electrode used as transducer for the biosensor fabrication. (ii) Just after applying potentiostatic conditions to the solution in presence of the monomer and the mediator, the pyrrole begins to polymerize, forming a thin-layer of polypyrrole; and (iii) beginning to growth a three-dimensional polypyrrole membrane entrapping the redox mediator. (iv) In the next step, the enzyme GOX is entrapped in a second PPy membrane electrogenerated by applying the same conditions that in the first step. Therefore, two layers are obtained: a thinner one entrapping the mediator and a thicker one with the enzyme.



Figure S5. Current (black line) and accumulation charge (red line) profile recorded during the amperometric electrogeneration of the (A) PPy/ferrycianide and (B) PPy/GOX membranes.

Ag/AgCl pseudo-reference: short-term stability test.



Figure S6. Potential profile recorded during the stability tests along 12 hours for the three compared reference electrodes. The top part of the plot has been magnified to show the variation of the Ag/AgCl pseudo-reference when compared with the commercial golden standard. Au pseudo-reference electrode showed higher potential variation than Ag/AgCl pseudo-reference and the golden standard.

Electrochemical Measurement of Individual (bio)Sensors. Activation and cleaning of gold microelectrodes.



Figure S7. Cyclic voltammograms recorded in 0.1 M KCl 1mM potassium ferricyanide after the activation of the gold microelectrode positioned on the ME-LoC versus the Ag/AgCl pseudo-RE (red line) and an external double-junction Ag/AgCl RE (black line). The voltammogram recorded with an external gold microelectrode as WE is plotted using a blue line. The electrochemical cell in this last experiment was completed using a commercial Pt CE and a commercial Ag/AgCl RE.