Rolled-Up Nanomembrane Sensors: Enabling Multi-Scale Monitoring from Molecules to Embryos

Mariana Medina Sánchez
Pallavi Jha, Friedrich Striggow, Maryam Jebari, Ronald Naumann
CIC nanoGUNE, Tolosa Hiribidea, 76, 20018
San Sebastian, Gipuzkoa
m.medina@nanogune.eu

Rolled-up microelectrodes represent a cutting-edge class of electrodes that offer significant advantages over traditional planar designs, including more uniform field distribution and the ability to mimic confined microenvironments. Their 3D structure increases surface area and stability, making them ideal for applications in photonics, energy storage, and biosensing [1,2]. These features have also enabled advancements in biological research, such as DNA detection[3], immune cell analysis[4], and drug response studies[5].

Building on these advantages, we introduce a miniaturized electrical impedance tomography (µEIT) platform featuring a 30 µm-diameter microtube with a strain-engineered electrode array. This design leverages a bilayer structure with variable intrinsic stresses, which causes the layers to naturally roll up upon release from the substrate. The bilayer consists of an inert silicon layer and a "stressed" silicon nitride layer, producing optically transparent microtubes for real-time analyte visualization [6]. EIT measurements are conducted by applying alternating currents to adjacent electrode pairs and recording surface voltages from the remaining electrodes. The resulting data is processed into conductivity maps using a fidelity-based reconstruction algorithm. The sensor successfully differentiates silica and Janus microparticles by detecting variations in spatial conductivity. In a biological application, we confirmed the necrosis of HeLa cancer cells by observing an increase in low-conductivity regions in the conductivity map, indicating cell swelling and increased permeability to the low-conductivity PBS solution (Figure 1a). Complete cell disintegration led to a total loss of conductivity.

To broaden the platform's capabilities, we refined the fabrication process to optimize tube geometry for larger specimens, such as organoids and embryos, and integrated the system with microfluidic setups. The improved protocol employs dry etching for precise control of the rolling process and SiO_2 passivation to enhance fluid stability, while also being scaled to wafer-level production. Using this approach, we monitored murine embryos progressing from the 4-cell stage to blastocysts and compared them with blocked or non-viable counterparts, revealing impedance changes that precede detectable differences under optical microscopy (Figure 1b,c).

The upgraded tubular electrodes, interfaced with a custom PCB, enable real-time, label-free, multiparametric analysis of small sample volumes, positioning them as a versatile tool for a wide range of biological applications.

References

[1] O.G. Schmidt, K. Eberl, Nature, 410(6825), 2001
[2] E. Smith, W. Xi, et l., Lab on a Chip, 11, 2012
[3] M. Medina-Sánchez, B. Ibarlucea, et al., Nano Lett, 16(7), 2016
[4] A. Egunov, M. Medina-Sánchez, O. G. Schmidt, et al., Small, 17(5), 2021
[5] E. Ghosh, A. Egunov, M. Medina-Sánchez, et al., Frequenz, 76, 2022
[6] S. Weiz, P. Jha, M. Medina-Sánchez, et al., Adv. Mater. Tech., 8(23), 2023

Figures

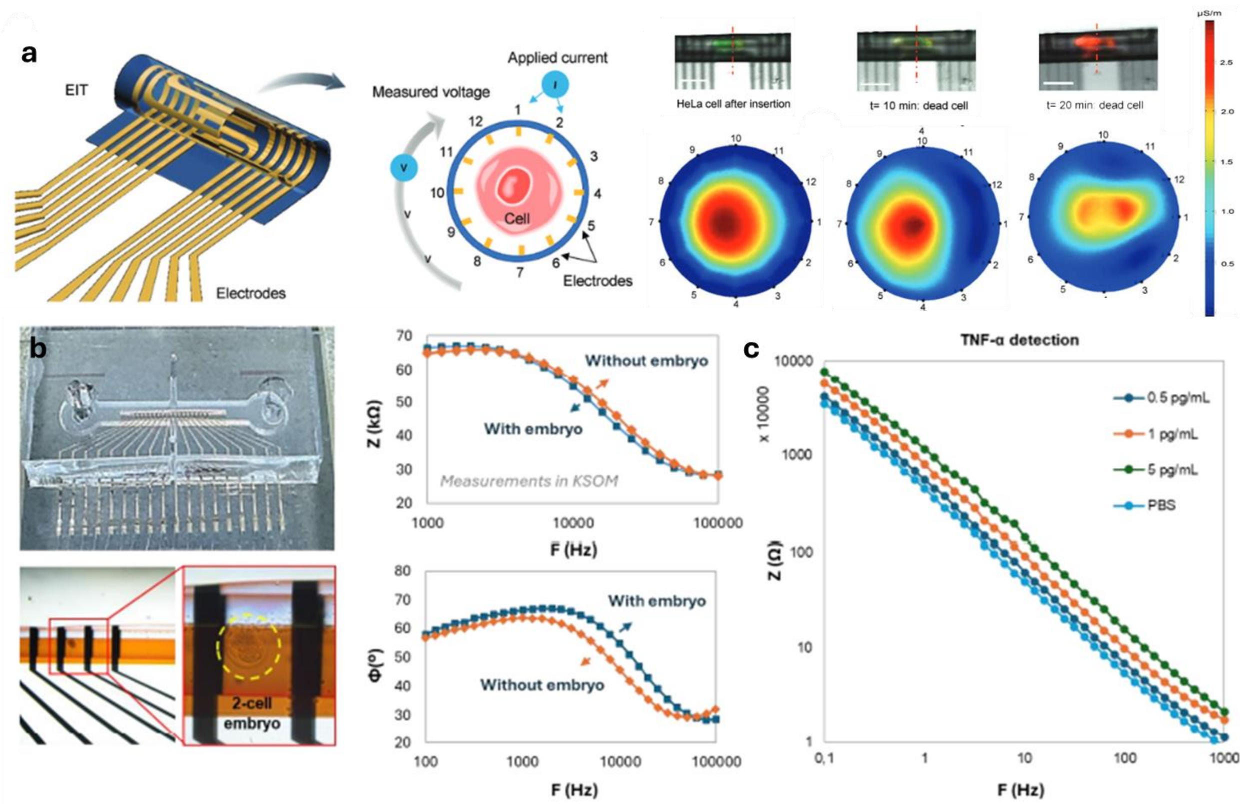

Figure 1: (a) Schematic of the rolled-up microtomography setup and measurement parameters, together with representative results for a HeLa cell undergoing necrosis. Green staining indicates a viable cell and its corresponding impedance tomography image, while red staining marks dead cells, associated with a decrease in conductivity likely caused by membrane rupture. Measurements done at 0.01X PBS. (b) Preliminary results on the fabrication of a microfluidic electrochemical impedimetric sensor for monitoring developing embryos in their native culture medium (KSOM), along with (c) molecular analyses for evaluating embryo implantation potential.