Advancing 3D Impedance Tomography for *In-Vitro* models

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Three-dimensional in vitro models, such as organoids and spheroids, have redefined biomedical research and drug development by more accurately replicating tissue complexity than conventional two-dimensional cultures. They enable tissue differentiation, disease progression, and drug response, but analysis remains difficult when seeking high-quality information across their full depth without damage. Micro-Electrical Impedance Tomography (µEIT), a label-free and non-destructive imaging modality, addresses this challenge by enabling non-invasive imaging while preserving tissue integrity [1].

In this study, we present the design of a µEIT platform for analyzing 3D *in-vitro* models. The system comprises three main modules: a 3D measurement interface, a signal acquisition unit, and an imaging unit. The measurement interface is a cubic biocompatible chamber with micro-electrodes integrated on each sidewall. During operation, the chamber is filled with culture medium, and the *in-vitro* model is placed inside for imaging. The signal acquisition unit features a reconfigurable switching matrix that controls current injection and voltage sensing, with the acquired data transmitted to the imaging unit for 3D impedance reconstruction. The platform operates over a frequency range of 1–100 kHz with current amplitudes of 10–100 µA.

To reconstruct 3D images, the platform employs time-differential EIT (TD-EIT), which reduces modeling and electrode-related errors by subtracting measurements at two time points. Conventional Gauss–Newton (GN) methods provide accurate reconstructions but are computationally expensive due to large Jacobian and Hessian matrices, especially in 3D EIT applications. To address this, we propose a matrix-free GN (MF-GN) method, which avoids explicit matrix storage and reduces computation complexity. Computation efficiency is further improved through adaptive meshing, applying a dense grid to the region of interest and a coarser grid to the background, ensuring high spatial resolution while minimizing cost.

An in-house prototype of the µEIT Cube was validated across a range of targets, demonstrating its capability to resolve both structural detail and dielectric contrast. In experiments with hydrogels and cerebral organoids, the system successfully distinguished the samples from the surrounding culture medium, confirming its applicability to biological models. Tests with multilayer targets, such as pomegranate seeds, further demonstrated accurate reconstruction of internal layers with distinct dielectric properties, closely matching the ground truth. Collectively, these results highlight the µEIT Cube's potential for 3D imaging of complex biological systems.

In conclusion, we present a non-invasive, label-free MEA-based platform for real-time, in-depth imaging of 3D *in-vitro* models, achieved through the integration of rapid measurement techniques and advanced reconstruction algorithms.

References:

[1] Deng, J., Renders, J., Meenaketan, B. L. P., Ebrahimi Takalloo, S., Braeken, D., De Beenhouwer, J., and Sijbers, J. (2024). IEEE Sensors Journal 24, 24452-24465.