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A bioimpedance-based sensing system for monitoring cellular dynamics in a 3D culture environment

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There is currently an increasing interest in developing sensitive analytical methods for real-time monitoring of the entire process of tissue engineering, starting from a bare 3D polymer scaffold, to cell attachment, growth and differentiation, up to the formation of vascularised organ-on-a-chip systems.

Bioimpedance has shown to be a powerful tool for the study and modeling of biological systems both in vivo and in vitro, establishing a physical correlation between bioelectrical measurements and tissue growth characteristics.

In this work, a bioimpedance-based 3D culture Lab-On-A-Chip (LOC) system is presented which is designed and optimized to investigate cellular dynamics occurring under in vitro tissue growth conditions. The novelty of this device is to enable label-free monitoring of real cell dynamics in a more physiological microenvironment mimicking the complex network of interactions taking place among cells and their matrix.

Since the important electrical characteristics of an electrode/tissue system are primarily determined by the electrode configuration, simplified finite element models were used to optimize electrode density and orientation within the 3D chip to enhance measurement sensitivity. Based on the simulation results, a prototype chip was developed with two opposite couples of vertical rectangular plate electrodes in a three-terminal configuration where current-carrying (CC) and pick-up (PU) electrodes could be switched between different positions to extend a positive sensitivity field to the whole bulk scaffold volume.

To demonstrate proof-of-concept, the bioimpedance-based LOC system was evaluated by growing different concentrations of mesenchymal stem cells embedded within a 3D gelatin scaffold. Preliminary results indicate that the presented device has a high potential for real-time monitoring of the entire process of tissue engineering without affecting cell viability.

Since different combinations of CC and PU electrodes can be exploited, this system will pave the way towards electrical impedance tomography applications enabling imaging of the changes occurring in 3D cell culture environments.