Nano Innovation 2023 Rome, 18-22 September Conference & Exhibition

# Detection of copper ions in Organ-on-Chip platforms via Anodic Stripping Voltammetry

E. Sciurti[1], C. T. Prontera[1] , C. De Pascali[1], L. Giampetruzzi[1], L. Blasi[1], V. Esposito[1], A. Calogiuri[1], D. Bellisario[1], P. A. Siciliano[1], L. Francioso[1]

[1]Institute for Microelectronics and Microsystems, Lecce, Italy.

Microfluidic devices known as Organ-on-Chip (OoC), which host living organs mimicking in vivo conditions, benefit greatly from the sensors integration, enabling the monitoring of specific chemical-physical parameters that can be correlated with biological processes. Real-time ions monitoring directly in cell culture systems represents a significant investigation tool to understand ion regulation and distribution in the body.

Copper is an essential trace mineral fundamental for our survival: dietary copper (largely in the form of $Cu^{2+}$) is absorbed by intestinal epithelium and its management and regulation is fundamental to preserve copper homeostasis in the whole body[1]. Imbalance of copper concentrations can be linked to specific pathologies.

Hence, real-time monitoring of $Cu^{2+}$ concentrations in cell culture media can be an important tool to study the processes of copper transport and uptake. Electrochemical methods are cheap, easy and fast and, in particular, anodic stripping voltammetry (ASV) is a powerful technique for trace analysis of metal ions, with low detection limits, good sensitivity, and selectivity [2].

In this study, the performance of ASV for copper detection in the complex cell culture media was evaluated, and a medium pre-treatment protocol of acidification was tested to improve the voltammetric signals intensity. First, the potential of the developed acidification protocol was evaluated by performing measurements with a real intestinal epithelial monolayer of Caco-2 cells in a Transwell® culture system.

Then, a microfluidic device was engineered in order to enable an automatic acidification of the cell culture medium in a separate sensing chamber without affecting the cell culture environment. A custom silicon microelectrode was integrated in the sensing compartment to perform a continuous ion monitoring in real-time.

To evaluate the integrity and differentiation of the intestinal epithelial monolayer Trans-Epithelial Electrical Resistance (TEER) data were recorded in chip via impedance spectroscopy analysis, across a selected spectrum of frequencies ($10–10^5$ Hz), and fitted with an equivalent electrical circuit.

The obtained microfluidic chip could be exploited to monitor the copper or different ions concentration in an organ-on-chip model; these functionalities represent a great opportunity for the strategic high-throughput experiments demand on biological systems, with conditions close to those in vivo.

[1] 1. Reznik, N.; Gallo, A.D.; Rush, K.W.; Javitt, G.; Fridmann-Sirkis, Y.; Ilani, T.; Nairner, N.A.; Fishilevich, S.; Gokhman, D.; Chacón, K.N.; et al. Intestinal Mucin Is a Chaperone of Multivalent Copper. Cell 2022, 185, 4206-4215.e11. https://doi.org/10.1016/j.cell.2022.09.021

[2] A.J. Borrill, N.E. Reily, J. V. Macpherson, Addressing the practicalities of anodic stripping voltammetry for heavy metal detection: A tutorial review, Analyst. 144 (2019) 6834–6849. https://doi.org/10.1039/c9an01437c

**Bio-sketch**

Elisa Sciurti was born in Zurich, Switzerland, in 1991. She received the M.Sc. degree in biology from the University of Salento, Lecce, Italy, in 2016, and the Ph.D. degree in Materials and Structural Engineering and Nanotechnology from the University of Salento and Italian Institute of Technology (IIT-CBN), Lecce, Italy, in 2020. Since 2021, she has been a Postdoctoral Fellow with the Institute for Microelectronics and Microsystems (IMM), National Research Council (CNR), Lecce. Her research interest focuses on the development of electrochemical sensors for biomedical applications, Lab-on-a-chip devices and energy storage systems.