Development of *in vitro* biomimetic environments for the regeneration of the nervous tissue

Antonis Kordas[1,*], Maria Farsari[1], and Anthi Ranella[1]

[1] Institute of Electronic Structure and Laser, Foundation for Research and Technology-HELLAS (FORTH/IESL), N. Plastira 100, Vassilika Vouton, 70013, Heraklion, Crete, Greece
[*]Corresponding author email: antkor89@iesl.forth.gr

The field of Tissue Engineering (TE) revolves around the recovery of lost function of tissues due to causes such as trauma or disease. Strategies that implement the use of cells from patients as the donor have been developed to mimic the native Extra-Cellular Matrix (ECM) of the damaged site for the creation of functional autografts that will be surgically inserted in the organism and restore normal tissue activity. A prominent case of TE application is the restoration of the nervous system. We demonstrate the development of *in vitro* environments that implement scaffolds with specific topographies that guide the elongation of axons of neurons and will be used as *in vitro* experimental models for the study of neurodegenerative diseases and development of counter-strategies. Scaffolds were fabricated via Two-Photon Polymerization (2PP) and the approach was enhanced with strategies such as co-culturing (Figure 1C-D) [1] and electrical stimulation (Figure 1G-H). The combination of scaffold topography and the aforementioned approaches had a clear effect towards axon guidance and functional neural networks, while avoiding toxicity, contaminations and cell death, showcasing the ability of the proposed models to achieve biomimesis.

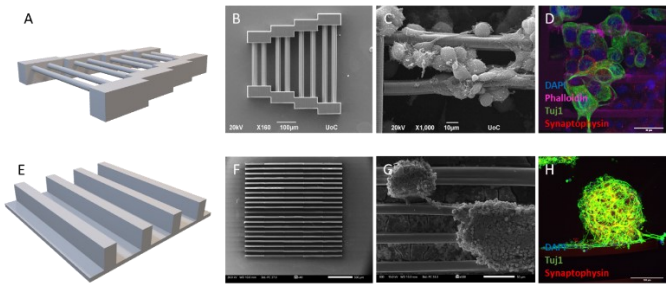

Figure 1: Development of *in vitro* biomimetic environments combining scaffolds fabricated with 2PP with co-culturing (**C-D**) and electrical stimulation (**G-H**). **A, E:** STL representations of the scaffolds. **B, F:** 2PP scaffolds. **C, D:** SEM and confocal images of co-cultures towards a functional network. **G, H:** SEM and confocal images of electrically stimulated NE-4C stem cells.

Acknowledgements: The implementation of this work was co-financed by Greece and the European Union (European Social Fund-ESF) through the Operational Programme «Human Resources Development, Education and Lifelong Learning» in the context of the Act "Enhancing Human Resources Research Potential by undertaking a Doctoral Research" Sub-action 2: IKY Scholarship Programme for PhD candidates in the Greek Universities.

References:

[1] A. Kordas, P. Manganas, A. Selimis, G.D. Barmparis, M. Farsari, A. Ranella, Development of an Oriented Co-Culture System Using 3D Scaffolds Fabricated via Non-Linear Lithography, Materials (Basel). 15 (2022) 4349. https://doi.org/10.3390/ma15124349.