A fluidic and visualization platform for long-term and real-time electrophysiological monitoring of 3D Human neural tissues at air-liquid interface

HEPIA RA&D

Poster ID: F-082

Adrien Roux[*1], Marc O. Heuschkel[1], Shaginth Sivakumar[1], João Pinheiro Marques[1], Loris Gomez Baisac[1], and Luc Stoppini[1]

[1] Tissue Engineering Group, HEPIA HES-SO University of Applied Sciences and Arts Western Switzerland, Geneva, Switzerland.

*Corresponding and presenting author: adrien.roux@hesge.ch

EUROoCS CONFERENCE 2024

Introduction :

The development of organoids requires the adaptation of several readouts specifically developed for 3D tissues. The possibility to grow organoids on Micro-Electrode Arrays (MEA) is limited by the need to immobilize the tissue on it and to keep proper oxygenation at the same time. The use of an Air-Liquid Interface (ALI) and the continuous perfusion of medium are two strategies to maintain sufficient oxygenation of long-term 3D cultures. Lack of oxygenation leads to a necrotic darkened center in the organoids, which is visible by brightfield microscopy.

Our laboratory has established protocols to generate reproducible 3D neural tissues (containing neurons and glial cells) and to culture it for long periods of time (up to more than two years) under rotation [1]. A data acquisition system for electrophysiological monitoring of the 3D tissues on ALI MEA devices has also been developed in-house and was previously reported [2]. A novel platform based on two additional optimized modules, a Visualization unit and a Fluidic unit, has been developed recently. These previous developments in combination with this recently developed dedicated imaging and perfusion platform allow performing long-term (for more than 2 months) non-invasive and real-time electrophysiological monitoring of 3D neural tissues.

Biology and Technology :

The Fluidic unit contains one to four pumps and one to four pinch valves, which enable the change of medium and the injection of sample/test compounds in a controlled manner. All parts of the resulting 3D neural tissue monitoring system are controlled by a computer. Additionally, the user interfaces of the fluidics and the visualization unit are also available on a tablet. All the units of this system can also function independently.

The main challenges addressed by this platform relate to maintaining ALI conditions, avoiding contamination, air bubble formation, necrosis, and maintaining the electronic device in a humid incubator. This platform is already used successfully in 3 different laboratories specializing in biological informatics, pharmacology or toxicology, and has been used internally for an in vitro model of traumatic brain injury [3].

Figure 1 *Overview of the whole 3D neural tissue monitoring system.*

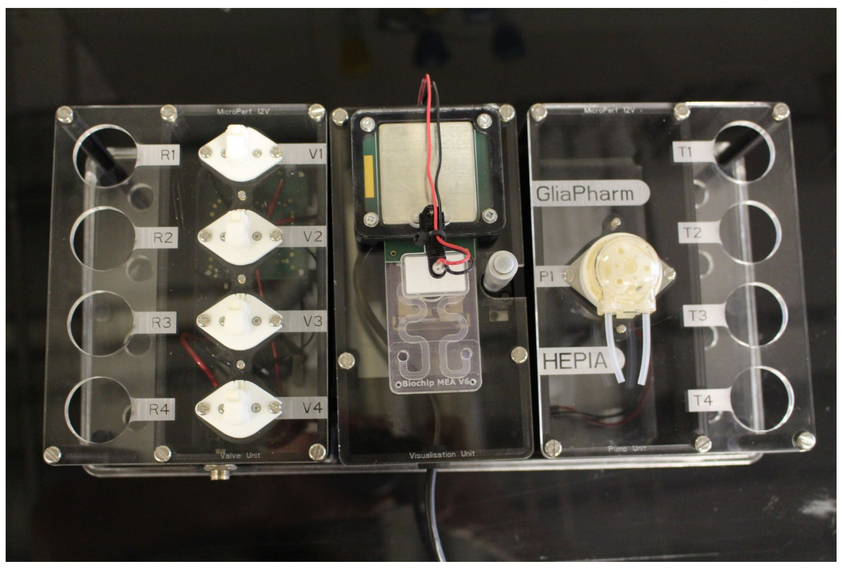

Figure 2 *Top view of a platform with 4 pinch valves and a single pump. This platform is currently used at GliaPharm SA.*

Figure 3 *User interface of the Fluidic unit of the platform.*

Figure 4 *MEA biochip composed of a porous membrane (yellow part of the device) comprising four recording areas with eight electrodes at each.*

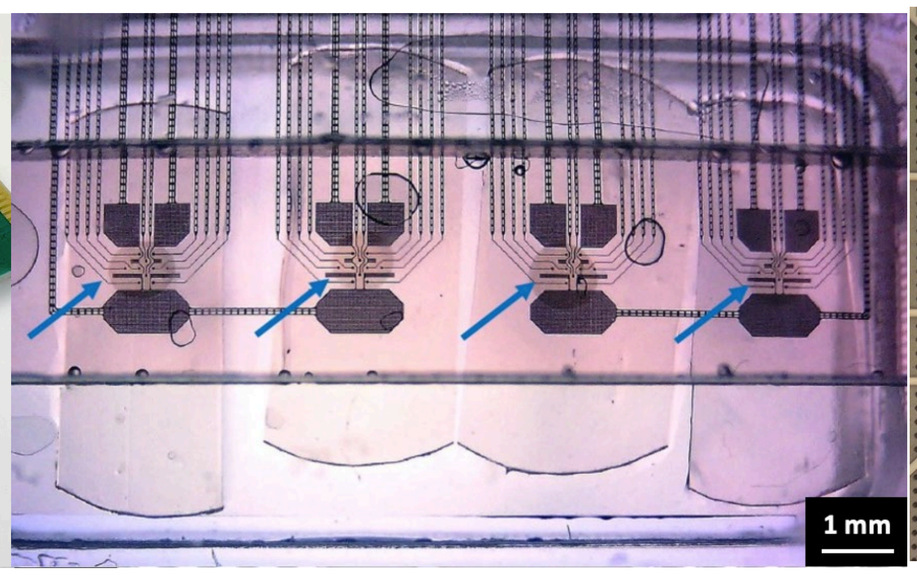

Figure 5 *Image taken from the visualization unit showing four independent 3D neural tissues at ALI (arrows) on the MEA biochip.*

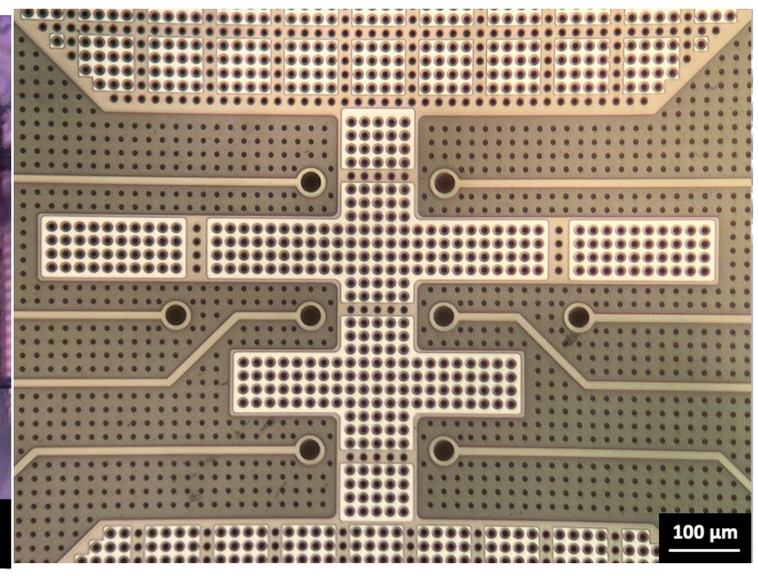

Figure 6 *Magnified view of one recording area composed of eight low impedance micro-electrodes coated with porous platinum black.*

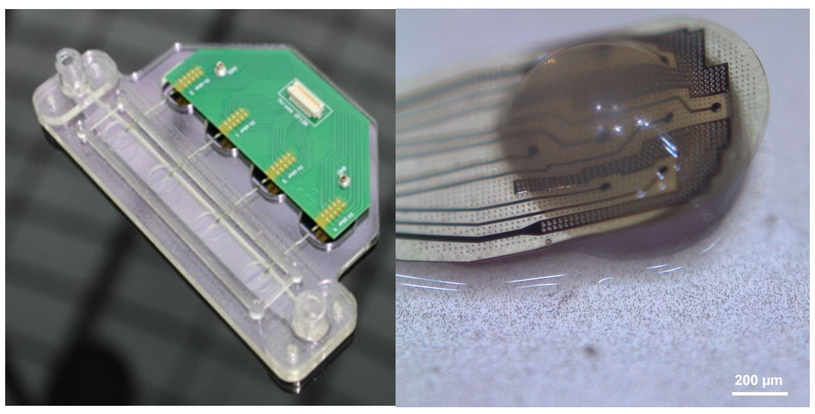

Figure 7 : Strip-MEA embedded between two neural tissues.

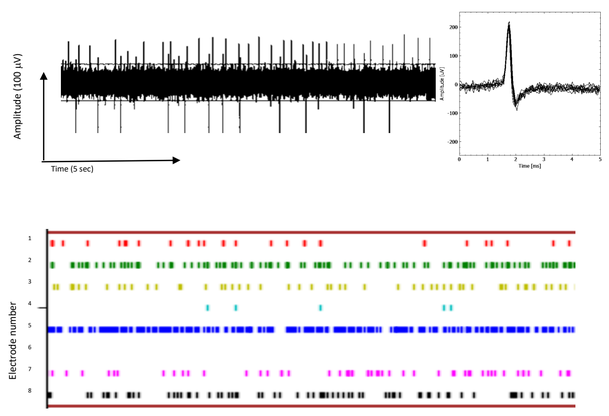

Figure 8 : Raw data recorded during 15 seconds at day 3 with the MEA platform showing spontaneous activities in the strip-MEA biochip.

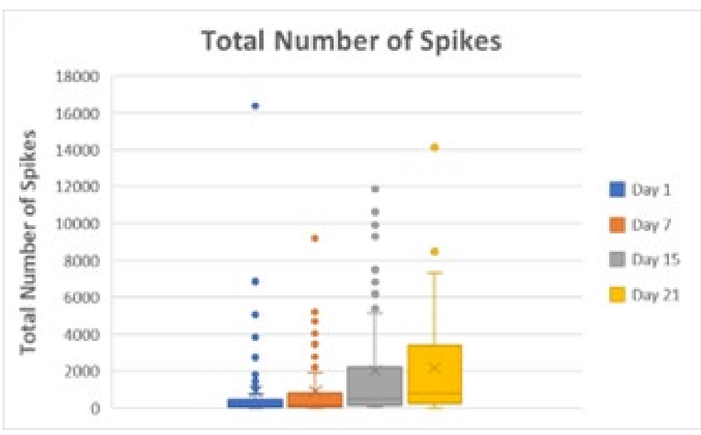

Figure 9 : Long term monitoring - Boxplots showing amplitudes of spikes peak-to-peak at days 1, 7, 15 and 21.

Conclusion : *HEPIA has built a fluidic platform suitable to welcome several type of MEA biochips. This platform allows long term monitoring, drug injection or medium change.*

Acknowledgments
Supported by the HES-SO (Delemont, Switzerland) (Grants: MicroPerf and Coat&Check).

References

[1] S. Govindan et al., Frontiers in Bioengineering and Biotechnology (2021)
[2] R. Wertenbroek, et al., IEEE Transactions on Biomedical Circuits and Systems (2021)
[3] C. Loussert-Fonta et al., Frontiers in Neuroscience. (2023)
[4] L. Stoppini et al., Frontiers in Cellular Neuroscience (2024)

h e p i a
Haute école du paysage, d'ingénierie et d'architecture de Genève

campus biotech

Hes·so
Haute Ecole Spécialisée de Suisse occidentale