Deep Brain Stimulation and Astrocytic Dynamics: Advancing from 2D cultures to 3D Brain Organoids

João Pinheiro Marques[1†], A. Pautrat[2], E. Garretas[1], M. O. Heuschkel[1], L. P. Magistretti[2], A. Roux[1*]

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

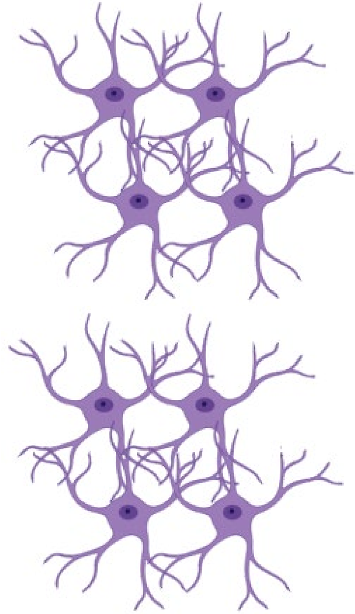
[2] Fonds de dotation Clinatec, Université Grenoble Alpes, Grenoble, France.

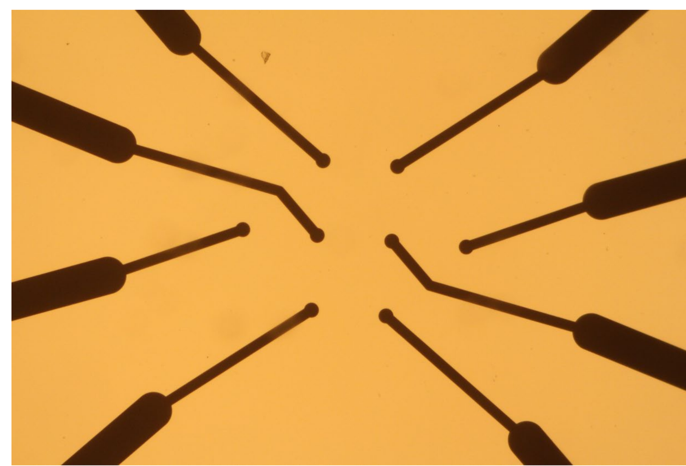
*Corresponding author: adrien.roux@hesge.ch † **presenting author**: joao.marques@hesge.ch

HEPIA RA&D

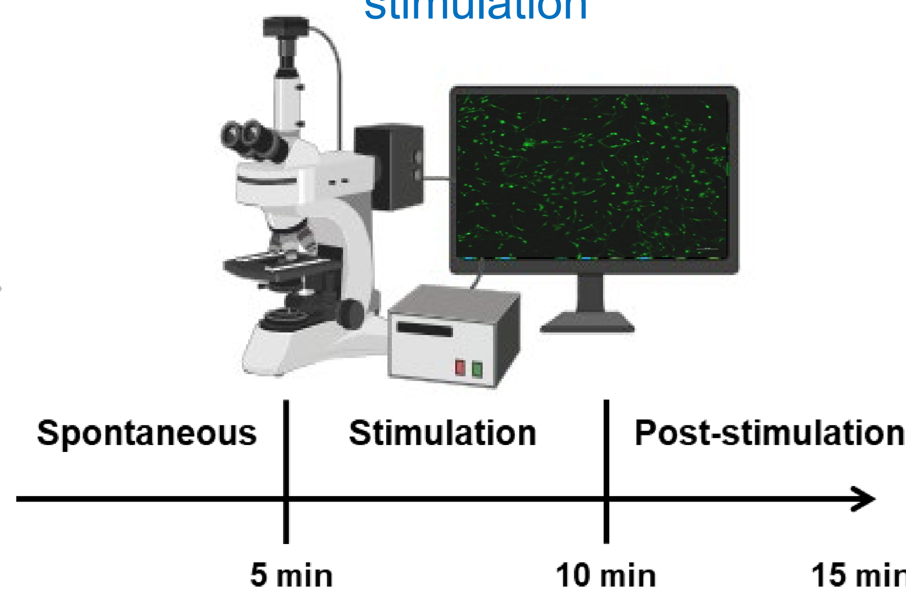
Introduction *: Deep Brain Stimulation (DBS) is an established neuromodulation technique with application extending from movement disorders like Parkinson's disease to major depression, chronic pain, and refractory epilepsy. While it offers symptom relief, the mechanisms underlining its therapeutic effects remain unclear, affecting efficacy and side effects. Traditionally, DBS has been viewed as a modality targeting neurons but mounting evidence indicates that astrocytes exhibit dynamic changes during stimulation, suggesting a critical role of astrocytes in mediating local and network-level DBS effects. To aid researchers evaluate the effects of DBS on astrocytes, we have developed tools dedicated to study astrocytic calcium dynamics during DBS in vitro and validated them using human induced pluripotent stem cell (hiPSC)-derived astrocytes on glass micro-electrode arrays (MEAs).*

Human iPSC-derived astrocytes

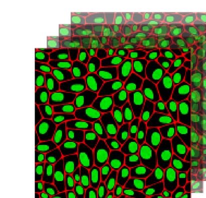


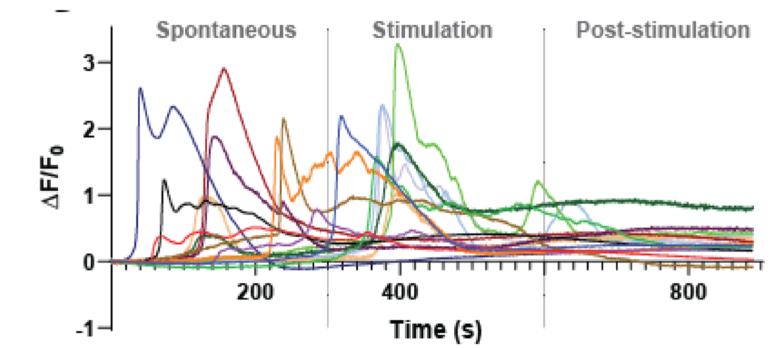


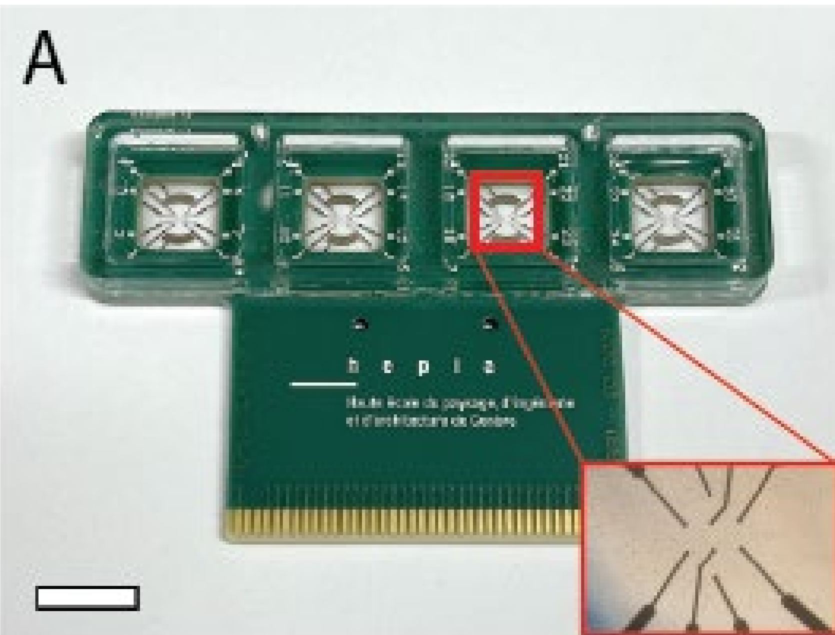
Calcium imaging during electric stimulation



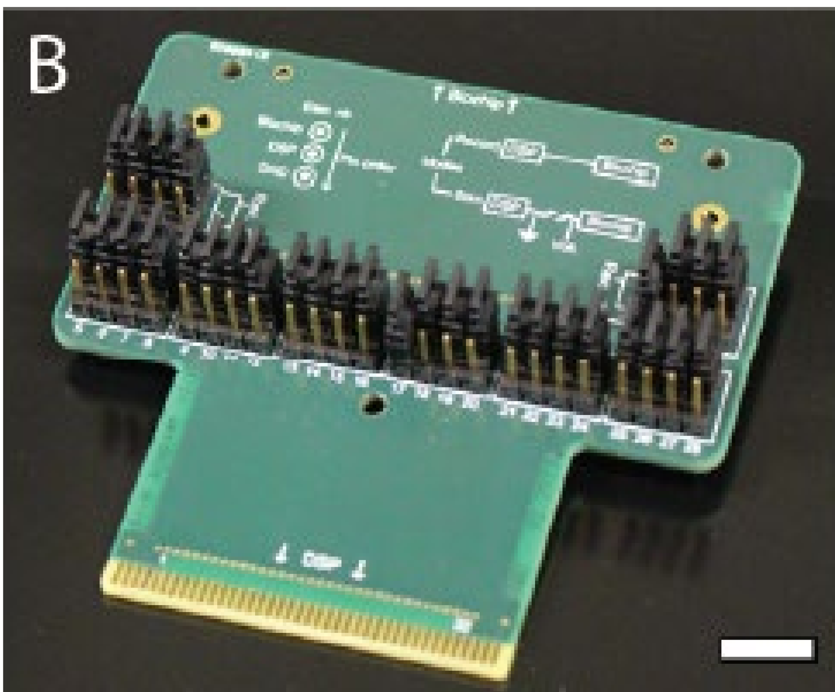
Analysis pipeline



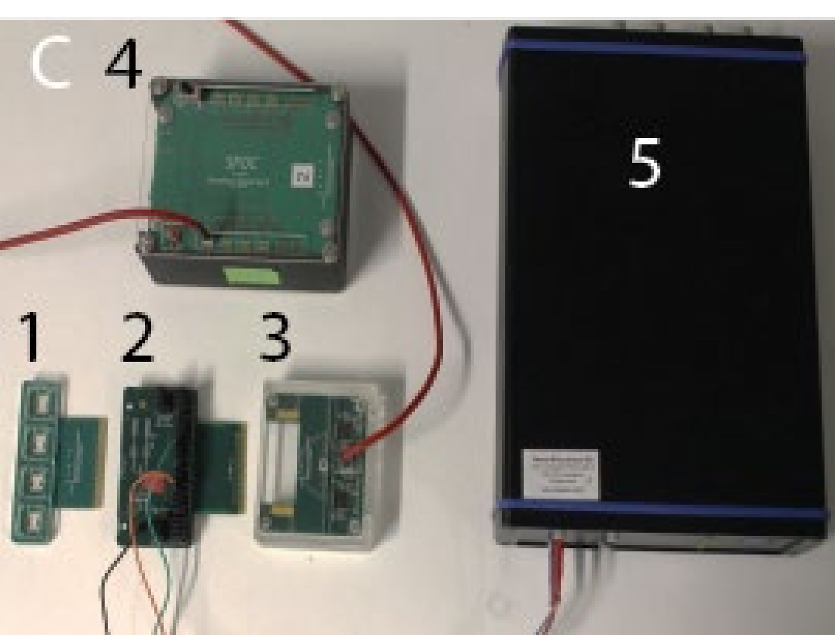




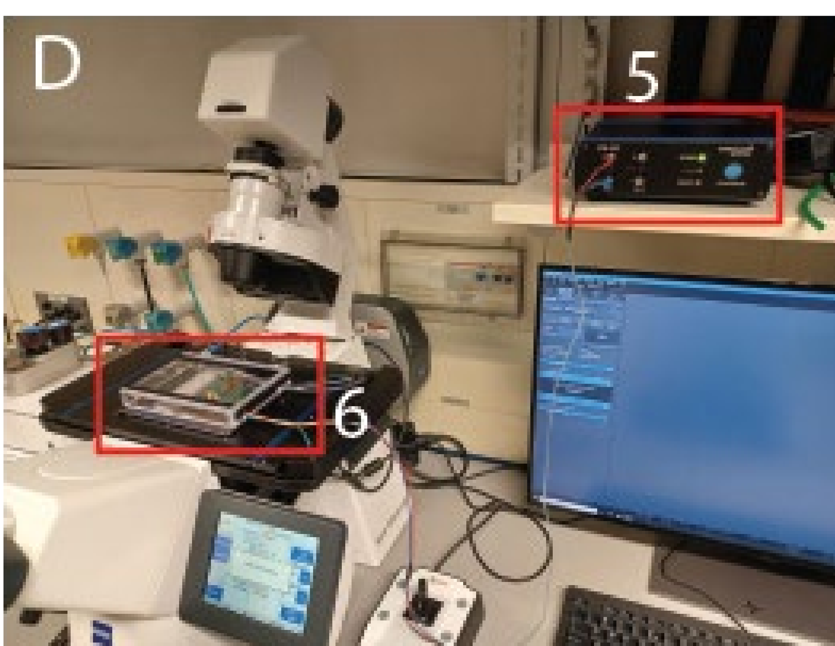
Experiments were conducted using hiPSC-derived astrocytes cultured on custom-made transparent MEAs, called MEA32-4x8. Scale bar: 1cm.



Custom stimulation interface connects the MEA32-4x8 to the constant current stimulator. Scale bar: 1cm.

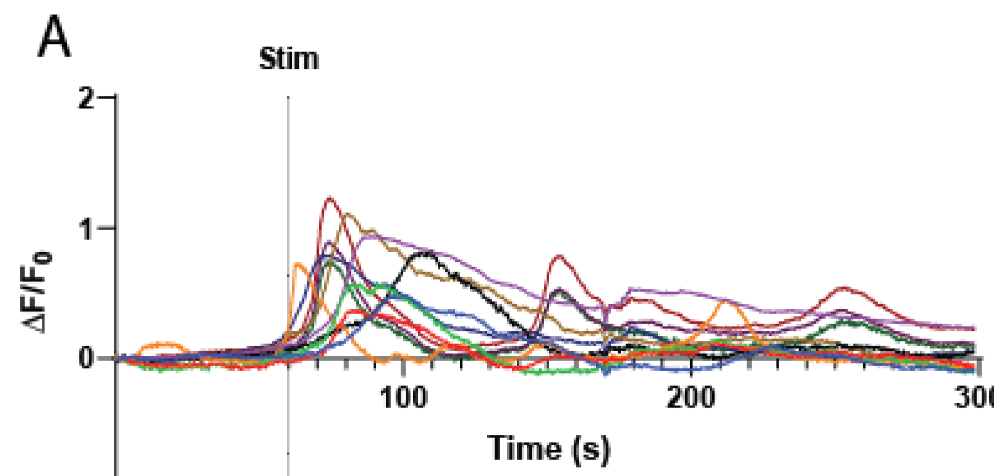


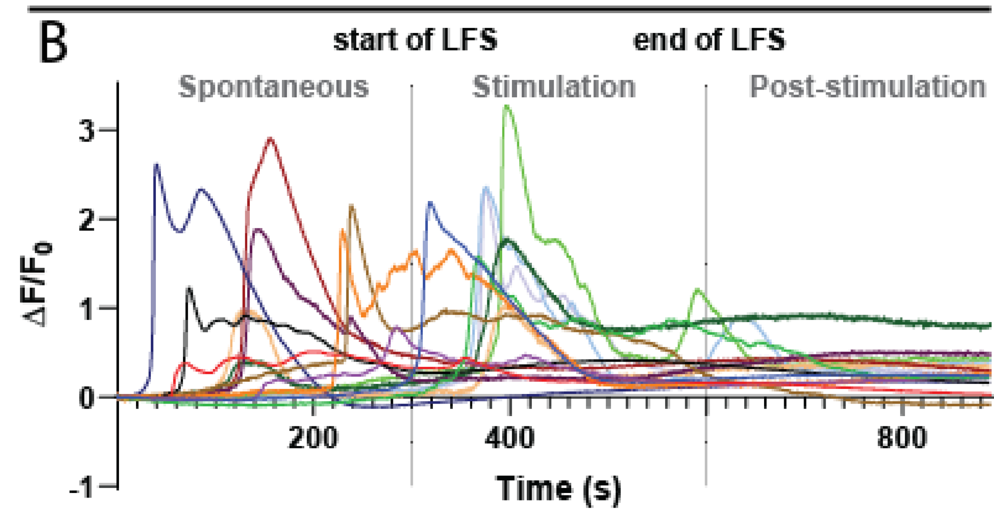
1) *MEA32-4x8*
2) *Stimulation interface*
3) *32-channel signal amplifier*
4) *SPOC data acquisition system*
5) *Constant current stimulator*

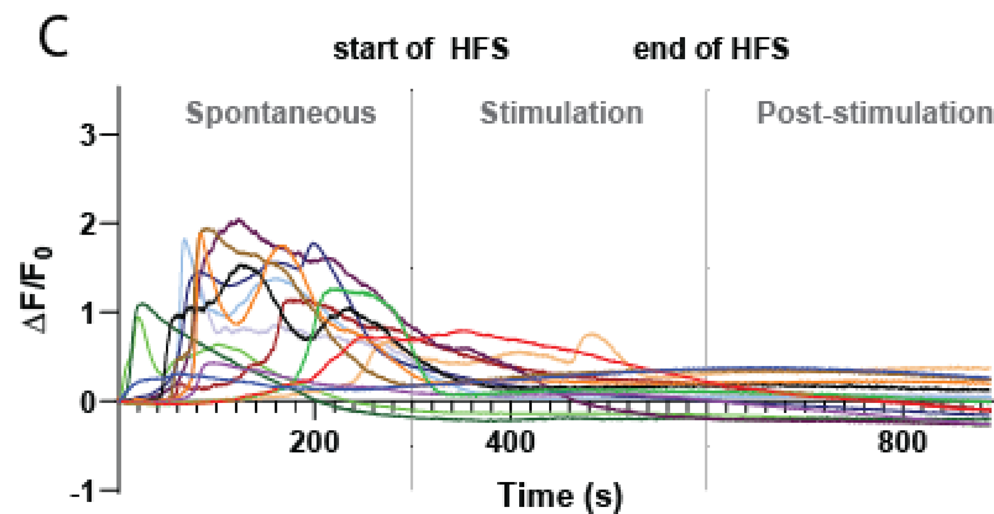


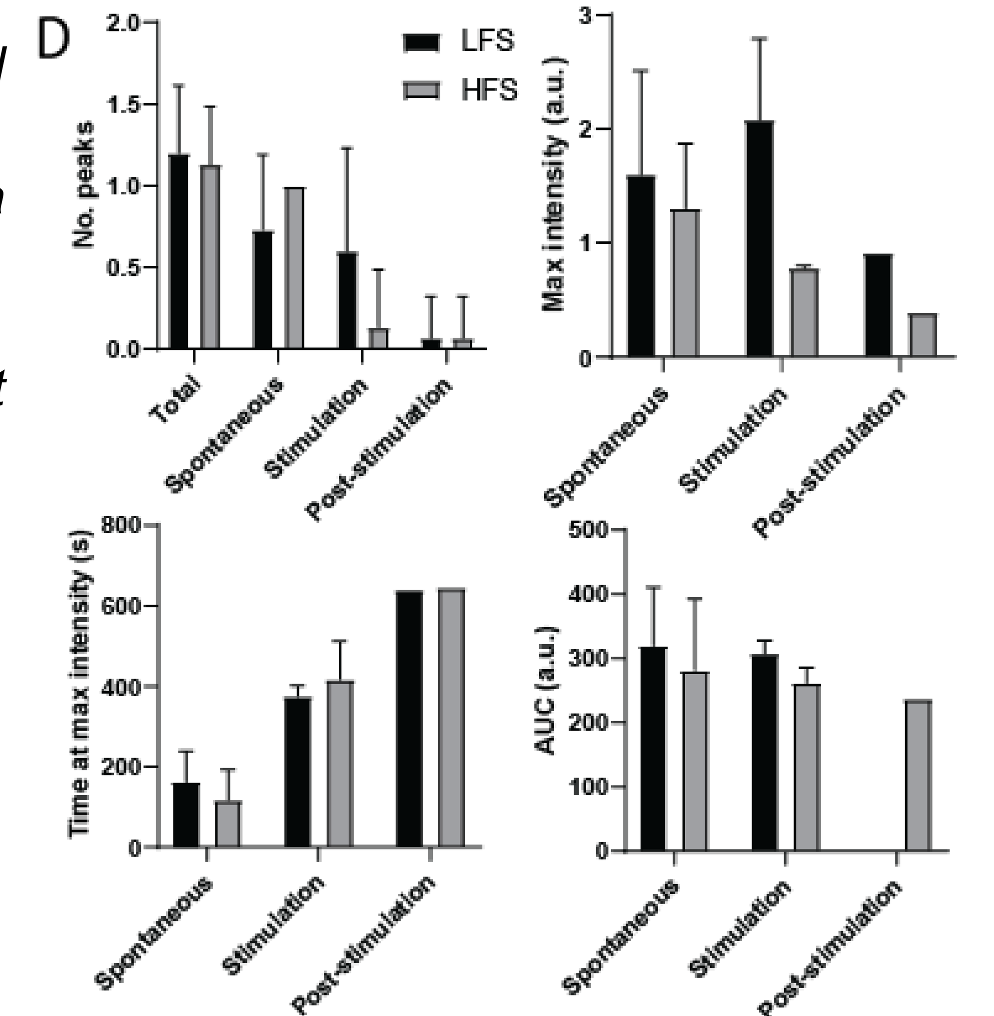
MEA32-4x8 and stimulation interface (6) are compatible with fluorescence microscopes.

5) Constant current stimulator

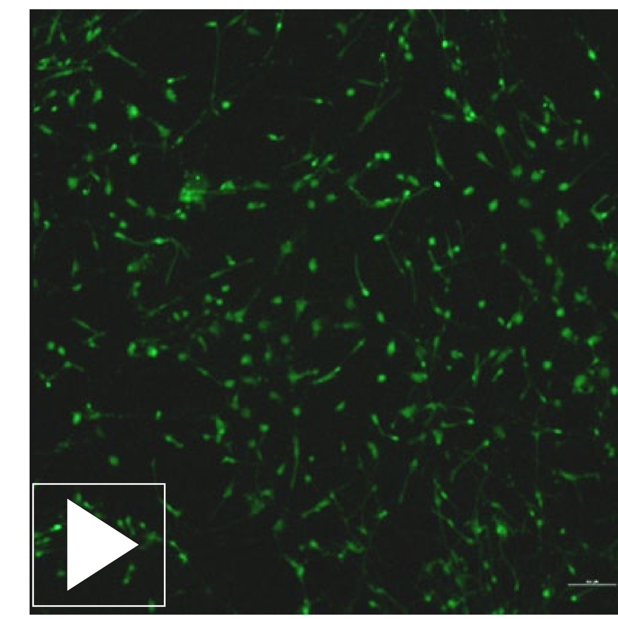




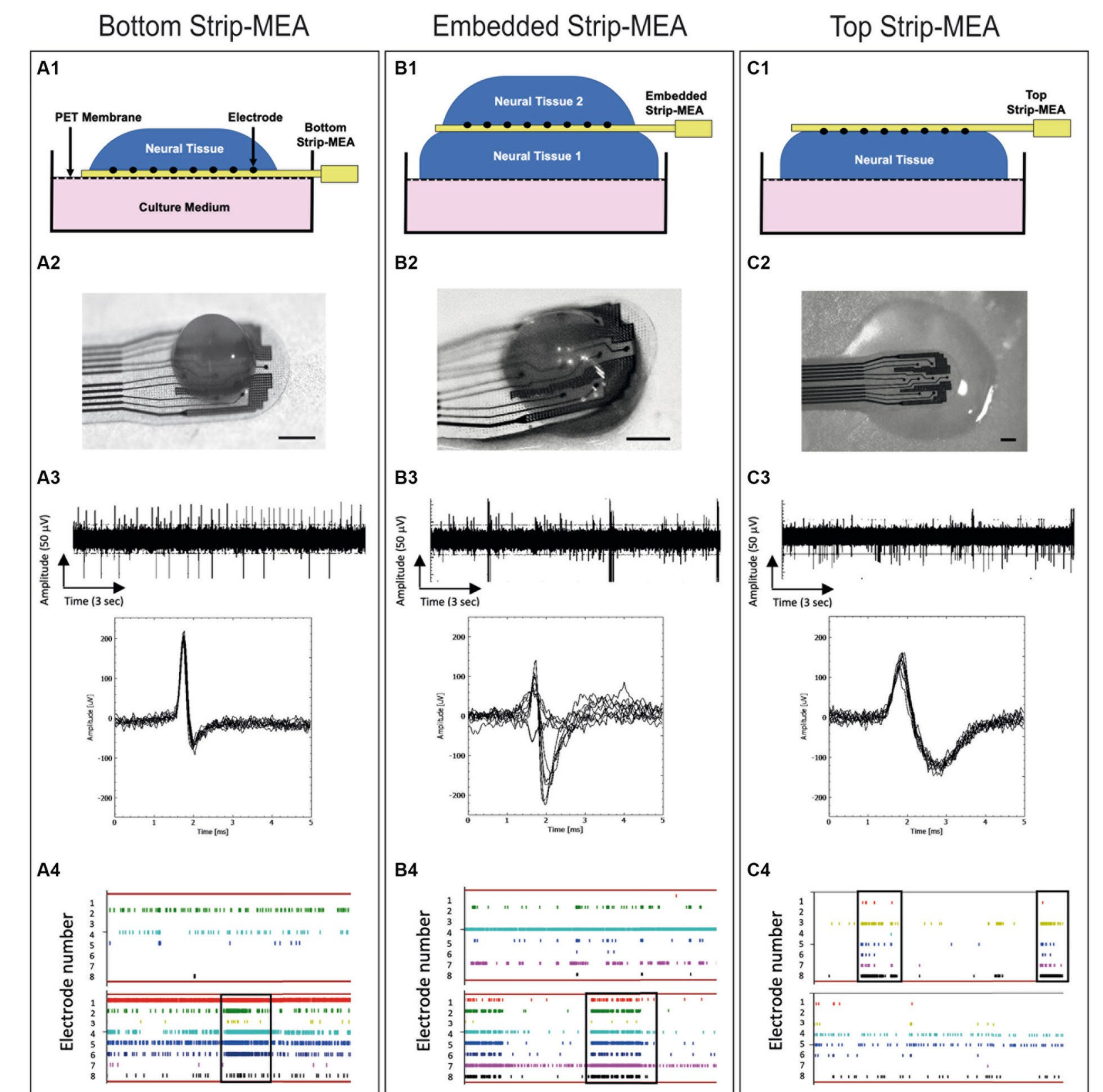




A) Fluorescence intensity changes over 5 min of 10 astrocytes stimulated once at 60 s. B, C) Fluorescence intensity changes of 15 astrocytes before, during and after Low Frequency Stimulation or High Frequency Stimulation. D) Parameters measured using our own Fluorescence_analyser script. Error bars represent standard deviation.



Scan to play video



Schematic views and pictures of different recording configurations of the Strip-MEA; examples of raw data recorded from 3D neural tissues; and raster plots showing neural activities recorded over time. From: Stoppini L, et al. Versatile micro-electrode array to monitor human iPSC derived 3D neural tissues at air-liquid interface. Front Cell Neurosci. 2024 May 9;18:1389580.

Conclusions *: Here we demonstrate the capabilities of the developed tools to electrically stimulate cells, acquire calcium imaging data and analyse it in a semi-automated manner. Additionally, we have previously developed technology capable of recording and electrically stimulate 3D tissues. We intend to integrate our tools developed to assess 2D cellular calcium dynamics with our 3D MEA technology to research effects of DBS on specific structures of brain organoids.*

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

campus biotech

FONDS CLINATEC

Hes·so Haute Ecole Spécialisée de Suisse occidentale