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In vitro neural tissue testing platform using Micro-Electrode Arrays

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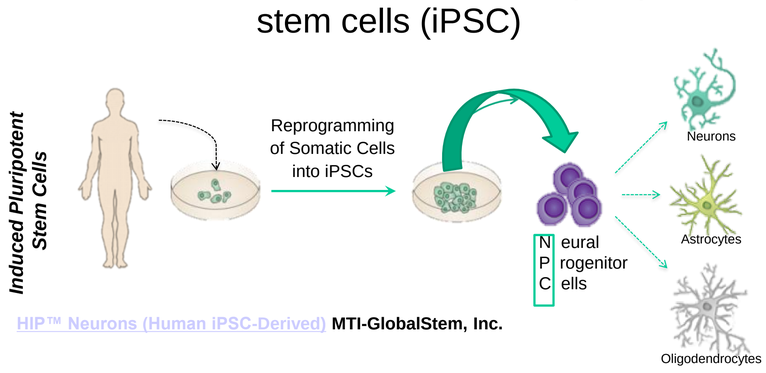
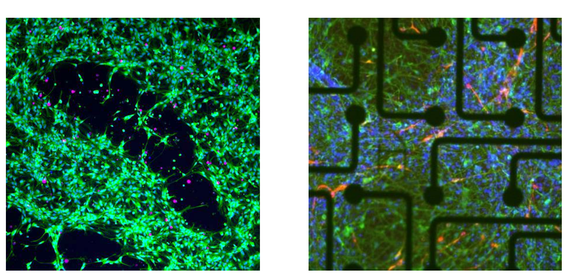
Today, drug discovery and toxicity assessment of compounds/molecules is still lacking efficient methods and biological models allowing relevant long-term effects of compounds to be discovered and evaluated, especially when linked to the brain. A novel electrophysiology platform addressing this need by *in vitro* monitoring of 3D tissues derived from human iPS cells has been developed. As it generates very large amounts of data, efficient and fast data analysis methods allowing relevant feature extraction have been developed.

In vitro human tissue model: 2D and 3D cell/tissue cultures from iPS cells

Neural tissue derived from human pluripotent stem cells (iPSC)

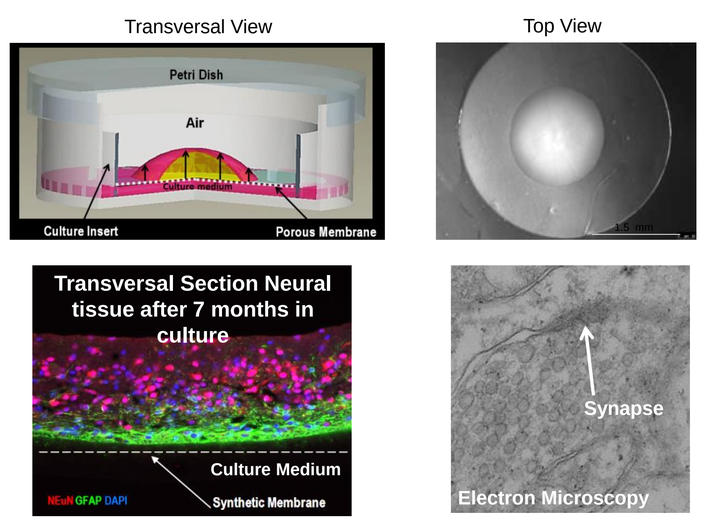


2D neural tissue derived from human pluripotent stem cells (iPSC) can be cultured in dishes.

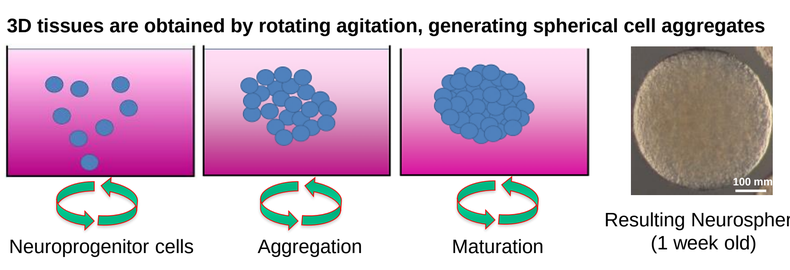


Immunolabelling of neuronal cells with anti-Tub3 (Green) and anti-GFAP (red) antibodies

3D neural tissues are cultured over very long time periods at air-liquid interface on porous membranes.



3D tissues are obtained by rotating agitation, generating spherical cell aggregates

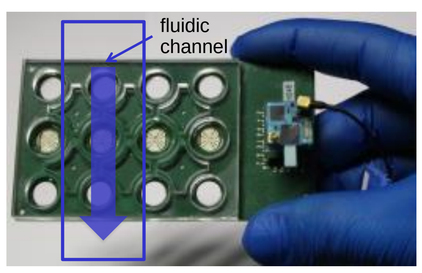


Neuroprogenitor cells — Aggregation — Maturation — Resulting Neurosphere (1 week old)

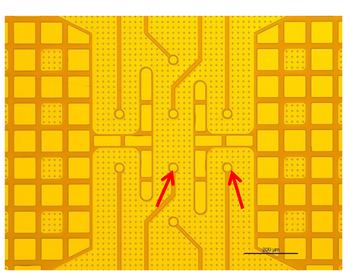
Electrophysiology recording system based on Micro-Electrode Arrays (MEA)

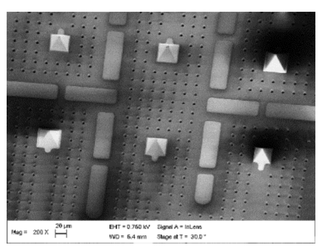
Microfabricated porous MEA devices integrating 2D or 3D platinum electrodes geometries.

Wellplate format MEA device

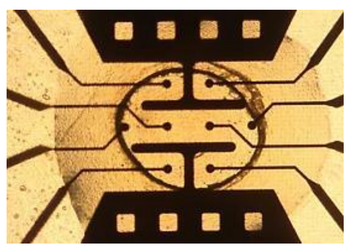


Micro-electrodes (arrows) on porous polyimide membrane (thickness 8µm)





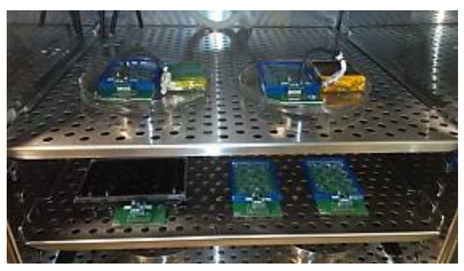
3D pyramidal electrode geometry



3D neurosphere on MEA

Data acquisition of electrical activity with stand alone WiFi system

WiFi Receiver — Headstage amplifier

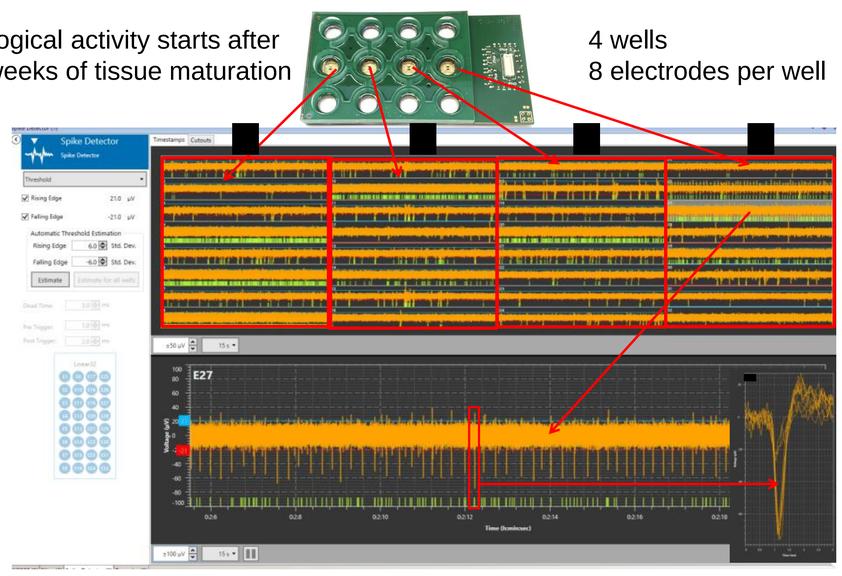


Several devices located in an incubator

Display of typical electrical signals recorded from the 32-channel data acquisition system (raw data)

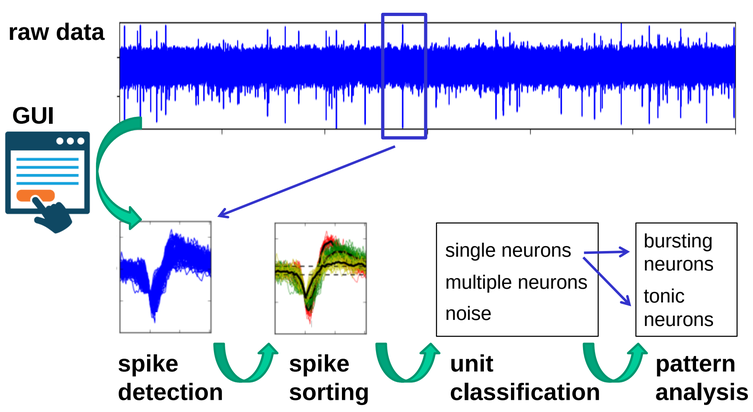
Biological activity starts after 6-8 weeks of tissue maturation

4 wells
8 electrodes per well

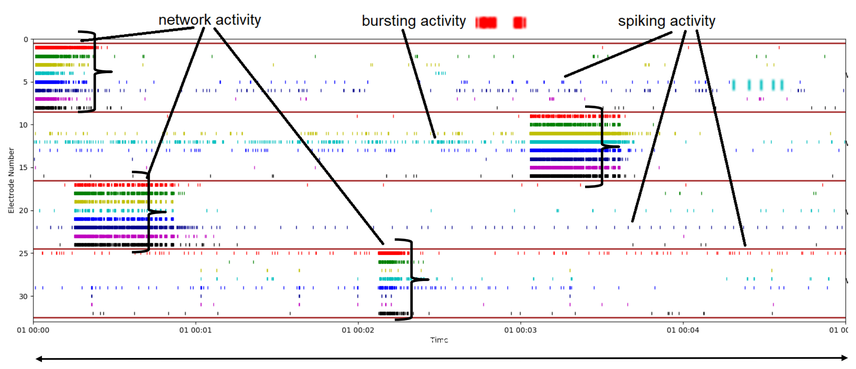


Data analysis tools and biological results

Semi-automated high throughput data analysis platform to reduce data analysis burden.

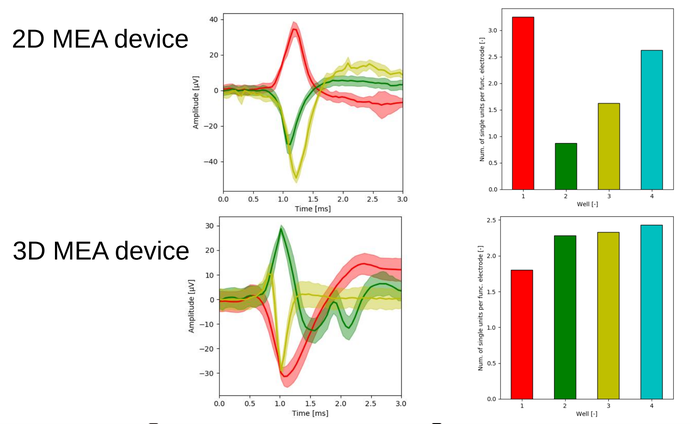


Data analysis and feature extraction from activity raster plots.



- Mean firing frequency of **spikes** (single/multiple neurons)
- Mean frequency of **burst activity**
- Mean frequency in **network activity**
- Duration mean of **network activity**

Typical biological signal shapes and activity levels from 2D and 3D MEA devices.



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