

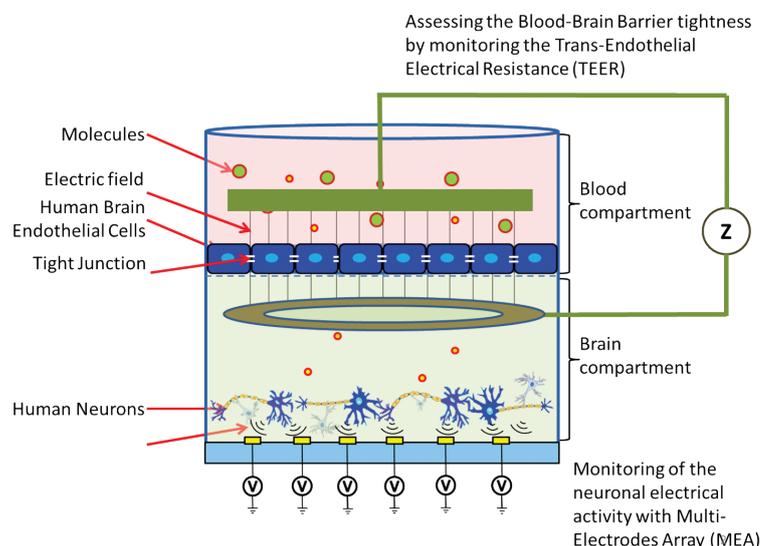
MEASURE

Integrated monitoring of the *in vitro* Neurovascular Unit

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Brief description

The main objective of this project was to develop an innovative “one step” *in vitro* assay technology for assessing human Blood Brain Barrier (BBB) integrity and effects on human neural tissues. This model is adapted to assess not only acute exposures to compounds but also repeated exposures (mimicking chronic treatment) to compounds, since most of central nervous system treatments require the latter type of exposures to be efficient or to show neurotoxicity.



Representation of the *in vitro* model of the Neurovascular Unit with its non-invasive monitoring

As the world’s population is aging, diseases of the central nervous system (CNS) become an increasing threat for global health as the total annual cost resulting from CNS diseases is quickly escalating. The development of drugs against CNS has one of the highest failure rates and longest development times. One reason for this poor success is that CNS drugs have to cross the blood brain barrier (BBB) before reaching the neural tissue. This complexity is worsened by the fact that there is currently no *in vitro* system to simultaneously test whether a substance can cross the human BBB and adequately affect the adjacent human neural tissue.

The project MEASURE addresses this problem. We have developed a device allowing the tissue engineering of an artificial human neurovascular unit (NVU), i.e. an *in vitro* model comprising both the neural tissue and the BBB. This device allows the simultaneous monitoring of the two components of the model and their pharmacological testing. This innovative solution aims at increasing the success rate of CNS drug development by facilitating and speeding up the drug discovery process and screening potential neurotoxic molecules present in our environment.

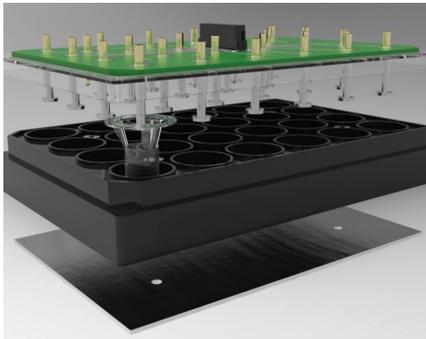
This device combines a system to simultaneously record neuronal activity with a system to measure the blood-brain barrier permeability. A Micro-Electrode Array (MEA) unit allows the electrophysiological recording of neural cultures sitting at the bottom of a standard 24-well plate and a Trans Endothelial Electrical Resistance (TEER) unit allowing the recording of the electrical impedance of a cultured BBB positioned just above.

The device is a unique standalone system able to work autonomously in an incubator, data being transmitted wirelessly or stored locally within the device. The device is also versatile and amenable for MEA recording, TEER recording or both simultaneously.

Key points

The innovative solution was to combine in a standalone device a system to measure the impedance of the barrier integrity to obtain the Trans Endothelial Electrical Resistance (TEER) and to record simultaneously *in vitro* the neuronal activity of neurons with a Micro-Electrode Array (MEA) unit.

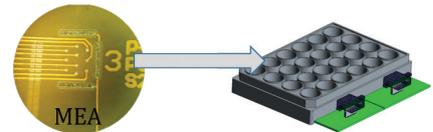
The novelty of this device is to combine two non-invasive measurements of the neurovascular unit, but each part of the device (MEA and TEER) can also be used independently, increasing the potential use.



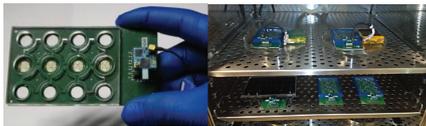
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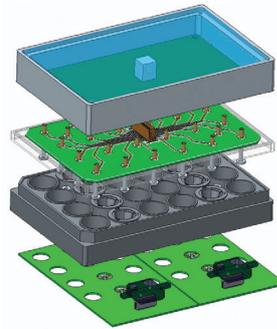
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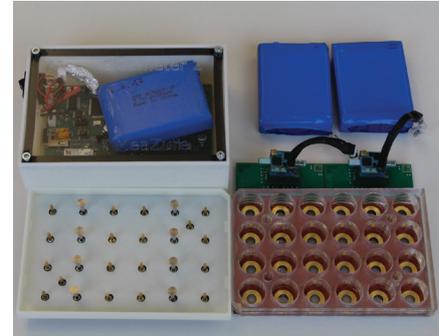
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Output

Our innovative integrated *in vitro* system has been presented in several international conferences. An invention announcement has been filed at Unitec (Technology transfer structure from HEPIA) and a process for the commercialization of the TEER device has started.

This works also led to several new projects such as a collaboration with private companies (Vivent), a public institution (Agroscope), a not for profit organization (Wyss Center) and a HES-SO project (Spike on Chip).

Special equipment

The electronic Xilinx Zynq-7000 has been developed by EIA-FR and the know-how based on Zync architecture with this system could be implemented in other projects.

The TEER device is compatible with other *in vitro* biological barriers such as the intestinal barrier or the respiratory epithelium.

Légendes

- 1 - Computer Assisted Design of the TEER device showing the cell insert inside the plate with electrodes.
- 2 - Picture of the TEER device with Electronic software and cell culture plate containing the electrodes.
- 3- Computer Assisted Design of the MEA device showing the network of electrodes inside the well plate.
- 4 - Picture of the standalone MEA device (Left) and its application in a cell culture incubator (Right).
- 5 - Computer Assisted Design of the MEAZURE device showing the MEA and the TEER part.
- 6 - Picture of the prototype of the MEAZURE device to measure the TEER and the electrophysiology.