Why Biologists need microtechnology : The example of "Organ-on-a-Chip"

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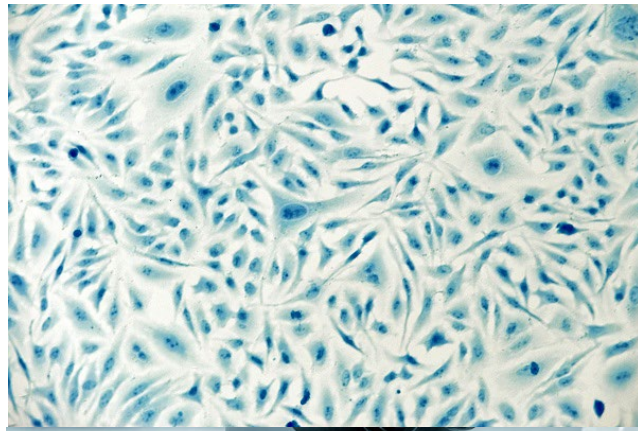
EPHJ, 15th September 2021

Scientific pitch - inSTI institute

L'avenir est à créer

Traditional cell culture for biologists

- "**Cell culture**" refers mainly to the culturing of animal cells mainly on **Petri dishes** to maintain the sterility
- **Incubator** to reproduce the physiological environment
- Cell culture **medium** to provide nutriments
- Readouts : optical (**Microscopy)** and biochemical (sampling by **pipetting)**



Evolution: Increasing the throughput

- by miniaturisation & standardisation
- by multiplexing
- by automation

6/12/24/48/96-wellplate

384-wellplate

Integration in Robotic platform

Automatic pipetting

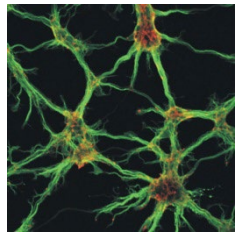
1536-wellplates

Robust, highly reproducible, low cost, quick tests
But => Low predictivity on Human

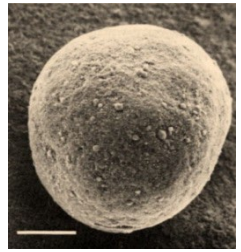
New Trend : move to more predictive models

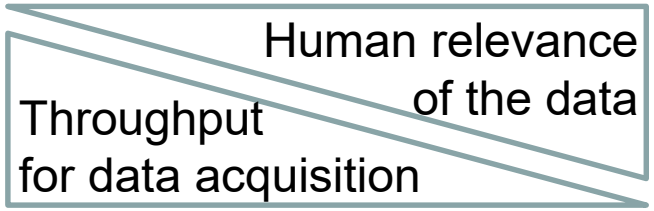
- **More functional readouts :** integration of electronics and use of bio-informatic tools to analyse the recorded data
- **Cells from Human origin :** avoid the inter-species extrapolation
- **More complex cellular model :** co-cultures, 3D tissue models, long term culture…. to better mimic organs

Simple Cell Models (2D)



Engineered Tissue (3D)



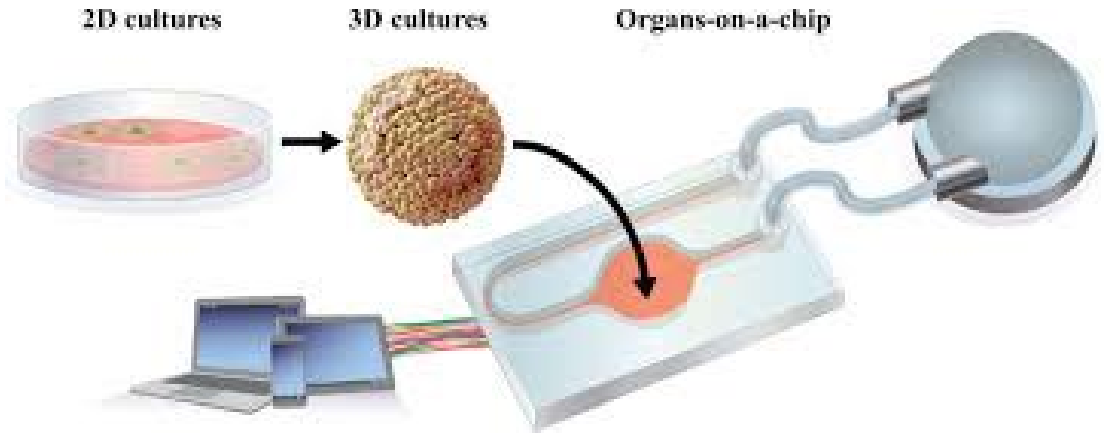


Results in **high content information**
Organ on Chip

What is an «organ on a chip» ?

Composed of:

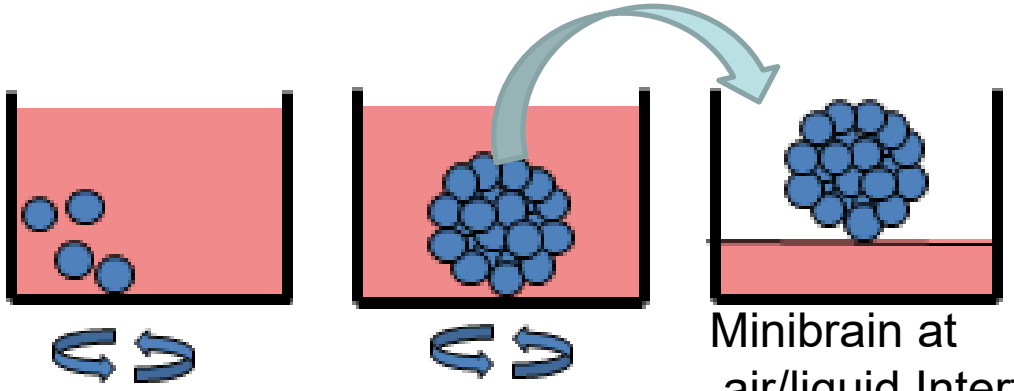
1. **Biology**: Cell types (2D, **3D**, co-culture, organoid)
2. **Biochip**: Microsystem (miniaturisation, fluidics, electronics)
3. **Readout:** External instrumentation and software



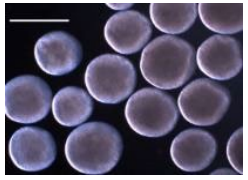
A device that recreates the natural physiology and mechanical forces that cells experience in the human body

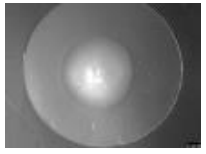
Biology : example of "minibrains"

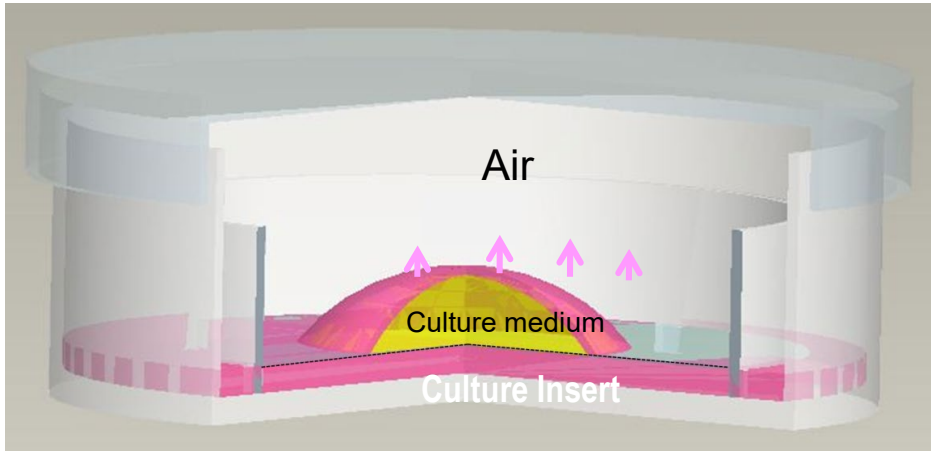
Auto-aggregation by orbital agitation



Minibrain at
air/liquid Interface

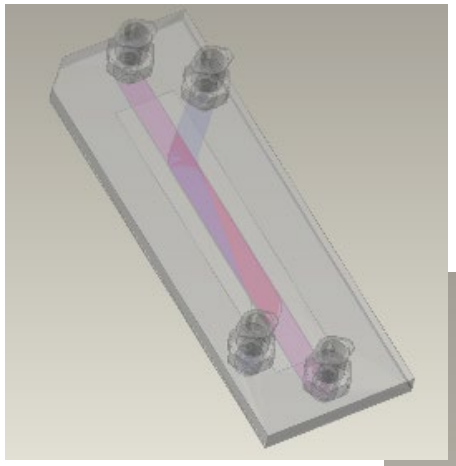


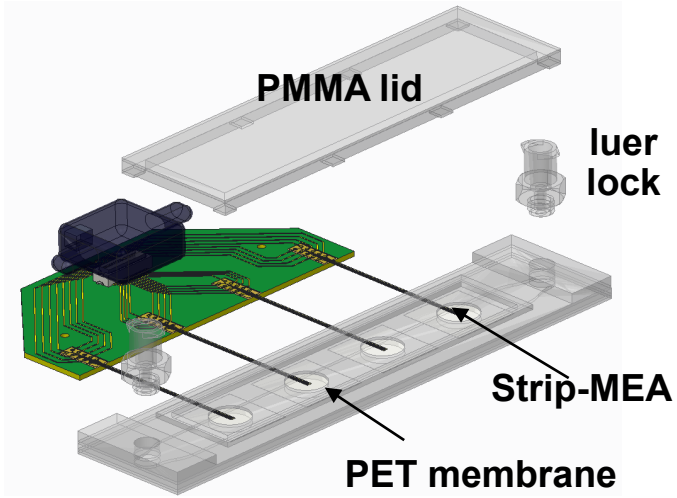


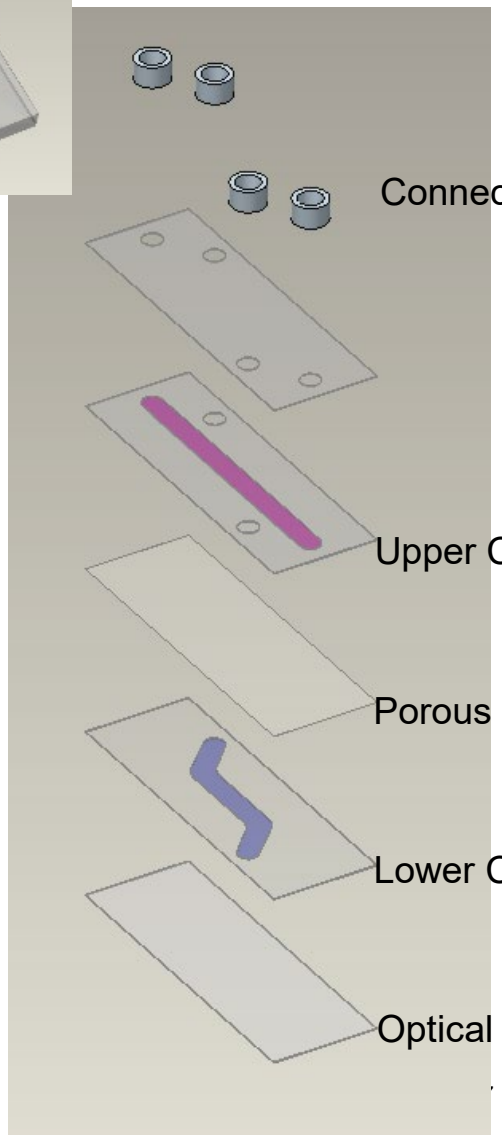


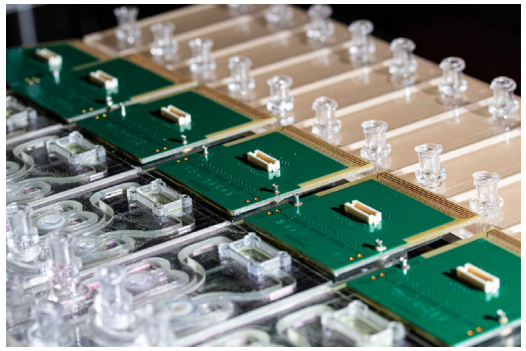
Biochip

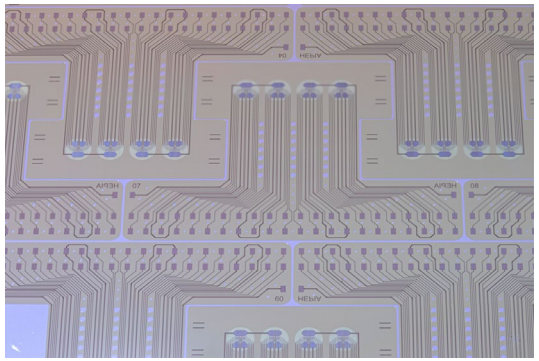
- Fluidic channels + connectors
- Biocompatible materials
- Prototype vs production
- Integration of sensors

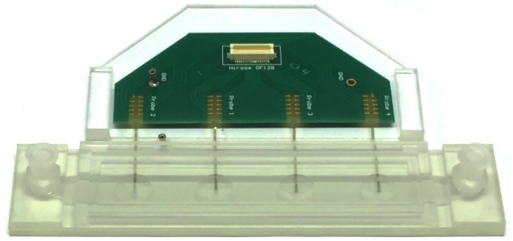








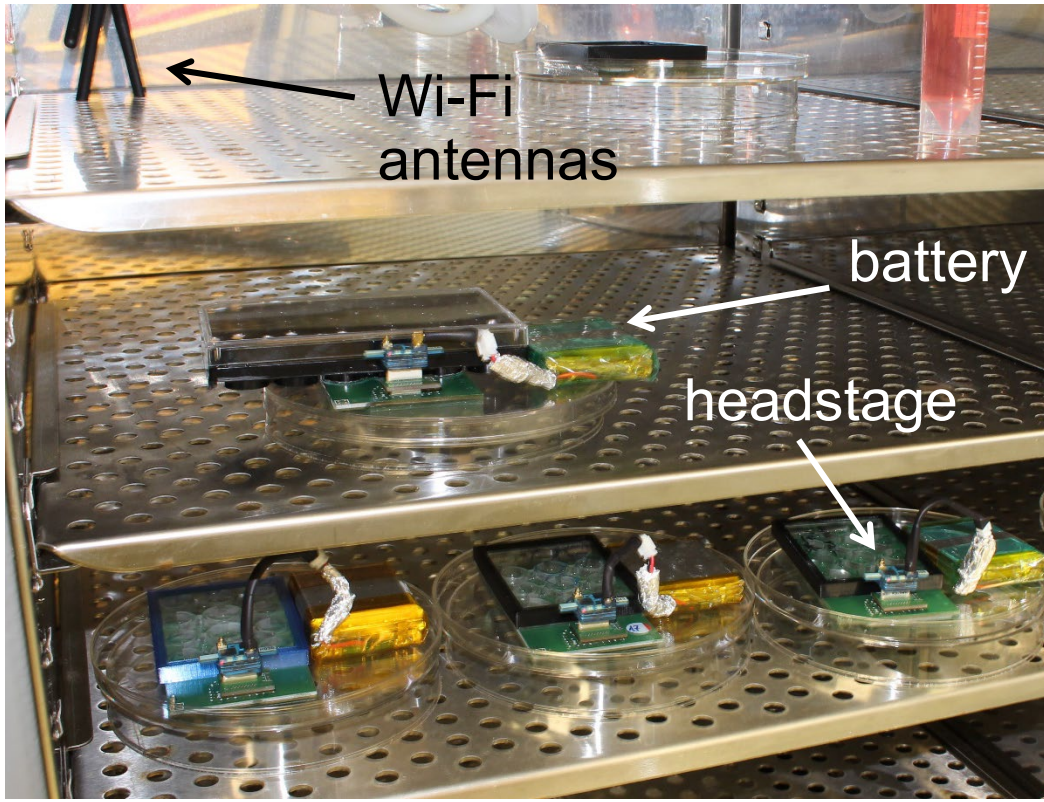


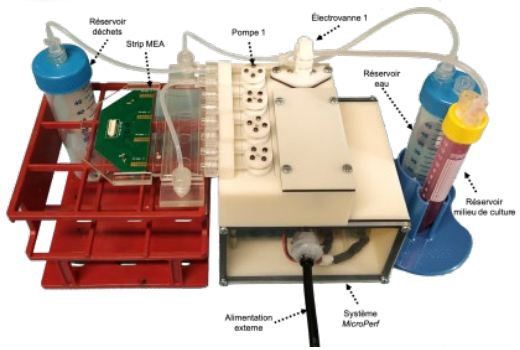


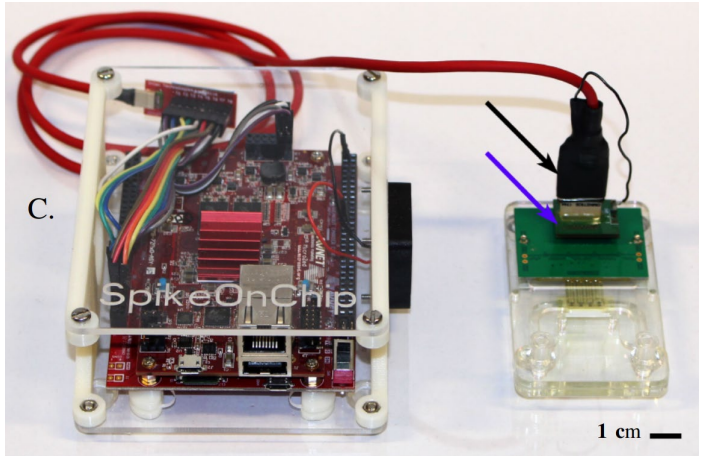
Readouts

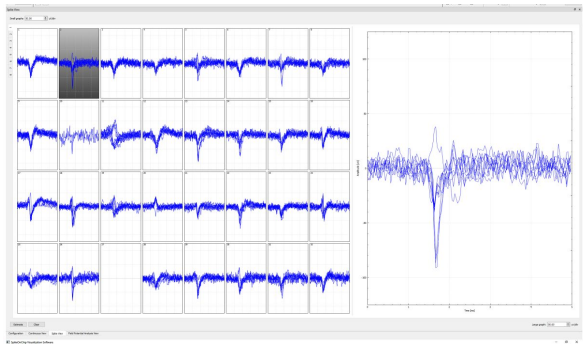
- Fluidic system (pumping and sampling)
- Visualisation system (real time)
- Electrical activity monitoring
- Specific software for data analysis

Remote control

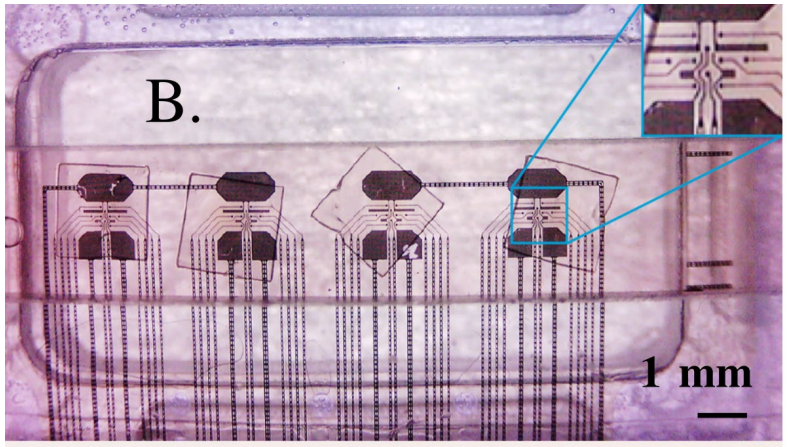




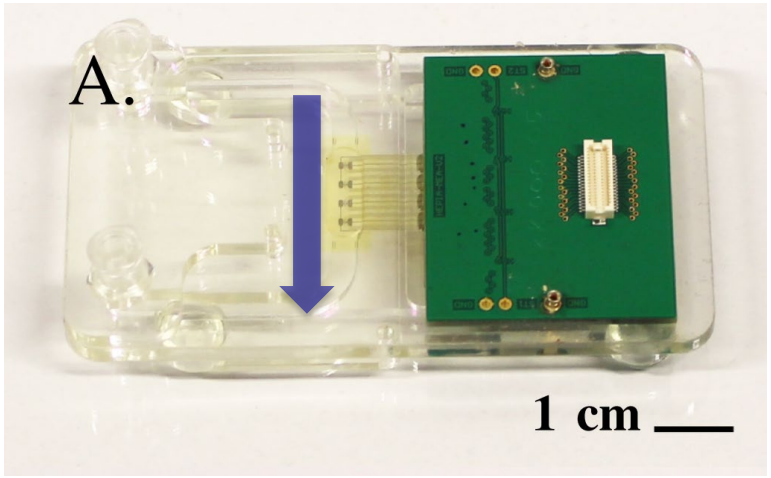




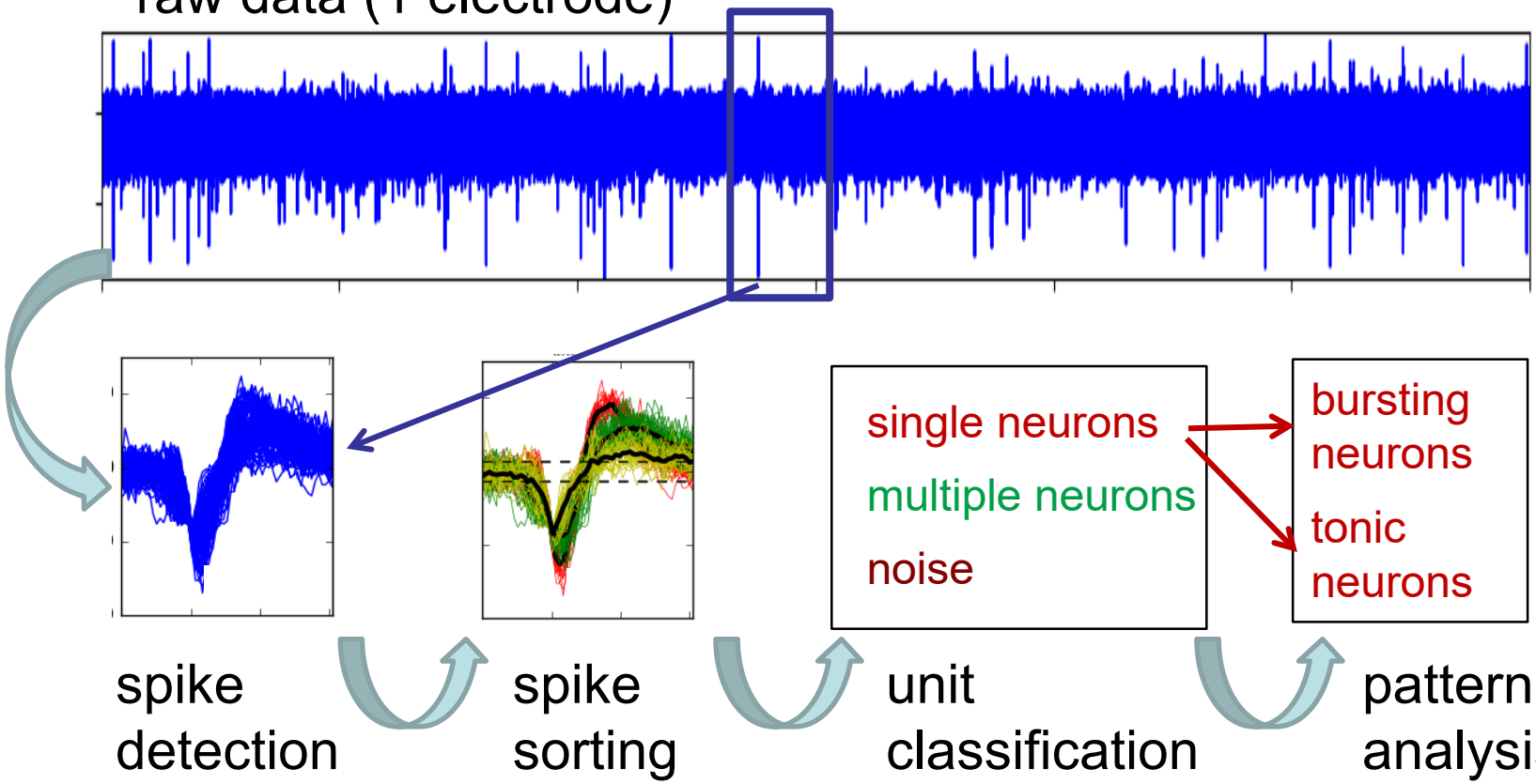
Minibrain electrical signal: acquisition & analysis



fluidic channel



raw data (1 electrode)



Generation of 15Gb every hour
=> Efficient data analysis needed

To conclude

- **To increase of predictivity, the trends are**
  - to use Human cells (iPS derived) and to increase the complexity of the cellular *in vitro* model (3D, co-culture)
  - To use more technology for functional readout (Organ-on-Chip)
- **Remaining technical challenges :**
  - Provide oxygenation to large organoids
  - Increase throughput of organ-on-chips to test more conditions
  - Improve data analysis with the help of AI

Best alternative to animal models (Replacement)

Acknowledgments to the Bio-engineering team

h e p i a

Haute école du paysage, d'ingénierie et d'architecture de Genève
Tissue Engineering Lab

Hes·so GENÈVE
Haute Ecole Spécialisée de Suisse occidentale

campus biotech

The Team of biologist:

Adrien Roux (Biologist)
Luc Stoppini (Neurobiologist)
Laetitia Nikles (Bio Lab technician)
Elia Ribeiro (Lab technician trainee)
Alexandra Laszlo (Biomedical student)
Pauline Kieffer (Biologist trainee)

The Team of engineer:

Marc Heuschkel (Microfabrication)
Loris Gomez Baisac (Microtechnology Engineer)
Cyril Iseli (data scientist & IA)
Grégoire Bouiller (Electronic Engineer)
Shaginth Sivakumar (Microtechnology Engineer)
Lisa Safasada (Engineer Trainee)