Samples of work: Comics as a tool to communicate neuroscience

The WP1 presents Inverting models: from observations to causes
(a look into Task 1.16)

**Synapses** are fundamental to the transmission of signals through the brain. When these synapses fail, it can have serious effects on the functioning of the brain. This is called SYNAPTOPATHY.

**Synaptopathies** are found in many neurological disorders, like Alzheimer's, Parkinson, Schizophrenia and EPILEPSY. As synapses form the connections of neuronal circuitry, understanding their dysfunction can help understand the processes behind these brain disorders.

In WP1 we study synaptopathies present in EPILEPSY by taking DATA obtained from individuals and using mathematical modelling to describe the synaptic signalling taking place in the brain.

From the observations, that measure the consequences of synaptopathies, we want to understand the CAUSES. We work with data from pediatric patients, obtained as part of their on-going treatments. This gives us a unique opportunity to look into synaptopathies that unfold during neural development.

Can we infer the CAUSES? (a description of the synapses dysfunction)

**Dynamic Causal Model**

- abnormal ↔ synaptopathies
- brain dynamics

In a **FORWARD MODEL**, one tries to describe observations that are the effect of certain CAUSES.

**What we are doing is inverting this, we are looking for the CAUSES of what we are OBSERVING.**

To do this, we use the observations to tune the PARAMETERS of our MODEL.

Richard Roach
King's College London

Karl Friston
University College London

Great Ormond Street Hospital
(One of UK's leading centers in pediatric epilepsy surgery)
It's like listening to a band playing behind a curtain and trying to identify which instrument are producing the music...

But in our case, we are listening to the music produced by the brain. That is, the fluctuations in electromagnetic signals that we see in the EEG recordings.

With our work, we aim at understanding and describing underlying synaptic processes observed in the EEG recordings.

This involves understanding better the different scales at which neurodevelopmental pathologies act on the brain, how they evolve and how they are affected by external factors.

Currently, roughly $\frac{2}{3}$ of epilepsy patients do not respond to medication, and some may respond to epilepsy surgery.

Our work can help identify who might benefit from surgery and plan surgery for each patient individually, drastically improving the well-being of our patients.

We will make our DATA available in EBRAINS and integrate our mathematical model in TVB platform.

In that way, our research can integrate other research done at WPI and we can all benefit from each other's experiences!
Understanding the architecture of the brain is fundamental in the HBP efforts to model the brain. This would not be complete without studying an actual human brain.

So far, most of what we know of the brain comes from mice and primates. Here we are going into uncharted territory. This is the first time that so many methods are put together to analyze a real human brain.

Oh, hi! I'm Roxana Kooijman, senior scientist at KNAW. Let me show you what I mean!

The human brain presents many challenges due to its size: it is huge! Many of the techniques used for mice and primates become more difficult or don't work on human brains.

We need to come up with new procedures & new tools!

We act quickly and with care to preserve the delicate tissue of the brain. It's a race against time!

We've teamed up with engineers to create a special 3D-printed container that allows the brain to sit for ~300 h for a high resolution scanner.

This data is important for analysis, but also as reference for later reconstruction of the brain.

* KNAW: Netherlands Institute for Neuroscience, Amsterdam
* Neuroimaging Center, CEA, Paris region
* Cyril Poen, Neurospin
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In FZJ, we cut very thin sections of the brain, which are mounted in glass. Then, the sections undergo PLI** in Markus Axer’s lab. Here, I integrate previously obtained data into PLI.

Then, the sections go into many many many large **EPI TUBES**!

I use a cell-staining technique called **CHROMOGENIC MULTIPLEX IMMUNOHISTOCHEMISTRY**. This is the use of **ANTIBODIES** to tag **PROTEINS** in certain cell-types using **COLOR**. This allows us to map the location of molecularly defined cell types.

All our efforts to analyze this one human brain will generate the first ever rigorous, high-resolution, cell-type specific **ATLAS** of the human brain, together with its integral **CONNECTOME**!

WP1 develops the brain reference framework **EBRAINS**, into which all these various pieces of information (geometry, connectivity, cyto-organization) are integrated. They serve to constrain brain models, and are accessible to neuroscience and medical communities.

* Forschungszentrum Jülich.  ** Polarized light imaging
The WP1 presents Philosophy of Science & brain modeling

In the search for a better understanding of the brain's functioning via brain simulation, the in-silico experiments done at WP1 are an unprecedented opportunity to study brain diseases like epilepsy.

As part of these efforts, neuroscientists have teamed up with philosophers of science and neuroethicists at Uppsala University in Sweden to examine the biological realism of brain simulations, and the societal and ethical aspects of building in-silico twins of human brains.

Our approach to study the brain models built in WP1 starts by defining the concepts that are used: brain, virtual brain, simulation, etc. What does it mean to make in-silico copies of brains? What does the human brain mean? Because of this, we can identify a first key challenge: the validity of brain simulations.

“The brain exists as a concept in our minds, but in reality, each individual brain is unique in its function, behavior and how it coordinates responses to external stimuli.”

Network Model

Now, when we look at specific experiments, we see that there are many technological and methodological challenges to predict behavior using brain simulations. A particularly successful method is the use of network models, that relate brain signals to behavior.

However, there are many limitations coming from environmental aspects. How well can a brain simulation predict behavior in different contexts?

ENVIRONMENTAL CONDITIONS

A particularly successful method is the use of network models, that relate brain signals to behavior.

* This comic is part of a series in WP1 (Human Multiscale Brain Connectome) of the Human Brain Project (HBP).
From a philosophical point of view, RELIABILITY is a constraint to the data production phase of an experiment.

**Question**
- Hypothesis 1
- Hypothesis 2
- Null hypothesis

**Data**

**Experimental process**

**Validity** is an experiment's capacity to support the conclusions drawn from it.

Complete fidelity between a virtual brain and a real, living brain may be an ideal, but still out of reach with the current knowledge and technology.

However, with the Virtual Brain, we have in front of us a unique opportunity for testing modifying different parameters in the model. This gives a sufficiently reliable framework to test hypotheses using real data.

The Virtual Brain
- Modelling at different scales
- Cellular
- Molecular
- System
- Ability to tune different parameters
- Validation through clinical trials

I'm the model of

Now, why is it important to discuss all these concepts?

The first philosophical and scientific goal is to deepen knowledge and understanding. Additionally, clear and transparent communication is crucial to producing a realistic and meaningful discussion about the research carried out in WP4 and its ethical and societal impact.

In this context, **CONCEPTUAL CLARITY** is key for the communication of research.

It allows to set realistic expectations and avoid unfounded concerns, hype and misuses. Then, we can help build solid interdisciplinary collaborations as well as relationships of trust between society and the scientific communities.

*This comic is part of a series in WP4 (Human Multiscale Brain Connectome) of the Human Brain Project (HoE).*