Generative modelling of brain dynamics: From principles to applications

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1089
Educational Course - Full Day (8 hours)
SEC Centre
Room: Boisdale

The use of modelling to infer brain connectivity has become one of the most important themes in human brain mapping. Recently, very large and concerted efforts to build in silico models of brain structure, function and its dynamics – in unprecedented details – have emerged (e.g., Human Brain Project, The Virtual Brain). Concurrently, a huge variety of high quality and data extensive repositories have been established both in healthy (e.g., HCP and UK Biobank) and clinical populations (e.g., ADNI, ENIGMA, ABIDE, ABCD). These modelling platforms and databases are largely open-access providing a highly rich combination and exciting new opportunities – all ready to be exploited – to extend, enrich and enhance our understanding of network organization of the brain. This means that in silico generative modelling techniques can now be tested with: i) increasingly high spatio-temporal resolution data coming from multiple modalities; ii) less noisy measurements due to advances in artefact removal techniques; and iii) large sample sizes allowing to probe for individual differences paving the way, to move beyond group analysis, towards normative models and precision medicine.

This educational workshop will provide the critically needed overview of the basic principles, assumptions, strengths, limitations, and applications of a few of the representative suite of generative modelling techniques. It will provide attendees an access to the much required, and highly sought after training and resources that will enable them to independently conceptualize, implement, validate and interpret these modelling techniques and their outcomes.

Objective

The main learning objective of this educational workshop is to teach attendees the basic principle, guidelines, practices, implementation and applications of some of the representative generative modelling techniques in order to extend our mechanistic understanding of the brain's structural and functional network organization. As learning outcomes of this workshop, attendees will learn:

1. How to specify and estimate models of brain structure and function using dynamical systems theory
2. How to apply these generative modelling techniques to clinical populations to estimate, compare, validate and

interpret their outcomes
3. Thoroughly understand strengths, assumptions and limitations of existing generative modelling techniques

Target Audience

The target audience will be trainees (Masters, PhD and Postdocs), faculty members, and industry practitioners, with a background in psychology, neuroscience, radiology, medicine, engineering, computer science and physics, hence catering to the requirements of basic, applied, and clinical scientists with a spectrum of previous experience.

Presentations

Dynamic causal modelling: Basic principles

In this educational lecture, dynamic causal modelling (DCM) will be presented to attendees assuming no or little previous knowledge of modelling brain dynamics. DCM is a Bayesian framework to model causal interactions among brain regions and it operationalizes hypothesis testing using model comparison. It uses a system of differential equations to describe evolution of neuronal activity and a biophysical – haemodynamic – model that links the neuronal activity to the observed BOLD signal. While the framework will be presented from the point of view of functional MRI, the basic principles also apply to other modalities like EEG/MEG (which will further be reinforced in accompanying lectures on these modalities, see below). A demo will also be given, together with scripts and instructions will be provided on how to run them.

Learning outcomes:
By the end of the lecture, attendees will be able to
1. place DCM in the image analysis pipeline
2. state the difference between structural, functional and effective connectivity
3. explain how a generative model helps to separate the BOLD signal into neuronal activity (effective connectivity), haemodynamics and noise
4. explain the interpretation of the parameters in the neuronal formula in DCM for fMRI and
5. explain how parameter estimates and the log model evidence are used to test hypotheses

Presenter

Adeel Razi, Monash University Clayton, Victoria
Australia

Dynamic causal modelling: Applications

Having learnt the basic principles behind dynamic causal models (DCM), this lecture will focus on its applications to clinical and cognitive neuroscience. Participants will learn about the usefulness of DCM in answering questions about the brain circuitries underpinning cognitive (dys)function in the typical brain and in clinical populations.

Learning outcomes:
Participants will learn about how to map alternative theoretical models to empirically testable hypotheses using M/EEG and fMRI.

Presenter

Marta Garrido, University of Melbourne Melbourne, Victoria
Australia

Dynamic causal modelling of synaptic pathology in epilepsy

Whilst most causes of epilepsy - such as genetic mutations, or brain lesions - are persistently impacting neuronal and local microcircuit function, we observe epileptic seizures by definition only intermittently in the epileptic brain. Generative models of brain dynamics, such as neural mass models of networked excitatory and inhibitory neuronal populations, can link pervasive synaptic pathophysiology and their intermittently expressed dynamic signatures quantitatively.

In this talk we will review one particular strategy of fitting such neural mass models to empirical neurophysiological recordings using dynamic causal modelling (DCM). This approach allows inference of the underlying synaptic pathology resulting in dynamic abnormalities in neurophysiological recordings in patients with epilepsy caused by a number of different conditions ranging from single receptor alterations as seen in NMDA receptor encephalitis, to extensive changes in structural brain networks in tuberous sclerosis.

Learning outcomes:
Following this course the participants will be able to identify research questions addressable with DCM, contrast different approaches of modelling epileptic brain dynamics to the DCM framework, and consider how fluctuations in synaptic pathology can be captured using hierarchically constrained, time-varying parameterisations of dynamic causal models.

Presenter

Richard Rosch, King College London London, London
United Kingdom

Simulating deep brain stimulation with The Virtual Brain

During this lecture, participants will shortly be introduced to the general principles of the neuroinformatics platform The Virtual Brain (thevirtualbrain.org) and will then use it to simulate the effects of deep brain stimulation (DBS). The Virtual Brain can be used to simulate the effects of different diseases on brain dynamics as well as to explore treatment options in silico. We will focus on the use case of patients suffering from Parkinson’s disease and compare different settings as well as placements of the DBS electrodes virtually.

Presenter

Jil Meier, Charité – Universitätsmedizin Berlin Berlin, Berlin
Germany

Responsible full brain modeling with clinical translation

Over the past decade we have demonstrated that the fusion of subject-specific structural information of the human brain with mathematical dynamic models allows building biologically realistic brain network models, which have a predictive value, beyond the explanatory power of each approach independently. The network nodes hold neural population models, which are derived using mean field techniques from statistical physics expressing ensemble activity via collective variables. Our hybrid approach fuses data-driven with forward-modeling-based techniques and has been successfully applied to explain healthy brain function and clinical translation including aging, stroke and epilepsy. Here we illustrate the workflow along the example of epilepsy: we reconstruct personalized connectivity matrices of human epileptic patients using Diffusion Tensor weighted Imaging (DTI). Subsets of brain regions generating seizures in patients with refractory partial epilepsy are referred to as the epileptogenic zone (EZ). During a seizure, paroxysmal activity is not restricted to the EZ, but may recruit other healthy brain regions and propagate activity through large brain networks. The identification of the EZ is crucial for the success of neurosurgery and presents one of the historically difficult questions in clinical neuroscience.

However, estimations of model parameters are a huge challenge due to neurodegeneracy and identifiability issues and have been referred to as the key obstacle to progress in neuroscience (Frégnac, 2017). A responsible treatment of these issues demands the use of proper estimates of confidence and diagnostics of performance of the inference, which is provided by latest techniques in Bayesian inference, in particular Hamiltonian Monte Carlo techniques. The example of epilepsy nicely underwrites the predictive value of personalized large-scale brain network models. The workflow of end-to-end modeling is an integral part of the European neuroinformatics platform EBRAINS and enables neuroscientists worldwide to build and estimate personalized virtual brains.

Presenter

Viktor Jirsa, Aix-Marseille Université Marseille, Marseille
France

Linear spectral graph models of brain activity

Many computational approaches exist that can couple a large array of non-linear neural masses via the brain's anatomic connectome. Due to their non-linearity, complexity and long simulation times, these approaches tend to lack easy interpretability, and make parameter inference challenging. Further, the role played by the connectome can only be assessed indirectly. It is also emerging that linear approximations of such coupled systems may equal or exceed narrowly-circumscribed performance metrics in selected scenarios.

In this lecture I will present recent advances in linear models, which can typically be expressed by closed form solutions that obviate the need for massive simulations and therefore make model inference far simpler and less ill-posed. I will show how both fMRI and MEG data can be correctly recapitulated by such a model, which we call Spectral Graph Model (SGM). Most importantly, SGM-type models are able to directly and simultaneously predict the spatial and spectral distribution of M/EEG data using only a few global parameters - something that is usually not possible with coupled NMMs. These models can be decomposed into eigenmodes or harmonic modes (see also: lecture by K Glomb). The lecture will include sharable code and a short tutorial on how to use it to fit to empirical M/EEG regional power spectra.

Learning outcomes:

1. Understand the general concept of graph Laplacian and its eigenmodes
2. Be able to write a simple linear rate equation that serves as a generative model of resting state fMRI, EEG and MEG
3. Understand how the rate equation directly leads to the SGM
4. Learn how to use the public SGM code in modeling resting state data

Presenter

Ashish Raj, UCSF San Francisco, CA
United States

From waves to harmonic modes

The idea that wave phenomena play a role in macroscopic electrophysiological activity is not new. Brain activity is thought to propagate along the cortical surface as well as through white matter long range connections, forming varied dynamical patterns. In this talk, I will introduce some basic models of such waves and how they have been used to understand brain activity measured with EEG, for example through the concept of harmonic modes. I will also show how the notion of a continuous wave can be extended to graphs and allow for a new interpretation of harmonic modes in network neuroscience.

Learning outcomes:

1. gain an understanding of the basic equations that describe diffusion and standing waves
2. know the principles of how these equations have been and are being applied to understand M/EEG activity
3. get familiar with how diffusion and standing waves are described on graphs and how that is applied to brain networks

Presenter

Katharina Glomb, Berlin Institute of Health/Charite
Brain Simulation Section
Berlin
Germany

Generative modelling of brain function using turbulence

Turbulence is a special dynamical state driving many physical systems by way of its ability to facilitate fast energy/information transfer across scales. These qualities are important for brain function, but it is currently unknown if the brain also exhibits turbulence as a fundamental organisational principle. Using large-scale neuroimaging empirical data from 1003 healthy participants, we demonstrate amplitude turbulence in human brain dynamics. Furthermore, we build a whole-brain model with coupled oscillators to demonstrate that the best fit of our model to the data corresponds to a region of maximally developed amplitude turbulence, which also corresponds to maximal sensitivity to the processing of external stimulations (information capability). The model shows the economy of anatomy by following the Exponential Distance Rule of anatomical connections as a cost-of-wiring principle. This establishes a firm link between turbulence and optimal brain function. Overall, our results

reveal a novel way of analysing and modelling whole-brain dynamics that for the first time ever establishes turbulence as a fundamental basic principle of brain organisation.

Presenter

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