Project title: Continuous mechanistic modelling of dynamic brain activity in neuropsychiatric disorders

Project reference: DT4H_11_2023

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Aim of the project

The objective of this project is to use state-of-the-art machine learning (or artificial intelligence - AI) to simulate dynamic brain activity and use this to build tailored, simulations of neuropsychiatric disorders within individual brains. These models will be updated over time (through integration of longitudinal data) to improve mechanistic understanding of the heterogeneity of these disorders and their treatments. The project will leverage:

- Geometric deep learning on cortical surface domains
- Transformers
- Functional magnetic resonance imaging (fMRI)
- Large imaging collections of cohorts with schizophrenia, autism spectrum disorder, depression and anxiety.

Project description

The human brain is an immensely complex structure, composed of approximately 86 billion interconnected neurons, working together to coordinate a myriad of cognitive processes at any one moment of time. Neuroscientists now have a good understanding of the cellular and molecular functioning of individual neurons – at the microscale - and can map general functional processes to different areas of the brain - at the macroscale. However, comprehensive understanding of how cognition arises from complex neuronal networks, and how this is disrupted in the case of neuropsychiatric disorders remains largely unknown.

Recently researchers have begun to use artificial intelligence (AI) to simulate sub-processes of the human brain. For example, Whittington et al [1] used Transformer networks to simulate spatial planning within the hippocampus. Other groups have shown that the activations of AI models trained to model language can replicate patterns of brain activity measured from functional magnetic resonance imaging (fMRI) of the human brain [2].

In our lab we have been developing novel AI tools that can precisely encode the complex patterns of brain structure and function within individual brains [3,4,5]. These methods have been shown to significantly improve the precision with which neurodevelopmental and cognitive phenotypes may be predicted from structural and functional MRI data [3,4], as well as model how the brains of individual neonates develop over time or change as a result of increasing prematurity [5].

Recently we have extended these models to encode the functional dynamics of human brains engaged in a movie watching task. In this way it is possible to predict how individual brains should respond when engaged in a task from just observing it at rest. This will allow us to start asking mechanistic questions regarding the impact of different neuropsychiatric conditions, by allowing us to disentangle natural variability (for example due to structural differences in brain organisation, or brain state, e.g., the effect of mind wandering) from variation that is specific to the clinical phenotype. It will also allow us to explore mechanisms underlying the large, reported variability in the link between behavioural and neural patterns associated with different neuropsychiatric disorders.

Task fMRI (tfMRI) has been used for some time now to build mechanistic understanding of a range of neuropsychiatric disorders. For example, studies of autism spectrum disorder (ASD) have investigated how individuals make inferences of others' intensions, process emotion, biological motion, spatial attention and recognize facial expressions [6]. By contrast, schizophrenia is reported to impact working memory and executive function, and such tasks have been used to investigate individuals' response to treatment [7]

This project will build tailored simulations of human brain dynamics from fMRI. These will be used predict how an individual's brain will respond to cognitive tasks, conditioned on disease status, response to treatment, age and sex. Such neurological digital twins could improve mechanistic understanding of neuropsychiatric conditions to ultimately lead to better in silico modelling of the effects of different treatments.

The most suitable candidate for this project would have a background in maths, physics or engineering and enthusiasm for neuroscience.

[1] Whittington, JCR. ICLR 2022 https://openreview.net/pdf?id=B8DVo9B1YE0
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[3] Dahan, Simon, *International Conference on Medical Imaging with Deep Learning*. PMLR, 2022. https://proceedings.mlr.press/v172/dahan22a.html
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[5] Fawaz, Abdulah, et al. "Surface Generative Modelling of Neurodevelopmental Trajectories." *bioRxiv* (2023): 2023-10. https://link.springer.com/chapter/10.1007/978-3-031-12053-4_35
[6] Dichter, Gabriel S. "Functional magnetic resonance imaging of autism spectrum disorders." *Dialogues in clinical neuroscience* (2022).
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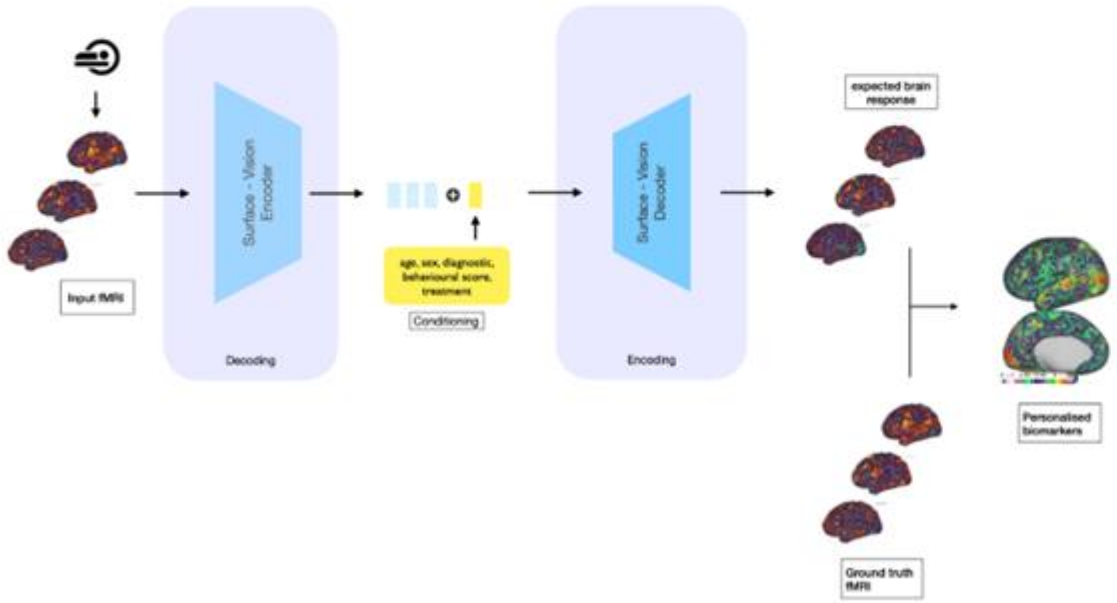
Input fMRI
Surface - Vision Encoder
Decoding
age, sex, diagnostic, behavioural score, treatment
Conditioning
Surface - Vision Decoder
Encoding
expected brain response
Personalised biomarkers
Ground truth fMRI