Workshop on

Responsible Research and Innovation in EBRAINS

Collection of Cases

Introduction:

- Select a case
- Select a speaker to present the groups reflections
- Select someone to take notes, and prepare slides for later presentation
- 40 minute breakout rooms

Prepare a short presentation for the plenary, covering:

- Short overview of key aspects of the case
- What ethical/ social / legal issues can arise in this case?
- How can these issues / concerns be addressed?
- Who is responsible?
- for what?
- How is it to be realised?
- In your experience of HBP or general research practice, do these issues arise in research practice? Are they appropriately addressed?
- What support would the researchers need to address these issues? Is this available in the HBP / EBRAINS? What else would be required?

Case 1 - **Sharing Neuroimaging Data on EBRAINS**

Prof Z and their team has collected a large dataset of fMRI (Functional Magnetic Resonance Imaging) data. These data were collected from patients at a clinic at a hospital in Spain, every patient was provided with information regarding the study by their doctor, who also took them through the informed consent process prior to any study procedure. This study was approved by the local ethics committee at the hospital.

After the data were collected, it was pseudonymized by removal of all obvious personal identifying features, and the masking of physical characteristics (facial features, skull shape) aside from those required to retain the scientific utility of the data itself. Each patient has been assigned a unique identifying number, and Prof Z's team store the collected data, and any associated metadata, securely and separately on a server at their local institution in Spain.

Prof Z and their team are now looking to share this fMRI data through the EBRAINS knowledge graph. They want the data to be publicly available to allow them to publish their results in academic journals, and so that the data they have collected can be re-used by other scientists. EBRAINS will curate the data, host it on a platform which is accessible across the globe, and provide access to the data to scientists both within and outside the European Union. As this human data is pseudonymised, it will be made accessible through the EBRAINS Human Data Gateway, which tracks user access, and requires anyone who wants to access the data to agree to certain terms and conditions.

Case 2 - Using Human Data from EBRAINS

Dr Y is a neuroscientist at a private research institution in Australia. They are developing machine learning algorithms which they hope will assist in brain tumor diagnosis. In order to develop these algorithms, Dr Y will require a large amount of neuroimaging data on which to train them. Dr Y has heard about EBRAINS, and how it could be a resource for scientists looking to gain access to such data.

Dr Y applies for access to the pseudonymised human data available through the EBRAINS knowledge graph. Doing so requires them to provide certain details about themselves during the user registration process, and then for them to agree to a Data Use Agreement. The Data Use Agreement stipulates how the data they access can be used and further shared.

Having now gained access to the neuroimaging data available through EBRAINS, Dr Y downloads a dataset of brain images available through the EBRAINS knowledge graph. This dataset was collected from patients in a clinic in the Netherlands in 2019.

Dr Y downloads this dataset to their local machine at their institution in Australia, they use it to train their machine learning algorithms and once they have finished their research activity, they plan to delete the data from their system.

Case 3 - Collecting and Sharing Non-human Primate Data

Dr X is a postgraduate researcher at a university in the United States, they are conducting research into object recognition. In order to gain an understanding of how identifying and classifying objects is reflected in brain activity, Dr X is utilising some non-human primate subjects (NHP), from whom they are collecting brain activity data whilst they perform a few perception and object manipulation tasks. Dr X and their colleagues collect data from a total of 8 NHP subjects in lab conditions.

The study is approved by their local research ethics committee, and Dr X and their colleagues obtain the appropriate licenses and training to conduct the study at their institution.

Now that the data is collected and analysed, Dr X wants to publish their results in academic journals – and so they are looking for platforms to host their data. They have chosen EBRAINS as a site which could provide this service. Their data will be available openly to anyone across the globe, users accessing non-human animal data on EBRAINS are not required to agree to a Data Use Agreement, and no log-in is required.

Case study 4: The Virtual Brain

Epilepsy is a serious brain chronic disease affecting approximately 50 million people worldwide (WHO). It has significant human and material impact through economic, ethical, social and health care implications resulting in high burden for both individuals and society. While therapies and treatments are available, their success is importantly shaped by individual brain variability.

The creation of computational models of the brain (central to the European Human Brain Project (HBP)) is intended to address this issue by enabling personalised therapies and treatments for brain diseases such as epilepsy. As stated in the project's proposal, "...a "digital twin" of the brain can be used clinically for patient-specific hypothesis testing and treatment discovery. It provides a qualitative advance beyond the state of the art and opens up novel avenues in research and innovation (e.g. early detection of trajectories of brain disease manifesting on different levels of brain organisation, personalised tracking of brain health and better stratification of patients) (SPECIFIC AGREEMENT 945539 — HBP SGA3, p 232).

The virtual brain illustrates a data driven approach to healthcare, where understanding "patient-specificity" becomes central for a number of reasons, notably the highly interactive (both internally and externally) and contextually and epigenetically shaped nature of the brain. Virtual brain modelling attempts to address the challenge presented by the variability and uniqueness of each brain by inferring the connectome (the whole set of connectivity between the nodes) from real data by white matter tracts reconstruction from dMRI and by fitting the model parameters with empirical functional data (i.e. real brain signals) to generate accurate and meaningful simulated signals.

Case 5: Indicators of consciousness

(Focus: Translational research)

Dr X is a clinician working in a Long Term Care Unit with patients with Disorders of Consciousness (DoCs) surviving traumatic accidents. He knows all the relevant clinical assessments protocols, from the Coma Recovery Scale – Revised to the Full Outline of Unresponsiveness and the Nociceptive Coma Scale Revised. He applies all these protocols with due diligence, but feels a growing sense of discomfort when talking with patients' families expressing their feeling and conviction that their loved ones are actually more conscious than he rates.

His discomfort arises from the awareness that current clinical approaches, even though prima facie reliable, are eventually unsatisfactory, as evidenced by the still high rate of misdiagnosis of DoCs.

Dr. X knows that attribution of consciousness to other subjects is *per se* inferential, and it becomes even more challenging in the case of behaviourally unresponsive or limitedly responsive subjects, like patients with DoCs. In fact, given the high rate of uncertainty surrounding both the definition and the clinical operationalization (i.e., the identification of relevant behavioural and/or neurophysiological data) of consciousness, it is crucial to remember that the absence of evidence of residual conscious activity is not evidence of its absence.

One possible strategy to improve diagnosis is suggested by recent EU and US Guidelines for DoCs: combining bedside examination, functional neuroimaging and EEG. But the clinics where dr X works does not have all needed technology available, and many results from relevant research are still at the stage-of-proof, i.e. not directly implementable in the clinics.

Dr X struggles to identify some "indicators of consciousness" in patients with DOCs, i.e. proxies for residual conscious activity, that might be translated into clinical settings.

Case 6: Neuro-robotics

(Focus: Technological exploitation of EBRAINS)

Work in WP3 promises to give an important contribution to the development of neuro-inspired robotic applications, which will likely result in new commercial products.
This will be pursued by emulating the architecture and operation of the brain that support human cognitive functions and applying them to address visuo-motor and cognitive problems in an embodied setting and on neuromorphic platforms.
One of the planned output of WP3 is “A biologically inspired functional cognitive architecture focusing on performance on the neuro-robotics platform and on real-world systems using simplified models of neurons and networks”, which promises to give rise to increasingly autonomous artificial agency as well as to robotic devices more embedded in the real world.