EBRAINS

EBRAINS Science Vision

25 April 2023

EBRAINS science vision is to revolutionize how neuroscience research is performed, changing the research culture from fragmented individual laboratory efforts to integrated platform research, ultimately leading to a better understanding of the brain and improving brain health and technology. We strive to be the premier digital infrastructure for neuroscience research by providing unique brain data of highest quality across multiple species, integrated with cutting-edge analysis, validation and curation tools and multiscale brain models that facilitate seamless interoperation and knowledge exchange. Researchers can build customized science workflows across the entire scientific value chain and generate new neuroscience knowledge that would be otherwise inaccessible, paving the way for innovative solutions to the most pressing challenges in neuroscience. Our ultimate goal is to accelerate the pace of scientific discovery, generate new insights into the brain, and translate these insights into tangible benefits for society.

EBRAINS mission is

- To enable cutting-edge research and innovation in neuroscience by continuously enhancing and maintaining our research infrastructure to the highest standard of excellence,
- To support a diverse and inclusive scientific program that serves the needs of a broad global community, fosters collaboration and cross-disciplinary research, and helps to drive transformative discoveries in the field of neuroscience.
- To develop strong and lasting partnerships with industry to promote knowledge transfer and accelerate the translation of research into new brain-based technologies and therapies.
- To be a neutral and authoritative voice for brain science, advocating for evidence-based policies that support fundamental research, and engaging with policymakers and stakeholders to promote awareness and understanding of the importance of neuroscience research.
- To provide world-class training and education opportunities for the next generation of scientists and engineers.
- To inspire and engage the public in brain science, fostering awareness, understanding, and support for neuroscience research and its potential to improve brain health and well-being for all.

EBRAINS as an open, sustainable, and portable RI

The science vision is accompanied by a technical vision for the EBRAINS research infrastructure (EBRAINS RI), making it more open, more sustainable, and more portable. Improved openness will make it easier for different scientific communities and other user groups to execute their workflows using RI research tools and services, and to access data and results via EBRAINS, even via other RIs. Planned measures include adopting Common Workflow Language (CWL) as a de facto standard. The improved sustainability goal reflects the need to reduce the complexity of the current HBP-legacy EBRAINS RI and so help to address the associated cost and reliability issues. Portability is a means of improving sustainability, but it is also desirable for other reasons. Portability will permit Research Tools and Services, and Platform Services, to be run on a wider range of Base Infrastructure services, giving EBRAINS a wider choice of suppliers. Increased portability also offers solutions for users working with sensitive patient data. Privacy and ethical considerations make it difficult to move such data to the RI's research tools and services. Portability allows an alternative approach: moving the research tools and services to the patient data. This “EBRAINS in a box” approach would allow researchers to install and run RI tools and services within the same protected environment that their data is stored in.

EBRAINS Workflows and overall Methodology

EBRAINS supports the building of customizable science workflows in a digital environment. To do so, we identify a multilateral network of key services, which are grouped in service categories Data, Health Data, Atlas, Modelling and Simulation, and Validation and Inference. A sixth service category Embodiment is under development. The services are connected, allowing their interoperation and seamless exchange of information to assure an uninterrupted scientific value chain from data through model to validation.

Two principal structures support the building of workflows in EBRAINS. The first is the EBRAINS knowledge space, which provides integration of data and models in the same reference space. The second is the EBRAINS knowledge loop, which provides interoperability of data, models and tools, together with compute and storage resources, enabling scientists to build workflows making use of a large range of services.

EBRAINS supports two major types of workflows. Clinically oriented workflows typically cover many key services and emphasize the macroscopic (system) level of brain organization, whereas preclinical workflows involve mechanistic investigations in fundamental neuroscience, often covering few key services, emphasizing the microscopic level of brain organization.

EBRAINS also fully supports digital twin investigative methodology[1], which has been advocated as a vision for digital brain research by the Human Brain Project (HBP) researchers and is now being refined with inputs from across neuroscience community, as a driver for the development of novel neurotechnologies and optimisation of diagnostic and therapeutic processes.

EBRAINS knowledge space and knowledge loop

EBRAINS knowledge space provides integration of data and models in the same reference space for multiple species (human, rat and mouse). Brain data are generated in many laboratories and are of highly variable nature spanning many scales (micrometres to centimetres). Data and multiscale brain models are curated and annotated with structured metadata, represented in the same common brain reference space and made accessible through brain atlases as well as via semantic search in the EBRAINS Knowledge Graph. Data include cellular, synaptic, connectome and functional brain data, including imaging data, and are homogenized in space across brain regions and cortical areas and layers. For instance, transcriptomic data on human cell types are matched to the protein expression levels by determining receptor densities across layers. The representation of atlas regions and areas is well advanced, including neocortical areas, hippocampus, basal ganglia, and cerebellum.

Research data are interpolated and filled in when becoming available. Nonlinear spatial transformations further allow the use of different brain templates. Functional imaging data including multi-electrode recordings, Local Field Potential (LFP), stereotactic and scalp electroencephalography (EEG), magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), including multi-modal imaging, are curated and co-registered in the same space for individual subjects and cohorts, in rest and task paradigms, and health and disease conditions (such as epilepsy, neurodegenerative diseases).

[1] https://zenodo.org/record/7764003#.ZEi_0OxBzlY

Unique for EBRAINS, models across scales are in the same reference space and matched to data. For each brain region, detailed cellular models of human neurons are available including the cortex, hippocampus, cerebellum and basal ganglia. These models are architecturally specific for a given brain region. On a larger spatial scale, mean-field models are provided capturing population level activity, tuned to reproduce the local-circuit features of each brain region. On the full brain scale, the mean-field models simulate entire brain regions (cerebral cortex, hippocampus, cerebellum and basal ganglia) embedded in the network connect by multiscale connectomes. All data and models can be compiled and extracted from atlas services (including brain volume, parcellation, structural and functional connectivity, regional characterisations).

EBRAINS knowledge loop enables interoperability of data, models and tools, which are represented in the common brain reference space. A first fundamental step of interoperation is the mapping of data upon model parameters, represented in ontologies, allowing for adequate queries via the atlas services. Multiscale models operate on molecular, cellular, multicircuit and brain network scales and are simulated by simulation engines optimized for its scale (Neuron, NEST, The Virtual Brain (TVB)). The simulators are interoperable via co-simulation technologies and can be used simultaneously, enabling simulations of regions of interest at fine scales, without loss of the residual network (simulated at coarser scales). Propagation of causal influences of neuroscience data across scales is provided by mean field algorithms. Mappings across source and sensor spaces are provided by state-of-the-art forward solutions for modalities of brain imaging (LFP, EEG, MEG, fMRI) and brain stimulation (deep brain stimulation (DBS), transcranial direct current/magnetic stimulation (TDCS/TMS), Temporal Interference (TI)). Empirical and simulated data are fed in data processing frameworks, which provide functionality in signal analysis, cross-validation, and statistical and causal inference. These environments comprise latest machine learning and artificial intelligence technologies (eg, Bayesian inference, Monte Carlo Markov Chain (MCMC), simulation-based inference (SBI), Dynamical Causal Modeling (DCM)) and provide the EBRAINS user with enhanced mechanistic identifiability and uncertainty quantification. Simulations and inference are computationally expensive and are fully supported by high performance and supercomputing resources available in EBRAINS. The loop from empirical data, the formulation of mechanisms and models, simulation of data in source and sensor space, the analysis and validation, and finally the inference of underlying causes establishes the EBRAINS knowledge loop (see Figure 1). It provides the skeleton for building customized clinical and pre-clinical workflows, as well as enables the use of digital twin methodology. Notably clinical translation benefits from this loop, where individual data inform brain models and define virtual twins with predictive power on the subject-specific level.

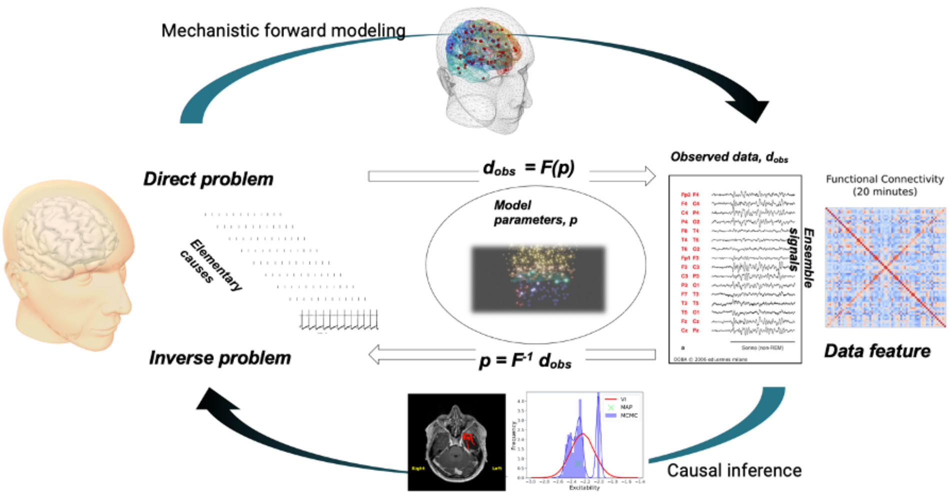

Figure 1: EBRAINS Knowledge loop comprises the sequence patient – data – model – validation – inference – patient (D'Angelo & Jirsa TINS 2022). The loop is illustrated from the left clockwise: Elementary causes generate brain dynamics and subsequently observed data. The causes are mechanistically modelled and observed data dobs are expressed as functions of model parameters p. The models are validated against data features. Causal inference makes predictions about likely mechanistic causes in the observed data set, setting the basis for personalized medicine ("back to the patient").

Examples demonstrating the added value of integration in the EBRAINS ecosystem comprise:

- **Data augmentation:** linking brain imaging data to a digital twin provides a computational extension of the visible range of neural sources, e.g., epileptogenic brain areas can be identified outside of the range of brain areas that are clinically accessible.
- **Early detection:** integrating multiple imaging modalities in same reference space enhances capacity to identify anomality in structural and functional data, e.g., lesions invisible in 3T-MRI become identifiable.
- **Across-species investigations:** systematically parametrized computational morphing of rodent neurons to human neurons quantifies the information processing capacity of the respective circuits and identifies relevant morphological features.
- **Cross-validation:** sophisticated tools of cross-validation and inference become more accessible to the non-expert by seamless integration in workflow.

Principles underlying EBRAINS architecture and key services

EBRAINS provides the digital infrastructure to operate the **key services,** which are **loosely connected** and **fully interoperable.** The services are organized in a multilateral network, in which interoperation of all services supports the building of customizable workflows. This strategy has the benefit, in that it allows the academic partners to take advantage of the integration of the service into the EBRAINS infrastructure (technical support and guidance, access to large user community, etc), but at the same time preserves the identity and autonomy of each service. Key services stand out by a high maturity of software, high degree of integration within EBRAINS, existing large user community, and their central role in representative use cases. The **key services** establish the service core of EBRAINS, which is maintained and continuously improved aspiring a high level of excellence, interoperability, and user support.

EBRAINS service core comprises the service categories

- Data
- Health Data
- Atlas
- Modelling & Simulation (with the major simulation ecosystems TVB, Nest, Neuron)
- Validation & Inference

A sixth service category Embodiment is under development. The service core is embedded in an **ecosystem of support services**, critical to enable the workflows of the service core and providing additional and/or improved functionality. Focus of EBRAINS is the integration of services, which will naturally help to advance individual service quality, increase size of user community, etc. The maintenance and increase of quality of a service is the responsibility of the service provider. Priority for EBRAINS will be **a service coverage of the whole scientific value chain**. The involvement of communities, which are relevant to, but not directly part of EBRAINS services is necessary. This concerns data acquisition, neurotechnology and future computing technologies (such as quantum and neuromorphic computing).

Digital Twins in neuroscience

EBRAINS aims to contribute to the emergence of a consolidated European ecosystem of digital twins for healthcare by fully enabling the digital twin of the brain with applications in medicine. The HBP consortium has also developed a scientific vision for the coming decade of digital brain research[2], providing a detailed scientific framework for current and future development of EBRAINS. The science vision paper has been published on Zenodo allowing the community at large to identify points of convergence and contribute to the paper, thereby shaping the scientific concept together. The essential components of this vision comprise the engineering concept of digital twin and translate it to neuroscience. A digital twin comprises three components: the physical object, its virtual counterpart and the data flow back and forth between the two. The empirical brain data are passed to its digital twin, and information and processes from the twin model are passed to the physical brain in the real world.

Evolution of the Science Vision

The Science Vision of EBRAINS is a living document that will be evolving with the time. As an ongoing process in 2023, EBRAINS captures the inputs of the community and works closely with its EBRAINS Science and Technology Committee[3], in support of the development of a scientific 10-year roadmap.

Concluding remarks

As illustrated above, **EBRAINS is ready to contribute to understanding the brain and defeating brain disorders.** Optimizing brain health for paramount to ensuring human health and well-being Brain health is also central to achieving global commitments[4] such as the new Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031, the World Health organization (WHO)'s Triple Billion targets, the United Nations Sustainable Development Goals (SDGs) and the 2021 Geneva Charter for Well-being. Improving **Brain health has direct impact in achieving Goal 3 of the SDGs: Ensure healthy lives and promote well-being for all at all ages**. It has also important secondary effects on other SDGs, for example by keeping more children and young people in school. Ensuring that people living with mental illness are included in other development interventions also improves mental health and reinforces the principle of leaving no one behind. **The challenges are global, and the response should therefore be of the same calibre.**

[2] https://zenodo.org/record/7764003#.ZEi_0OxBzIY
[3] https://ebrains.eu/news/ebrains-announces-estc/
[4] https://news.un.org/en/story/2022/08/1124272