**HP** Human Brain Project

# An extensive guide to the tools developed

HP | Human Brain Project

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Cover picture 1:
*Nerve fibres of a human brain section visualised by Polarized Light Imaging (PLI). Colours represent 3D fibre orientations highlighting pathways of individual fibres and tracts.*

Cover picture 2:
*A connectivity matrix of the whole brain. The x and y axes denote regions; the colours represent different intensities of connections.*

Left:
*Cytoarchitecture of the auditory cortex of the human brain*

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# Digital tools have enabled a new era of brain research



Katrin Amunts
Scientific Director of the
Human Brain Project

"Tool building has been
at the core of the
Human Brain Project
from the very beginning."

You can learn more about HBP research breakthroughs in:

"Human Brain Project – A closer look at scientific advances".

When we talk about the many achievements of the Human Brain Project, we often focus on what we have learnt about the brain and how this new knowledge is translated into treatments for patients or into advances in artificial intelligence. What stands behind all these breakthroughs is less frequently in the spotlight: the work of the technicians, programmers, engineers and developers that makes today's advanced neuroscience possible in the first place. With this book, we want to provide an insight into this rarely highlighted work: the plethora of scientific tools developed within the Human Brain Project.

During its ten-year runtime, the project has not only generated an impressive array of new scientific insights into the brain, medical approaches and neuro-inspired technological advances, but it has also set strong emphasis on designing research technologies on a large scale, and in a standardised, combinable and science-driven way.

In fact, tool building has been at the core of the Human Brain Project from the very beginning – always with the higher aim of advancing brain research. We have consistently asked ourselves: which technologies do we need at this point in time to better understand the human brain?

To us, the answer derives from considering the nature of the human brain: a complex system organised on multiple scales in space and time. To understand such a system, we need to take the different scales into account – how signals are transmitted by tiny molecules, how individual nerve cells are structured and work together, how different parts of the brain are connected on the whole-brain level and how the activity of brain networks results in specific functions and behaviour.

This cannot be achieved using only one method or one single approach. What's more, different methods and approaches cannot simply be considered in isolation, because they describe structures and processes that are inter-connected in the real-life object. Multiple approaches need to be integrated into one system to understand how the different pieces fit together. Consequently, the HBP has combined diverse approaches in a highly integrative way – an endeavour that has been enabled by a change of research culture towards close collaboration across disciplines and by the development of enabling technologies.

Research tools are usually developed based on the needs of individual research teams in order to tackle specific scientific questions. Eventually, these tools become more broadly useful and are shared with the community. At this point, they have the potential to change the way research is carried out and give the field a boost, just like, for example, a new telescope. This process is called co-design and has to be science-driven.

The co-design of hundreds of advanced scientific tools in the HBP has only been possible thanks to the strong scientific and technological core of the project.

To be truly useful for understanding a multi-scale system, different tools must be able to communicate with each other, be compatible and interoperable. To enable this, we have built a common platform – EBRAINS (European Brain ReseArch INfrastructureS). The research infrastructure hosts the different tools under one umbrella and not only enables a variety of approaches but also the merging of approaches and results of different research groups.

EBRAINS is the result of a development that started with 12 interacting technical and scientific sub-projects. These led to the first release of six independent platforms in 2016. Our work to make them compatible for scientific cross-platform workflows led to the HBP Joint Platform in 2019 – with increased integration ultimately resulting in EBRAINS as a collaborative Research Infrastructure listed on the selective ESFRI Roadmap. Like the brain itself, the infrastructure development has to be malleable so that it can evolve over time to address new challenges.

An active infrastructure not only requires technology, but also people who provide the interface between researchers and providers. In our case, these are the Scientific Liaison Unit (SLU) and the High-Level Support Team (HLST). And an infrastructure needs training – not only did the HBP develop technology for the community, but it also ran the HBP Education Programme, where digital neuroscience was taught to the next generation of researchers, with more than 6,000 participants over the years.

Combining tools, pipelines and complex workflows of different groups, even over long distances and at large scale is today not only possible but is in fact the new standard of digital brain research. This also means that not everyone has to build everything on their own. If you have a big idea, now, it's much easier to put it into practice and to build on the work of others using the same building blocks.

Ten years of HBP have established a new basis for collaborative brain science. The project has yielded tangible results that will shape the future: novel research technologies of the highest calibre and a new generation of scientists that is highly adept at using them and has learned to flexibly look beyond single scales and methods. The newly founded community routinely collaborates across borders of disciplines and states – across scales, and at scale.

*Katrin Amunts*

To better understand the complex system of the human brain, HBP researchers have developed and combined methods on different levels – from the molecular to the cellular to the whole-brain scale.

# Why brain science needs
# shared infrastructures



Jan Bjiaalie
University of Oslo,
HBP Infrastructure
Operations Director



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Athena Research Center,
HBP Software
Development Director

Ten years ago, the Human Brain Project set out to employ advanced Information and Communication Technologies to meet one of the greatest challenges of the 21st century: understanding the complexity of the human brain.

Studying the brain as a multi-scale system requires researchers to combine their knowledge and approaches and to integrate different types of data from multiple spatial and temporal scales into a common reference space. The requirement for advanced technological solutions is exemplified by the amount of data generated by high-resolution imaging technologies, which reaches the terabyte to petabyte range. The ability to store, share and analyse such data is critical for advancing our understanding of the brain.

We have come a long way since the beginning of the HBP. In 2013, the field of neuroscience was only just starting to use high-performance computing (HPC) and advanced digital tools at scale. In the meantime, we have witnessed an explosion of new technologies that have revolutionised the way we study the brain. The HBP has ushered in a new era of digital brain research, building a large interdisciplinary community that includes neuroscientists and engineers who work together in a highly collaborative way. This has resulted in the development of an impressive number of technologically mature digital tools, including those for atlasing, modelling and simulation, data analysis and visualisation.

Brain research and technological developments have been spurring each other on. The ever-increasing technological demands of brain research have driven the development of cutting-edge computing technology, whether it is in traditional supercomputing or brain-inspired neuromorphic computing systems, while, conversely, technological progress is allowing neuroscientists to ask ever more challenging and visionary questions. The digital tools that we have developed in the HBP have already allowed us to solve problems that were once thought intractable.

This book presents a snapshot of the current status of these tools, all of which are openly accessible to the entire scientific community, to enable the continuation of a highly collaborative and systematic effort to study the brain as pioneered by the HBP.

To provide these tools via one common platform and to facilitate large-scale collaboration, the HBP has built the EBRAINS digital infrastructure. Importantly, many of the scientific tools have been made compatible with each other on this platform, thereby enabling users to combine multiple tools into unified complex workflows. The open platform offers free access not only to digital tools but also to data, models and services as a lasting contribution of the HBP to scientific progress.

Key to this progress are reproducibility and replicability, which are intimately dependent on robust digital tools. Hence, EBRAINS sets high standards on the quality of such tools, including their documentation, versioning methodology, and overall maintenance and support. Accessing tools from a single platform has the additional advantage that users can learn how to use different tools much faster because they are already familiar with the interface.

It is important to note that the tools that you will find in this book are only the tip of the iceberg: they are built upon a foundational layer of technologies, services and computing infrastructures that are less visible (ideally, completely invisible) to the end user. Many of the tools that the HBP offers to the community via the EBRAINS platform rely on powerful supercomputing as well as cloud and multi-petabyte storage systems, which are provided by the Fenix infrastructure – a federation of six of Europe's leading supercomputing centres. Through Fenix, brain researchers from all over Europe can now access these resources much more easily. The infrastructure has been developed for the HBP, but it is versatile enough to be already used by many research groups from other communities. The Human Brain Project has brought together brain researchers and computer scientists and engineers building a strong interdisciplinary community that drives the advancement of digital brain research. At an even more fundamental level, it has also brought us closer as Europeans.

We would like to encourage you to explore the tools that have been developed in the HBP and make full use of them for your research. Let's build on these foundations to push the boundaries of our knowledge even further!

*Jan Bjaalie, Yannis Ioannidis, Thomas Lippert*



Thomas Lippert
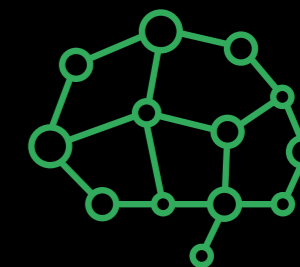Jülich Supercomputing
Centre, Leader of HBP
Computing Services

"The digital tools that we have developed in the HBP have already allowed us to solve problems that were once thought intractable."

# EBRAINS

# Service Categories

The brain is a multi-scale system, and, consequently, our methods must strive to become multi-scale as well. The EBRAINS Research Infrastructure makes it possible to connect digital research tools within common frameworks, to allow the many excellent tools displayed in this book to be combined into multi-scale research workflows. As these integrated efforts advance, collaboration across deeply ingrained borders of different sub-disciplines and often siloed communities is becoming ever more seamless. This is the unique benefit of an integrated infrastructure - it helps us connect scales, efforts and people.

EBRAINS will remain available as a lasting contribution of the HBP to global scientific progress. All researchers are welcome to join the EBRAINS community.
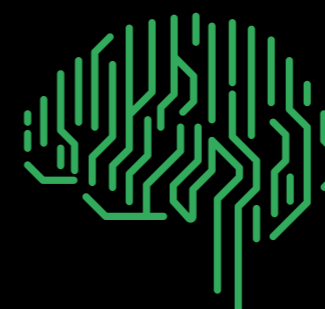
## Data and Knowledge

EBRAINS Data and Knowledge services facilitate sharing of and access to research data, computational models and software. These services revolve around an expert-driven Knowledge Graph which combines metadata ingestion pipelines, human-user input and multiple quality assurance processes to help contributors and users by ensuring data consistency and quality.

## Atlases

Brain atlases provide spatial reference systems for neuroscience, giving the ability to navigate, characterise and analyse information on the basis of anatomical location. Atlases define the shape, location and variability of brain regions in common coordinate spaces and allow interpretation, integration and comparison of observations and measurements collected from different sources and different brains.

## Simulation

Simulation is a powerful instrument for understanding the human brain, which is a complex dynamic system with a multi-scale architecture. Understanding the complexity and versatility of the brain and the variations between different brains are major scientific challenges that are driving the development of simulation technology.

## Brain-Inspired Technologies

EBRAINS offers brain-inspired tools and services to understand and leverage the computational capabilities of spiking neural networks. In contrast to standard deep neural networks, which consume considerable amounts of energy, spiking neural networks shed light on the human brain's ability to continuously learn and express higher cognitive functions while consuming much less power.

## Medical Data Analytics

The Medical Data Analytics service currently hosts the Medical Informatics Platform (MIP), a unique EBRAINS platform providing advanced analytics for diagnosis and research in clinical neuroscience.
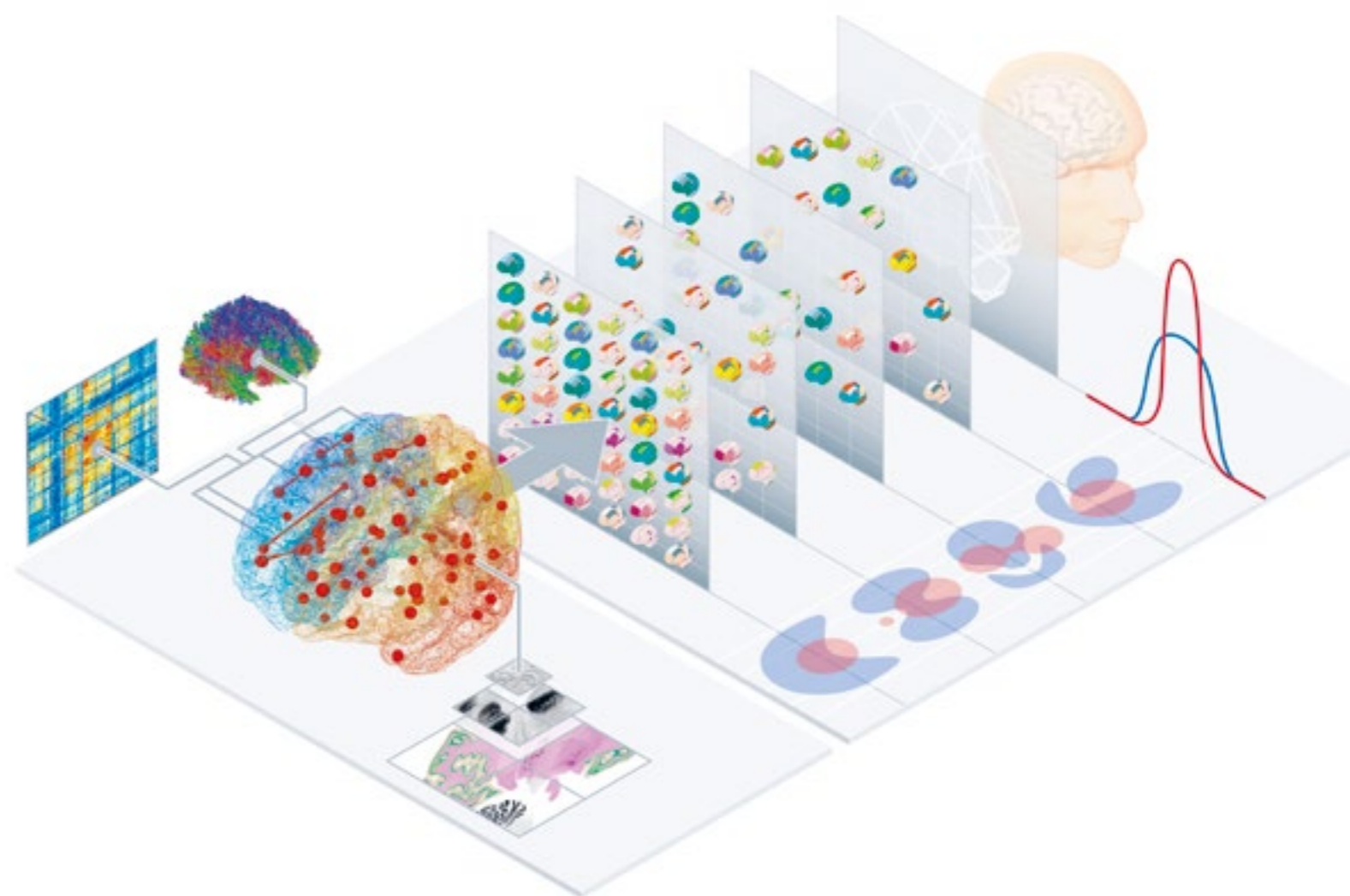
# The EBRAINS showcases

## Building a cohort of virtual brains to unravel the relationship between structure and function

HBP scientists are using advanced simulation and atlasing tools together with a large dataset from a population-based cohort study to identify mechanisms underlying brain ageing.

The following showcases demonstrate how the tools and services developed in the HBP and offered to the community via its EBRAINS infrastructure enable innovative and complex scientific workflows to address some of the most challenging questions in neuroscience.

HBP-developed tools are highlighted with a small arrow (→). More detailed descriptions of the individual tools can be found from page 30.



*Workflow for simulating ageing in a cohort of virtual brains*

Every human brain is different. Yet, despite variations in structure and activity, different brains can maintain similar functionality, for example, perceiving a sound or processing language. The reason for this is that one function can be based on different configurations – different patterns of neural activity. This phenomenon of multiple configurations leading to the same result is present in many complex systems and is called "degeneracy", or in the case of the brain "neurodegeneracy".

In brain research, relating structural variability to functional variability in a clear, unambiguous fashion is very difficult due to neurodegeneracy. A structural change may cause loss of function in one person's brain but have no or little consequences in another individual. For two patients with identical symptoms, a drug may be efficient for one patient and have no effects for the other.

As we age, our brain structure changes and this has functional consequences, but due to neurodegeneracy the consequences of a specific structural change can vary across individuals. This makes it difficult for researchers to pinpoint which structural change is responsible for which functional change such as cognitive decline. To take variability and neurodegeneracy into account, many different brains need to be studied.

"The ideal dataset to better understand ageing mechanisms would be both vast and longitudinal: a large cohort of people whose brains have been scanned at multiple timepoints as they age," says HBP researcher Gorka Zamora-López from Universitat Pompeu Fabra (UPF) in Barcelona. "To date, nobody has produced such a dataset. So, can we understand variability with less data at our disposal? Could brain simulation fill the gaps? How much data is enough?"

## Exploring brain differences in large datasets

With the help of advanced simulation tools, HBP teams from UPF, Aix-Marseille Université (AMU), Forschungszentrum Jülich (FZJ) and University of Düsseldorf (UDUS) have set out to disentangle the mechanisms that affect brain function during ageing. Simulation enables the researchers to test hypotheses about specific causalities, e.g., whether a specific structural change indeed causes a certain functional outcome. To this end, the researchers build virtual brain models based on a large dataset and then simulate the ageing process – on a much shorter timescale than it happens for humans.

"Where does healthy ageing stop and pathological ageing begin? How can we push the onset of pathological ageing further in the future? Can we stop it? These questions are being tackled with this work. It cannot be done only experimentally, we need model-based approaches in order to get answers from the best data available," says Viktor Jirsa, leader of the HBP's work package on the human multiscale brain connectome,
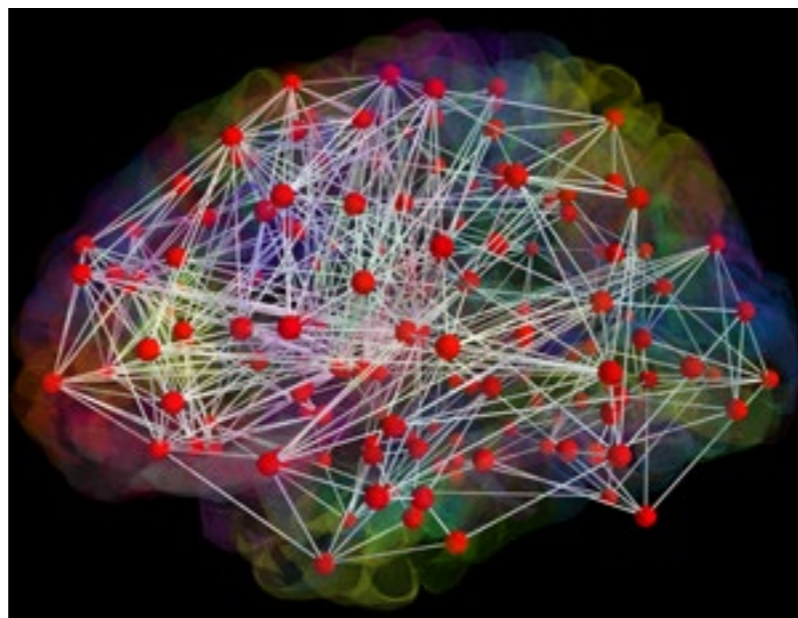


*The Virtual Brain enables computational models of the brain on the network scale.*

Director of Research at Centre national de la recherche scientifique (CNRS) and Director of the Institut de Neurosciences des Systèmes (INS) of Inserm and AMU.

The researchers made use of a large dataset derived from the population-based cohort study "1000BRAINS" carried out at FZJ. The study includes more than 1,000 participants aged 55-85 who have been examined by magnetic resonance imaging (MRI), generating an unprecedented amount of data on brain connectivity, both structural and functional. Systematically analysing this data, the researchers identified specific structural changes associated with ageing.

Based on the detailed dataset about structural variability, the researchers have generated virtual brain models in order to simulate the functional consequences of structural changes associated with ageing. Their work is enabled by a link between the HBP's Multilevel Human Brain Atlas and The Virtual Brain (TVB) simulator – a platform for constructing and simulating personalised brain network models.

In order to build the virtual brain models, the researchers extracted data from the data management system →EBRAINS Knowledge Graph using the →siibra-python software. siibra-phyton enables structured access to spatial properties of brain regions from the microstructure to the whole-brain level as well as access to regional data features from different modalities such as cytoarchitecture, densities of neurotransmitter receptors and functional data.

Through siibra-python, the researchers combined the connectivity data with spatial maps of neurotransmitter receptor densities linked to the Multilevel Human Brain Atlas. The receptor maps provide important microstructural information about different brain regions – the local organisation on a functional level. Combining this micro-scale data with the data at the whole-brain connectome level from the 1000BRAINS

study allowed the researchers to build more precise models. They then used the simulation tool →TVB EBRAINS to build whole-brain virtual models based on this empirical structural and functional data.

The HBP researchers set out to test the hypothesis that structural changes associated with ageing lead to a decline in cognitive performance. To this end, they virtually aged a brain model by introducing the specific structural changes and then simulated brain activity during this virtual ageing process. Analysing the patterns of brain activity, they observed the same functional changes that they found across the ageing process in the empirical data of the participants of the 1000BRAINS study. The results support the hypothesis that the specific structural degeneration was indeed responsible for a cognitive decline – at least on a group level.

To understand whether this effect could also be observed on the individual level, the researchers generated an entire cohort of virtual brains, each based on the data from one single subject of the 1000BRAINS study. As expected, they found that the individual structural changes led to the hypothesised functional effects, confirming the group-level prediction. But they also correctly predicted functional decline to be more pronounced in some than in others, despite the same amount of structural change. The researchers attribute this finding to neurodegeneracy.

## Simulating brain ageing

The virtual ageing involves the simulation of brain activity in many different network nodes in parallel over a relatively long time period of 10 to 20 minutes (equivalent to the time of MRI measurements performed in the study participants at resting state). The models are based on multiple combinations of different parameters and simulations are run for hundreds of subjects in parallel. To handle this large amount of data and massive parallelisation, the team used a special backend of TVB called →RateML, which employs high-performance computing.

To make their workflow easier to use, a set of modular graphic components and software solutions called →TVB Widgets was developed by the software company Codemart in co-design with the HBP team at AMU. Among other features, the TVB Widgets allow users to interactively navigate the EBRAINS Knowledge Graph and enable them to generate plots by providing parameters interactively rather than writing them into code. "The TVB Widgets we have developed for this study make our tools more accessible to a larger number of people," says AMU researcher Jan Fousek.

Next, the HBP researchers want to add a longitudinal dimension to their study by including MRI measurements of the same individuals taken several years later. So far, the ageing effects have been studied by correlating structural and functional changes with the age of the subjects. Having data from several

timepoints will provide valuable information about the effects of ageing on an individual level.

Beyond ageing, the researchers aim to apply their model to study further factors that affect brain structure and function. "We used age as the first factor to be implemented, because data on this is abundantly available and could thus serve as a test case. And age is a factor for which at least some theories exist on how it might affect the brain in a systematic way," explains Svenja Caspers, deputy leader of the work package and Director of the Institut für Anatomie I of the Heinrich Heine University Düsseldorf and leader of the 'Connectivity' group at FZJ.

"The virtual model has enabled us to prove theories that we could previously only suspect to be true. Now that we have this working model, we would like to widen our view and integrate other factors as well," says Caspers. The team is now studying how lifestyle factors such as smoking, alcohol consumption, social integration and nutrition affect the brain using data from the 1000BRAINS study. "Being able to predict on an individual level how a certain lifestyle affects the brain would be invaluable for medicine, because it would allow physicians in the long run to provide patients with personalised recommendations to slow down or even prevent cognitive decline," says Caspers.

## Moving towards personalised medicine

The scientists expect that, ultimately, a better understanding of degeneracy and brain variability will assist in the effort to deliver personalised brain medicine also for patients with disorders such as Alzheimer's disease or dementia. In fact, the virtual models can be used in many different contexts to test various hypotheses about the brain.

"Our work demonstrates one way how these digital tools can be combined to answer a specific scientific question. What is exciting is that, like LEGO® bricks, the tools we have built in the HBP can be mixed and matched in many different ways to build something new that serves your specific purpose, and different components of our toolbox are interoperable," says Fousek.

The researchers plan to integrate the technical implementation of their workflow with the virtual epileptic patient (see p. 61) in order to provide the simulation tools within one framework including a common space in the EBRAINS →Collaboratory. This will facilitate the usage of the model to address a larger variety of scientific questions to decode the complex connection between brain structure and function.

# Improving epilepsy care using HBP-developed simulation tools

| Research tools have empowered the translation from basic neuroscience into clinical applications.

As well as helping us to understand a disease or neurological condition, virtually modelling the brain can also provide tools for better therapy. An example is epilepsy, which affects more than 50 million people globally. Epilepsy is a matter of brain excitability: abnormal electrical activity in certain zones of the brain can lead to life-altering seizures. The brain dynamics of a person who has epilepsy can be extremely complex.

One third of all epileptic patients develop resistance to drugs. For these patients, the surgical removal of the areas of the brain where the seizures emerge becomes the only treatment option. These areas are called the epileptogenic zones and they vary from patient to patient. How does a surgeon know where exactly this zone is? How far does it reach into the patient's brain; what is its shape?

Removing a piece of brain matter always requires careful decision making – generally, you want to remove as little as possible, but inadvertently keeping part of the unhealthy tissue could negate the whole operation. Clinicians estimate the seizure-inducing areas by inserting electrodes into the brain, taking stereo-electroencephalography (SEEG) readings. This established procedure, however, may not provide the full picture of the extension of the area. Currently, only 60% of patients are seizure-free after the surgical removal.

In order to more precisely detect the epileptogenic zone and better inform clinicians, researchers in the HBP have employed whole-brain simulation: generating whole-brain, personalised, virtual brain models of epileptic patients using the individual measured brain data. In extensive tests, the scientists have confirmed that these computer models are indeed able to predict patient-specific brain activity dynamics and effects of changes in the brain. For the clinic, that could mean letting the models act as virtual patients, replicating as accurately as possible the real seizure dynamics. HBP researchers at the Institut de Neurosciences des Systèmes (INS) in Marseille use The Virtual Brain (TVB) simulation platform to investigate these dynamics.
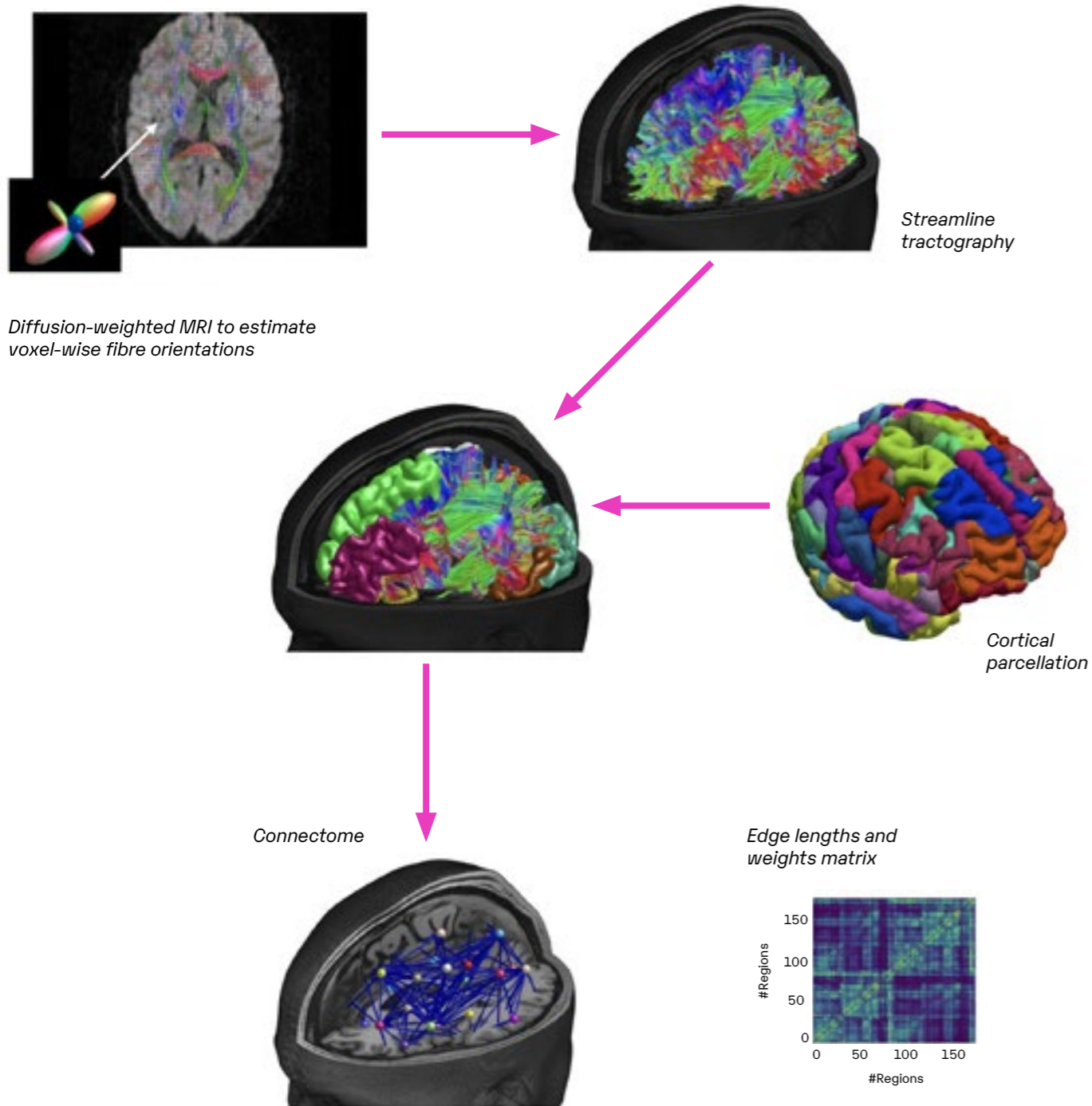
## Reconstructing a brain

TVB is an ecosystem for whole-brain network simulation and offers a family of tools capable of approximating the human brain into a network of 60 to 500 nodes. Each node represents a distinct neural mass of hundreds of thousands of neurons characterised by various parameters, of which one is excitability, relevant to seizure generation.

The researchers start from empirical imaging data of the patient's brain using structural and diffusion MRI. This data is processed through the →TVB Image Processing Pipeline and inserted into →TVB EBRAINS. "This process gives us a delineation of each node but also the strength of the connection between each node – the so-called connectome," explains Jan Paul Triebkorn, computational scientist at the INS.

*Patient-specific brain imaging data are combined with computational models to locate the epileptic zone.*

*Diffusion-weighted MRI to estimate voxel-wise fibre orientations*

*Streamline tractography*

*Cortical parcellation*

*Connectome*

*Edge lengths and weights matrix*

*Generating the personalised connectome of the brain of a patient for TVB*

The thickness of the fibres and closeness between each node increase the likelihood that the seizure will spread in a particular direction, and this varies from one individual to another.

Once TVB EBRAINS has assigned and connected the nodes, it is a matter of refining the set of excitability parameters assigned to each node. Using the →TVB Inversion tool, which employs the Bayesian EBRAINS pipeline, the researchers fine-tune the parameters iteration after iteration to match the original SEEG recordings of the patient as accurately as possible. This

specific workflow, tailored to TVB by the researchers, is called Bayesian Virtual Epileptic Patient (→BVEP). It simulates thousands of possible seizure-spread patterns (a "taxonomy of seizures", described by mathematical equations), and, using probabilistic machine learning to quantify the amount of uncertainty of each pattern, eventually arrives at the closest match with the one recorded in the patient.

"We estimate the uncertainty caused by hidden variables and aim to refine our estimates through Bayesian inference, which is a process that updates the statisti-

cal probability of a certain event as more information becomes available," says computer scientist Meysam Hashemi. Simulating a few-second-long seizure in a single node might require a few seconds of computation, but the process has to be repeated for each node and has to take the interaction between connected nodes into account, bringing the overall time necessary to run a simulation for a single patient to roughly half a day. The researchers have provided Jupyter Notebooks in EBRAINS outlining all the steps for this pipeline.

## Reconstructing a brain from the simulator to the hospital

The researchers' aim is to provide clinicians with more precise predictions about the potential paths for treatment for each patient. The final result of the simulation process is a report that estimates the likelihood that each node, corresponding to a brain area, might be epileptogenic. This is visually matched with the brain scans of the patients, highlighting the areas which are the best candidates for removal.

TVB can pinpoint other areas than those which were initially expected, since they may have escaped detection during the original readings. The decision on what to remove, however, still rests with the clinician. "The doctors might provide us with relevant background information on the patients that we can use to refine the simulation. It's a highly collaborative process," says Triebkorn.

The methodology is currently undergoing a large-scale clinical trial in eleven French hospitals, involving almost 400 patients. The trial is called EPINOV and has been developed in collaboration with neurologists at the Timone Hospital in Marseille. Started in January 2019, EPINOV is expected to last four years and related studies have shown some promising preliminary results. "Physicists like myself work with theoretical equations all the time. It's exciting to see them given context and material applications that can help people's lives," says Hashemi.

## Reconstructing a brain with multi-scale co-simulation

TVB is a so-called whole-brain simulator, approximating tens of thousands of neurons to individual nodes, down to a single parameter. While this allows simulation of the excitability of nodes, it doesn't give information on why a particular node may be excitable. This is where other EBRAINS-integrated simulators, such as the →NEST Simulator, come into play.

The NEST Simulator is capable of modelling the activity of individual neurons in a smaller area and at much higher time-resolution. Normally, these two simulations would be incompatible, because they are

running at such different scales, but the HBP researchers wanted to run their simulation on multiple scales simultaneously.

To this end, another INS researcher, Lionel Kusch, in collaboration with the FZJ, has developed a method to run both TVB and NEST at the same time via the EBRAINS infrastructure, allowing for co-simulation (→Modular Science). When run on EBRAINS, the data of NEST is compatible with TVB. "Currently, no computer is powerful enough to simulate the whole brain at the microscale, but with co-simulation, we can zoom into an area of particular relevance, down to individual neuron activation, while keeping the whole picture of the brain in mind," says Hashemi. "Instead of resembling the brain as much as possible, we aim to selectively reduce the amount of relevant information for our predictions."

The researchers see potential in the digital tools developed within the HBP that goes beyond their current use for epilepsy. The process is flexible enough to be adapted to many scientific questions. Researchers could, for example, obtain data from the →EBRAINS Knowledge Graph or use their own dataset, process it with a dedicated pipeline, simulate brain connections using one of the different tools within TVB and then match the results with the HBP's Multilevel Human Brain Atlas thanks to the recently implemented integration of the →siibra-explorer tool.
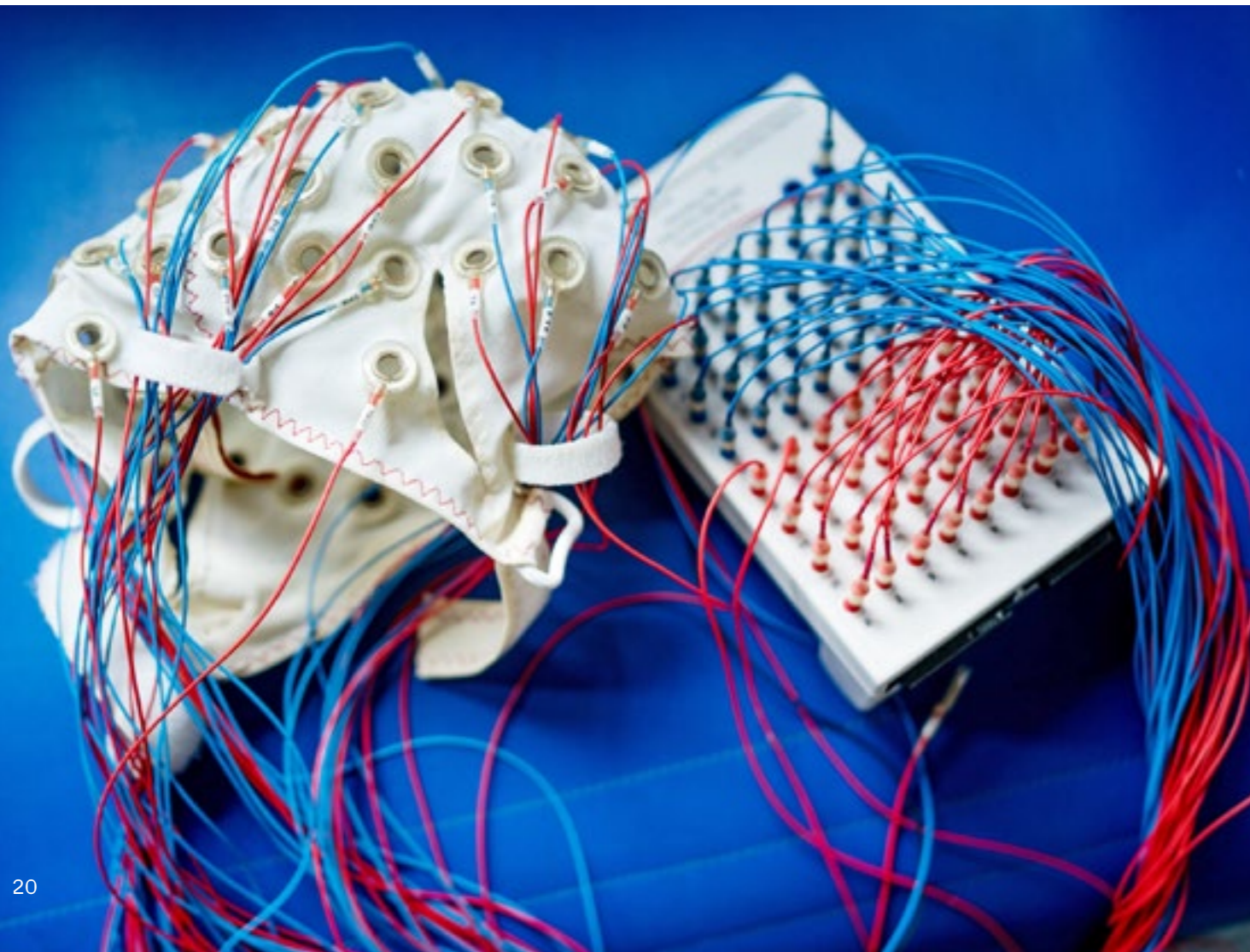
Even though the brain scans and medical data of the patients from the ongoing study are kept private to comply with regulations for sensitive medical data, other curated image and connectome datasets are publicly available and can be accessed through the EBRAINS Knowledge Graph, the starting point for many experiments in HBP.

"TVB has already been used for Alzheimer's, Multiple Sclerosis and for analysing resting states, and we anticipate further medical applications. Future advances in brain modelling will open a path to digital twin approaches in brain medicine," says INS Director Viktor Jirsa, who leads the research. Digital twins, a concept borrowed from engineering, are virtual representations of an object or a system, which can be used to simulate its behaviour and dynamics. Jirsa concludes: "Improvements are to be expected along two main lines: high resolution of the data and patient specificity. The integration of these factors has been made possible within the HBP, through the use of modelling software, computing power, brain atlases and datasets provided on the digital research infrastructure EBRAINS."

# New tools to measure levels of consciousness

> Innovative multi-scale modelling tools allow researchers to simulate micro- to whole-brain-scale networks and measure different states of consciousness.



*An EEG cap – magnetic stimulation and simultaneous EEG readings are used to determine the level of consciousness.*

How consciousness, and the loss thereof, are reflected in the brain has long been an open question in neuroscience.

Each year, about a million patients worldwide are sent to emergency services after a brain injury, but determining their levels of consciousness remains difficult. Understanding fundamental mechanisms that support consciousness is crucial for guiding diagnoses, determining treatment options and supporting better patient recovery following brain damage – and it is also key for better understanding our own existence.

Yet, exploring the neural underpinnings of a phenomenon like consciousness has proven to be an enormous challenge, due to the brain's complexity. While addressing these questions, HBP researchers have made significant advances using digital technologies. Their work and the digital tools they have developed are paving the way for a deeper understanding of human consciousness.

## Measuring consciousness levels

HBP scientists are working on new methods to detect states of consciousness directly from brain activity. A HBP team at the University of Milan has developed a tool called the Perturbational Complexity Index (→PCI), which supports non-invasive measurement of levels of consciousness.

In order to calculate this index, a weak magnetic pulse is applied to the head of a patient, momentarily perturbing spontaneous brain activity that is always present in the brain. The brain response to this pulse is simultaneously measured with EEG. In unconscious states, this response is not necessarily weaker, but rather less complex. In other words, the complexity of the brain's response is indicative of the level of consciousness of a person. The measurements are then compressed using an algorithm – cases with highly complex responses will have lower compressibility and vice versa.

This method has been tested and validated not only at the University of Milan but also in collaboration with HBP colleagues at the University Hospital of Liège, who are working to improve the clinical care in both intensive care and neuro-rehabilitation settings.

At the Coma Science Group in Liège, the researchers work on patients with disorders of consciousness after severe brain injury. "We assess them using fMRI and EEG and also test different treatments in computer simulations. In the HBP, we work mostly on model-based assessments of the different brain states that are associated with the levels of consciousness," Jitka

Annen, neurobiologist and postdoctoral researcher, explains.

The current gold standard for assessing these patients is through behavioural tests. However, patients can be misdiagnosed when these behavioural methods cannot detect covert signs of consciousness. Therefore, other objective measures such as the PCI or neuroimaging are important tools for improving diagnosis.

For example, diagnosis of brain states classically based on behaviour has roughly differentiated between "unresponsive wakefulness syndrome" (formerly known as "vegetative state") and a "minimally conscious state". Beyond behavioural methods, neuroimaging of electromagnetic and chemical signatures of neural activity has emerged as an important, quantitative tool to improve the resolution of neural activity related to the capacity for conscious processing. "With neuroimaging tools, we can identify patients in a minimally conscious state who, based on behaviour alone, would have been misdiagnosed as unresponsive," says Annen.

In this context, computational modelling is also a powerful tool to investigate brain dynamics in different consciousness levels and has a great potential for clinical applications.

## States of mind – from micro to macro

HBP neuroscientists have also drawn inspiration from physics, which has been successful in understanding the relationship between different scales. For example, when looking at states of matter, it is possible to see that changes at the microscopic scale determine macroscopic characteristics, such as being a solid, liquid, gas or plasma. When it comes to different brain states, there is also an interrelationship between micro-, meso- and macro-scale activity, but this has previously not been well understood.

"We can make an interesting analogy between states of matter and states in the brain to study the interaction between microscopic and macroscopic scales," says Jennifer S. Goldman, an EITN postdoctoral fellow and lead author of HBP studies at the Centre national de la recherche scientifique (CNRS) within Paris-Saclay University.

Now, HBP researchers at the Paris-Saclay University and the Aix-Marseille University (AMU) have made progress in understanding the multi-scale biological mechanisms regulating consciousness, using computational modelling to study spontaneous (background activity of a "resting brain") and evoked brain activity (responses to sensory stimuli or direct electromagnetic perturbation of the brain).

These new multi-scale models of brain networks allow researchers to integrate data across different scales of the brain – from the neurons to networks and the whole brain – and to simulate their dynamics. This

*MRI scan being carried out at the University of Liège*

group has recently shown that macroscopic, whole-brain-state transitions between spontaneous dynamical regimes associated with different levels of consciousness can be explained by shifts caused by molecular and cellular microscopic events.

In order to achieve an integrated understanding of neural activity patterns over several spatial scales, the HBP scientists in France have used a class of models called "mean-field models", which are built using statistics from microscopic-scale data. They used these models to describe the activity of neurons at the level of a population, moving to the large scale in a typical bottom-up construction of a whole-brain model.

For this construction of a whole-brain model from the ground up, the theorists started at the neuron level, with a biophysical model called Adaptive Exponential (AdEx) integrate-and-fire. Next was the level of neuronal population, or the mesoscale, which was captured by mean-field models of networks of AdEx neurons, each representative of a tiny area of brain tissue, like a pixel in a camera.

The next step, towards macroscopic scale, was to integrate the mean-field models to model phenomena at the scale of several brain areas, up to the entire brain. For that, they used →TVB EBRAINS as a simulation platform, incorporating the mean-field model into a large network of mean-field units constrained by the entire human brain connectome, to create the →TVB-AdEx.

These new TVB-AdEx models can simulate microscopic processes, like changes in spike frequency adaptation – the synchronised periods of silence and activity observed in neural assemblies during unconsciousness. Simulating microscopic changes and observing the effects on the macroscopic whole-brain scale, the team found they were able to capture both the slow-wave dynamics, which are typical of unconscious states, and the irregular dynamics, present in conscious states, on the whole-brain level.

In other words, making changes at the microlevel could reproduce brain-state dependent dynamics at the whole-brain macrolevel. "If we change the spike frequency adaptation, or do other manipulations at the microscopic scale in the model, we can see the emergence of global rhythms that are associated with sleep or wakefulness, the more synchronous or asynchronous regimes. We study the emergence of different patterns based on these microscopic changes," says Goldman.

## Clinical advances

The researchers found that the model responds to stimuli in the same way human subjects do in experiments. "We discovered that, just like in the experimental data, if we give an external stimulus to the simulated brain, the response depends on the state of activity exhibited by the model," says Alain Destexhe, research director at CNRS within Paris-Saclay University, who supervised this work.

With their new plugins for TVB platform, the researchers demonstrated a scale-integrated understanding of different states of consciousness and some of their underlying mechanisms.

The CNRS team is now investigating the effect of drugs and anaesthetics, by integrating their action on different synaptic receptor types, and how this micro-scale action can lead to the emergence of different macro-scale activity states, for example, how anaesthetics can switch brain activity to slow-wave dynamics.

The personalisable models used in this research currently rely on anatomical data that can be non-invasively obtained from humans using imaging techniques. These models will serve as substrates for the development of subject-specific models of human brain activity, including restful and waking states, as well as sleep, anaesthesia and coma, to aid future advances in personalised medicine.

"In the future, more detailed patient data – genomic, proteomic or metabolomic data – can be included to improve the accuracy and predictive power of personalised models," says Goldman.

"This is the first time that we have the tools to predict global changes in brain activity following changes at the level of synaptic receptors, which can be applied to anaesthesia, drug actions, pathologies, or even to predict ways to restore consciousness in patients suffering from brain lesions," says Destexhe.

The researchers also used the model to simulate the measurement of levels of consciousness as done with the Perturbational Complexity Index (→PCI) developed in Milan: By running their simulation through the →TVB-AdEx model, the researchers demonstrated that inducing wake-like asynchronous states was accompanied by high PCI after stimulation. The reproduction of experimental PCI results validates the model, besides offering a view of micro- and mesoscale that is not seen in the PCI experiments.

"This is an incredibly exciting time, because we now have scientific tools to really investigate this centuries-old question that has previously been contemplated in religion and philosophically," says Goldman. "Such work offers integrated insights into sleep and wakefulness that are relevant for everyone, while supporting a better understanding of the multi-scale mechanisms underlying insomnia, other sleep disorders, anaesthesia and head trauma."

Especially exciting is the close connection between modelling and clinical experiments. "Such a thorough multiscale exploration is unique and provides a solid mechanistic background for our method to detect consciousness," says PCI developer Marcello Massimini.

*conscious-like dynamics*    *unconscious-like dynamics*
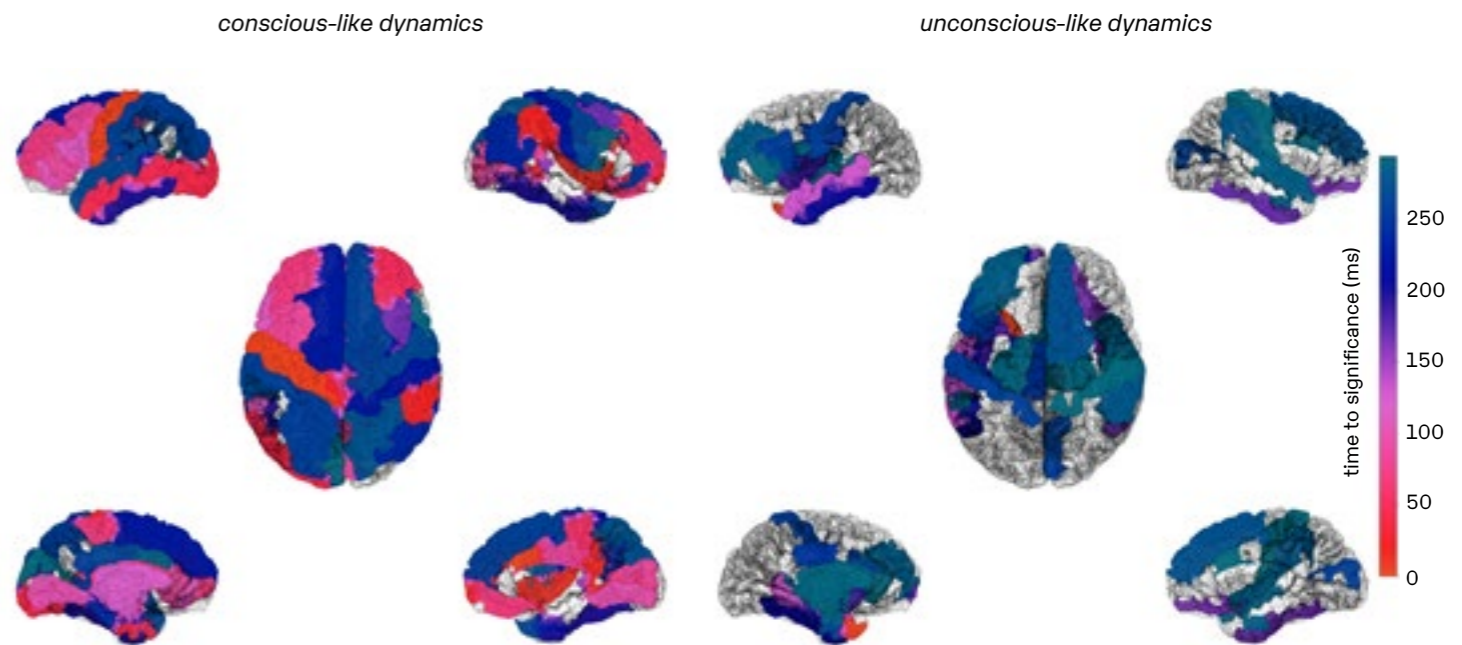


*Simulated human brain activity during conscious-like and unconscious-like brain states. Colour bar represents the time of earliest significant change of neural firing rate in response to stimulation.*

# Why artificial brains need a body

> Human cognition is grounded in bodily experiences within the physical world. Cognitive scientists have discovered the combined use of brain modelling and robotics as a new path to emulate this interaction.

Today's AI is impressive but strangely disembodied. Many cognitive functions that we previously thought exclusive to biological brains now get solved by large language models, image recognition systems and more – but these hyper-specialised models have no bodily experience whatsoever and lack environmental interaction.

The same is true for many computer models of the brain used by neuroscientists. While they represent high-resolution brain networks of massive complexity and prove to be predictive and useful even for clinical work, how much can such "brains in a jar" really tell us about the richness of real-life cognition – where mind and brain interact with a body as well as an environment at all times? How do these systems compare to biological brains?

Such are the questions that have led brain modellers and experimentalists to robotics. In order to study "embodied cognition", the HBP community has pioneered new scientific tools that allow connecting virtual brain models and robotic bodies.

The research is mainly driven by neuroscientific questions, but giving robots a better brain opens up opportunities for technologists as well.

## Robots coming to their senses

From neuroscience we know that familiar places can be recognised most accurately if information from different senses is combined. While it is easy for humans and animals to do this, artificial steering systems of robots still struggle with this task.

A HBP team led by neuroscientist Cyriel Pennartz from the University of Amsterdam emulated this process by simulating multisensory navigation with a neural network model they named MultiPredNet. The network is based on predictive coding, a theory of how the brain uses prediction and representation to navigate the world more efficiently.

"It's a unique situation," says Pennartz. "We were able to say: here's an interesting model of perception based on neurobiology, and it would be great to test it
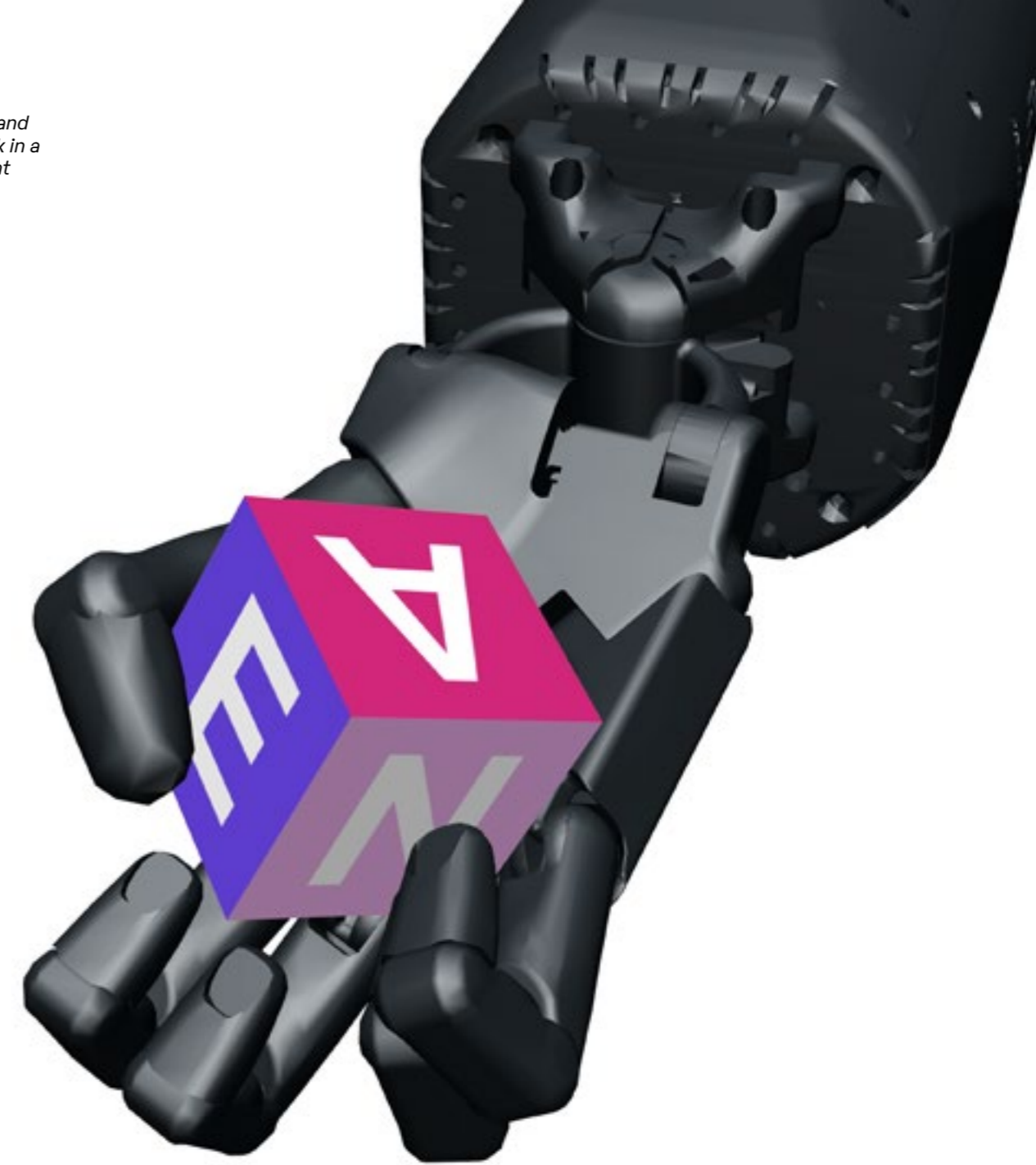
on a larger scale with supercomputers and embodied in a robot. Doing this is normally very complicated, with many technical hurdles, but the HBP and EBRAINS made it possible for us."

On the EBRAINS infrastructure, Pennartz and roboticists of the Bristol Robotics Laboratory (BRL) were able to devise a custom-made experiment and share both the methods and all data with the community through the →EBRAINS Knowledge Graph. First, the MultiPredNet was built from real-life data of rodents, implemented as a spiking neural network of interconnected models of cortical structures of the rat. The network was then connected to a robotic rat-like body with 24 artificial whiskers and two cameras as eyes, the so-called WhiskEye robot.

The team used the HBP's →Neurorobotics Platform (NRP) to create a fully virtual version of their robot, which allowed for the running of many experiments in parallel using different parameters. The NRP is a web-based robotics and neuroscience research tool enabling the design of virtual robots coupled to spiking neural network simulators.

"What we were able to reproduce for the first time in an artificial system of this scale is how the brain makes predictions across different senses – in this case tactile and visual information," Pennartz explains. "You can predict and represent how something will feel from looking at it and vice versa your brain can generate a visual image – like visual imagery – solely based on tactile input." The researchers showed that the brain-de-

rived solution can combine visual and tactile information more robustly than previous artificial systems, and that the robot can use this combined information for place recognition and navigation more efficiently than in prior, artificial networks.

The group is now moving on to enhance the cognitive capabilities of larger predictive coding models, such as parsing the environment into different objects, and recognising the same object from different viewing angles.

The algorithm is able to recognise places even when one of the sensors – visual or tactile – momentarily "drops-out", akin to the way humans or animals are able to navigate their environment even with incomplete or changing information from the different senses.

And it is extensible so that further senses can be included in the future. The virtual robot and environments are accessible on the NRP for further open testing.

## Lending artificial brains a hand

Another team based at Maastricht University supervised by Mario Senden and Rainer Goebel designed an experiment to explore how the brain determines the versatility of the human hand. Every day, we manipulate objects with a high degree of dexterity – whether we're typing on a computer, playing a musical instrument or even just turning a key to unlock a door. While these tasks may seem simple, in-hand object manipulation engages a large-scale brain network encompassing sensory, association and motor regions. To explore such sensory-motor processes, the cognitive neuroscientists developed a dedicated tool called →AngoraPy, short for "Anthropomorphic Goal-Driven Responsive Agents in Python". AngoraPy enables neuroscientists to build and train neural network models with a brain-derived architecture in ecologically valid settings using reinforcement learning and goal-driven modelling.

To add biological constraints and more closely mimic the biological neural network in the human brain, the →siibra-python tool is used, an interface that lets programmers easily integrate brain data from the HBP's Multilevel Human Brain Atlas into models. The brain-based model was trained on the supercomputer CSCS, with access provided through the Fenix Infrastructure, and learned how to perform complex hand movements and manipulate objects.

The research team connected their network to a virtual robotic hand to study how the human brain orchestrates complex manual movements. Tonio Weidler from Maastricht University, who developed AngoraPy, explains: "If you want to model behaviour, and not just pure perception, you need to map between sensory input and the optimal movement, for instance, in the joints of your hand, on a millisecond scale."

The scientists are giving the model challenges of increasing sophistication. While the earliest iteration simply focused on learning to touch index finger and thumb, the model is now capable of using its 92 virtual touch sensors and finger joints to quickly reorient a virtual block to any given orientation without dropping it, and it is displaying human-like dexterity behaviour in doing so.

Although the scientists first used the tool to better understand dexterity, AngoraPy is open and can enable experiments with any kind of anthropomorphic robot and for any kind of task. "Goal-driven models were rarely used before in sensorimotor computational neuroscience," explains Weidler. "Going forward, researchers can create them without dealing with the technical challenges – this is all now only a few lines of code."
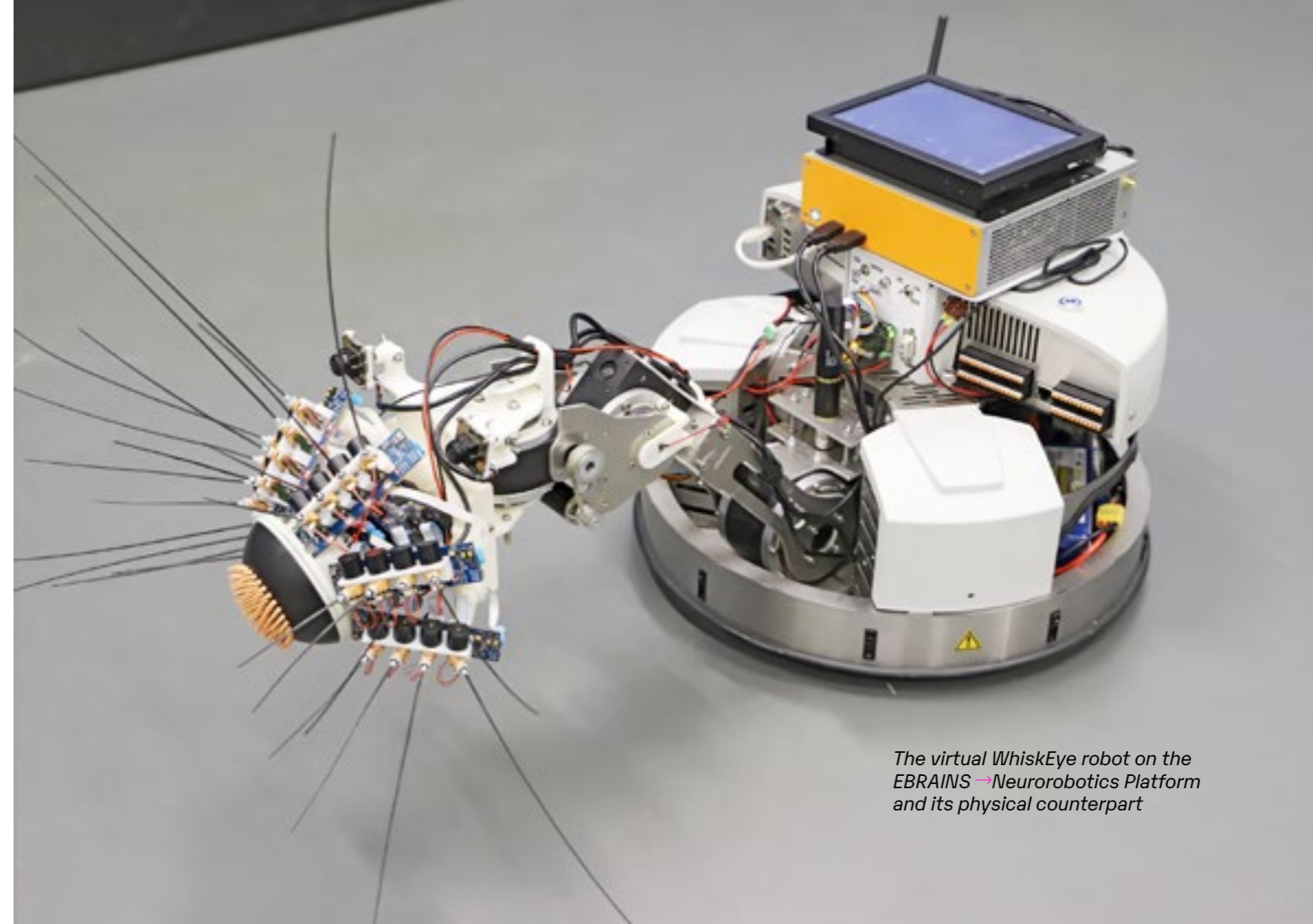
## Safe interaction between robots and humans

With robotics becoming a new tool for neuroscientific research, will robots in industry also benefit? This is what a team of HBP brain, robotics and AI researchers now explore. In particular, they are addressing the challenges of safe human-robot interaction. The team has set up a virtual factory floor of robots and begun integrating many models developed by the different groups in the HBP. This way, researchers will in the future be able to connect any new brain model quickly to a body and carry out so-called "cobotics" experiments virtually.

In a first demonstration, brain network models of motor function (cerebellar, spinal cord and musculo-skeletal systems), perception, planning and memory were all successfully integrated into a single simulation and connected to a robotic arm using the NRP's Integrated Behavioural Architecture (IBA). Additionally, the team added capacitive sensors to enable collision-aware robot navigation in close proximity to humans.

The platform even integrates one of the major brain-inspired technologies of the HBP: for very large network models it can be deployed on the →SpiNNaker neuromorphic supercomputer. Brain-inspired computers like SpiNNaker and →BrainScaleS are important tools for fast network simulation in real-time scenarios, such as robotic control, where calculation and output have to be in lockstep with each other.

Michael Zechmair from Maastricht University is working on the integration of the architecture: "All individual building blocks – vision, localisation, embodiment, motor control and planning – have value in themselves. We learn a lot by putting them together in a modular, flexible system where anyone can simulate real-life situations, drawing inspiration from multiple contributions to neuroscience and robotics."
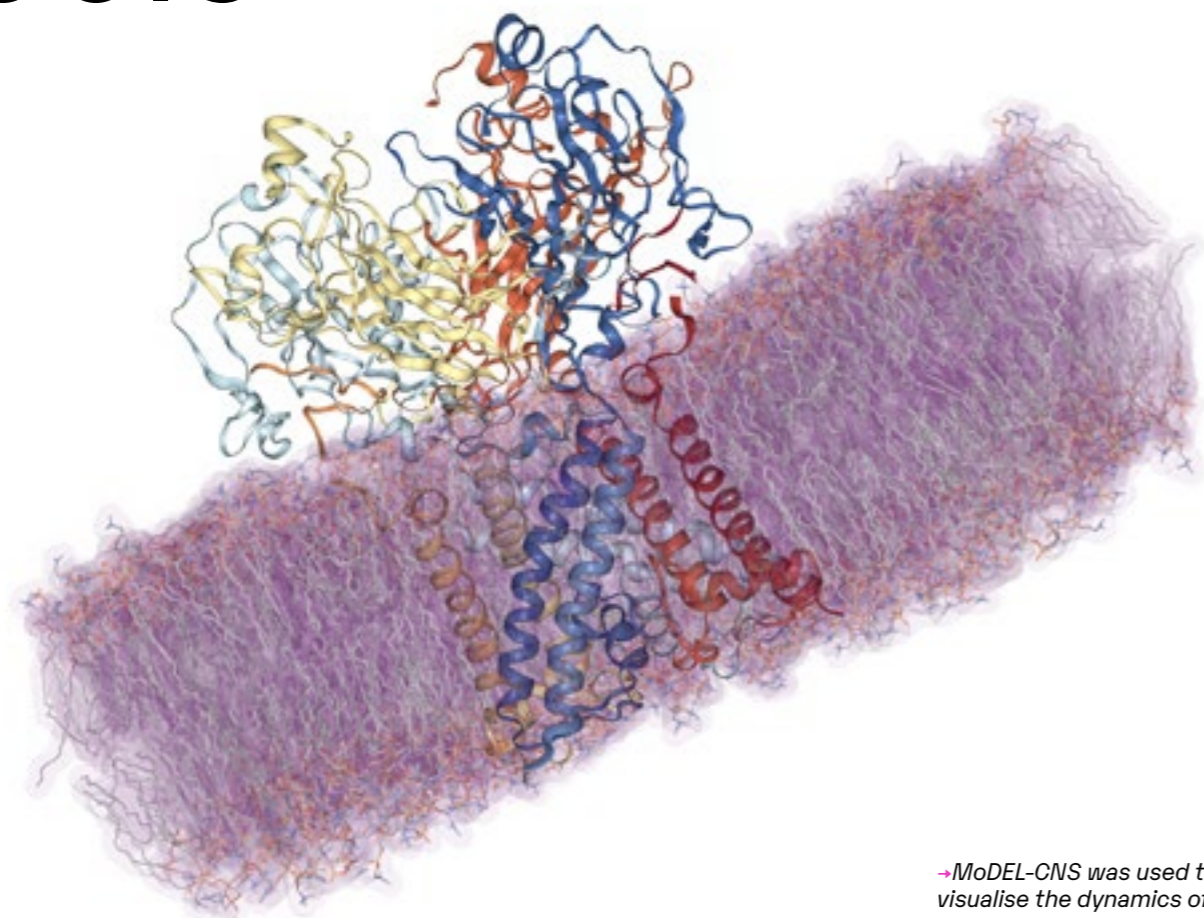




*The virtual WhiskEye robot on the EBRAINS →Neurorobotics Platform and its physical counterpart*

# Guide to HBP tools

The HBP aims to better understand the brain as a multi-level system. To this end, HBP researchers have developed digital tools that facilitate the study and integration of insights from different scales of the brain.

On the following pages, you will find a comprehensive snapshot of the current set of these tools. We are using the word tool here for brevity and include software and services, middleware and even hardware platforms. These tools span a range of different research methods, from data management to simulation to core infrastructure tools that facilitate integration and collaboration. All of the tools included in this book have been designed to facilitate brain research, and their development has – fully or partly – been funded by the HBP. Some tools were newly developed and conceptualised within the HBP, others were developed further within the project.

We introduce each tool with an up-to-date description, which has kindly been provided by the tool developers. The tools are sorted in chapters according to the spatial scale of the brain that they are typically applied to – from the molecular to the whole-brain scale to embodiment. In line with the multi-scale approach of HBP research, the largest chapter comprises tools that can be applied to and integrate multiple spatial scales. The chapter on transversal tools includes tools that are required for overarching activities such as collaboration, ethics, responsible research, data storage and (high-performance) computing.

If you are searching for a specific tool, please refer to the multiple indices at the end (p. 96), where you can find all the tools sorted by different methods, including spatial scale and application method and in alphabetical order, to make it easy for you to find any tool depending on your specific need.

To directly access and download individual tools, please visit:

humanbrainproject.eu/tools

**HBP TOOLS**

- Whole-brain-scale tools
- Cellular- and subcellular-scale tools
- Transversal tools
- Embodiment tools
- Molecular-scale tools
- Network-scale tools
- Multi-scale tools

# Molecular-scale tools



*→MoDEL-CNS was used to visualise the dynamics of a membrane protein involved in neuronal function.*

DATA ANALYSIS | SIMULATION | VISUALISATION

## Database of atomistic molecular dynamics of COVID–19-related proteins

### BioExcel-CV19

Platform
Web application
Web service
Data store
Compute cluster
Cloud/VM

BioExcel-CV19 is a platform designed to provide web access to atomistic-MD trajectories for macromolecules involved in COVID-19. The project is part of the open access initiatives promoted by the worldwide scientific community to share information about COVID-19 research. The BioExcel-CV19 web server interface presents the resulting trajectories, with a set of quality control analyses and system information. All data produced by the project are available to download from an associated programmatic access API.

DATA ANALYSIS

## Package to analyse protein-protein interaction networks

### BioNAR

Software library
Workflow tool
Desktop

Biological Network Analysis in R (BioNAR) combines a selection of existing R protocols for network analysis with newly designed original methodological features to support step-by-step analysis of biological/biomedical networks. BioNAR supports a pipeline approach where many networks and iterative analyses can be performed. BioNAR helps to achieve a number of network analysis goals that are difficult to achieve anywhere else, e.g., choosing the optimal clustering algorithm from a range of options based on independent annotation enrichment; predicting a protein's influence within and across multiple sub-complexes in the network and estimating the co-occurrence or linkage between meta-data at the network level.

→ McLean et al. (2023). bioRxiv 2023.02.08.527636.

DATA ANALYSIS | SIMULATION | VISUALISATION

## Software library for interoperable biomolecular simulation workflows

### BioBB

Software library
Software suite
Workflow tool
Compute cluster
Cloud/VM

The BioExcel Building Blocks (BioBB) software library is a collection of Python wrappers on top of popular biomolecular simulation tools. The library offers a layer of interoperability between the wrapped tools, which makes them compatible and prepares them for direct interconnection to build complex biomolecular workflows. Building and sharing complex biomolecular simulation workflows just require joining and connecting BioExcelBuilding Blocks together. Biomolecular simulation workflows built using the BioBB library are integrated in the →Collaboratory Jupyter lab infrastructure, allowing the exploration of dynamics and flexibility of proteins related to the central nervous system.

→ Andrio et al. (2019). Sci. Data 6:169.

SIMULATION | VISUALISATION

## Web-server for the preparation, running and analysis of CGMD simulations

### CGMD Platform

Platform
Web application
Web service
Compute cluster

Recent advances in Coarse-Grained Molecular Dynamics (CGMD) simulations have allowed longer and larger simulations of the molecular dynamics of biological macromolecules and their interactions. The CGMD Platform is dedicated to the preparation, running and analysis of Coarse-Grained Molecular Dynamics simulations. In its current version, the platform expands the implementation of the Martini force field for membrane proteins to also allow the simulation of soluble proteins using both the Martini and SIRAH force fields. Additionally, it offers an automated protocol to retrieve an atomic system from a coarse-grained description through a back mapping procedure.

→ Marchetto et al. (2020). Molecules 25: 5934.

DATA ANALYSIS | SIMULATION | VISUALISATION

## Database and server platform designed to efficiently generate and parameterise bioactive conformers of ligands binding to neuronal proteins

### CNS-ligands

Platform
Web application
Web service

Data store
Compute cluster
Cloud/VM

The project is part of the Parameter generation and mechanistic studies of neuronal cascades using multi-scale molecular simulations of the HBP. Central nervous system (CNS) conformers are generated using a powerful multilevel strategy that combines a low-level (LL) method for sampling the conformational minima and high-level (HL) ab initio calculations for estimating their relative stability. A CNS database presents the results in a graphical user interface, displaying small molecule properties, analyses and generated 3D conformers. All data produced by the project are available to download.

DATA ANALYSIS | SIMULATION | VISUALISATION

## Web access to atomistic MD trajectories for relevant signal transduction proteins

### MoDEL-CNS

Platform
Web application
Web service

Data store
Compute cluster
Cloud/VM

Molecular Dynamics Extended Library-CNS (MoDEL-CNS) is a database and server platform designed to provide web access to atomistic MD trajectories for relevant signal transduction proteins. The project is part of the service for providing molecular simulation-based predictions for systems neurobiology of the HBP. MoDEL-CNS expands the MD Extended Library database of atomistic MD trajectories with proteins involved in CNS processes, including membrane proteins. The MoDEL-CNS web server interface presents the resulting trajectories, analyses and protein properties. All data produced are available to download.

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SIMULATION | VISUALISATION

## Automatic set-up of MM/CG simulations for hGPCR/ligand complexes

### Hybrid MM/CG Webserver

Web application
Web service
Workflow tool

Molecular Mechanics/Coarse-Grained (MM/CG) simulations help predict ligand poses in human G Protein-Coupled Receptors (hGPCRs) for pharmacological applications. This approach allows for the description of the ligand, the binding cavity and the surrounding water molecules at atomistic resolution, while coarse-graining the rest of the receptor. The web server automatises and speeds up the simulation set-up of hGPCR/ligand complexes. It also allows for equilibration of the systems, either fully automatically or interactively. The results are visualised online, helping the user to identify possible issues and modify the set-up parameters. This framework allows for the automatic preparation and running of hybrid molecular dynamics simulations of molecules and their cognate receptors.

→ Schneider et al. (2020). Front. Mol. Biosci. 7:576689.

SIMULATION | VISUALISATION

## Web-based tool to study protein-protein interactions

### PIPSA

Software suite
Web application
Desktop
Compute cluster

Protein Interaction Property Similarity Analysis (PIPSA) enables the comparison of the electrostatic interaction properties of proteins. It permits the classification of proteins according to their interaction properties. PIPSA may assist in function assignment and in estimating binding properties and enzyme kinetic parameters.

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DATA ANALYSIS | VISUALISATION

## Analysis of protein-ligand interactions along MD trajectories

### MD-IFP

Desktop application
Workflow tool
Desktop
Compute cluster

Molecular Dynamics-Interaction Fingerprint (MD-IFP) is a Python workflow for the generation and analysis of protein-ligand interaction fingerprints from molecular dynamics trajectories. If used for the analysis of Random Acceleration Molecular Dynamics (RAMD) trajectories, it can help to investigate dissociation mechanisms by characterising transition states as well as the determinants and hot-spots for dissociation. As such, the combined use of →τRAMD and MD-IFP may assist the early stages of drug discovery campaigns for the design of new molecules or ligand optimisation.

→ Kokh et al. (2020). J. Chem. Phys. 153(12):125102.

SIMULATION

## Brownian dynamics simulation of molecular diffusion and association

### SDA 7

Software suite
Web application
Compute cluster

Simulation of Diffusional Association version 7 (SDA 7) can be used to carry out Brownian dynamics simulations of the diffusional association in a continuum aqueous solvent of two solute molecules, e.g., proteins, or of a solute molecule to an inorganic surface. SDA 7 can also be used to simulate the diffusion of multiple proteins, in dilute or concentrated solutions, e.g., to study the effects of macromolecular crowding.

DATA ANALYSIS

## Synaptic proteins integrated from 57 studies and respective protein-protein interactions

### Synaptic proteome database in SQLite

Desktop application
Data store

Integration of 57 published synaptic proteomic datasets reveals a stunningly complex picture involving over 7,000 proteins. Molecular complexes were reconstructed using evidence-based protein-protein interaction data available from public databases. The constructed molecular interaction network model is embedded into an SQLite implementation, allowing queries that generate custom network models based on meta-data including species, synaptic compartment, brain region and method of extraction.

→ Sorokina et al. (2021). Sci. Rep. 11:9967.

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DATA ANALYSIS

## Bioconductor package for assessing the synaptic protein database

### Synaptome.db

Software library
Data store
Desktop

The Synaptome.db bioconductor package contains a local copy of the synaptic proteome database. On top of this it provides a set of utility R functions to query and analyse its content. It allows for extraction of information for specific genes and building the PPI graph for gene sets, synaptic compartments and brain regions.

→ Sorokina et al. (2022). Bioinform. adv. 2(1):vbac086.

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DATA ANALYSIS | SIMULATION | VISUALISATION

## Estimation of protein-ligand dissociation rates from RAMD simulations

### τRAMD

Software library
Desktop application
Workflow tool
Compute cluster

The τ-Random Acceleration Molecular Dynamics (τRAMD) technique makes use of RAMD simulations to compute relative residence times (or dissociation rates) of protein-ligand complexes. In the RAMD method, the egress of a molecule from a target receptor is accelerated by the application of an adaptive, randomly oriented force on the ligand. This enables ligand egress events to be observed in short, nanosecond timescale simulations without imposing any bias regarding the ligand egress route taken. If coupled to the →MD-IFP tool, the τRAMD method can be used to investigate dissociation mechanisms and characterise transition states.

→ Kokh et al. (2021). J. Chem. Theory Comput. 17(10):6610-6623.
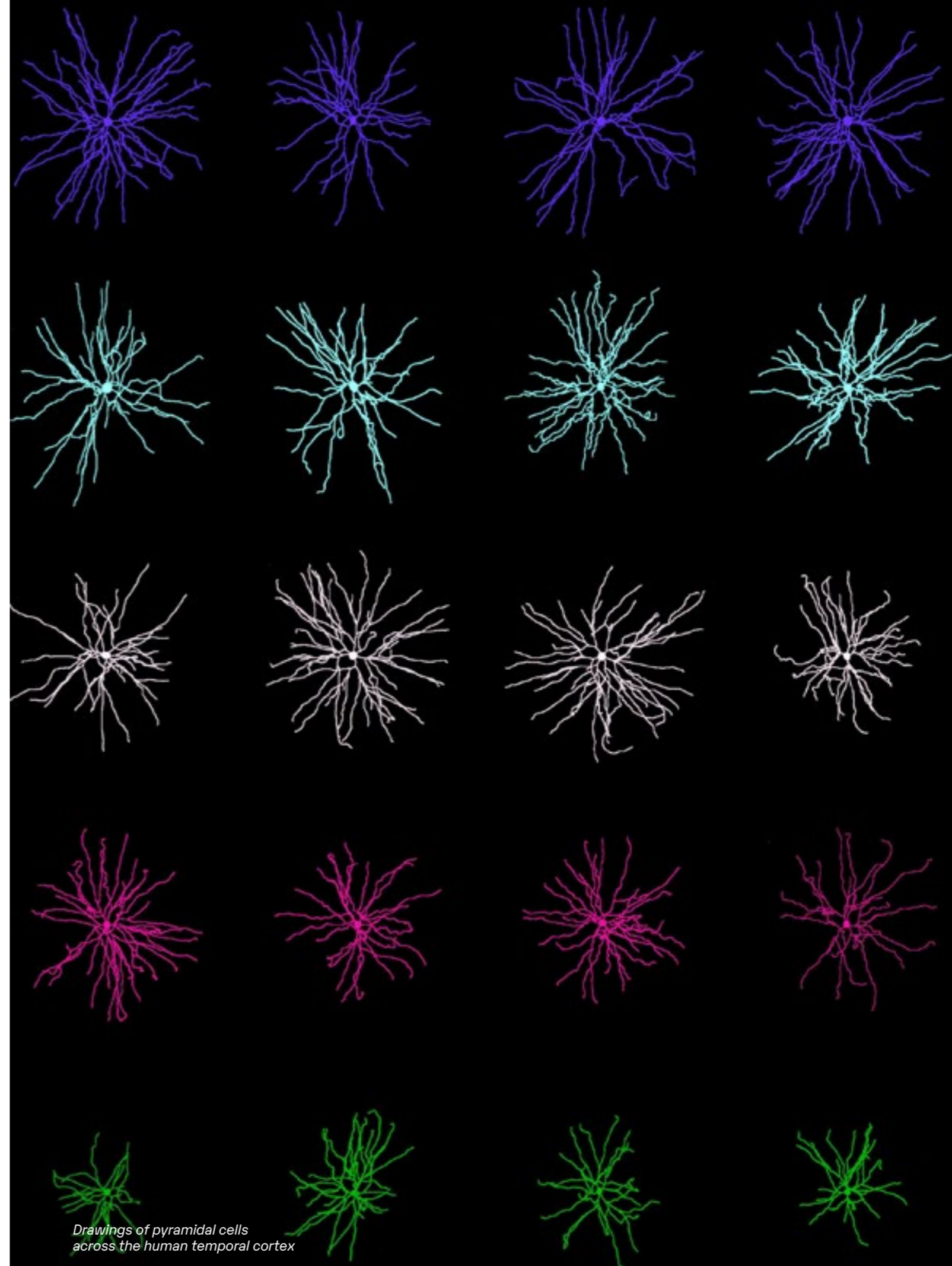


*Drawings of pyramidal cells across the human temporal cortex*

# Cellular- and sub-cellular-scale tools
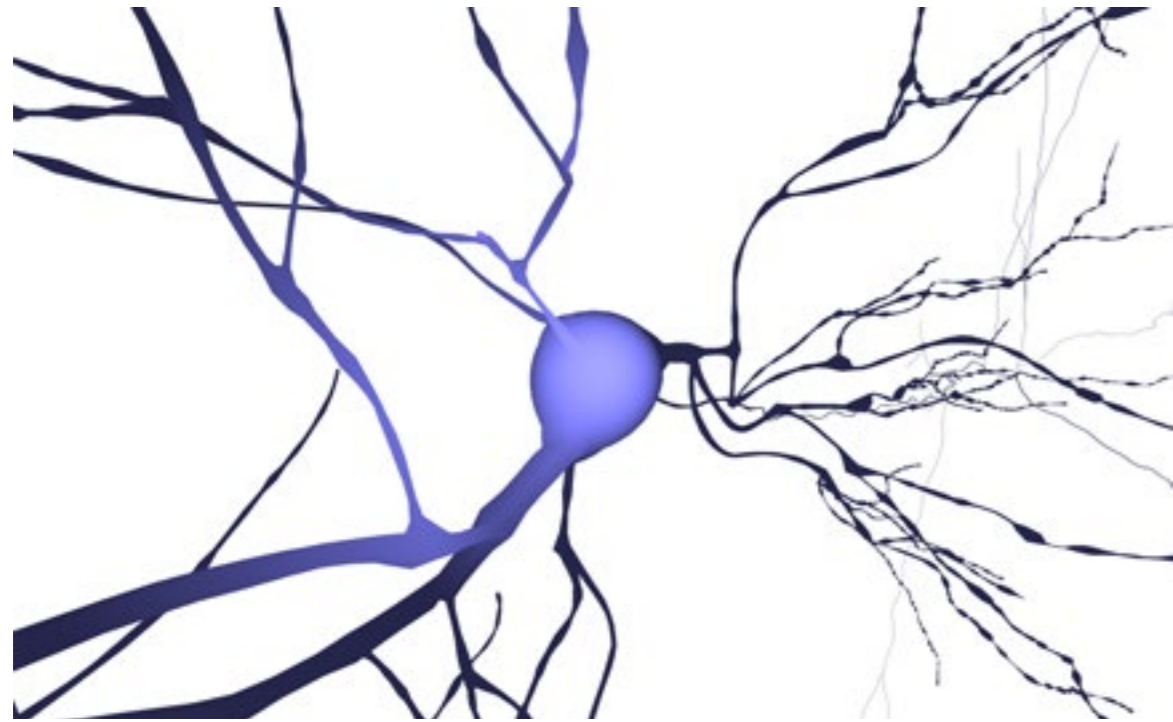


*Detailed morphology of a single neuron from the hippocampus visualised using →NeuroTessMesh*

SIMULATION

## Simulation software library for neuron models with complex morphologies

### Arbor

Software library
Desktop application
Workflow tool
Middleware

Infrastructure component
Compute cluster
Cloud/VM
Web application

Arbor is a simulation software library for neuron models with complex morphologies — from single cells to large distributed networks. Developed entirely inside the HBP, it enables running large-scale simulations on any HPC, including those available through EBRAINS. Arbor provides performance portability for native execution on all HPC architectures. Optimised vectorised code is generated for Intel, AMD and ARM CPUs, NVIDIA and AMD GPUs, and support will be added for new architectures as they become available. Model portability is easier due to an interface for model description independent of how Arbor represents models internally.  Interoperability with other simulation engines is enabled via API for spike exchange and the output of voltages, currents and model state.

→ Akar et al. (2019). 10.1109/EMPDP.2019.8671560:274-282.

SIMULATION | VISUALISATION

## Comprehensive tool for building single cell models using Arbor

### Arbor GUI

Desktop application
Workflow tool
Middleware

Arbor graphical user interface (GUI) strives to be self-contained, fast and easy to use.
· Design morphologically detailed cells for simulation in Arbor.
· Load morphologies from SWC .swc, NeuroML .nml, NeuroLucida .asc.
· Define and highlight Arbor regions and locsets.
· Paint ion dynamics and bio-physical properties onto morphologies.
· Place spike detectors and probes.
· Export cable cells to Arbor's internal format (ACC) for direct simulation.
· Import cable cells in ACC format.

This project is under active development and welcomes early feedback.

SIMULATION

## Interact with single cell models through a web application

### BlueNaaS-SingleCell

Web application

BlueNaaS-SingleCell is an open source web application. It enables users to quickly visualise single cell model morphologies in 3D or as a dendrogram. Using a simple web user interface, single cell simulations can be easily configured and launched, producing voltage traces from selected compartments.

SIMULATION

## Web environment for the simulation of brain molecular networks

### BlueNaaS-Subcellular

Web application
Web service

BlueNaaS-Subcellular is a web-based environment for creation and simulation of reaction-diffusion models. It allows the user to import, combine and simulate existing models derived from other parts of the pipeline. It is integrated with a number of solvers for reaction-diffusion systems of equations, and can represent rule-based systems using BioNetGen. Additionally, it supports simulation of spatially distributed systems using STEPS (stochastic engine for pathway simulation), providing spatial stochastic and deterministic solvers for simulation of reactions and diffusion on tetrahedral meshes. It includes some visualisation tools such as a geometry viewer, a contact map and a reactivity network graph.

BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Streamlined electrophysiological data analysis

### BluePyEfe

Software library
Desktop
Compute cluster
Cloud/VM

BluePyEfe eases the process of reading experimental recordings and extracting batches of electrical features from these recordings. It combines trace reading functions and features extraction functions from the eFel library.
BluePyEfe outputs protocols and features files in the format used by BluePyOpt for neuron electrical model building.

→ Reva et al. (2022). bioRxiv 2022.12.13.520234.

SIMULATION

## Optimised simulator library for NEURON Simulator

### CoreNEURON

Software library
Desktop application
Compute cluster

In order to adapt NEURON to evolving computer architectures, the compute engine of the NEURON simulator was extracted and optimised as a library called CoreNEURON. CoreNEURON is a compute engine library for the NEURON simulator optimised for both memory usage and computational speed on modern CPU/GPU architectures. Some of its key goals are to: 1) Efficiently simulate large network models, 2) Support execution on accelerators such as GPU, 3) Support optimisations such as vectorisation and cache-efficient memory layout.

→ Awile et al. (2022). Front. Neuroinform. 16:884046.
→ Kumbhar et al. (2019). Front. Neuroinform. 13:63.

BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Extensible framework for data-driven model parameter optimisation that wraps and standardises several existing open-source tools

### BluePyOpt

Software library      Desktop
Software suite        Compute cluster
                      Cloud/VM

The Blue Brain Python Optimisation Library (Blue-PyOpt) simplifies the task of creating and sharing data-driven model parameter optimisations, and the associated techniques and knowledge. This is achieved by abstracting the optimisation and evaluation tasks into various reusable and flexible discrete elements according to established best practices.
Further, BluePyOpt provides methods for setting up both small- and large-scale optimisations on a variety of platforms, ranging from laptops to Linux clusters and cloud-based computer infrastructures.

→ Van Geit et al. (2016). Front. Neuroinform. 10:17.

BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Automatically extract features from time series data

### eFEL

Software library
Desktop
Compute cluster
Cloud/VM

Electrophys Feature Extraction Library (eFEL) allows neuroscientists to automatically extract features from time series data recorded from neurons (both in vitro and in silico). Examples include action potential width and amplitude in voltage traces recorded during whole-cell patch clamp experiments. Users can provide a set of traces and select which features to calculate. The library will then extract the requested features and return the values.

→ Reva et al. (2022). bioRxiv 2022.12.13.520234.

SIMULATION

## Web application that displays CLS scientific use cases and creates an environment to run them flawlessly

### bsp-usecase-wizard

Web application
Embedded hardware

The Cellular Level Simulation (CLS) interactive workflows and use cases application guides users through the resolution of realistic scientific problems. They are implemented as either front-end or full stack web applications or Python-based Jupyter Notebooks that allow the user to interactively build, reconstruct or simulate data-driven brain models and perform data analysis visualisation. Web applications are freely accessible and only require authentication to EBRAINS when specific actions are required (e.g., submitting a simulation job to a HBP HPC system). Jupyter Notebooks are cloned to the lab.ebrains.eu platform and require authentication via an EBRAINS account.

DATA ANALYSIS | SIMULATION | VISUALISATION

## Build biophysically detailed NEURON models of individual cells

### Hodgkin-Huxley Neuron Builder

Web application
Workflow tool

The Hodgkin-Huxley Neuron Builder is a web application that allows users to interactively go through an entire NEURON model building pipeline of individual biophysically detailed cells.
The workflow consists of three steps:
1. Electrophysiological feature extraction from voltage traces
2. Model parameter optimisation via HPC systems
3. In silico experiments using the optimised model cell.

→ Bologna et al. (2022). Front. Neuroinform. 16:991609.

DATA ANALYSIS | VISUALISATION

## Segmentation of neurons and neurites in chronic calcium imaging datasets

SpecSeg is a toolbox that segments neurons and neurites in chronic calcium imaging datasets based on low-frequency cross-spectral power. The pipeline includes a graphical user interface to edit the automatically extracted ROIs, to add new ones or delete ROIs by further constraining their properties.

→ de Kraker et al. (2022). Cell Rep. Methods 2(10):100299.

### Leveltlab/SpectralSegmentation

Software suite
Workflow tool
Desktop
Cloud/VM

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SIMULATION

## GPU-based tool to generate realistic phantoms of the brain microstructure

Using a spherical meshing technique that decomposes each microstructural item into a set of overlapping spheres, the phantom construction is made very fast while reliably avoiding the collisions between items in the scene. This novel method is applied to the construction of human brain white matter microstructural components, namely axonal fibres, oligodendrocytes and astrocytes. The algorithm reaches high values of packing density and angular dispersion for the axonal fibres, even in the case of multiple white matter fibre populations and enables the construction of complex biomimicking geometries including myelinated axons, beaded axons and glial cells.

→ Ginsburger et al. (2019). Neuroimage 193:10-24.

### MEDUSA

Desktop application

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DATA ANALYSIS | SIMULATION

## Python and C++ library for reading and writing neuronal morphologies

MorphIO is a library for reading and writing neuron morphology files. It supports the following formats: SWC, ASC (also known as neurolucida), H5. There are two APIs: mutable, for creating or editing morphologies, and immutable, for read-only operations. Both are represented in C++ and Python. Extended formats include glia, mitochondria and endoplasmic reticulum.

### MorphIO

Software library
Desktop

---

DATA ANALYSIS

## Toolbox for morphology editing

MorphTool is a Python toolkit designed for editing morphological skeletons of cell reconstructions. It has been developed to provide helper programmes that perform simple tasks such as morphology diffing, file conversion, soma area calculation, skeleton simplification, process resampling, morphology repair and spatial transformations. It allows neuroscientists to curate and manipulate morphological reconstruction and correct morphological artifacts due to the manual reconstruction process.

### MorphTool

Software library
Workflow tool
Desktop

---

BRAIN-INSPIRED TECHNOLOGY | SIMULATION | VISUALISATION

## Python library for the analysis and simplification of morphological neuron models

NEural Analysis Toolkit (NEAT) allows for the convenient definition of morphological neuron models. These models can be simulated through an interface with the NEURON simulator or analysed with two classical methods: (i) the separation-of-variables method to obtain impedance kernels as a superposition of exponentials and (ii) Koch's method to compute impedances with linearised ion channels analytically in the frequency domain. NEAT also implements the neural evaluation tree framework and an associated C++ simulator to analyse sub-unit independence. Finally, NEAT implements a new method to simplify morphological neuron models into models with few compartments, which can also be simulated with NEURON.

### NEAT

Software library
Desktop

→ Wybo et al. (2021). eLife 10:e60936.

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DATA ANALYSIS | SIMULATION | VISUALISATION

## Python package for working with electrophysiology data

Neo implements a hierarchical data model well adapted to intracellular and extracellular electrophysiology and EEG data. It improves interoperability between Python tools for analysing, visualising and generating electrophysiology data by providing a common, shared object model. It reads a wide range of neurophysiology file formats, including Spike2, NeuroExplorer, AlphaOmega, Axon, Blackrock, Plexon, Tdt and Igor Pro and writes to open formats such as NWB and NIX. Neo objects behave just like normal NumPy arrays, but with additional metadata, checks for dimensional consistency and automatic unit conversion. Neo has been endorsed as a community standard by the International Neuroinformatics Coordinating Facility (INCF).

### Neo

Software library
Desktop
Compute cluster

→ Garcia et al. (2014). Front. Neuroinform. 8:10.

VISUALISATION

## Web-based visualisation of electrophysiology data

### Neo Viewer

Software library
Web application
Web service
Infrastructure component
Mobile

Neo Viewer consists of a REST-API and a Javascript component that can be embedded in any web page. Electrophysiology traces can be zoomed, scrolled and saved as images. Individual points can be measured off the graphs. Neo Viewer can visualise data from most of the widely used file formats in neurophysiology, including community standards such as NWB.

SIMULATION

## Simulator for modelling individual neurons and networks of neurons

### NEURON

Software library
Desktop application
Compute cluster

The NEURON simulation environment is used in laboratories and classrooms around the world for building and using computational models of neurons and networks of neurons. Users can build and simulate models using Python, HOC, and/or NEURON's graphical interface. NEURON provides tools for conveniently building, managing and using models in a way that is numerically sound and computationally efficient. It is particularly well-suited to problems that are closely linked to experimental data, especially those that involve cells with complex anatomical and biophysical properties.

→ Awile et al. (2022). Front. Neuroinform. 16:884046.

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DATA ANALYSIS | VISUALISATION

## Extract an ensemble of electrophysiological features from neural activity

### NeuroFeatureExtract

Web application
Workflow tool

NeuroFeatureExtract is a web application that allows users to extract an ensemble of electrophysiological properties from voltage traces recorded upon electrical stimulation of neuronal cells. The main outcome of the application is the generation of two files – features.json and protocol.json – that can be used for later analysis and model parameter optimisations via the Hodgkin-Huxley Neuron Builder application.

→ Bologna et al. (2021). Front. Neuroinform. 15:713899.

ATLASES | DATA ANALYSIS | SIMULATION | VISUALISATION

## Tool enabling Imaris-Neurolucida interoperability generating a connected 3D mesh and tracing

### Neuronize v2

Software suite
Desktop application
Workflow tool

Neuronize v2 has been developed to generate a connected neural 3D mesh. If the input is a neuron tracing, it generates a 3D mesh from it, including the shape of the soma. If the input is data-extracted with Imaris Filament Tracer (a set of unconnected meshes of a neuron), Neuronize v2 generates a single connected 3D mesh of the whole neuron (also generating the soma) and provides its neural tracing, which can then be imported into tools such as Neurolucida, facilitating the interoperability of two of the most widely used proprietary tools.

→ Velasco et al. (2020). Front. Neuroanat. 14:585793.

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DATA ANALYSIS

## Python toolkit for the analysis and processing of neuron morphologies

### NeuroM

Software library
Desktop
Compute cluster
Cloud/VM

The Neuronal Morphology Analysis Tool (NeuroM) is a Python toolkit for the analysis and processing of neuron morphologies. It allows the extraction of various information about morphologies, e.g., the segment lengths of a morphology via the segment_lengths feature. More than 50 features can be extracted.

DATA ANALYSIS

## Collection of tools to repair morphologies

### NeuroR

Software library
Desktop
Compute cluster

NeuroR is a collection of tools to repair morphologies. This includes cut plane detection, sanitisation (removing unifurcations, invalid soma counts, short segments) and "unravelling": the action of "stretching" the cell that has been shrunk due to the dehydratation caused by the slicing.

VISUALISATION

## Visualise circuits with large numbers of neurons with detailed morphologies

### NeuroTessMesh

Desktop application
Workflow tool
Infrastructure component

NeuroTessMesh takes morphological tracings of cells acquired by neuroscientists and generates 3D models that approximate the neuronal membrane. The resolution of the models can be adapted at the time of visualisation. You can colour-code different parts of a morphology, differentiating relevant morphological variables or even neuronal activity. NeuroTessMesh copes with many of the problems associated with the visualisation of neural circuits consisting of large numbers of cells. It facilitates the recovery and visualisation of the 3D geometry of cells included in databases, such as NeuroMorpho, and allows approximation of missing information such as the soma's morphology.

→ Garcia-Cantero et al. (2017). Front. Neuroinform. 11:38.

SIMULATION

## Run benchmarks and validation tests for multi-compartment neural network simulations

### NSuite

| | |
|---|---|
| Software library | Desktop |
| Framework | Compute cluster |
| Workflow tool | Cloud/VM |

NSuite is a framework for maintaining and running benchmarks and validation tests for multi-compartment neural network simulations on HPC systems. NSuite automates the process of building simulation engines, and running benchmarks and validation tests. NSuite is specifically designed to allow easy deployment on HPC systems in testing workflows, such as benchmark-driven development or continuous integration. The development of NSuite has been driven by the need (1) for a definitive resource for comparing performance and correctness of simulation engines on HPC systems, (2) to verify the performance and correctness of individual simulation engines as they change over time, and (3) to test that changes to an HPC system do not cause performance or correctness regressions in simulation engines.

VISUALISATION

## Interactive exploration of the detailed microanatomy of pyramidal neurons

### Pyramidal Explorer

Desktop application
Workflow tool
Infrastructure component

PyramidalExplorer is a tool to interactively explore and reveal the detailed organisation of the microanatomy of pyramidal neurons with functionally related models. Possible regional differences in the pyramidal cell architecture can be interactively discovered by combining quantitative morphological information about the structure of the cell with implemented functional models. The key contribution of this tool is the morpho-functional-oriented design, allowing the user to navigate within the 3D dataset, filter and perform content-based retrieval operations to find the spines that are alike and dissimilar within the neuron, according to particular morphological or functional variables.

→ Toharia et al. (2016). Front. Neuroanat. 9:159.

DATA ANALYSIS | SIMULATION | VISUALISATION

## Jupyter Notebook application that allows construction, configuration and simulation of single-cell models

### Single Cell Model (Re)builder Notebook

Web application
Workflow tool

The Single Cell Model (Re)builder Notebook is a web application, implemented via a Jupyter Notebook on EBRAINS, which allows users to configure the →Blue-PyOpt to re-run an optimisation with their own choices for the parameters range. The optimisation jobs are submitted through Neuroscience Gateway.

DATA ANALYSIS | SIMULATION

## Toolset for data-driven building of subcellular biochemical signaling pathway models

### Subcellular model building and calibration tool set

| | |
|---|---|
| Software library | Desktop |
| Software suite | Workflow tool |
| Framework | Compute cluster |

The toolset includes interoperable modules for: model building, calibration (parameter estimation) and model analysis. All information needed to perform these tasks (models, experimental calibration data and prior assumptions on parameter distributions) are stored in a structured, human- and machine-readable file format based on SBtab. The toolset enables simulations of the same model in simulators with different characteristics, e.g., STEPS, NEURON, MATLAB's Simbiology and R via automatic code generation. The parameter estimation can include uncertainty quantification and is done by optimisation or Bayesian approaches. Model analysis includes global sensitivity analysis and functionality for analysing thermodynamic constraints and conserved moieties.

→ Eriksson et al. (2022). Elife 11:e69013.
→ Santos et al. (2022). Neuroinformatics 20(1):241-259.

DATA ANALYSIS | SIMULATION | VISUALISATION

## Jupyter Notebook application to fit single synaptic events

### Synaptic Events Fitting

Web application
Workflow tool

The Synaptic Events Fitting is a web application, implemented in a Jupyter Notebook on EBRAINS, that allows user to fit synaptic events using data and models from the →EBRAINS Knowledge Graph (KG). The user can select, download and visualise experimental data from the KG and then select the data to be fitted. A mod file is then selected (local or default) together with the corresponding configuration file (including protocol and the name of the parameters to be fitted, their initial values and allowed variation range, exclusion rules and an optional set of dependencies). The fitting procedure can run on Neuroscience Gateway. The user can fetch the fitting results from the storage of the HPC system to the storage of the Collab or analyse the optimised parameters.

→ Lupascu et al. (2020). Front. Cell. Neurosci. 14:173.

SIMULATION | DATA ANALYSIS | VISUALISATION

## Configure and test different synaptic plasticity mechanisms and protocols on single-cell models

### Synaptic Plasticity Explorer

Web application
Workflow tool

The Synaptic Plasticity Explorer is a web application implemented via a Jupyter Notebook on EBRAINS. Through an intuitive GUI, it allows configuration and testing of different synaptic plasticity models and protocols on single-cell optimised models. The Explorer is available in the EBRAINS Model Catalog and consists of two tabs: "Config", where the user can specify the plasticity model to use and the synaptic parameters, and "Sim", where the recording location, weight's evolution and number of simulations to run are defined. The results are plotted at the end of the simulation and the traces are available for download.

VISUALISATION

## Spatial and temporal navigation, analysis and interaction with simulation data

### ViSimpl

Desktop application
Workflow tool
Infrastructure component

ViSimpl integrates a set of visualisation and interaction components that provide a semantic view of brain data with the aim of improving its analysis procedures. ViSimpl provides 3D particle-based rendering that visualises simulation data with their associated spatial and temporal information, enhancing the knowledge extraction process. It also provides abstract representations of the time-varying magnitudes, supporting different data aggregation and disaggregation operations and giving focus and context clues. In addition, ViSimpl provides synchronised playback control of the simulation being analysed.

→ Galindo et al. (2020). Neurocomputing 400:309-321.
→ Galindo et al. (2016). Front. Neuroinform. 10:44.

"The HBP tool with the greatest potential, in my view, is the EBRAINS Knowledge Graph. It is the single point of truth for any neuroscientist with respect to data models. It is a place for everyone to browse, understand what is there, and pick something to test."



Sofia Karvounari

is part of the Technical Coordination team of the HBP. Based in Athena Research Center (Greece), her responsibilities include working with scientists to find more standardised ways of defining digital workflows, and being able to execute those workflows in more than one technical setting.

# Network-scale tools
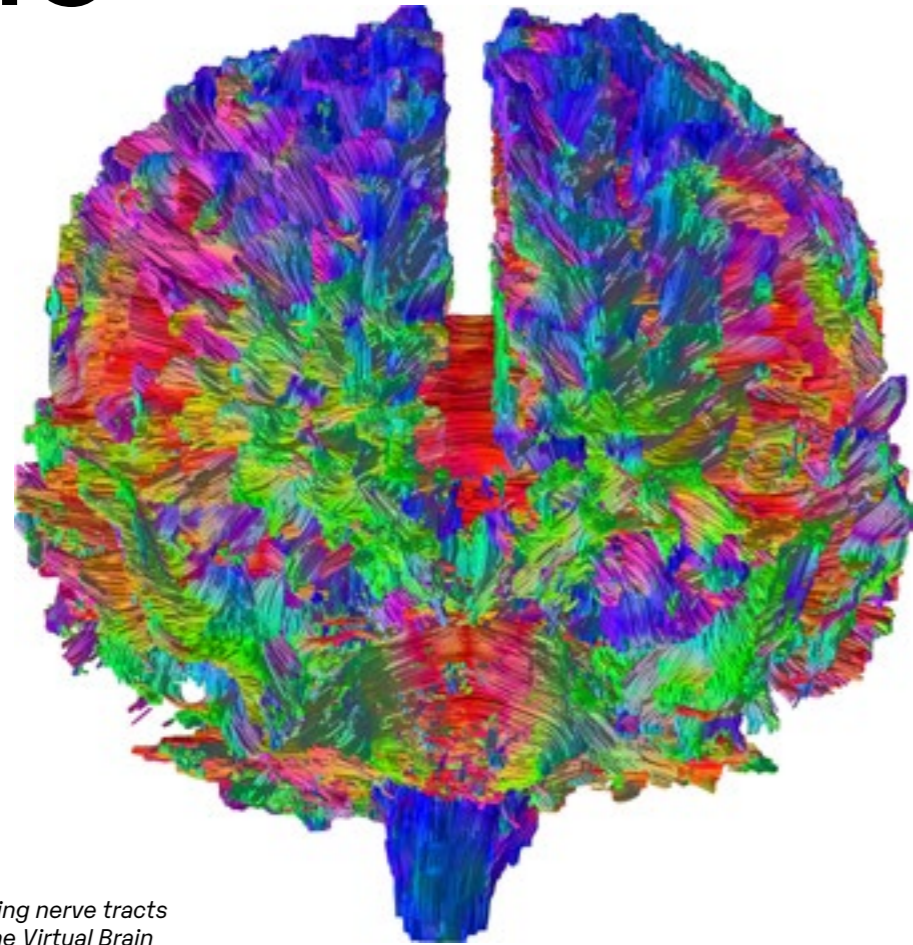


*Tractography representing nerve tracts of the human brain in The Virtual Brain (→TVB EBRAINS).*

SIMULATION

## Data structure schema for neural network computational models

A data structure schema for neural network computational models that aims to be generically applicable to all kinds of neural network simulation software, mathematical models, computational models and data models, but with a focus on dynamic circuit models of brain activity.

→ Roehri et al. (2021). Neuroinformatics 19(4):639–647.
→ Jegou et al. (2022). Neurosci. Inform. 2(2):100072.

## BIDS Extension Proposal Computational Model Specifications

Framework
Data store

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BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Blue Brain Python Cell Model Management

### BluePyMM

Software library
Desktop
Compute cluster
Cloud/VM

When building a network simulation, biophysically detailed electrical models (e-models) need to be tested for every morphology that is possibly used in the circuit. With current resources, e-models are not re-optimised for every morphology in the network. In a process called Cell Model Management (MM), we test if an existing e-model matches a particular morphology "well enough". It takes as input a morphology release, a circuit recipe and a set of e-models, then finds all possible (morphology, e-model)-combinations (me-combos) based on e-type, m-type and layer as described by the circuit recipe, then calculates the scores for every combination. Finally, it writes out the resulting accepted me-combos to a database, and produces a report with information on the number of matches.

→ Reva et al. (2022). bioRxiv 2022.12.13.520234.

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BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Neuromorphic computing system – accelerated analogue electronic emulation of neuron, synapse and plasticity models

### BrainScaleS

| | |
|---|---|
| Software suite | |
| Hardware system | |
| Platform | Desktop |
| Workflow tool | Compute cluster |
| Infrastructure component | Cloud/VM |
| Web service | Embedded hardware |

Emulate spiking neural networks in continuous time on the BrainScaleS analogue neuromorphic computing system. Models and experiments can be described in Python using the PyNN modelling language, or in hxtorch, a PyTorch-based machine-learning-friendly API. The platform can be used interactively via the EBRAINS JupyterLab service or EBRAINS HPC; in addition, the NMPI web service provides batch-style access. The modelling APIs employ common data formats for input and output data, e.g., neo.

→ Pehle et al. (2022). Front. Neurosci. 16:795876.

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SIMULATION

## Organised workflows for neural circuit reconstruction and simulation at different levels of detail

### BSB

Framework
Workflow tool
Desktop
Compute cluster

The Brain Scaffold Builder (BSB) reconstructs realistic neural circuits by placing and connecting fibres and neurons with detailed morphologies or only simplified geometrical features. Configure your model the way you need. Interfaces with several simulators (→Core-NEURON, →Arbor, →NEST) allow simulation of the reconstructed network and investigation of the structure-function-dynamics relationships at different levels of resolution. The "scaffold" design allows an easy model reconfiguration reflecting variants across brain regions, animal species and physio-pathological conditions without dismounting the basic network structure. The BSB provides effortless parallel computing both for the reconstruction and simulation phase.

→ De Schepper et al. (2022). Commun. Biol. 5:1240.

DATA ANALYSIS

## Adaptable and reusable pipeline for analysing cortical wave activity

### Cobrawap

Software library
Workflow tool
Desktop

Compute cluster
Cloud/VM

Cobrawap is an adaptable and reusable software tool to study wave-like activity propagation in the cortex. It allows for the integration of heterogeneous data from different measurement techniques and simulations through alignment to common wave descriptions. Cobrawap provides an extendable collection of processing and analysis methods that can be combined and adapted to specific input data and research applications. It enables broad and rigorous comparisons of wave characteristics across multiple datasets, model calibration and validation applications, and its modular building blocks may serve to construct related analysis pipelines.

→ Gutzen et al. (2022). arXiv:2211.08527.
→ Capone et al. (2023). Commun. Biol. 6:266.

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SIMULATION

## Cerebral cortex simulation framework

### CxSystem2

Framwork
Desktop
Compute cluster

CxSystem2 is a cerebral cortex simulation framework, which operates on personal computers. The CxSystem enables easy testing, and build-up of diverse models at single-cell resolution and it is implemented on the top of the Python-based Brain2 simulator. The CxSystem interface comprises two csv files – one for anatomy and technical details, the other for physiological parameters.

→ Garnier Artiñano et al. (2023). Front. Comput. Neurosci. 17:1011814.
→ Andalibi et al. (2019). Neural. Comput. 31 (6): 1048–1065.
→ Hokkanen et al. (2019). Neural. Comput. 31:1066-1084.

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DATA ANALYSIS | VISUALISATION

## Python library to analyse spike data and neuronal population activity

### Elephant

Software library
Desktop
Compute cluster
Cloud/VM

The Electrophysiology Analysis Toolkit (Elephant) is a Python library that provides a modular framework for the analysis of experimental and simulated neuronal activity data, such as spike trains, local field potentials, and intracellular data. Elephant builds on the Neo data model to facilitate usability, enable interoperability, and support data from dozens of file formats and network simulation tools. Its analysis functions are continuously validated against reference implementations and reports in the literature. Visualisations of analysis results are made available via the Viziphant companion library. Elephant aims to act as a platform for sharing analysis methods across the field.

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SIMULATION | VISUALISATION

## Creation of nerve fibre models based on mathematical functions with visualisation

### FAConstructor

Desktop application
Middleware

Fiber Architecture Constructor (FAConstructor) allows a simple and effective creation of fibre models based on mathematical functions or the manual input of data points. Models are visualised during creation and can be interacted with by translating them in 3D space.

→ Bazeille et al. (2021). Neuroimage 245:118683.

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BRAIN-INSPIRED TECHNOLOGY | SIMULATION | VISUALISATION

## Collection of repositories for applications of fast spike-based sampling

### Fast sampling with neuromorphic hardware

Software library
Software suite
Hardware system

Framework
Workflow tool
Infrastructure component

Compared to conventional neural networks, physical model devices offer a fast, efficient, and inherently parallel substrate capable of related forms of Markov chain Monte Carlo sampling. This software suite enables the use of a neuromorphic chip to replicate the properties of quantum systems through spike-based sampling.

→ Czischek et al. (2022). SciPost Phys. 12:039.
→ Klassert et al. (2022). iScience 25(8):104707.

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SIMULATION

## Fiber Architecture Simulation Toolbox for 3D-PLI

### fastPLI

Desktop application

fastPLI is an open-source toolbox based on Python and C++ for modelling myelinated axons, i.e., nerve fibres, and simulating the results of measurement of fibre orientations with a polarisation microscope using 3D-PLI. The fastPLI package includes the following modules: nerve fibre modelling, simulation, and analysis. All computationally intensive calculations are optimised either with Numba on the Python side or with multi-threading C++ algorithms, which can be accessed via pybind11 inside the Python package. Additionally, the simulation module supports the Message Passing Interface (MPI) to facilitate the simulation of very large volumes on multiple computer nodes.

→ Matuschke et al. (2021). J. Open Source Softw. 6(61):3042.

ATLASES | DATA ANALYSIS

## Fiber orientation analysis in volumetric microscopy

### Foa3D

Desktop application
Workflow tool
Compute cluster

3D Fiber Orientation Analysis (Foa3D) is a tool for multiscale nerve fibre enhancement and orientation analysis in high-resolution volume images acquired by two-photon scanning or light-sheet fluorescence microscopy, exploiting brain tissue autofluorescence or exogenous myelin stains. Its image processing pipeline is built around a 3D Frangi filter that enables the enhancement of fibre structures of varying diameters and the generation of accurate 3D orientation maps in both grey and white matter. Foa3D features the computation of multiscale orientation distribution functions that facilitate the comparison with orientations assessed via 3D-PLI or 3D PS-OCT and the validation of mesoscale dMRI-based connectivity information.

→ Sorelli et al. (2023). Sci. Rep. 13:4160.

DATA ANALYSIS

## Functional connectivity analysis and group-level statistics of neurophysiological data

### Frites

Software library
Workflow tool
Desktop
Compute cluster

Frites allows the characterisation of task-related cognitive brain networks. Neural correlates of cognitive functions can be extracted both at the single brain area (or channel) and network level. The toolbox includes time-resolved directed (e.g., Granger causality) and undirected (e.g., Mutual Information) functional connectivity metrics. In addition, it includes cluster-based and permutation-based statistical methods for single-subject and group-level inference.

→ Combrisson et al. (2022). J. of Open Source Softw. 7(79):3842.

SIMULATION

## Python module for calculating brain signals from simulated neural activity

### LFPy

Software library
Desktop application
Compute cluster

LFPy is an open-source Python module linking simulated neural activity with measurable brain signals. This is done by enabling calculation of brain signals from neural activity simulated with multi-compartment neuron models (single cells or networks). LFPy can be used to simulate brain signals like extracellular action potentials, local field potentials (LFP), and in vitro MEA recordings, as well as ECoG, EEG and MEG signals. LFPy is well integrated with the NEURON simulator and can, through a LFPykit, also be used with other simulators like →Arbor. Through the recently developed extensions hybridLFPy and LFPykernels, LFPy can also be used to calculate brain signals directly from point-neuron network models or population-based models.

→ Hagen et al. (2018). Front. Neuroinform. 12:92.

DATA ANALYSIS | SIMULATION

## Python and C++ interface to the SONATA format

### libsonata

Software library
Desktop
Compute cluster

libsonata allows circuit and simulation config loading, node set materialisation and access to node and edge populations in an efficient manner. It is generally a read-only library, but support for writing edge indices has been added.

BRAIN-INSPIRED TECHNOLOGY | DATA ANALYSIS | SIMULATION | VISUALISATION

## Library that couples NEST simulations with interactive visualisation and analysis applications

### Monsteer

Software library
Framework          Desktop
Web service        Compute cluster
Workflow tool      Web application

Monsteer is a library for interactive supercomputing in the neuroscience domain. It facilitates the coupling of running simulations (currently NEST) with interactive visualisation and analysis applications. Monsteer supports streaming of simulation data to clients (currently limited to spikes) as well as control of the simulator from the clients (also known as computational steering). Monsteer's main components are a C++ library, a MUSIC-based application and Python helpers.

SIMULATION

## Co-simulation tool for computational neuroscience

### MUSIC

Software library
Framework          Desktop
Middleware         Compute cluster

Multi-Simulation Coordinator (MUSIC) is a communication framework in the domain of computational neuroscience and neuromorphic computing which enables co-simulations, where components of a model are simulated by different simulators or hardware. It consists of an API and C++ library which can be linked into existing software with minor modifications. MUSIC enables the communication of neuronal spike events, continuous values and text messages while hiding the complexity of data distribution over ranks, as well as scheduling of communication in the face of loops. MUSIC is light-weight with a simple API.

"What is exciting is that, like LEGO® bricks, the tools we have built in the HBP can be mixed and matched in many different ways to build something new that serves your specific purpose, and different components of our toolbox are interoperable."

## Jan Fousek

works on implementation and scientific and technical coordination of EBRAINS showcases and whole-brain modelling contributions to a live paper on responsiveness. As a member of the The Virtual Brain (TVB) Facility Hub of Aix-Marseille University, he participates in the EBRAINS technical coordination and assists with formulation and execution of use cases building on the TVB EBRAINS services. He has contributed to the development of →TVB EBRAINS, →TVB Widgets and other TVB tools as well as three different EBRAINS showcases.

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SIMULATION | VISUALISATION

### NEST Desktop is a web-based GUI application for NEST Simulator

## NEST Desktop

Web application
Desktop application
Cloud/VM

NEST Desktop comprises GUI components for creating and configuring network models, running simulations and visualising and analysing simulation results. NEST Desktop allows students to explore important concepts in computational neuroscience without the need to first learn a simulator control language. This is done by offering a server-side →NEST simulator, which can also be installed as a package together with a web server providing NEST Desktop as visual front-end. Besides local installations, distributed setups can be installed, and direct use through EBRAINS is possible. NEST Desktop has also been used as a modelling front-end of the Neurorobotics Platform.

→ Spreizer et al. (2021) eNeuro 8(6):ENEURO.0274-21.2021.

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BRAIN-INSPIRED TECHNOLOGY | SIMULATION

### Large-scale spiking neural network simulator

## NEST Simulator

Software suite
Desktop application
Compute cluster
Cloud/VM

NEST is used in computational neuroscience to model and study behaviour of large networks of neurons. The models describe single neuron and synapse behaviour and their connections. Different mechanisms of plasticity can be used to investigate artificial learning and help to shed light on the fundamental principles of how the brain works. NEST offers convenient and efficient commands to define and connect large networks, ranging from algorithmically determined connections to data-driven connectivity. Connections can be created between neurons using numerous synapse models from STDP to gap junctions.

→ Jordan et al. (2018). Front. Neuroinform. 12:2.

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SIMULATION

### NEST modelling language and code generation tool for neurons and synapses

## NESTML

Software library
Workflow tool
Desktop
Compute cluster

NEST modelling language (NESTML) is a domain-specific language for neuron and synapse models. These dynamic models can be used in simulations of brain activity on several platforms, in particular →NEST Simulator.
NESTML combines an easy to understand, yet powerful syntax with good simulation performance by means of code generation (C++ for NEST Simulator) but also flexibly supports other simulation engines including neuromorphic hardware.

→ Linssen et al. (2023). Zenodo 10.5281/zenodo.7648958.

DATA ANALYSIS | VISUALISATION

## Python library for gene regulatory network learning

NeurogenPy is a Python package for working with Bayesian networks. It is focused on the analysis of gene expression data and learning of gene regulatory networks, modelled as Bayesian networks. For that reason, at the moment, only the Gaussian and fully discrete cases are supported. The package provides different structure learning algorithms, parameter estimation and input/output formats. For some of them, already existing implementations have been used, with bnlearn, pgmpy, networkx and igraph being the most relevant used packages. This project has been conceived to be included as a plugin in the EBRAINS interactive atlas viewer, but it may be used for other purposes.

### NeurogenPy

Software library
Web application

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DATA ANALYSIS | MEDICAL DATA ANALYSIS

## Covariance estimator for brain functional connectivity analysis

Population Shrinkage Covariance Estimator (PoSCE) is a functional connectivity estimator of fMRI time-series. It relies on the Riemannian geometry of covariances and integrates prior knowledge of covariance distribution over a population.

→ Rahim et al. (2019). Med. Image Anal. 54:138-148.

### PoSCE

Software library

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BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Remote access to EBRAINS neuromorphic computing systems

The Neuromorphic Computing Job Queue allows users to run simulations/emulations on the →SpiNNaker and →BrainScaleS systems by submitting a →PyNN script and associated job configuration information to a central queue. The system consists of a web API, a GUI client (the Job Manager app) and a Python client. Users can submit scripts stored locally on their own machine, in a Git repository, in the →EBRAINS Knowledge Graph, or in EBRAINS Collaboratory storage (→Collaboratory Drive/→Collaboratory Bucket service). Users can track the progress of their job and view and/or download the results, log files and provenance information.

### Neuromorphic Computing Job Queue

| Software library | |
| --- | --- |
| Web application | Middleware |
| Web service | Desktop |
| Workflow tool | Cloud/VM |

---

SIMULATION

## Simulator-independent language for building neuronal network models

A model description written with the PyNN (pronounced "pine") API and the Python programming language runs on any simulator that PyNN supports (currently NEURON, →NEST and Brian 2) as well as on the →BrainScaleS and →SpiNNaker neuromorphic hardware systems. PyNN provides a library of standard neuron, synapse and synaptic plasticity models, verified to work the same on different simulators. PyNN also provides commonly used connectivity algorithms (e.g. all-to-all, random, distance-dependent, small-world) but makes it easy to provide your own connectivity in a simulator-independent way. PyNN transparently supports distributed simulations using MPI.

### PyNN

| Software library | |
| --- | --- |
| Hardware system | Desktop |
| Middleware | Compute cluster |

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SIMULATION

## Improved code generation engine for NMODL replacing the original nrnivmodl

NEURON MODeling Language (NMODL) Framework is designed with modern compiler and code generation techniques. It provides modular tools for parsing, analysing and transforming NMODL; it provides an easy-to-use, high-level Python API; it generates optimised code for modern compute architectures including CPUs and GPUs; it provides flexibility to implement new simulator backends; and it supports full NMODL specification.

→ Kumbhar, P. et al. (2020). Computational Science – ICCS 2020. Lecture Notes in Computer Science 12137.

### NMODL Framework

Software library
Desktop application
Compute cluster

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BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Helper library for spike-based sampling in PyNN-supported neural simulators

Spike-based sampling, sbs, is a software suite that takes care of calibrating spiking neurons for given target distributions and allows the evaluation of these distributions as they are produced by stochastic spiking networks.

→ Korcsak-Gorzo et al. (2022). PLoS Comput. Biol. 18(3):e1009753.

→ Petrovici et al. (2016). Phys. Rev. E. 94(4-1):042312.

### sbs: Spike-based sampling

| Software library | Workflow tool |
| --- | --- |
| Software suite | Desktop |
| Framework | Compute cluster |

SIMULATION

## Generate realistic connectivity using touch detection and simulate large-scale neuron networks

### Snudda

Desktop application
Workflow tool
Compute cluster

Snudda ("touch" in Swedish) allows the user to set up and generate microcircuits where the connectivity between neurons is based on reconstructed neuron morphologies. The touch detection algorithm looks for overlaps of axons and dendrites and places putative synapses where they touch. The putative synapses are pruned, removing a fraction to match statistics from pairwise connectivity experiments. If needed, Snudda can also use probability functions to create realistic microcircuits. The Snudda software is written in Python and includes support for supercomputers. It uses ipyparallel to parallelise network creation and NEURON as the backend for simulations. Install using pip or by directly downloading.

→ Hjorth et al. (2021). Neuroinform. 19:685–701.

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ATLASES | DATA ANALYSIS | MEDICAL DATA ANALYSIS

## AI-based tool for semantic segmentation of neuronal somas

### SomaSegmenter

Software library
Desktop application
Workflow tool
Compute cluster

SomaSegmenter allows neuronal soma segmentation in fluorescence microscopy imaging datasets with the use of a parametrised version of the U-Net segmentation model, including additional features such as residual links and tile-based frame reconstruction.

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BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Million-core neuromorphic computer supported by spiking neural network (SNN) simulation software

### SpiNNaker

Hardware system
Platform

Infrastructure component
Desktop
Cloud/VM

SpiNNaker is a neuromorphic computer with over a million low-power, small-memory ARM cores arranged in chips, connected together with a unique brain-like mesh network and designed to simulate networks of spiking point neurons. Software is provided to compile networks described with PyNN into running simulations and to extract and convert results into the neo data format, as well as providing support for live interaction with running simulations. This allows integration with external devices such as real or virtual robotics as well as live simulation visualisation. Scripts can be written and executed using Jupyter for interactive access.

→ Rowley et al. (2019). Front. Neurosci. 13:231.
→ Rhodes et al. (2018). Front. Neurosci. 12:816.

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DATA ANALYSIS | SIMULATION | VISUALISATION

## Interactive visualisation, visual data analytics, coordinated multiple views, 3D visualisation, neuronal network simulation, spiking neurons, spatiotemporal patterns, data analysis workflow

### VIOLA

Web application

VIsualization Of Layer Activity (VIOLA) is an interactive, web-based tool to visualise activity data in multiple 2D layers such as the simulation output of neuronal networks with 2D geometry. As a reference implementation for a developed set of interactive visualisation concepts, the tool combines and adapts modern interactive visualisation paradigms, such as coordinated multiple views, for massively parallel neurophysiological data. The software allows for an explorative and qualitative assessment of the spatiotemporal features of neuronal activity, which can be performed prior to a detailed quantitative data analysis of specific aspects of the data.

→ Senk et al. (2018). Front. Neuroinform. 12:75.

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> "The EBRAINS infrastructure has really helped me in promoting the data, the analyses and the models that we are developing in our lab."

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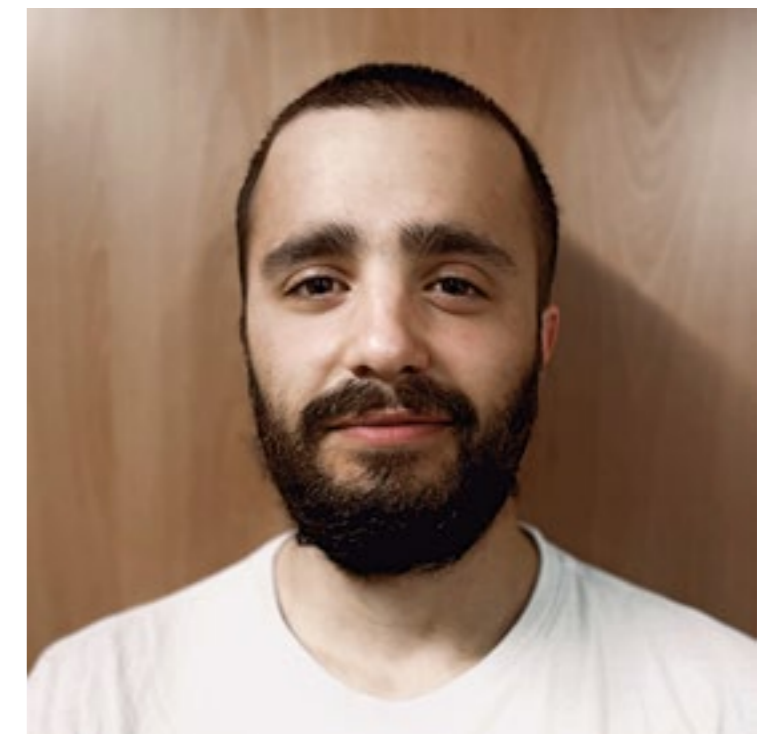


**Arnau Manasanch**

works at August Pi i Sunyer Biomedical Research Institute (IDIBAPS) in Barcelona. He is the technical coordinator of the HBP's scientific work package on consciousness and cognition. In this role, he is responsible for the coordination and integration of the package data, models and scientific software applications into EBRAINS, the digital research infrastructure of the HBP. His work involved tools such as →Neo, →Cobrawap, →TVB EBRAINS, →NEST Simulator and →ViSimpl.

# Whole-brain-scale tools



*Simulation in The Virtual Brain
(→TVB EBRAINS)*

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DATA ANALYSIS | VISUALISATION

## Web-based application to explore large fMRI datasets and inter-subject alignments

Brain Cockpit is a web app comprising a Typescript front-end and a Python back-end. It is meant to help explore large surface fMRI datasets projected on surface meshes and alignments computed between brains, such as those computed with Fused Unbalanced Gromov-Wasserstein (fugw) for Python.

### Brain Cockpit

Web service
Web app

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DATA ANALYSIS | MEDICAL DATA ANALYSIS | SIMULATION

## Probabilistic framework designed for inferring the spatial map of epileptogenicity in a personalised large-scale brain model

The Bayesian Virtual Epileptic Patient (BVEP) relies on the fusion of structural data of individuals, a generative model of epileptiform discharges and state-of-the-art probabilistic machine learning algorithms. It uses a self-tuning Monte Carlo sampling algorithm, and deep neural density estimators for reliable and efficient model-based inference at source and sensor levels data. The Bayesian framework provides an appropriate patient-specific strategy for estimating the extent of epileptogenic and propagation zones of the brain regions to improve outcome after epilepsy surgery.

### BVEP

Framework
Workflow tool
Compute cluster

→ Wang et al. (2023). Sci. Transl. Med. 15(680): eabp8982.
→ Sip et al. (2021). PLoS Comput. Biol.17(2): e1008689.
→ Hashemi et al. (2023). Neural Netw. 163:178-194.

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DATA ANALYSIS | MEDICAL DATA ANALYSIS | VISUALISATION

## De-identifying MRIs

AnonyMI is an MRI de-identification tool that uses 3D surface modelling in order to de-identify MRIs while retaining as much geometrical information as possible. It can be run automatically or manually, which allows precise tailoring for specific needs. AnonyMI is distributed as a plug-in of 3D Slicer, a widely used, open-source, stable and reliable image-processing software. It leverages the power of this platform for reading and saving images, which makes it applicable on almost any MRI file type, including all the most commonly used formats (e.g., DICOM, Nifti, Analyze, etc.).

→ Mikulan et al. (2021). Hum. Brain Mapp. 42:5523–5534.

### AnonyMI

Software library
Desktop

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ATLASES | DATA ANALYSIS

## Automatic registration of coronal brain section images to a 3D atlas using deep neural networks

DeepSlice is a deep neural network that aligns histological sections of mouse brain to the Allen Mouse Brain Common Coordinate Framework, adjusting for anterior-posterior position, angle, rotation and scale. At present, DeepSlice only works with tissue cut in the coronal plane, although future versions will be compatible with sagittal and horizontal sections.

→ Carey et al. (2022). bioRxiv 2022.04.28.489953.

### DeepSlice

Software library
Framework
Web application
Web service
Desktop

SIMULATION

## Mean-field-based method for forward estimation of LFP-MEG signals

### Feed-forward LFP-MEG estimator from mean-field models

Software library
Framework
Desktop

This tool was developed to calculate the local field potentials (LFP) and magnetoencephalogram (MEG) signals generated by a population of neurons described by a mean-field model. The calculation of LFP is done via a kernel method based on unitary LFPs (the LFP generated by a single axon), which was recently introduced for spiking-networks simulations and that we adapt here for mean-field models. The calculation of the magnetic field is based on current–dipole and volume–conductor models, where the secondary currents (due to the conducting extracellular medium) are estimated using the LFP calculated via the kernel method and where the effects of medium inhomogeneities are incorporated.

→ Tesler et al. (2022). Front. Comput. Neurosci. 16:968278.

ATLASES

## Fully automated and general-purpose brain segmentation algorithm

This is a scheme for training and applying the Factorisation-based Image Labelling (FIL) framework. Some functionality from SPM12 is required for handling images. After training, labelling a new image is relatively fast because optimising the latent variables can be formulated within a scheme similar to a recurrent Residual Network (ResNet).

→ Yan et al. (2021). Front. Neurosci. 15: 10.3389/fnins.2021.818604.

### FIL

Software suite
Desktop

DATA ANALYSIS

## Functional alignment and template estimation library for fMRI data

This library is meant to be a light-weight Python library that handles functional alignment tasks (also known as hyperalignment). It is compatible with and inspired by Nilearn. Alternative implementations of these ideas can be found in the pymvpa or brainiak packages.

→ Bazeille et al. (2021). Neuroimage 245:118683.

### FMRALIGN

Software library

ATLASES | VISUALISATION

## Pan-and-zoom type viewer displaying image series with overlaid atlas delineations

LocaliZoom is a pan-and-zoom-type viewer displaying high-resolution image series coupled with overlaid atlas delineations. It has different operating modes:

· Display series with atlas overlay. Both linear and nonlinear alignments are supported (created with →QuickNII or →VisuAlign).

· Create markup which can be exported as MeshView point clouds or to Excel for further numerical analysis.

### LocaliZoom

Web application
Workflow tool

ATLASES | VISUALISATION

## 3D viewer of brain atlas parcellations with solid mesh cutting

MeshView is a web application for real-time 3D display of surface mesh data representing structural parcellations from volumetric atlases, such as the Waxholm Space atlas of the Sprague Dawley rat brain. Key features: orbiting view with toggleable opaque/transparent/hidden parcellation meshes, rendering user-defined cut surface as if meshes were solid objects, rendering point-clouds (simple type-in, or loaded from JSON). The coordinate system is compatible with →QuickNII.

### MeshView

Web application
Workflow tool

ATLASES

## Group-wise diffeomorphic registration and segmentation of medical images

The Multi-Brain (MB) model has the general aim of integrating a number of disparate image analysis components within a single unified generative modelling framework. Its objective is to achieve diffeomorphic alignment of a wide variety of medical image modalities into a common anatomical space. This involves the ability to construct a "tissue probability template" from a population of scans through group-wise alignment. The MB model has been shown to provide accurate modelling of the intensity distributions of different imaging modalities.

→ Brudfors et al. (2020) Lecture Notes in Computer Science 12263. Springer, Cham. 10.1007/978-3-030-59716-0_25.

### Multi-Brain

Software library
Compute cluster
Desktop

ATLASES | MEDICAL DATA ANALYSIS | VISUALISATION

## Analytical solution for multimodal imaging data using multiple atlases

### NEURO-CONNECT

Software suite
Platform
Web application

The NEURO-CONNECT platform provides functions to integrate multimodal brain imaging information in a unifying feature space. Thus, Surface-Based Morphometry (SBM), Functional Magnetic Resonance Imaging (fMRI) and Diffusion Tensor Imaging (DTI) can be combined and visualised at the whole-brain scale. Moreover, multiple brain atlases are aligned to match research outcomes to neuroanatomical entities. The datasets are appended with →openMINDS metadata and thus enable integrative data analysis and machine learning.

→ Rechberger et al. (2022). Front. Aging Neurosci. 14:10.3389/fnagi.2022.832828

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ATLASES | DATA ANALYSIS

## Standalone image analysis tool for quantification of labelled features in brain section images

### Nutil

Software suite
Desktop application
Workflow tool

Nutil aims to simplify the pre-and-post processing of 2D brain section image data from mouse, rat and other small animal models. It can be used to preprocess images in preparation for analysis and used as part of the QUINT workflow to perform spatial analysis of labelled features relative to a reference brain atlas.

→ Groeneboom et al. (2020). Front. Neuroinform. 14:37.
→ Yates et al. (2019) Front. Neuroinform. 13:75.

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DATA ANALYSIS | SIMULATION

## Metadata, schema, annotations, The Virtual Brain (TVB)

### openMINDS metadata for TVB-ready data

Software library

Jupyter Python notebook with code and commentaries for creating openMINDS metadata version 1.0 in JSON-LD format for ingestion of TVB-ready data in →EBRAINS Knowledge Graph.

→ Schirner et al. (2022). Neuroimage 251:1053-8119.

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DATA ANALYSIS | MEDICAL DATA ANALYSIS | BRAIN-INSPIRED TECHNOLOGY

## Index measuring brain complexity EEG response to TMS perturbation

### PCI

Software library
Workflow tool
Desktop, compute cluster

The notebook allows the computation of the Perturbational Complexity Index (PCI) Lempel-Ziv and PCI state transitions. In order to run the examples, a wake and sleep data set needs to be provided in the Python-MNE format.

→ Comolatti et al. (2019). Brain Stimul. 12(5):1280-1289.
→ Casali et al. (2013). Sci. Transl. Med. 5:198ra105-198ra105.

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ATLASES | DATA ANALYSIS

## Serial section aligner to volumetric atlases

### QuickNII

Desktop application
Workflow tool

QuickNII is a tool for user-guided affine registration (anchoring) of 2D experimental image data, typically high-resolution microscopic images, to 3D atlas reference space, facilitating data integration through standardised coordinate systems.

Key features:

· Generate user-defined cut planes through the atlas templates, matching the orientation of the cut plane of the 2D experimental image data, as a first step towards anchoring of images to the relevant atlas template

· Propagate spatial transformations across series of sections following anchoring of selected images

→ Puchades et al. (2019). PLoS One 14(5):e0216796.

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SIMULATION

## Whole-brain network model generator for TVB on HPC

### RateML

Software library
Workflow tool
Infrastructure component
Desktop
Compute cluster

RateML enables users to generate whole-brain network models from a succinct declarative description, in which the mathematics of the model are described without specifying how their simulation should be implemented. RateML builds on NeuroML's Low Entropy Model Specification (LEMS), an XML-based language for specifying models of dynamic systems, allowing descriptions of neural mass and discretised neural field models, as implemented by TVB simulator. The end user describes their model's mathematics once and generates and runs code for different languages, targeting both CPUs for fast single simulations and GPUs for parallel ensemble simulations.

→ van der Vlag et al. (2022). Front. Netw. Physiol. 2:826345.

DATA ANALYSIS

## Retrieve a proxy of the haemodynamic response function (HRF) from resting-state (rs) fMRI

### rsHRF

Software library
Workflow tool
Desktop

Compute cluster
Cloud/VM

This toolbox is aimed at retrieving the onsets of pseudo-events triggering an haemodynamic response from resting-state fMRI BOLD signals. It is based on point process theory and fits a model to retrieve the optimal lag between the events and the HRF onset, as well as the HRF shape, using different shape parameters or combinations of basis functions.
Once the HRF has been retrieved for each voxel/vertex, it can be deconvolved from the time series (for example, to improve lag-based connectivity estimates), or one can map the shape parameters everywhere in the brain (including white matter) and use it as a pathophysiological indicator.

→ Wu et al. (2021). Neuroimage 244:118591.

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MEDICAL DATA ANALYSIS | SIMULATION

## TVB simulation engine for end-to-end personalised brain simulation in EBRAINS

### TVB EBRAINS

Framework
Web application
Compute cluster
Cloud/VM

TVB EBRAINS is the principal full brain network simulation engine in EBRAINS and covers every aspect of realising personalised whole-brain simulations on the EBRAINS platform. It consists of the simulation tools and adaptors connecting the data, atlas and computing services to the rest of the TVB ecosystem and Cloud services available in EBRAINS. As such, it allows the user to find and fetch relevant datasets through the →EBRAINS Knowledge Graph and Atlas services, construct the personalised TVB models and use the HPC systems to perform parameter exploration, optimisation and inference studies.

→ Schirner et al. (2022). Neuroimage 251:1053-8119.
→ Jirsa et al. (2021). 10.1007/978-1-4614-7320-6_100682-1.

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DATA ANALYSIS | SIMULATION

## Pipeline rendering data TVB-simulation-ready

### TVB Image Processing Pipeline

Software library
Workflow tool

TVB Image Processing Pipeline takes multimodal MRI data sets (anatomical, functional and diffusion-weighted MRI) as input and generates structural connectomes, region-average fMRI time series, functional connectomes, brain surfaces, electrode positions, lead field matrices and atlas parcellations as output. The pipeline performs preprocessing and distortion-correction on MRI data as well as white matter fibre bundle tractography on diffusion data. Outputs are formatted according to two data standards: a TVB-ready data set that can be directly used to simulate brain network models and the same output in BIDS format.

→ Schirner et al. (2022). NeuroImage 251:1053-8119.

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DATA ANALYSIS | MEDICAL DATA ANALYSIS | SIMULATION

## Performing inference over parameters of The Virtual Brain

### TVB Inversion

Software library
Desktop
Compute cluster
Cloud/VM

The TVB Inversion package implements the machinery required to perform parameter exploration and inference over parameters of The Virtual Brain simulator (→TVB EBRAINS) . It implements Simulation-Based Inference (SBI), which is a Bayesian inference method for complex models, where calculation of the likelihood function is either analytically or computationally intractable. As such, it allows the user to formulate with great expressive power both the model and the inference scenario in terms of observed data features and model parameters. Part of the integration with TVB entails the option to perform numerous simulations in parallel, which can be used for parameter space exploration.

→ Jirsa et al. (2023). Lancet Neurol. 22(5):443-454.
→ Hashemi et al. (2020). Neuroimage 217:116839.

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SIMULATION | VISUALISATION

## The Virtual Brain available as EBRAINS Cloud Service

### TVB Web App

Software suite
Web application
Cloud/VM

The Virtual Brain (TVB) Web App provides The Virtual Brain Simulator as an EBRAINS Cloud Service with an HPC back-end. Scientists can run intense personalised brain simulations without having to deploy software. Users can access the service with their EBRAINS credentials (single sign on). TVB Web App uses private/public key cryptography, sandboxing and access control to protect personalised health information contained in digital human brain twins while being processed on HPC. Users can upload their connectomes or use TVB-ready image-derived data discoverable via the →EBRAINS Knowledge Graph. Users can also use containerised processing workflows available on EBRAINS to render image raw data into simulation-ready formats.

→ Schirner et al. (2022). NeuroImage 251:1053-8119.

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DATA ANALYSIS | SIMULATION | VISUALISATION

## Graphic components and software solutions supporting EBRAINS showcases and workflows

### TVB Widgets

Software library
Workflow tool
Infrastructure component
Web application

In order to support the usability of EBRAINS workflows, TVB Widgets has been developed as a set of modular graphic components and software solutions, easy to use in the →Collaboratory within the JupyterLab. These GUI components are based on and under open source licence, supporting open neuroscience and features like:
· Setup of models and region-specific or cohort simulations
· Selection of data sources and their links to models
· Querying data from →siibra and the →EBRAINS Knowledge Graph
· Deployment and monitoring jobs on HPC resources
· Analysis and visualisation
· Visual workflow builder for configuring and launching TVB simulations

ATLASES

## Nonlinear refinement of registration performed by the QuickNII tool

### VisuAlign

Desktop application
Workflow tool

VisuAlign is a tool for user-guided nonlinear registration after →QuickNII of 2D experimental image data, typically high-resolution microscopic images, to 3D atlas reference space, facilitating data integration through standardised coordinate systems.
Key features:
· Generate user-defined cut planes through the atlas templates, matching the orientation of the cut plane of the 2D experimental image data, as a first step towards anchoring of images to the relevant atlas template
· Propagate spatial transformations across series of sections following anchoring of selected images

→ Puchades et al. (2019) PLoS One 14(5):e0216796.

ATLASES | DATA ANALYSIS

## Atlas-based anatomical analysis of individual MRIs

### voluba-mriwarp

Desktop application
Workflow tool

Warping whole brain MRI scans to a standardised space like ICBM MNI152 2009c nonlinear asymmetric space enables integration into the detailed anatomical context of the Multilevel Human Brain Atlas on EBRAINS. However, reasonable registration requires various steps that need optimisation. voluba-mriwarp is a desktop application that aims to simplify this workflow. It automatically applies a set of predefined parameters to perform skull stripping and registration to MNI152 space on a human whole-brain MRI scan. The warping result can then be utilised to perform detailed analysis of brain regions on the input scan by connecting to the →siibra toolsuite.

ATLASES

## Web version of QuickNII

### WebAlign

Web service
Workflow tool
Web application

WebAlign is the web version of →QuickNII. Presently, it is available as a community app in the →Collaboratory. Features include:
· Spatial registration of sectional image data
· Generation of customised atlas maps for your sectional image data

ATLASES

## Web version of VisuAlign

### WebWarp

Web service
Workflow tool
Web application

WebWarp is the web version of →VisuAlign. Presently, it is available as a community app in the →Collaboratory. Features include:
· Nonlinear refinements of atlas registration by →WebAlign of sectional image data
· Generation of customised atlas maps for your sectional image data

> "Thanks to the HBP, we have been able to develop and openly share tools enabling brain section image analyses. Based on feedback from users worldwide, we added new features and made the tools even more reliable."



**Maja A. Puchades**

coordinates a mixed team of software developers and scientists in the Neural Systems Laboratory at the University of Oslo and is deputy leader of a HBP task. Her team has developed tools that allow for the analysis of brain section image data and the integration into reference brain atlases, including →QuickNII, →VisuAlign, →Nutil, →QCAlign, →MeshView, →LocaliZoom, →DeepSlice, →WebAlign and →WebWarp.

# Embodiment tools

*The WhiskEye robot*
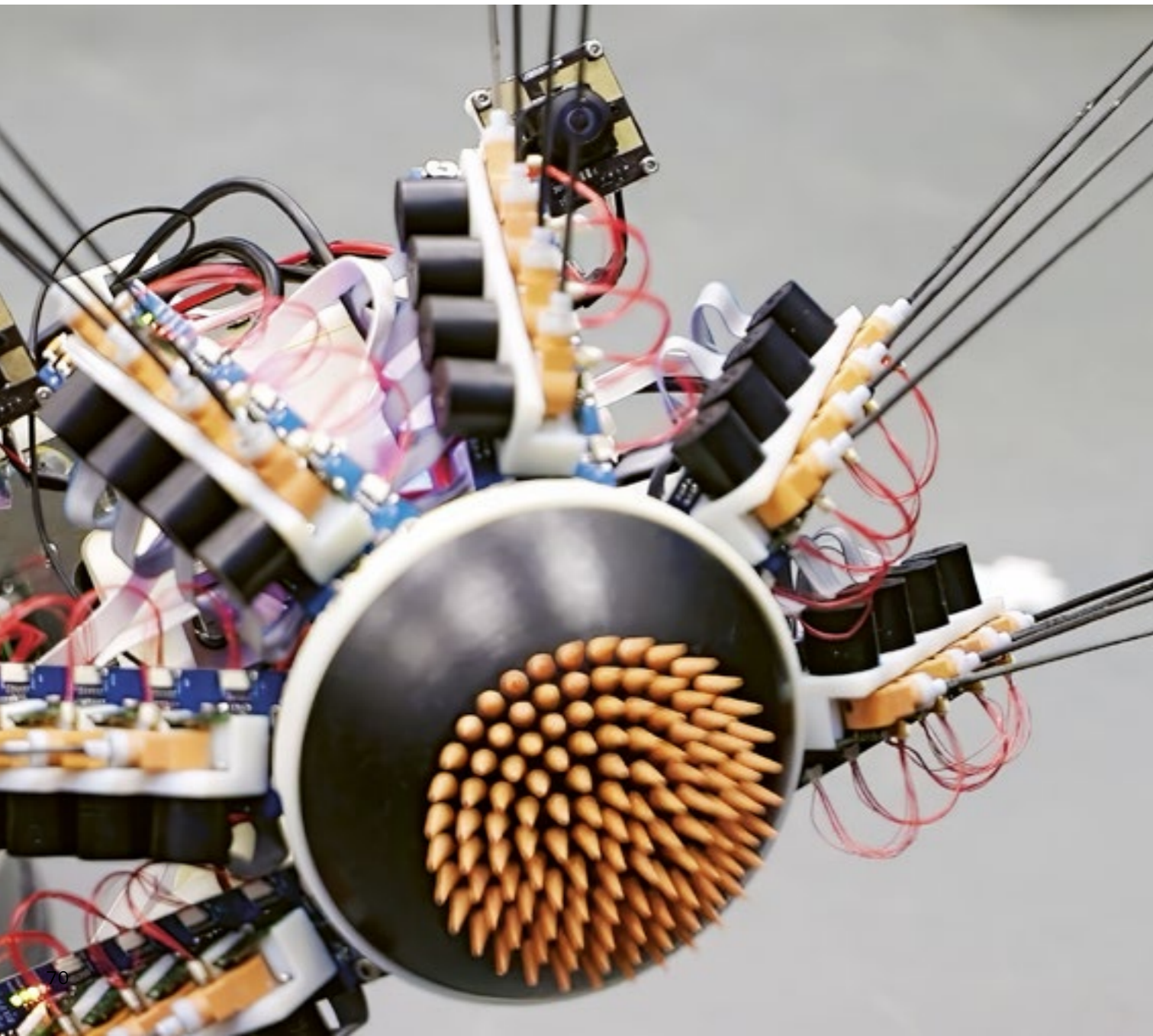


BRAIN-INSPIRED TECHNOLOGY

## Toolbox for goal-driven deep sensorimotor modeling in neuroscience

### AngoraPy

Software library
Framework
Desktop

Compute cluster
Cloud/VM

AngoraPy is an open-source Python library that helps neuroscientists build and train goal-driven models of the sensorimotor system. The toolbox comprises state-of-the-art machine learning techniques under the hood of an easy-to-use API. With the help of deep reinforcement learning, the connectivity required for solving complex, ecologically valid tasks can be learned autonomously, obviating the need for hand-engineered or hypothesis-driven connectivity patterns. With AngoraPy, neuroscientists can train custom deep neural networks on custom sensorimotor tasks.

BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## HBP service for embodied simulation connecting brain models to body models

### Neurorobotics Platform

Platform
Desktop application
Compute cluster
Cloud/VM

The Neurorobotics Platform (NRP) is an integrative simulation framework that enables in silico experimentation and embodiment of brain models inside virtual agents interacting with realistic simulated environments. Entirely Open Source, it offers a browser-based graphical user interface for online access. It can be installed locally (Docker or source install). It can be interfaced with multiple spike-based neuromorphic chips (SpiNNaker, Intel Loihi). You can download and install the NRP locally for maximum experimental convenience or access it online in order to leverage the HBP High-Performance Computing infrastructure for large-scale experiments.

SIMULATION

## Graphical tool to design robotic and musculoskeletal simulation models

### Neurorobotics Platform Robot Designer

Software library
Workflow tool
Desktop

The Robot Designer is a plugin for the 3D modeling suite Blender that enables researchers to design morphologies for simulation experiments on the →Neurobotics Platform as well as other platforms. This plugin helps researchers design and parameterise models with a Graphical User Interface, simplifying and speeding up the design process. It includes design capabilities for musculoskeletal bodies as well as robotic systems, fostering not only the understanding of biological motions and enabling better robot designs, but also enabling true neurorobotic experiments that consist of biomimetic models such as tendon-driven robots or a transition between biology and technology.

→ Feldotto et al. (2022). Front. Neurorobot. 16:856727.

# Multi-scale tools
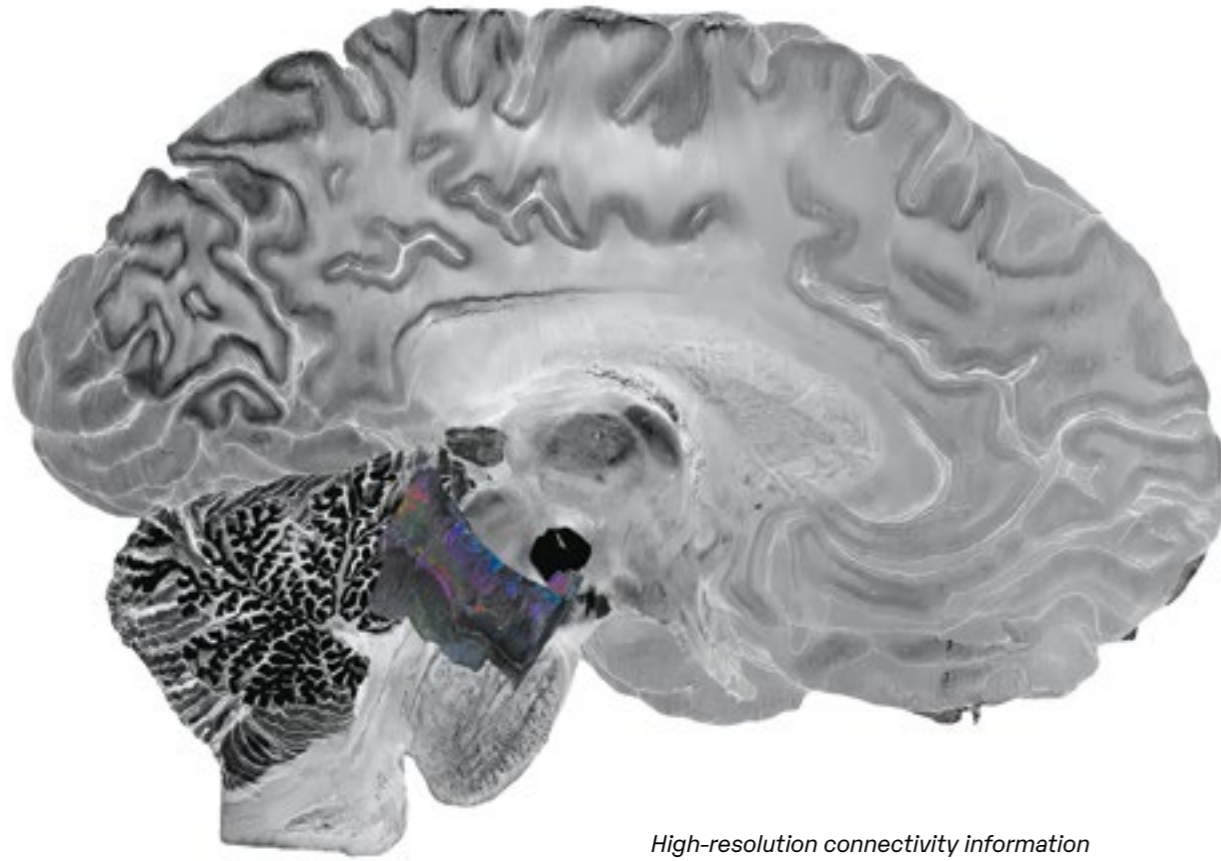


*High-resolution connectivity information of the hippocampus is integrated into the cytoarchitectonic human brain atlas that can be explored using the →siibra tools.*

BRAIN-INSPIRED TECHNOLOGY | VISUALISATION

## High-fidelity, large-scale, interactive and photorealistic visualisation platform for scientific data

Brayns is a large-scale scientific visualisation platform based on Intel OSPRAY that performs CPU Ray-tracing and uses an extension-plugin architecture. The core provides basic functionalities that can be reused and/or extended in plugins, which are independent and can be loaded or disabled at start-up. This simplifies the process of adding support for new scientific visualisation use cases, without compromising the reliability of the rest of the software. Brayns counts with braynsService, a rendering backend which can be accessed over the internet and streams images to connected clients. Already made plugins include CircuitExplorer, DTI, AtlasExplorer, CylindricCamera and MoleculeExplorer.

→ Eilemann et al. (2017). In: Kunkel et al. (eds.) Lecture Notes in Computer Science 10524: 662-675.

### Brayns

Software library
Web application
Desktop application
Web service

Workflow tool
Compute cluster
Cloud/VM
Mobile

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BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Brion allows read/write access to Blue Brain data structures

Brion is a C++ project for read and write access to Blue Brain data structures, including BlueConfig/CircuitConfig, Circuit, CompartmentReport, Mesh, Morphology, Synapse and Target files. It also offers an interface in Python.

→ Dai et al. (2020). PLoS Comput. Biol. 16(2):e1007696.

### Brion

Software library
Workflow tool
Desktop
Compute cluster
Cloud/VM

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VISUALISATION

## Preprocessing large 2D/3D images for fast access

The Image Service takes large 2D (and 3D) images and preprocesses them to generate small 2D tiles (or 3D chunks). Applications consuming image data (viewers or other) can then access regions of interest by downloading a few tiles rather than the entire large image. Tiles are also generated at coarser resolutions to support zooming out of large images. The service supports multiple input image formats.

The serving of tiles to apps is provided by the →Collaboratory Bucket service (based on OpenStack Swift object storage), which provides significantly higher network bandwidth than could be provided by any VM.

### EBRAINS Image Service

Web application
Web services
Workflow tool
Cloud/VM

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VISUALISATION

## Software to make multi-panel plotting in Matplotlib easier

Plotting tool to make plotting with many subfigures easier, especially for publications. After installation, gridspeccer can be used from the command line to create plots.

→ Göltz et al. (2021). Nat. Mach. Intell. 3(9):823-835.
→ Haider et al. (2021). Adv. Neural Inf. Process. Syst. 34:17839-17851.

### gridspeccer

Software library
Desktop

BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Cartesian Genetic Programming (Cgp) in pure Python

### Hal-Cgp

Software library
Framework

Hal-Cgp is an extensible pure Python library implementing Cgp to represent, mutate and evaluate populations of individuals encoding symbolic expressions targeting applications with computationally expensive fitness evaluations. It supports the translation from a CGP genotype, a two-dimensional Cartesian graph, into the corresponding phenotype, a computational graph implementing a particular mathematical expression. These computational graphs can be exported as pure Python functions, in a NumPy-compatible format, SymPy expressions or PyTorch modules. The library implements a mu + lambda evolution strategy to evolve a population of individuals to optimise an objective function.

→ Schmidt et al. (2020). Zenodo 10.5281/zenodo.3889162.

DATA ANALYSIS | MEDICAL DATA ANALYSIS | SIMULATION

## GDPR, sensitive data, health data, security, privacy, cloud, medical, clinical, virtual research environment

### Health Data Cloud

Platform
Infrastructure component
Cloud/VM

The Health Data Cloud (HDC) provides EBRAINS services for sensitive data as a federated research data ecosystem that enables scientists across Europe and beyond to collect, process and share sensitive data in compliance with EU General Data Protection Regulations (GDPR). The HDC is a federation of interoperable nodes. Nodes share a common system architecture based on the Charité Virtual Research Environment (VRE) and Indoc Pilot technology, enabling research consortia to manage and process data, and making data discoverable and sharable via the →EBRAINS Knowledge Graph.

→ Schirner et al. (2023). Nat. Commun. 14(1):2963
→ Schirner et al. (2022). Neuroimage 251:118973.

DATA MANAGEMENT | MEDICAL DATA ANALYSIS

## Simplified iEEG data analysis and sharing

### Human Intracerebral EEG Platform

| | |
|---|---|
| Software suite | Workflow tool |
| Framework | Middleware |
| Platform | Infrastructure component |
| Web application | Desktop |
| Web service | Compute cluster |
| Data store | Cloud/VM |

The Human Intracerebral Platform (HIP) is an open-source platform designed for collecting, managing, analysing and sharing multi-scale iEEG data at an international level. Its mission is to assist clinicians and researchers in improving research capabilities by simplifying iEEG data analysis and interpretation. The HIP integrates different software, modules and services necessary for investigating spatio-temporal dynamics of neural processes in a secure and optimised fashion. The interface is browser-based and allows selecting sets of tools according to specific research needs.

SIMULATION

## Middleware enabling in-transit data access to NEST, TVB and Arbor

### Insite

Software suite
Middleware
Desktop
Compute cluster

Insite enables users to access data via the in-transit paradigm for →NEST, →TVB and →Arbor simulations. Compared to the traditional approach of offline processing, in-transit paradigms allow accessing of data while the simulation runs. This is especially useful for simulations that produce large amounts of data and are running for a long time. In-transit allows the user to access only parts of the data and prevents the need for storing all data. It also allows the user early insights into the data even before the simulation finishes. Insite provides an easy-to-use and easy-to-integrate architecture to enable in-transit features in other tools.

→ Krüger et al. (2022). In: Anzt et al. (eds.) High Performance Computing 13387: 295-305.

VISUALISATION

## Interactive visualisations for multimodal brain and head image data

### Interactive Brain Atlas Viewer

Software library
Web application
Desktop
Mobile

The Interactive Brain Atlas Viewer provides various kinds of interactive visualisations for multi-modal brain and head image data: different parcellations, degrees of transparency and overlays. The Viewer provides the following functions and supports data from the following sources: EEG, white matter tracts, MRI and PET 3D volumes, 2D slices, intracranial electrodes, brain activity, multiscale brain network models, supplementary information for brain regions and functional brain networks in multiple languages. It comes as a web app, mobile app and desktop app.

→ Schirner et al. (2022). Neuroimage 251:118973.

DATA ANALYSIS | ATLASES

## Cytoarchitecture linked to gene expression to study multilevel human brain organisation

### JuGEx

Desktop application
Web service
Web application

Decoding the chain from genes to cognition requires detailed insights into how areas with specific gene activities and microanatomical architectures contribute to brain function and dysfunction. The Allen Human Brain Atlas contains regional gene expression data, while the Julich Brain Atlas, which can be accessed via →siibra, offers 3D cytoarchitectonic maps reflecting interindividual variability. Julich Brain Gene Expression (JuGEx) offers an integrated framework that combines the analytical benefits of both repositories towards a multilevel brain atlas of adult humans. JuGEx is a new method for integrating tissue transcriptome and cytoarchitectonic segregation.

→ Bludau et al. (2018). Brain Struct. Funct. 223:2335–2342.

DATA MANAGEMENT

## Data discoverability portal and encyclopaedia for neuroscience

### KnowledgeSpace

Platform
Web service

KnowledgeSpace (KS) is a globally-used, data-driven encyclopaedia and search engine for the neuroscience community. As an encyclopaedia, KS provides curated definitions of brain research concepts found in different neuroscience community ontologies, Wikipedia and dictionaries. The dataset discovery in KS makes research datasets across many large-scale brain initiatives universally accessible and useful. It also promotes FAIR data principles that will help data publishers to follow best practices for data storage and publication. As more and more data publishers follow data standards like →openMINDS or DATS, the quality of data discovery through KS will improve. The related publications are also curated from PubMed and linked to the concepts in KS to provide an improved search capability.

SIMULATION

## Gradient-free hyper-parameter optimisation library for HPC

### L2L

Software library          Infrastructure component
Workflow tool             Desktop
Middleware                Compute cluster

L2L is an easy-to-use and flexible framework to perform parameter and hyper-parameter space exploration of mathematical models on HPC infrastructure. L2L is an implementation of the learning-to-learn concept written in Python. This open-source software allows several instances of an optimisation target to be executed with different parameters in an massively parallel fashion on HPC. L2L provides a set of built-in optimiser algorithms, which make adaptive and efficient exploration of parameter spaces possible. In contrast to other optimisation toolboxes, L2L provides maximum flexibility in the way the optimisation target can be executed.

→ Yegenoglu et al. (2022). Front. Comput. Neurosci. 16:885207.

MEDICAL DATA ANALYSIS  |  VISUALISATION

## Software to visualise large volumetric datasets

### Livre

Framework
Desktop application
Workflow tool
Compute cluster

The Large-scale Interactive Volume Rendering Engine (Livre) is an out-of-core, multi-node, multi-GPU, OpenGL volume rendering engine to visualise large volumetric datasets. It provides the following major features to facilitate rendering of large volumetric datasets:

· Visualisation of pre-processed UVF format volume datasets
· Real-time voxelisation of different data sources (surface meshes, BBP morphologies, local field potentials, etc.) through the use of plugins
· Multi-node, multi-GPU rendering (only sort-first rendering)

→ Eilemann et al. (2017). International Conference on High Performance Computing: 662–675.

BRAIN-INSPIRED TECHNOLOGY  |  DATA ANALYSIS  |  MEDICAL DATA ANALYSIS

## Secure federated data analysis for collaborative initiatives

### MIP

Software suite            Web service
Framework                 Cloud/VM
Platform                  Data store
Web application           Infrastructure component

The Medical Informatics Platform (MIP) is an open-source platform enabling federated data analysis in a secure environment for centres involved in collaborative initiatives. It allows users to initiate or join disease-oriented federations with the aim of analysing large-scale distributed clinical datasets. For each federation, users can create specific data models based on well-accepted common data elements, approved by all participating centres. MIP experts assist in creating the data models and facilitate coordination and communication among centres. They provide advice and support for data curation, harmonisation and anonymisation, as well as data governance, especially with regards to Data Sharing Agreements and ethical considerations.

→ Redolfi et al. (2020). Front. Neurol. 11:1021.
→ Amunts et al. (2019). PLoS Biol. 17(7):e3000344.

DATA ANALYSIS  |  SIMULATION

## Tools for structured model validation

### Model Validation Service

Software library          Middleware
Web application           Desktop
Web service               Compute cluster
Workflow tool             Cloud/VM

The HBP/EBRAINS Model Validation Service is a set of tools for performing and tracking validation of models with respect to experimental data. It consists of a web API, a GUI client (the Model Catalog app) and a Python client. The service enables users to store, query, view and download: (i) model descriptions/scripts, (ii) validation test definitions and (iii) validation results. In a typical workflow, users will find models and validation tests by searching the Model Catalog (or upload their own), run the tests using the Python client in a Jupyter notebook, with simulations running locally or on HPC, and then upload the results.

SIMULATION

## Set of Python packages containing tools for model validation

### Model Validation Test Suites

Software library
Software suite
Desktop
Compute cluster

As part of the HBP/EBRAINS model validation framework, we provide a Python Software Development Kit (SDK) for model validation, which provides: (i) validation test definitions and (ii) interface definitions intended to decouple model validation from the details of model implementation. This more formal approach to model validation aims to make it quicker and easier to compare models, to provide validation test suites for models and to develop new validations of existing models. The SDK consists of a collection of Python packages all using the sciunit framework: HippoUnit, MorphoUnit, NetworkUnit, BasalUnit, CerebUnit, eFELUnit, HippoNetworkUnit.

→ Sáray et al. (2021). PLoS Comput. Biol. 17(1):e1008114.
→ Gutzen et al. (2018) Front. Neuroinform. 12:90.

"Work that took me two days in the past now takes me only ten minutes. I work with the human brain atlas on EBRAINS, which includes enormously large data and requires supercomputers. Now, I can access and work with the data from anywhere in the world – and so can any researcher in brain science."

### Nicola Palomero-Gallagher

from Forschungszentrum Jülich and the University of Düsseldorf leads a research group studying neurotransmitter receptors. The team produces receptor density maps that can be found on the →EBRAINS Knowledge Graph and are integrated into the HBP's Multilevel Human Brain Atlas, which can be accessed using the →siibra tools.
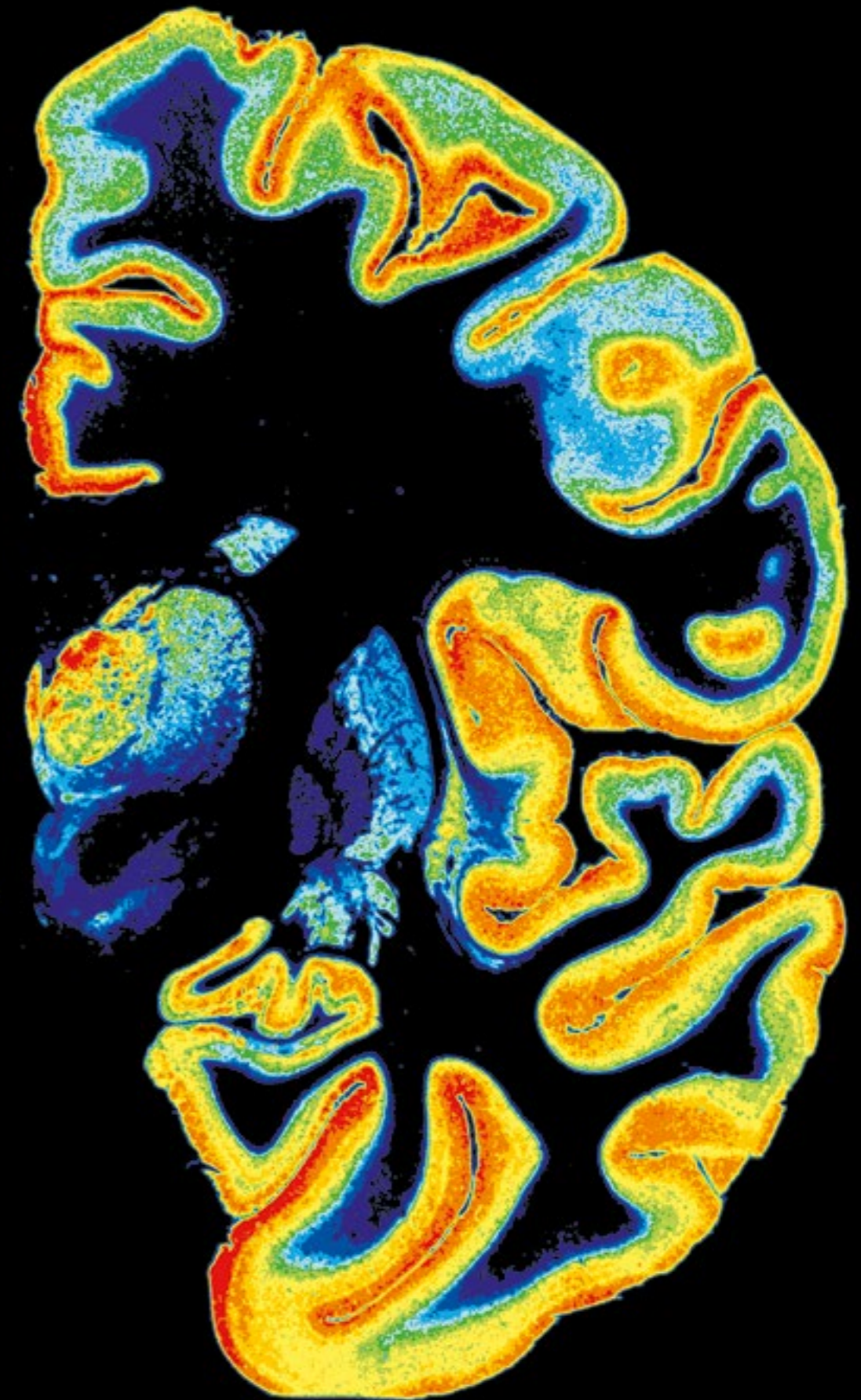
low ▭ high

*Autoradiograph of a right hemisphere showing the receptor density distribution of the GABAB-receptor from low (blue) to high (red).*

SIMULATION

## Multi-scale co-simulation on laptops and supercomputers

## Modular Science

Middleware
Desktop
Compute cluster

Modular Science is a middleware that provides robust deployment of complex multi-application workflows. It contains protocols and interfaces for multi-scale co-simulation workloads on high-performance computers and local hardware. It allows for synchronisation and coordination of individual components and contains dedicated and parallelised modules for data transformations between scales. It offers insight into both the system level and the individual subsystems to steer the execution, to monitor resource usage, and system health & status with small overheads on performance. It comes with a number of neuroscience co-simulation use cases including →NEST-TVB, →NEST-Arbor, →LFPy and the →Neurorobotics Platform.

→ Schirner et al. (2022). Neuroimage 251:118973.
→ Klijn et al. (2019). International Conference on HPCS: 305-31.

ATLASES | DATA ANALYSIS

## Brain slices with pieces of neurite are aligned to form a complete morphology

## Morphology alignment tool

Software library
Web application
Workflow tool
Desktop

Starting with serial sections of a brain in which a complete single morphology has been labelled, the pieces of neurite (axons/dendrites) in each section are traced with Neurolucida or similar microscope-attached software. The slices are then aligned, first using an automated algorithm that tries to find matching pieces in adjacent sections (Python script) and second using a GUI-driven tool (web-based, JavaScript). Finally, the pieces are stitched into a complete neuron (Python script). The neuron and tissue volume are then registered to one of the EBRAINS-supported reference templates (Python script). The web-based tool can also be used to align slices without a neuron being present.

ATLASES | DATA ANALYSIS | VISUALISATION

## Intuitively navigate high-resolution 2D image series

## Multi-Image-OSD

Web service
Workflow tool
Web application

Multi-Image-OSD has browser-based classic pan and zoom capabilities. A collection of images can be displayed as a filmstrip (Filmstrip Mode) or as a table (Collection Mode) with adjustable numbers of rows and columns. The tool supports keyboard and/or mouse navigation options, as well as touch devices. Utilising the open standard Deep Zoom Image (DZI) format, it is able to efficiently visualise very large brain images in the gigapixel range, allowing the user to zoom from common, display-sized overview resolutions down to the microscopic resolution without downloading the underlying, very large image dataset.

DATA ANALYSIS | SIMULATION | VISUALISATION

## Tool for multiscale modelling of brain circuits using Python/NEURON

## NetPyNE

Software suite
Web application

NetPyNE provides programmatic and graphical interfaces to develop data-driven multiscale brain neural circuit models using Python and NEURON. Users can define models using a standardised JSON-compatible, rule-based, declarative format. Based on these specifications, NetPyNE will generate the network in →NEURON, enabling users to run parallel simulations, optimise and explore network parameters through automated batch runs and use built-in functions for visualisation and analysis (e.g., generate connectivity matrices, voltage traces, spike raster plots, local field potentials and information theoretic measures). NetPyNE also facilitates model sharing by exporting and importing standardised formats: NeuroML and SONATA.

→ Dura-Bernal et al. (2019). eLife 8:e44494.

VISUALISATION

## Neural circuit navigation at different abstraction levels using schematic representations

## NeuroScheme

Desktop application
Workflow tool
Infrastructure component

NeuroScheme uses schematic representations, such as icons and glyphs, to encode attributes of neural structures (neurons, columns, layers, populations, etc.), alleviating problems with displaying, navigating and analysing large datasets. It manages hierarchically organised neural structures; users can navigate through the levels of the hierarchy and hone in on and explore the data at their desired level of detail. NeuroScheme has currently two built-in "domains", which specify entities, attributes and relationships used for specific use cases: the "cortex" domain, designed for navigating and analysing cerebral cortex structures; and the "congen" domain, used to define the properties of cells and connections, create circuits of neurons and build populations.

→ Pastor et al. (2015). CEIG 10.2312/ceig.20151208.

BRAIN-INSPIRED TECHNOLOGY |
MEDICAL DATA ANALYSIS | SIMULATION

## Efficient identification of neurostimulation through scalable optimisation of personalised simulations

## NeuroScOPeS

Desktop application
Web service            Compute cluster
Workflow tool          Cloud/VM

NeuroScOPeS is a modular framework for multi-scale simulation of neurostimulation strategies in personalisable neuroanatomical and biophysical models. The goal is to efficiently identify effective and safe neurostimulation parameters to selectively target individual neural substrates corresponding to specific treatment modalities such as pain reduction or movement support. A specific use-case exists in clinical decision support and therapy design of spinal cord stimulation for movement support. The framework is extendable to other treatment modalities of spinal cord stimulation and other neurostimulation strategies.

DATA ANALYSIS | VISUALISATION

## Web platform for neuroscientific data analysis

### NeuroSuites

Web services
Web application

NeuroSuites is a web-based platform designed to handle large-scale, high-dimensional data in the field of neuroscience. It offers neuroscience-oriented applications and tools for data analysis, machine learning and visualisation, while also providing general-purpose tools for data scientists in other research fields. NeuroSuites requires no software installation and runs on the backend of a server, making it accessible from various devices. The platform's main strengths include its defined architecture, ability to handle complex neuroscience data and the variety of available tools.

→ Moreno-Rodríguez et al. (2023). Front. Neuroinform. 17:1092967.

SIMULATION | VISUALISATION

## Scalable, real-time rendering tool to visualise neuronal cable model-based simulations

### RTNeuron

Desktop application
Workflow tool
Infrastructure component
Software library

The main utility of RTNeuron is twofold: (i) the interactive visual inspection of structural and functional features of the cortical column model and (ii) the generation of high-quality movies and images for presentations and publications.
RTNeuron provides a C++ library with an OpenGL-based rendering backend, a Python wrapping and a Python application called rtneuron. RTNeuron is only supported in GNU/Linux systems. However, it should also be possible to build it on Windows systems. For OS/X it may be quite challenging and might require changes in OpenGL-related code.

→ Pastor et al. (2015). CEIG 10.2312/ceig.20151208.

ATLASES | DATA ANALYSIS

## Quality control support for the QUINT workflow

### QCAlign software

Desktop application
Workflow tool

The QUINT workflow enables spatial analysis of labelling in series of brain sections from mouse and rat based on registration to a reference brain atlas.
The QCAlign software supports the use of QUINT for high-throughput studies by providing information about:
· The quality of the section images used as input to the QUINT workflow
· The quality of the atlas registration performed in the QUINT workflow
· QCAlign also makes it easier for the user to explore the atlas hierarchy and decide on a customised hierarchy level to use for the investigation

→ Gurdon et al. (2023). bioRxiv 2023.02.27.530226

ATLASES

## Automatically learns shape and appearance models for datasets of 3D scans

### Shape & Appearance Modelling

Software suite
Desktop
Compute cluster

Shape & Appearance Modelling is a framework for automatically learning shape and appearance models for medical (and certain other) images. The algorithm was developed with the aim of eventually enabling distributed privacy-preserving analysis of brain image data, such that shared information (shape and appearance basis functions) may be passed across sites, whereas latent variables that encode individual images remain secure within each site. These latent variables are proposed as features for privacy-preserving data mining applications.

→ Ashburner et al. (2019). Med. Image Anal. 55:197-215.

DATA ANALYSIS

## Region-wise Connectivity-Based Psychometric Prediction

### Region-wise CBPP using the Julich Brain Atlas

Data store
Desktop
Compute cluster

Many studies have investigated the relationships between interindividual variability in brain connectivity and behavioural phenotypes by utilising connectivity-based prediction models. We showed that an approach based on the combination of whole-brain and region-wise connectivity-based psychometric prediction (CBPP) can provide insight into the predictive model, and hence brain-behaviour relationships, by offering interpretable patterns. We applied this approach using the Julich Brain Atlas with the resting-state functional connectivity and psychometric variables from the Human Connectome Project dataset, illustrating each brain region's predictive power for a range of psychometric variables. As a result, a psychometric prediction profile was established for each region.

→ Wu et al. (2021). Cereb. Cortex 31(8):3732–3751.

ATLASES

## Retrieve atlas (meta)data over RESTful API

### siibra-api

Web service
Middleware
Desktop
Cloud/VM

siibra-api provides an HTTP wrapper around →siibra-python, allowing developers to access essential functionalities over HTTP protocol. This includes access to parcellations, reference templates and multimodal data features. Deployed on the EBRAINS infrastructure, developers can access the centralised (meta)data on atlases regardless of the programming language.

ATLASES | VISUALISATION

## Browser-based viewer for visual exploration of EBRAINS atlases

### siibra-explorer

Web application
Desktop
Mobile

The interactive atlas viewer siibra-explorer allows exploration of the different EBRAINS atlases for the human, monkey and rodent brains together with a comprehensive set of linked multimodal data features. It provides a 3-planar view of a parcellated reference volume combined with a rotatable overview of the 3D surface. Several templates can be selected for navigating through the brain from MRI-scale to microscopic resolution, allowing inspection of terabyte-size image data. Anatomically anchored datasets reflecting aspects of cellular and molecular organisation, fibres, function and connectivity can be discovered by selecting brain regions from parcellations, or zooming and panning the reference brain. siibra-explorer also allows annotation of brain locations as points and polygons.

→ Zachlod et al. (2023). Biol. Psychiatry 93(5):471–479.

BRAIN-INSPIRED TECHNOLOGY | SIMULATION

## Python toolbox for co-simulation of The Virtual Brain (TVB) with spiking networks simulators

### TVB-Multiscale

Software library
Desktop
Cloud/VM

TVB-Multiscale is a Python toolbox aimed at facilitating the configuration of multiscale brain models and their co-simulation with TVB and spiking network simulators (currently →NEST, →NetPyNE (NEURON) and ANNarchy). A multiscale brain model consists of a full brain model formulated at the coarse scale of networks of tens up to thousands of brain regions, and an additional model of networks of spiking neurons describing selected brain regions at a finer scale. The toolbox has a user-friendly interface for configuring different kinds of models for transforming and exchanging data between the two scales during co-simulation.

→ Meier et al. (2022). Exp. Neurol. 354:114111.
→ Schirner et al. (2022). Neuroimage 251:118973.

ATLASES | DATA ANALYSIS | VISUALISATION

## A comprehensive Python library for working with EBRAINS atlases

### siibra-python

Software library
Compute cluster

siibra-python is a Python client to a brain atlas framework that integrates brain parcellations and reference spaces at different spatial scales and connects them with a broad range of multimodal regional data features. It aims to facilitate programmatic and reproducible incorporation of brain parcellations and brain region features from different sources into neuroscience workflows. Also, siibra-python provides an easy access to data features on the →EBRAINS Knowledge Graph in a well-structured manner. Users can preconfigure their own data to use within siibra-python.

DATA ANALYSIS | VISUALISATION

## Graphical meta-framework to design interactive and coordinated views applications for data visualisation

### VMetaFlow

Framework
Web application
Infrastructure component

VMetaFlow (formerly, Meta Language for Visualization) is an abstraction layer placed over existing visual grammars and visualisation declarative languages, providing them with interoperability mechanisms. The main contribution of this research is to provide a user-friendly system to design visualisation and data processing operations that can be interconnected to form data analysis workflows. Visualisations and data processes can be saved as cards. Cards and workflows can be saved, distributed and reused between users.

→ Cosmin-Toader et al. (2022). IEEE Access 10:94545–94559.

SIMULATION

## Simulation of GPCR signal transduction pathways with system biology models

### SSB toolkit

Software library
Software suite
Workflow tool
Desktop

The Structural Systems Biology (SSB) toolkit is an open-source Python library to simulate mathematical models of the signal transduction pathways of G protein-couple receptors (GPCRs). By merging structural macromolecular data with systems biology simulations, the framework allows simulation of the signal transduction kinetics induced by ligand-GPCR interactions, as well as the consequent change of concentration of signalling molecular species, as a function of time and ligand concentration. Therefore, this tool allows the investigation of the subcellular effects of ligand binding upon receptor activation, deepening the understanding of the relationship between molecular ligand-target interactions and higher-level cellular and physiological or pathological response mechanisms.

→ Ribeiro et al. (2022). bioRxiv 2022.11.08.515595

DATA ANALYSIS | ATLASES

## Interactive alignment of high-resolution volumes to 3D reference atlases

### voluba

Web service
Web application
Workflow tool

A common problem in high-resolution brain atlasing is spatial anchoring of volumes of interest from imaging experiments into the detailed anatomical context of an ultra-high-resolution reference model like BigBrain. The interactive volumetric alignment tool voluba is implemented as a web service and allows anchoring of volumetric image data to reference volumes at microscopical spatial resolutions. It enables interactive manipulation of image position, scale, orientation, flipping of coordinate axes and entering of anatomical point landmarks in 3D. The resulting transformation parameters can be downloaded or used to view the anchored image volume in an atlas context and create spatial metadata for FAIR data sharing.

DATA ANALYSIS

## A browser-based interactive learning and segmentation toolkit

webilastik brings the popular machine learning-based image analysis tool ilastik from the desktop into the browser. Users can perform semantic segmentation tasks on their data in the cloud. webilastik runs computations on federated EBRAINS HPC resources and uses EBRAINS infrastructure for data access and storage. webilastik makes machine learning-based image analysis workflows accessible to users without deep knowledge of image analysis and machine learning. webilastik is part of the QUINT workflow for extraction, quantification and analysis of features from rodent histological images.

### webilastik

Web application
Web service
Workflow tool

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DATA ANALYSIS | VISUALISATION

## A tool designed to stitch large volumetric images

ZetaStitcher is a Python package designed to stitch large volumetric images, such as those produced by light sheet fluorescence microscopes. It is able to quickly compute the optimal alignment of large mosaics of tiles thanks to its ability to perform a sampling along the tile depth, i.e., pairwise alignment is computed only at certain depths along the thickness of the tile. This greatly reduces the amount of data that needs to be read and transferred, thus, making the process much faster. ZetaStitcher comes with an API that can be used to programmatically access the aligned volume in a virtual fashion as if it were a big NumPy array, without having to produce the fused 3D image of the whole sample.

### ZetaStitcher

Software library
Workflow tool
Desktop
Compute cluster

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"My lab and I are enthusiastic users of the HBP online tools. Many of their built-in and unique features have been instrumental in making our work easier and, most importantly, more accurate and reproducible for other users in the field."

Michele Migliore

is Research Director at the Institute of Biophysics of the Italian National Research Council, and his lab has been using several HBP tools and workflows such as the →Hodgkin-Huxley Neuron Builder, →ViSimpl, →NEST Desktop, the EBRAINS Model Catalog, the →EBRAINS Knowledge Graph, the →Live Papers and others.

# Transversal tools
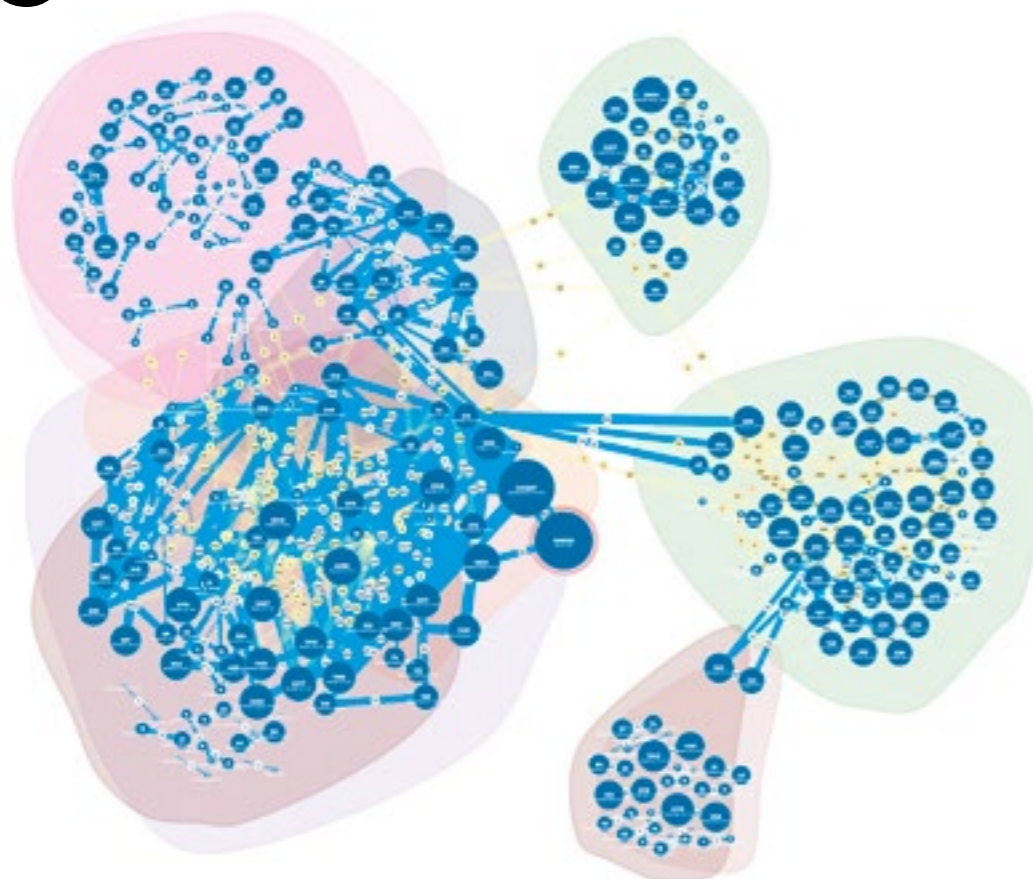


*Graphical overview of the continuously developing content of the →EBRAINS Knowledge Graph (derived from https://kg.ebrains.eu/statistics/)*

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ICT INFRASTRUCTURE

## Allows users to submit jobs on remote HPC systems using the EBRAINS authentication

The Service Account of the Cellular Level Simulation Interactive (CLSI) Workflows is a REST API service that allows developers to submit jobs on HPC systems and retrieve job results on behalf of EBRAINS users. These are not required to own any HPC account and only need EBRAINS credentials in order to be granted access to HPC resources via the Service Account.

## CLSI Service Account

Web service
Cloud/VM

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COLLABORATION | ICT INFRASTRUCTURE

## Object storage for EBRAINS users

## Collaboratory Bucket service

Web application
Webservice
Data store
Cloud/VM

The Bucket service provides object storage to EBRAINS users without them having to request an account on Fenix (the EBRAINS infrastructure provider) and storage resources there. This is the recommended storage for datasets that are shared by data providers, on the condition that these do not contain sensitive personal data. For sharing datasets with personal data, users should refer to the →Health Data Cloud. The Bucket service is better suited for larger files that are usually not edited, such as datasets and videos. For Docker images, users should refer to the EBRAINS Docker registry. For smaller files and files which are more likely to be edited, users should consider the →Collaboratory Drive service.

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COLLABORATION | ICT INFRASTRUCTURE

## File storage for EBRAINS users

## Collaboratory Drive

Web application
Web service
Data store
Cloud/VM

The Drive service offers users cloud storage space for their files in each collab (workspace). The Drive storage is mounted in the →Collaboratory Lab to provide permanent storage (as opposed to the Lab containers which are deleted after a few hours of inactivity). All files are under version control. The Drive is intended for smaller files (currently limited to 1 GB) that change more often. Users must not save files containing personal information in the Drive (i.e., data of living human subjects). The Drive is also integrated with the →Collaboratory Office service to offer easy collaborative editing of Office files online.

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COLLABORATION | ICT INFRASTRUCTURE

## Authentication service for all EBRAINS services

## Collaboratory IAM

Web application
Web service
Infrastructure component
Cloud/VM

The EBRAINS Collaboratory IAM allows the developers of different EBRAINS services to benefit from a single sign-on solution. End users will benefit from a seamless experience, whereby they can access a specific service and have direct access from it to resources in other EBRAINS services without re-authentication. For the developer, it is a good way to separate concerns and to offload much of the identification and authentication to a central service. The EBRAINS IAM is recognised as an identity provider at Fenix supercomputing sites. The IAM service also provides three ways of managing groups of users: as Units, Groups and Teams.

COLLABORATION | ICT INFRASTRUCTURE

## Cloud instance of JupyterLab with all EBRAINS tools pre-installed

### Collaboratory Lab

Web application
Cloud/VM

The Collaboratory Lab provides EBRAINS users with a user-friendly programming environment for reproducible science. EBRAINS tools are pre-installed for the user. The latest release is selected by default, but users can choose to run an older release to reuse an older notebook or try out the very latest features in the weekly experimental deployment. Official releases are produced by EBRAINS every few months. End users do not need to build and install the tools, and, more importantly, they do not need to resolve dependency conflicts among tools as this has been handled for them.

COLLABORATION

## Collaborative editing of Office documents

### Collaboratory Office

Web application
Web service
Cloud/VM

With the Office service, EBRAINS users can collaboratively edit Office documents (Word, PowerPoint or Excel) with most of the key features of the MS Office tools. It uses the open standard formats .docx, .pptx and .xlsx so that files can alternately be edited in the Collaboratory Office service and in other compatible tools including the MS Office suite.

COLLABORATION

## Framework and publication part of the Collaboratory

### Collaboratory Wiki

Platform
Web application
Web service
Infrastructure component
Cloud/VM

The Wiki service offers the user-friendly wiki functionality for publishing web content. It acts as a central user interface and API to access the other Collaboratory services. EBRAINS developers can integrate their services as an app which can be instantiated by users in their collabs. The Wiki is a good place to create tutorials and documentation and it is also the place to publish your work on the internet if you choose to do so.

ETHICS & SOCIETY

### EBRAINS Ethics & Society Toolkit

Platform
Web service
Mobile

The aim of the toolkit is to offer researchers who carry out cross-disciplinary brain research a possibility to engage with ethical and societal issues within brain health and brain disease. The user is presented with short introductory texts, scenario-based dilemmas, animations and quizzes, all tailored to specific areas of ethics and society in a setting of brain research. All exercises are reflection-oriented, with an interactive approach to inspire users to incorporate these reflections into their own research practices. Moreover, it is possible to gain further knowledge by utilising the links for relevant publications, teaching modules and the EBRAINS Community Space.

DATA MANAGEMENT

## Metadata management system to ensure FAIR principles in neuroscience

### EBRAINS Knowledge Graph

Software suite
Web application
Web service
Workflow tool
Cloud/VM

The EBRAINS Knowledge Graph (KG) is the metadata management system of the EBRAINS Data and Knowledge services. It provides fundamental services and tools to make neuroscientific data, models and related software FAIR. The KG Editor and API (incl. Python SDKs) allow annotation of scientific resources in a semantically correct way. The KG Search exposes the research information via an intuitive user interface and makes the information publicly available to any user. For advanced users, the KG Query Builder and KG Core API provide the necessary means to execute detailed queries on the graph database whilst enforcing fine-grained permission control.

COLLABORATION | ETHICS & SOCIETY

## Integration of Equality, Equity, Diversity and Inclusion in research content and collaboration

### EDI Toolkit

Web application
Workflow tool

The Equality, Equity, Diversity, Inclusion (EDI) Toolkit supports projects in integrating EDI in their research content and as guiding principles for team collaboration. It is designed for everyday usage by offering:
· Basic information
· Guiding questions, templates and tools to design responsible research
· Quick checklists, guidance for suitable structures and standard procedures
· Measures to support EDI-based leadership, fair teams and events

→ Grasenick et al. (2023). Zenodo 10.5281/zenodo.7756892.
→ Grasenick (2019). Zenodo 10.5281/zenodo.5575845.
→ Grasenick (2019). Zenodo 10.5281/zenodo.5236297.

DATA ANALYSIS | MEDICAL DATA ANALYSIS | SIMULATION

## openMINDS-aware Python client for the EBRAINS Knowledge Graph

### fairgraph

Software library
Desktop
Cloud/VM

fairgraph is a Python library for working with metadata in the →EBRAINS Knowledge Graph (KG), with a particular focus on data reuse, although it is also useful for registering and curating metadata. The library represents metadata nodes (also known as openMINDS instances) from the KG as Python objects. fairgraph supports querying the KG, following links in the graph, downloading data and metadata, and creating new nodes in the KG. It builds on →openMINDS and on the KG Core Python library.

---

ICT INFRASTRUCTURE

## Launching supercomputing jobs for service providers

### HPC Job Proxy

Framework
Infrastructure component
Compute cluster
Cloud/VM

The High Performance Computing (HPC) Job Proxy provides a simplified way for EBRAINS service providers to launch jobs on Fenix supercomputers on behalf of EBRAINS end users. The proxy offers a wrapper over the Unicore service, which adds logging, access to stdout/stderr/status, verification of user quota, and updating of user quota at the end of the job.

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ICT INFRASTRUCTURE

## Real-time check of the HPC Systems available to HBP users

### HPC Status Monitor

Web application
Web service
Workflow tool

The High Performance Computing (HPC) Status Monitor allows a real-time check of the availability status of the HPC Systems accessible from HBP tools and services and provides an instant snapshot of the resource quotas available to individual users on each system.

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DATA ANALYSIS | SIMULATION | VISUALISATION

## Tools for publishing Live Papers

### Live Papers

Web application
Cloud/VM

EBRAINS Live Papers are structured and interactive documents that complement published scientific articles. Live Papers feature integrated tools and services that allow users to download, visualise or simulate data, models and results presented in the corresponding publications. You can build interactive documents to showcase your data and the simulation or data analysis code used in your research, easily link to resources in community databases, interactively visualise electrophysiology data and neuronal reconstructions, launch EBRAINS simulation tools to explore single neuron models in your browser, share live papers pre-publication with anonymous reviewers during peer review and explore published Live Papers.

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SIMULATION

## Automatic selection and generation of integration schemes for systems of ordinary differential equations

### ODE-toolbox

Software library          Desktop
Workflow tool            Compute cluster

The Ordinary Differential Equation (ODE)-toolbox is a Python package that assists in solver benchmarking and recommends solvers on the basis of a set of user-configurable heuristics. For all dynamical equations that admit an analytic solution, ODE-toolbox generates propagator matrices that allow the solution to be calculated at machine precision. For all others, first-order update expressions are returned based on the Jacobian matrix. In addition to continuous dynamics, discrete events can be used to model instantaneous changes in system state, such as a neuronal action potential. These can be generated by the system under test as well as applied as external stimuli, making ODE-toolbox particularly well-suited for applications in computational neuroscience.

→ Linssen et al. (2022). Zenodo 10.5281/zenodo.7193350.

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DATA MANAGEMENT

## Community-driven, open-source metadata framework for neuroscience data

### openMINDS

Framework
Infrastructure component

The open Metadata Initiative for Neuroscience Data Structures (openMINDS) is composed of: (i) integrated metadata models adoptable by any graph database system (GDBS), (ii) a set of libraries of serviceable metadata instances with external resource references for local and global knowledge integration, and (iii) supportive tooling for handling the metadata models and instances. Moreover, the framework provides machine-readable mappings to other standardisation efforts (e.g., schema.org). With this, openMINDS is a unique and powerful metadata framework for flexible knowledge integration within and beyond any GDBS.

DATA ANALYSIS | SIMULATION | MEDICAL DATA ANALYSIS | VISUALISATION

## Web API for computational provenance metadata in the EBRAINS Knowledge Graph

### Provenance API

Web service
Middleware
Cloud/VM

The EBRAINS Provenance API is a web service that facilitates work with computational provenance metadata. Metadata are stored in the →EBRAINS Knowledge Graph (KG) using →openMINDS schemas. The Provenance API provides a somewhat simplified interface compared to accessing the KG directly and performs checks of metadata consistency. The service covers workflows involving simulation, data analysis, visualisation, optimisation, data movement and model validation.

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ICT INFRASTRUCTURE

## Centralised accounting of user quotas in EBRAINS services

### Quota manager

Framework
Web service
Cloud/VM

The Quota Manager enables each EBRAINS service to manage user quotas for resources EBRAINS users consume in their respective services. The goal is to encourage the responsible use of resources. It is recommended that all users (except possibly guest accounts) are provided with a default quota and that specific users have the option of receiving larger quotas based on their affiliation, role or motivated requests.

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ETHICS & SOCIETY

## Resources for anticipation, reflection and deliberation on research and innovation

### RRI Capacity Development Resources

Web service

A series of training resources developed to enable anticipation, critical reflection and public engagement/deliberation of societal consequences of brain research and innovation activities. These resources were designed primarily for HBP researchers and EBRAINS leadership and management, involving EBRAINS data and infrastructure providers. However, they are also useful for engaging the wider public with Responsible Research and Innovation (RRI). The resources are based on the legacy of over 10 years of research and activities of the ethics and society team in the HBP. They cover important RRI-related topics on neuroethics, data governance, dual-use, public engagement and foresight, diversity, research integrity, etc.

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ICT INFRASTRUCTURE

## Co-allocation of compute and data resources on multi-tiered storage clusters

### Slurm Plugin for Co-allocation of Compute and Data Resources

Middleware
Compute cluster

The Simple Linux Utility for Resource Management (Slurm) plugin enables the co-allocation of compute and data resources on a shared multi-tiered storage cluster by estimating waiting times when the high-performance storage (burst buffers) will become available to submitted jobs. Based on the current job queue and the estimated waiting time, the plugin decides whether scheduling the high-performance or lower-performance storage system (parallel file system) benefits the job's turnaround time. The estimation depends on additional information the user provides at submission time.

→ Lackner et al. (2019). 19th IEEE/ACM International Symposium on Cluster, Cloud and Grid Computing (CCGRID):321–330.

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VISUALISATION

## Multi-window, multi-user touch interface for large screens

### Tide

Software suite          Infrastructure component
Web application        Desktop
Middleware              Compute cluster

BlueBrain's Tiled Interactive Display Environment (Tide) provides multi-window, multi-user touch interaction on large surfaces – think of a giant collaborative wall-mounted tablet. Tide is a distributed application that can run on multiple machines to power display walls or projection systems of any size. Its user interface is designed to offer an intuitive experience on touch walls. It works just as well on non-touch-capable installations by using its web interface from any web browser.

→ Eilemann et al. (2017). International Conference on High Performance Computing: 662–675.

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DATA ANALYSIS | VISUALISATION

## Core communication system between Espina and DC Explorer, Pyramidal Explorer and Clint Explorer

### Vishnu 1.0

Software suite
Framework
Desktop application

DC Explorer, Pyramidal Explorer and Clint Explorer are the core of an application suite designed to help scientists to explore their data. Vishnu 1.0 is a communication framework that allows them to interchange information and cooperate in real-time. It provides a unique access point to the three applications and manages a database with the users' datasets. Vishnu was originally designed to integrate data for Espina.

# Indices

## By name

## By research method

# By scale

ABBREVIATIONS

| | |
|---|---|
| AMD | Advanced Micro Devices, Inc. |
| API | Application Programming Interface |
| brainiak | Brain Imaging Analysis Kit |
| BSP | Brain Simulation Platform |
| CPU | Central Processing Unit |
| DICOM | Digital Imaging and Communications in Medicine |
| DTI | Diffusion Tractography Imaging |
| ECoG | Electrocorticography |
| EEG | Electroencephalography |
| FAIR | Findability, Accessibility, Interoperability, and Reusability |
| fMRI | Functional magnetic resonance imaging |
| BOLD | Blood-oxygen-level-dependent |
| GPU | Graphics Processing Unit |
| GUI | Graphical User Interface |
| HBP | Human Brain Project |
| HPC | High-Performance Computing |
| HTTP | Hypertext Transfer |
| IAM | Identity and Access Management (from Collaboratory) |
| ICT | Information and Communications Technology |
| kg-core | Knowledge Graph Core |
| LFP | Local Field Potential |
| MEG | Magnetoencephalography |
| MPI | Message Passing Interface |
| MRI | Magnetic Resonance Imaging |
| PET | Positron Emission Tomography |
| PLI | Polarized Light Imaging |
| pymvpa | MultiVariate Pattern Analysis (MVPA) in Python |
| Python SDKs | Python software development kit |
| ResNet | Residual Neural Network |
| ROI | Region of Interest |
| Sbtab | Table format for Systems Biology |
| TMS | Transcranial Magnetic Stimulation |
| TVB | The Virtual Brain |
| VM | Virtual Machine |

# Partner institutions of the HBP
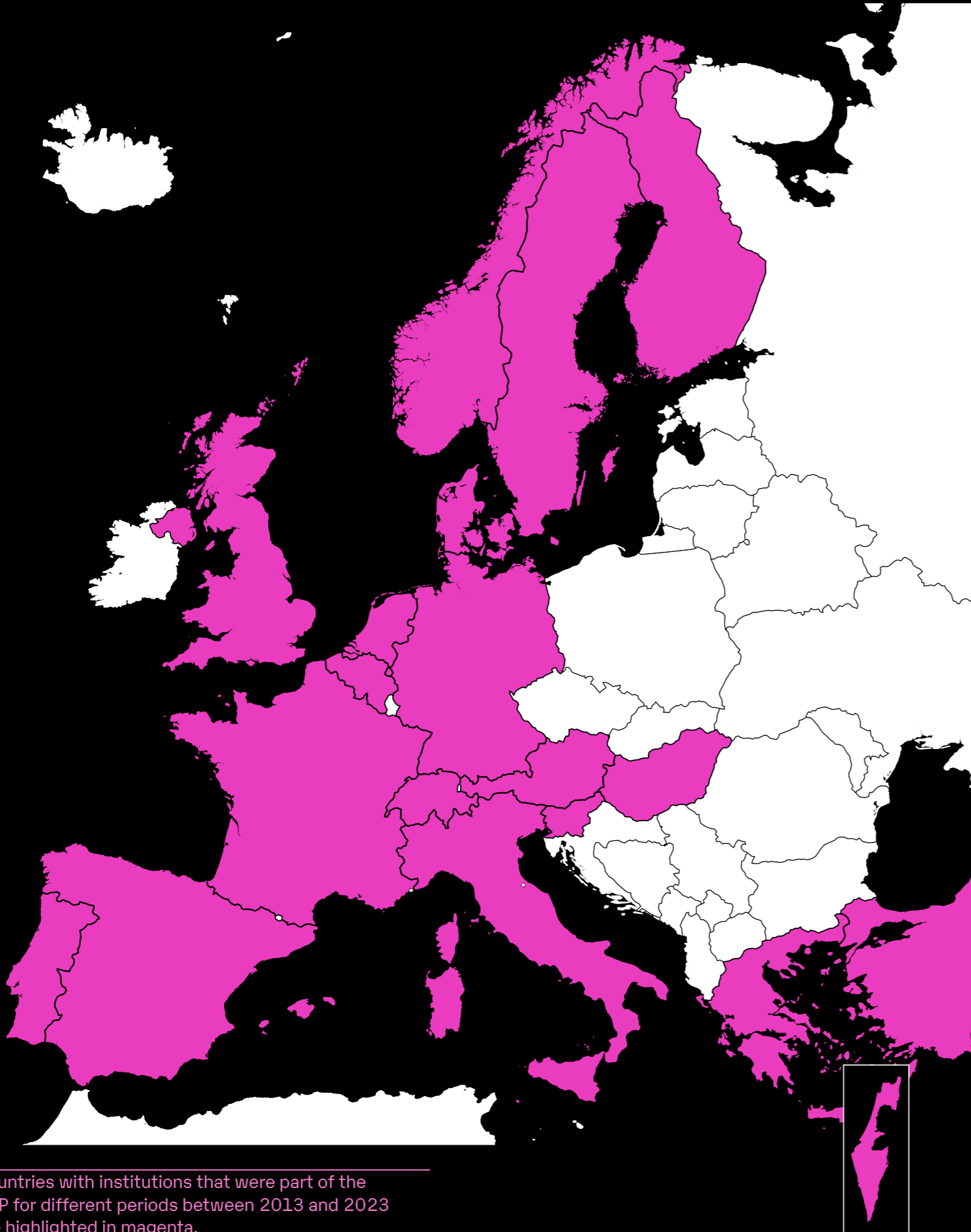


Countries with institutions that were part of the HBP for different periods between 2013 and 2023 are highlighted in magenta.

| Institution | Country |
|---|---|
| Aalto-Korkeakoulusäätiö | Finland |
| Academisch Ziekenhuis Leiden | Netherlands |
| AI2Life Srl | Italy |
| Alpine Intuition Sàrl | Switzerland |
| Athens University of Economics and Business - Research Center | Greece |
| Athina-Erevnitiko Kentro Kainotomias Stis Technologies Tis Pliroforias, Ton Epikoinonion Kai Tis Gnosis | Greece |
| Autonomyo Sàrl | Switzerland |
| Barcelona Supercomputing Center - Centro Nacional De Supercomputacion | Spain |
| Bauhaus Universität Weimar | Germany |
| Bergische Universität Wuppertal | Germany |
| Biomax Informatics AG | Germany |
| Bitbrain SL | Spain |
| Bloomfield Science Museum Jerusalem (BSMJ) | Israel |
| Cardiff University | United Kingdom |
| Centre Hospitalier Regional de Marseille Assistance Publique-Hopitaux Marseille | France |
| Centre Hospitalier Regional et Universitaire de Lille | France |
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| Consiglio Nazionale delle Ricerche | Italy |
| Consorci Institut d'Investigacions Biomediques August Pi i Sunyer | Spain |
| Consorzio Interuniversitario Cineca | Italy |
| Convelop - Cooperative Knowledge Design GMBH | Austria |
| Danmarks Tekniske Universitet | Denmark |
| De Montfort University | United Kingdom |
| Debreceni Egyetem | Hungary |
| Deutsches Zentrum für Neurodegenerative Erkrankungen EV | Germany |
| EBRAINS Association Internationale Sans But Lucratif | Belgium |
| Ecole Normale Supérieure | France |
| École polytechnique fédérale de Lausanne | Switzerland |
| Eidgenössische Technische Hochschule Zürich | Switzerland |
| Erasmus Universitair Medisch Centrum Rotterdam | Netherlands |
| Ethniko Kai Kapodistriako Panepistimio Athinon | Greece |
| European Brain Research Institute R Ita Levi-Montalcini Fondazione*EBRI | Italy |
| European Molecular Biology Laboratory | Germany |
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| Fundacio Institut de Bioenginyeria de Catalunya | Spain |
| General Equipment for Medical Imaging SA | Spain |
| Georg-August-Universität Göttingen Stiftung Öffentlichen Rechts | Germany |
| Heinrich-Heine-Universität Düsseldorf | Germany |
| Helsingin yliopisto | Finland |
| HITS GGMBH | Germany |
| Hochschule Stralsund | Germany |
| Hospices Cantonaux CHUV | Switzerland |
| Humboldt-Universität zu Berlin | Germany |
| Idryma Iatroviologikon Ereunon Akademias Athinon | Greece |
| Imperial College of Science, Technology and Medicine | United Kingdom |

| Institution | Country |
|---|---|
| Indoc Research Europe gGmbH | Germany |
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| Katholieke Universiteit Leuven | Belgium |
| King's College London | United Kingdom |
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| Kungliga Tekniska Hoegskolan | Sweden |
| L'Azienda Socio Sanitaria Territoriale (ASST) Grande Ospedale Metropolitano Niguarda | Italy |
| Laboratorio Europeo di Spettroscopie non Lineari | Italy |
| LabVantage Biomax GMBH | Germany |
| Linneuniversitetet | Sweden |
| Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V | Germany |
| Medical Research Council | United Kingdom |
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| Middlesex University Higher Education Corporation | United Kingdom |
| Norges Miljo-Og Biovitenskaplige Universitet | Norway |
| Oslo universitetssykehus HF | Norway |
| Österreichische Studiengesellschaft für Kybernetik | Austria |
| Politecnico di Milano | Italy |
| Politecnico di Torino | Italy |
| Rheinisch-Westfälische Technische Hochschule Aachen | Germany |
| Robotnik Automation S.L.L. | Spain |
| Ruprecht-Karls-Universität Heidelberg | Germany |
| Sabanci University | Turkey |
| Scuola Internazionale Superiore di Studi Avanzati di Trieste | Italy |
| Scuola Normale Superiore | Italy |
| Scuola Superiore di Studi Universitari e di Perfezionamento Sant'Anna | Italy |
| SICHH Swiss Integrative Center for Human Health SA | Switzerland |
| Stichting Katholieke Universiteit | Netherlands |
| Stichting VU-VUmc | Netherlands |
| Stiftung FZI Forschungszentrum Informatik am Karlsruher Institut für Technologie | Germany |
| Technical University of Crete | Greece |
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| The University of Manchester | United Kingdom |

| Institution | Country |
|---|---|
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| Universita degli Studi di Pavia | Italy |
| Universita degli Studi di Roma 'La Sapienza' | Italy |
| Università degli Studi di Torino | Italy |
| Universität Basel | Switzerland |
| Universität Bern | Switzerland |
| Universität Bielefeld | Germany |
| Universität Trier | Germany |
| Universität Zürich | Switzerland |
| Universitätsklinikum Aachen | Germany |
| Universitätsklinikum Bonn | Germany |
| Universitätsklinikum Freiburg | Germany |
| Universitätsklinikum Hamburg-Eppendorf | Germany |
| Universitätsmedizin Greifswald Körperschaft des öffentlichen Rechts | Germany |
| Universitat de Barcelona | Spain |
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| Universiteit Antwerpen | Belgium |
| Universiteit Gent | Belgium |
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| Universiteit van Amsterdam | Netherlands |
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| University College London | United Kingdom |
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| University of Hertfordshire | Netherlands |
| University of Leeds | United Kingdom |
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| University of Sheffield | United Kingdom |
| University of Surrey | United Kingdom |
| University of Sussex | United Kingdom |
| University of the West of England, Bristol | United Kingdom |
| Uppsala Universitet | Sweden |
| Weizmann Institute of Science | Israel |

The institutions listed above were core partners of the HBP for different periods between 2013 and 2023. In addition, 33 further organisations from 15 countries including Canada, Czechia, Lithuania, Luxembourg and the United States of America were associated members of the HBP in the context of Partnering Projects.

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