Discover EBRAINS A key enabler to advance brain science





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 Digital reconstruction of a circuit of neurons in the temporal lobe of the human brain, close-up from a large artwork on the upper limits before pia matter.

Image Credits: Scientific visualizations of neuronal complexes on the cover and pages 13, 15 and 22 by Nicolas Antille. Polarised light imaging (3D-PLi) images pages 8 and 18, from Dr. Markus Axer, IMN-1 Forschungszentrum Jülich.

The EBRAINS ambition

EBRAINS is a **new digital research infrastructure** (RI), created by the EU-funded Human Brain Project (HBP), that gathers an extensive range of data and tools for brainrelated research.

It draws on cutting-edge neuroscience, big data, computing, robotics and related technologies to help translate the latest scientific discoveries into innovation in medicine and industry, for the benefit of patients and society.

EBRAINS' ambition is to provide the scientific community at large with an open state-of-the-art capability that fosters collaborative brain science, opens the way to ground-breaking discovery and aims to secure Europe's leading position in the dynamically growing field of multidisciplinary brain research and its exploitation.

The need for a Digital Brain Research Infrastructure in Europe



The JUWELS Supercomputer located in Forschungszentrum Jülich is one of several computers located in five EU supercomputing centers providing services to EBRAINS. Advancing brain research in Europe responds to several societal, scientific, technological and economic needs and priorities.

Addressing a public health priority

Brain disorders are increasingly recognised as major causes of disability and death worldwide. Neurological disorders accounted for 276 million of Disability-Adjusted Life Years and 9 million deaths in 2016¹. In Europe, as many as 179 million are affected, at the economic cost of over 800 billion euros a year². As populations are growing and ageing, new knowledge is required to develop effective prevention and treatment solutions. This was underscored in the United Nations General Assembly report of December 2017, which stated that progress in reducing the burden of non-communicable diseases, including neurological and psychiatric disorders, had been insufficient to meet the UN Sustainable Development Goal targets by 2030. In addition, the World Health Organisation has recently drawn attention to the massive impact of the COVID-19 pandemic on mental health³.

Significant medical advances are needed to overcome brain health issues and alleviate their associated personal and socio-economic burden. Improved understanding of the brain is crucial for better prevention, diagnosis and treatment. The data, tools, services and resources made available by EBRAINS will help European researchers to contribute significantly to addressing what is sometimes referred to by health care professionals as the **"greatest health challenge of the 21st century"**.

EBRAINS will also bring its expertise to the development of the Shared European Brain Research Agenda, leading to the creation of a European Partnership for Brain Health, to which it aims to make a valuable contribution.

"In Europe, as many as 179 million are affected, at the economic cost of over 800 billion euros a year."

Lancet Psychiatry/JAMA Psychiatry

3. COVID-19 disrupting mental health services in most countries, WHO survey. World Health Organisation website press release, October 5 2020.

^{1.} Vigo, D. Thornicroft, G. Atun, R. Estimating the true global burden of mental illness. *Lancet Psychiatry*, February 2016. Walker, E.R. McGee, R.E. Druss, B. J. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. *JAMA* Psychiatry, April 2015.

^{2.} DiLuca, M. Olesen, J. The cost of brain diseases: a burden or a challenge? *Neuron*, June 2014.

Accelerating innovation through community-wide sharing of expertise

Digital tools to help unravel the complexity of the brain and create an environment promoting sharing of knowledge and convergence of viewpoints are **crucial to advancing modern neuroscience and accelerating innovation**.

EBRAINS is key to generating the **necessary synergy between research efforts that are often fragmented, across nations and between different scientific disciplines**; providing a unique, distributed digital research infrastructure for all of Europe and beyond. Its aim is to dramatically increase the efficiency and productivity of European research, by making findable, reusable data and state-of-the art digital research tools available to the scientific community within Europe, and offering them openly for use and expansion across the planet. The EBRAINS research infrastructure and its user community will accelerate collaborative scientific, clinical and industrial research across disciplines and borders.

EBRAINS will build on the Human Brain Project's international collaborations, which include the International Brain Initiative (which connects the HBP with national efforts in Australia, Canada, China, Japan, Korea and the USA), the Global Brain Consortium, the International Brain Laboratory and the International Brain Research Organisation. As such, EBRAINS will help to diffuse best practice in neuroscience and will be in the vanguard of Open Science.

No research infrastructure for brain scientists is currently available in Europe that is or could be similar to EBRAINS in its goals, multi-disciplinarity and level of technological development. Indeed, neuroscience lacks a research infrastructure of the kind available to other disciplines, such as biology (BBMRI, EMBRC, EU-OPENSCREEN and <u>INSTRUCT</u>), Life Sciences (<u>EATRIS</u>, <u>ECRIN</u>, <u>ELIXIR</u>, <u>Euro-Biolmaging</u> and <u>INFRAFRONTIER</u>) and highperformance computing (<u>PRACE</u>). EBRAINS will correct this imbalance and strengthen Europe's scientific position in the field.

In fact, **EBRAINS is a unique infrastructure worldwide**, in that it provides access to the most comprehensive set of brain data yet made available, along with an unprecedented array of digital resources for sharing, analysing and storing such data, using them to model and simulate the brain, and test the results in virtual neurorobotics experiments, using advanced high-performance computing capabilities.

EBRAINS' construction is guided by the principles of responsible research and innovation, and incorporates that responsibility by design, to ensure that processes and products of EBRAINS are socially acceptable, desirable and sustainable.

Insuring digital and technological progress

In the last decade, research into the brain and braininspired technology has emerged to take a prominent place on the world stage.

Leading scientific and industrial powers are already acting on the understanding that, in the future, their researchers' and industrialists' ability to master knowledge of the brain will be of enormous value. By setting up the Human Brain Project, Europe took an early lead in this race. It is now critical for Europe to capitalise on its achievements and invest in EBRAINS, to secure Europe's long-term leadership in digital neuroscience, brain medicine and brain-based technology.

EBRAINS aims to make a major contribution to **developing Europe's digital leadership**, by underpinning the development of braininspired Artificial Intelligence (AI) and other related technologies, including neurorobotics (robots controlled by functional neural models) and neuromorphic computing systems (with architectures that emulate that of the brain).

Brain-inspired artificial neural networks and learning algorithms are vibrant areas of AI research. Our ability to improve in this domain is conditional on gathering more and better data about the brain and its workings, analysing that data and applying the results in models, simulations and other forms of software, as well as hardware. This is what EBRAINS will help to achieve. The transfer of knowledge from brain research to information science and related technologies offers a unique opportunity to responsibly enrich and improve AI and robotics. EBRAINS is well-equipped to support that process, with its unrivalled scale, organisation, tools, data resources, test facilities and use-cases, which are resulting from most advanced neuroscientific research.

As such, EBRAINS will contribute to European excellence in the field of Artificial Intelligence. It will also cooperate closely with networks of Al researchers such as CLAIRE and ELLIS as well as platforms offering high-level services and resources, such as AI4EU.

"It is now critical for Europe to capitalise on its achievements and invest in EBRAINS, to secure Europe's long-term leadership in digital neuroscience, brain medicine and brain-based technology."

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What EBRAINS brings to the scientific community



3D Polarized Light Imaging (3D-PLI) technology is used to reveal the structural connectivity and fiber architecture in post mortem brains at microscopic resolution. EBRAINS aims at accelerating collaborative brain research with a comprehensive package of data, tools and facilities, including data sharing, atlasing, modelling, simulation, high-performance computing, big data analytics, neurorobotics, neuromorphic computing and others.

This package will grow over time, with useful new capabilities being added, to address the evolving requirements of the scientific community. Al functionalities, in particular, will be added to improve models and analysis of data sets.

A comprehensive set of multi-faceted data and tools

In neuroscience, there are numerous ways to generate data. At the same time, the data itself are highly complex, with multiple timeframes, multiple scales and multiple modes of gathering, including optical and electronic microscopy, magnetic resonance imaging, electroencephalography and electrical recordings of brain signals.

The data and models accessible via EBRAINS stand out in many ways, beyond basic characteristics such as their sheer volume. They are drawn from multiple sources, both within and outside the Human Brain Project.

In addition, there is data derived using multiple investigative techniques on a given biological sample, which yields insights unobtainable using a single method. A substantial portion of the data has been generated recently, using cutting-edge techniques developed within the Human Brain Project, such as 3D Polarised Light Imaging, which helps to reveal even long-range fibre connections that link different brain regions with microscopical resolution. These are almost impossible to detect using other methods, yet are key to understanding how higher brain functions are exercised. The large EBRAINS data sets are curated and can be searched, accessed, explored using EBRAINS' Knowledge Graph. The EBRAINS Knowledge Graph helps scientists find and share the data they need to make their next discovery. It is also built to connect them to the software and hardware tools that will help them analyse the data they have. The EBRAINS Knowledge Graph is a multi-modal metadata store that brings together information from different fields of brain research. At the core of the EBRAINS Knowledge Graph, a graph database tracks the linkage between experimental data and neuroscientific data science supporting more extensive data reuse and complex computational research than would be possible otherwise.

As for **EBRAINS Atlases**, they allow for brain data to be explored in 3D space. The data cover different species, including mouse, rat, non-human primate and human - in the latter case, both in vivo, from healthy subjects and patients, and post mortem. By tapping these various sources, researchers can use data from species that are more accessible experimentally to complement human data, which can be harder to obtain. Last but not least, the EBRAINS **Medical Informatics Platform** allows researchers to interrogate a large and growing volume of neurological clinical data: currently, more than 20,000 datasets, covering dementia, epilepsy, mental health and traumatic brain injury drawn from a growing number of participating hospitals (currently 30), while protecting patient anonymity. Great care is taken to ensure that data available through EBRAINS conform to the EU's high ethical standards and respects the "FAIR" **principles** (i.e. that they be Findable, Accessible, Interoperable, Reusable), which is both good science and EU policy. These scientific and technical advances need to be delivered in a way that reflects European values and principles, such as non-discrimination, fairness and privacy. In line with these ethical, privacy and quality standards, EBRAINS will develop a "Service for Sensitive Data", a platform for collecting, storing, analysing and sharing patient data, thereby contributing to the development of the European Health Data Space.

EBRAINS offers access to an extensive array of data



High-performance analytics and computing resources

The EBRAINS' IT infrastructure is built on the <u>Fenix</u> infrastructure. It allows researchers to exploit the powerful **high-performance analytics and computing resources** of Europe's leading supercomputing centres as "cloud"-type services.

FENIX, funded by the European ICEI project, is enabled by five leading European supercomputing centres, i.e. BSC, Barcelona Supercomputing Center, Spain, CEA, Commissariat à l'Energie Atomique et aux Energies Alternatives, France, CINECA, Consorzio Interuniversitario per il Calculo Automatic, Italy, CSCS, Centro Svizzero di Calculo Scientifico, Switzerland, and JSC, Jülich Supercomputing Centre, Germany.

Fenix provides **the full spectrum of services** required for advanced analytics, visualisation, modelling and computation such as scalable and interactive computing, co-located large scale data repositories and a high-speed interconnecting network. The EBRAINS IT infrastructure combines these with additional federation, facilitation and access services (authentication, authorisation, accounting, auditing, SSH Public Keys Management, Site Specific Usage and Reporting), providing frictionless access to all levels of the infrastructure

This represents a comprehensive digital infrastructure, covering all elements from the hardware to specific services for the neuroscience community. It also ensures that EBRAINS' IT infrastructure will remain highly dynamic, thanks to continuous adaptation and modernisation.

A unique pallet of expertise

To serve the scientific community, EBRAINS builds on the diverse expertise assembled by **a transdisciplinary community of researchers** united by the quest to understand the brain. This includes the over 500 scientists who have been working on the Human Brain Project in areas covering neuroscience, big data, computing, and robotics but also the associated researchers who have liaised with the project to co-explore new breakthrough areas, and spread excellence across Europe and internationally. In addition, the dozens of partnering projects the Human Brain Project teams up with have contributed to significant added value in terms of scientific, technological or innovation expertise and know-how.

EBRAINS objectives: three pillars

ADVANCING OUR SCIENTIFIC UNDERSTANDING OF THE BRAIN

"JOINING THE DOTS"

Addressing the major challenge for neuroscience: **"bridging the scales"** or understanding how the different levels of brain organisation – molecular, cellular, circuits, region, whole brain – work together.

ORGANISING THE DATA

Providing a combination of atlases and tools to better organise data, place it in its 3D anatomical context, allow users to search for it, harness it for digital brain reconstructions, and explore the relationship between structure and function.

MODELLING THE BRAIN

Linking mathematical brain models to observable behaviour through virtual closed-loop neurorobotic experiments, where the output of a simulated brain affects its environment through a simulated body and where these changes are, in turn, propagated back to the brain through simulated sensory organs.

HARNESSING THAT UNDERSTANDING TO DELIVER IMPROVED DIAGNOSIS AND TREATMENT OF DISEASES OF THE BRAIN

DRUG DISCOVERY

Improving screening of drug candidates and simulation of their binding in the brain.

DIAGNOSTICS

Better diagnosis and prognosis of neurological and psychiatric conditions.

SURGERY

Improved outcomes for neurosurgery, through better-targeted diagnosis and intervention.

PROSTHETICS

Prosthetics to overcome problems of the central nervous system, such as those affecting mobility or vision.

TRANSLATING IMPROVED KNOWLEDGE OF THE BRAIN INTO TECHNOLOGICAL ADVANCES

BRAIN-INSPIRED ICT

Neuromorphic computing systems that can outperform conventional ones in specific areas of application, not least in terms of reduced energy consumption.

BRAIN-INSPIRED ROBOTICS

More flexible, capable robotic systems, driven by brain-based controllers.

"BIOLOGICAL" AI

Offer biological "shortcuts" to improve AI, reducing current massive learning requirements.

VIRTUAL DESIGN & TESTING

Fully virtual design of brain-derived devices, via the EBRAINS simulation infrastructure. The development of robots and embedded systems can be decoupled from physical constraints, with multiple, realistic simulations performed on high-performance computers.



EBRAINS services available today

Scaffold data for the making of a visualization of the human brain.

EBRAINS services available today

EBRAINS currently offers the following categories of services, research capabilities and resources. They will continue to be fine-tuned, developed and expanded in the months and years to come building on the feedback, collaboration, needs and suggestions of the EBRAINS users.

The concept of combining these services is a game-changer, enabling brain researchers to tackle their questions effectively and allowing other disciplines to benefit from brain research. They offer open access to EBRAINS' databases and should enable rapid use of other facilities, such as those needed to model a brain disease process, link data to atlases and models, test brain models in a robotic embodiment, or run brain simulations in real time on neuromorphic systems.

EBRAINS' digital research infrastructure, includes a large number of software solutions provided to – and by - users. This requires **continuous** development in line with user needs. The hardware also needs to be upgraded roughly every six years, which is why EBRAINS' close partnership with Europe's leading supercomputing centres is so important. In addition, computing is undergoing significant technical changes, which any world-class research infrastructure will need to keep abreast of. The increased capabilities offered by High-Performance Computing have enabled the rapid development of deep learning networks. EBRAINS is an efficient vehicle for harnessing these evolving techniques and making them readily available to researchers.



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Towards breakthrough outcomes

A view of the central gyri of the human brain with a digital reconstruction of a neocortical circuit of neurons.

Towards breakthrough outcomes

EBRAINS will facilitate access to and the enrichment of research tools, allowing constantly **updated knowledge on brain function and brain-inspired AI to be shared across Europe**, leading to a considerable increase in the amount of scientific data, educational material and research produced by the communities.

Also, EBRAINS simulation services will enable a rapid change in how the brain research community manages and uses its data and, consequently, an **increase in research into multi-level brain** complexity (in space and time), laying the ground for related **new discoveries**. EBRAINS already supports a range of scientific outcomes and practical applications, and this will continue to evolve both within the Human Brain Project and beyond. Some examples are listed below.

NEUROSCIENTIFIC AND COMPUTING ADVANCES LEADING TO MEDICAL BENEFITS

Thanks to **EBRAINS Atlas** tools for combining, analysing and integrating brain data in 3D space, **interventions in patients' brains** will be better guided. In particular, thanks to the Human Brain Atlas, neurologists and neurosurgeons will be able to develop a wide range of tools for preparing personalised brain models for patients undergoing surgery. In their clinical practice, they will also be in the position to provide software for stereotaxic interventions, such as deep brain stimulation (DBS) in patients with Parkinson's, or to support surgery on brain tumours, by making available microstructurally plausible information on target brain regions.

TANGIBLE EXAMPLE

The Virtual Brain application available through EBRAINS is used to develop patient-specific individualised brain models and to help **improve surgical outcomes for epilepsy patients** who cannot be treated with drugs. A clinical trial called <u>EPINOV</u> is ongoing and planned to end in 2023.

Thanks to EBRAINS models and related simulations, new clinical measures will be explored to assess the level of consciousness in patients with **consciousness disorders** (e.g. comatose patients) and sets of information will be proposed for supporting prognosis and therapeutic decision-making.

TANGIBLE EXAMPLE

Using EBRAINS' large data sets and models, the Perturbation Complexity Index (PCI) for quantifying consciousness should offer **improved management of consciousness disorders** and inform ethical treatment decisions

Better identification of phenotypes, gene-phenotype and structure-function relationships will help improve prognosis and evaluation of the **likely impact of different therapies on individual patients, as well as new drug treatments.**

The access to ever-larger volumes of clinical data will help derive **more accurate disease signatures**, where today doctors make do with symptom-based ones with recognised shortcomings.

TANGIBLE EXAMPLES

An innovative epilepsy model developed through EBRAINS provides the basis for a **new classification of epilepsy seizures**, which could lead to better understanding of the disease.

Using EBRAINS's Medical Informatics Platform, researchers are exploring how to better define the **biological signature of Alzheimer's disease** and diagnostic biomarkers in order to quantify a patient's risk to develop the disease.

BRINGING BRAIN EXPERTISE TO INDUSTRY – SOME EXAMPLES

Virtual experiments on high-performance computers, including modelling and simulation of the brain, and neurorobotics, will allow to explore new brain science avenues and new industry-driven research will be launched on devices such as implants and prostheses .	EBRAINS-supported workflows that connect neural models with physical simulations will support advances of our understanding of mechanisms underlying motricity, with applications to spinal stimulation and neuro- rehabilitation .
Thanks to EBRAINS making available new, high-performance, closed-loop functions based on insights into human cognition , industry will be able to develop advanced prototypes for industrial robots, advanced autonomous driving systems, or prostheses for the visually impaired.	Finally, workflows supporting neural embodiment will be capitalised on to explore alternatives to deep learning's reliance on big data , helping to reduce costs and greatly expand the range of applications.



The EBRAINS ways of working

3D-Polarized Light Imaging reveals the "wiring" of the brain. Shown here are nerve fiber pathways in and near the Hippocampus. The different colors indicate the direction of fibers and fiber tracts in the tissue.

Commitment to open science

EBRAINS will support and contribute to the European Open Science Cloud (EOSC) initiative, providing links to tools, data and know-how developed in the Human Brain Project and will disseminate **open science best practices across the spectrum of brain science, medicine and technology**. EBRAINS is committed to developing new standards for the sharing of data related to brain research and helping researchers to follow the principles of open science. The **EBRAINS community exemplifies open science, co-creating research topics and projects, co-designing infrastructure development**, sharing data and knowledge, and collaborating in new combinations of disciplines, institutions and borders. A further distinguishing feature of EBRAINS is its commitment, through the contributions of the Human Brain Project, to the integration of ethical and sociological reflection, stakeholder and citizen engagement, and education in research.

Inclusive and "co-creating" EBRAINS community

EBRAINS is co-designed with its end-users. Scientists exploring a particular aspect of the brain work closely with software engineers to create and refine digital tools to support that work. This helps to ensure that its service offerings address real scientific needs, and do so effectively and reliably, helping other users to reproduce research results. The co-design of EBRAINS is an integral aspect of the responsibility by design approach pioneered by EBRAINS, which can serve as an exemplar for other infrastructures and research fields.

The EBRAINS Community is **organised to enable this bottom-up development**. Continuous user needs-based development of EBRAINS will be encouraged by various workshops and science incubation activities. EBRAINS will also provide researchers with scientific and technological support to help them advance and accelerate their discovery work, including in-depth support for tools and services, operations support, support for scientific use-case development and integration, and support for model curation. The EBRAINS ecosystem potentially includes every brain researcher and his/her own research, data and experiments. The highly inclusive EBRAINS Community will gather users and collaborators of all levels in a common collaborative environment which will maximise use of the EBRAINS RI to advance science.

Collaborators will include experts and scientists who are not necessarily users themselves, plus stakeholders, civil society organisations, funders, policy makers and others who can support and contribute to the execution of excellent research and innovation. The Community will embrace national sub-communities, plus international ones addressing specific scientific themes and areas of innovation. The EBRAINS Community will drive expansion of the RI user base and expand its geographic coverage, while helping to secure societal benefits from the work done using EBRAINS.

Geographically distributed, albeit unified, approach

Co-creation also translates in the way EBRAINS operates. No Member State can build or manage such a broad-scope research infrastructure on their own. Co-creation, collaboration and alignment are key factors of success and essential elements to create an efficient European Brain Research Area. This supports and explains EBRAINS' **distributed nature**, made possible by its digital underpinnings: while working towards a unified goal, the Partners providing RI and support services are spread across the participating Member States and will shortly form the National Nodes of EBRAINS. Germany has specialised facilities for human brain atlasing, neurorobotics and neuromorphic and highperformance computing, France for modelling

(The Virtual Brain), neuroimaging and medical applications, Belgium for clinical neuroscience, Norway and Greece for data management, Switzerland for brain simulation and medical informatics, the Netherlands for neurotechnology and cognition, etc. The National Nodes will also serve as competence centres, offering advice and expertise in using EBRAINS services. This distributed network of expertise is expandable and other countries are welcome and encouraged to join. **EBRAINS aims to be truly pan-European**, and to integrate "best-in-class" resources, creating synergy and building upon scientific developments nationally.

Coordination

EBRAINS as a research infrastructure is coordinated by the EBRAINS AISBL (Belgium), acting as the Central Hub, whose members currently include the Commissariat à l'énergie atomique et aux énergies alternatives (France), Forschungszentrum Jülich (Germany), the Consiglio Nazionale delle Ricerche (Italy), the Universitetet i Oslo (Norway), the Universidad Politécnica de Madrid (Spain), the Kungliga Tekniska Högskolan (Sweden) and the Ecole Polytechnique Fédérale de Lausanne (Switzerland). The EBRAINS AISBL is an international association, which aims to extend its reach across Europe and beyond. By joining the EBRAINS AISBL, members get the opportunity to participate in the co-development of the research infrastructure and be involved in the shaping of its future service offering.





12 HPC, FENIX (JUELICH)

Neuroscience data management hub (UiO)

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Building the long-term future

Inside a digital reconstruction of a circuit of neurons in the temporal lobe of the human brain.

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EBRAINS will capitalize on the work performed by the Human Brain Project teams in digital neuroscience, brain medicine and brain-inspired technology, and **will take it to the next level**.

The core mission of EBRAINS is to continue to serve the scientific and academic community to help them further boost research in brain science, combining neuroscience with modern ICT, and translate that knowledge into medical and technological progress and concrete implementation output, benefiting patients and society.

Examples of future focus areas, to be realised through new projects and partnerships, include:

- Enhanced modelling and simulation tools to better understand and manage medical conditions associated with behavioural or emotional dysfunction
- Technology development or the safe and secure use of patient data to generate robust profiles of brain disorders, including rare diseases
- Development of predictive models in mental disorders with the aim of improving classification and developing and applying targeted interventions
- Analysis and modelling of the brain-level mechanisms and networks that enable language acquisition, processing and their related disorders to derive neurobiologically informed concepts for language learning and language therapy.

In parallel to its role as a scientific enabler, EBRAINS will also seek to increasingly involve industrial companies as users of its research capabilities, and also as contributors to it, as co-developers of new tools and capabilities. In addition, cooperation with the business sector – ranging from international players to SMEs - will be leveraged to turn scientific and technological outputs into marketable products and services. Active partnerships will be established with companies in the Artificial Intelligence and pharmaceutical sectors, as well as in other fields, including among others medical devices, diagnostics and robotics, imaging and image processing, and information technology.



Building the long-term future

These are truly **exciting times for brain research**. Never before have we seen so many new territories opening in neuroscience, enabled by the rapid progress in digital technology, big data, computing and artificial intelligence. There is no doubt that by joining forces and expertise, trans-disciplinary teams will succeed in creating a paradigm shift in brain science. **And from these scientific breakthroughs should emerge unparalleled societal benefits**, with innovative treatment solutions for brain diseases and revolutionary brain-inspired technologies. Developing EBRAINS, **we are very proud to be part of this journey!**

A bright future for brain research





EBRAINS Brussels, Belgium

ebrains.eu info@ebrains.eu



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EBRAINS, International Non-Profit Association Chaussée de la Hulpe 166, "Glaverbel", 1st floor, Section b, 1170 Brussels, Belgium Company registration number 0740.908.863 - VAT BE 0740.908.863 Banque/bank/bank account: IBAN: BE31 7360 6257 3855-BIC: KREDBEBB