THE COMING DECADE OF DIGITAL BRAIN RESEARCH

A VISION FOR NEUROSCIENCE AT THE INTERSECTION OF TECHNOLOGY AND COMPUTING

EXECUTIVE SUMMARY

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Brain research has entered a new epoch. Large-scale, multidisciplinary collaboration and progressive digitalisation have enabled a new, multiscale approach to decode brain organisation. This transformation opens up entirely new opportunities for brain science, medicine and technology and will shape the decade to come.

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INTRODUCTION

The way brain research is carried out has changed fundamentally in recent years. Digital technologies and new instrumentation, tools and methods, are transforming the field. New large-scale collaborations, within Europe and globally, building on data and tool sharing, create synergies and serve as drivers for progress at a rate never seen before.

A research field that has previously been rather fragmented is now combining data and knowledge about different levels of brain organisation by utilizing new technologies and closely collaborating across disciplines and national borders. This enables a new multiscale approach that is key to understanding the brain – one of the most complex systems known to man.

The complexity of the brain is characterised by its organisation on multiple spatial (from molecules to the whole brain and body) and temporal (from milliseconds to an entire lifetime) scales that need to be considered in concert in order to uncover the basic principles of brain function.

Large-scale collaboration and the new multiscale approach of studying the brain have been facilitated by digital methods and computing including shared curated databases, advanced informatics, supercomputing, big data analytics, artificial intelligence as well as modelling and simulation methods. Digital platforms have been developed to enable neuroscientists to integrate data from different scales, to extract new insights from large amounts of heterogeneous data and to work collaboratively on a larger scale.

Notably, this digitalisation does not compete with wet-lab research or the development of novel experimental methods. On the contrary, huge advances in experimental data generation have, in fact, necessitated this next phase, which will be marked by new solutions to make the most of the data.

The transformation of the field has led to outstanding progress and opened up entirely new opportunities of advancing brain science, medicine and brain-inspired technologies. Moving forward, a systematic approach will be essential to meet pressing challenges of the next decade by making full use of these new opportunities. This systematic approach includes continuous large-scale, inter-disciplinary exchange and collaboration that starts with a joint vision for the future of digital brain research.

In this paper, we provide an overview of how digital neuroscience has developed, what characterises the current moment, the impact on medicine and technology and the advances we expect and envision for the coming decade.

THE HBP AND EBRAINS - NEUROSCIENCE, TECHNOLOGY AND MULTIDISCIPLINARY COLLABORATION

Few projects in the world have driven these developments as broadly and as deeply as the Human Brain Project (HBP). The HBP is a European Flagship project in the field of Future and Emerging Technologies. Started in 2013, it was one of the first large-scale research projects of neuroscience worldwide and played a pioneering role for digital brain research (Amunts et al., 2022)*.

The HBP followed a systematic approach of empowering the neuroscience community to take advantage of the most recent developments in computing, simulation, neuro-derived technologies and artificial intelligence. Experimental data, computational models and tools, instruments and dedicated hardware such as neuromorphic systems have been developed in the project and made available to the community to significantly speed up developments in brain medicine and research.

The consortium has developed and is operating EBRAINS as a collaborative research platform with the aim of bringing brain research to the next level through digital tools and computation and by further developing applications in medicine and neuro-derived technologies. EBRAINS is being developed by scientists for scientists. EBRAINS was selected for the European Strategy Forum on Research Infrastructures Roadmap (ESFRI), which aims to support a strategic approach to policy-making and to facilitate multilateral initiatives to optimise the use of research infrastructures, at the EU and international levels.

SCOPE OF THE POSITION PAPER

The new science of the brain combines high-quality basic research, data integration across multiple scales, large-scale collaboration and translation into applications. New computational techniques allow a better understanding of the brain, but at the same time open the door to a new level of complexity and new questions. It is crucial to assess, foresee and shape these changes, maximize opportunities and address challenges of the next decade for scientific research, technology and engineering, as well as ethics.

In 2022, the Science and Infrastructure Board of the HBP initiated an open and community-driven process that led to this position paper. A first version was published on Zenodo in March 2022. While the composition of collaborations in the HBP is broad, the input of the larger community beyond the HBP was crucial. Input from new authors led to 5 versions published in regular intervals and promoted for further comment on Zenodo. In the process the number of authors grew to 106. In April 2024 the final paper was published in the open-access journal *Imaging Neuroscience* (DOI: 10.1162/imag_a_00137)

By discussing views with the research community at large, this paper identifies points of convergence and common goals, and provides a scientific framework for current and future developments in digital brain research. With this collaborative approach we also outline an integration of reflection, dialogues and societal engagement on ethical and societal opportunities and challenges as part of future neuroscience research. We are convinced that digital brain research will continue to help drive progress in the transformation of brain models for Artificial Intelligence, including machine learning and deep learning, and for neuroscientific research at large. With the paper we also aim to inform and engage stakeholders, funding organizations and research institutions regarding these developments.

CURRENT STATE OF THE ART AND ACHIEVEMENTS OF DIGITAL NEUROSCIENCE

The changes described in this paper have precipitated a range of advances over the last decade.

The HBP has made available a high-resolution multiscale 'living' digital atlas of the human brain. This atlas allows for active interaction akin to Google Maps and multimodal analysis of selected areas, while the atlas' usability with the tool suite siibra allows data to be used in computer models by programmers and computational scientists.

Scaling up previously unconnected data-driven brain models has resulted in powerful multiscale co-simulation applications, and personalisation of such models has allowed for tailored diagnostics and prediction of therapeutic effects in individual patients. Employing the highly promising concept of brain and nervous system digital twins, next-generation personalised models will permit continuous updating with real-world data from patients.

Closely connected to the increasing sophistication of brain models is the development of brain-inspired A.I., which has resulted, for example, in the HBP-funded development of BrainScaleS and SpiNNaker, Europe's most powerful neuromorphic systems. Brain-derived A.I. algorithms have demonstrated remarkable capabilities emulating the brain, notably its energy- efficiency, high flexibility and plasticity, and the ability to learn from sparse data. Using models of cerebellar, hippocampal and sensory areas, scientists are building robots increasingly capable of exploring and learning from their environment, based on principles from embodied cognition.

Given these and other developments over the past decade, the authors of the position paper have defined goals for the next decade.

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RESEARCH TOPICS

Below "roadmap" draws estimates for different intersecting areas of research in the coming decade, going from (1) Near-term or current work, to (2) Middle-term, to (3) Long-term. It is based on the input that was gathered during the process of writing the position paper, but has been condensed and shortened.

MULTI-LEVEL BRAIN ATLAS AND HIGH-RESOLUTION BRAIN MODELS

1. Integrate data, from the whole-brain level to cells, into a comprehensive, high resolution brain atlas as basis to get a deeper understanding of general principles of brain organisation, to enable the prediction of missing features where the atlas is incomplete, and to guide comparative studies about interspecies similarities and differences.
2. Generate detailed, data-driven, multiscale models to study the role of variability in human brain organization during the lifespan, under different conditions.
3. Provide a sound answer on what the conditions of brain organisation and structure are to develop complex behaviours, intelligence and consciousness.

MULTI-LEVEL BRAIN MODELS AND SIMULATION

1. Multiscale integration of models, from local biophysical properties to whole brain models, including detailed bottom-up and top-down models. Models are driven and tuned by data and their predictions tested.
2. Model biologically realistic, complex brain functions using multiscale, whole-brain models – approaching digital twins for concrete use cases.
3. Apply model predictions to larger-scale use cases in basic science, medicine and A.I., which in turn drive model testing and sophistication ("productive loops").

BRAIN PLASTICITY, LEARNING AND ADAPTION DURING THE ENTIRE LIFESPAN

1. Identify and integrate the rules of plasticity, learning and adaptation into existing multilevel brain models.
2. Identify constraints of brain plasticity and tools to modulate it for the benefit of patients.
3. Reveal mechanisms of memory consolidation and translate this to medicine and technology.

NEUROMORPHIC BRAIN MODELS FOR BIO-INSPIRED ARTIFICIAL INTELLIGENCE

1. Develop training methods for spike-based deep neural networks using leaky-integrate-and-fire-based neuron models. Integrate complex hardware neuron models in simulation environments.
2. Develop hardware and training methods for large-scale and highly performant spiking network models using complex neuron models.
3. Integrate results from plasticity research to develop large-scale spiking networks with built-in learning capabilities.

COGNITION AND BEHAVIOUR	BRAIN AS PART OF THE BODY
1. Develop a coherent framework describing the mechanisms of cognitive functions using a multi-scale perspective, from sensory- and visuomotor to more complex cognitive functions. 2. Formulate a coherent framework for language, as a uniquely human complex cognitive function, integrating insights from linguistics and neuroscientific research using multilevel brain approaches, and using brain development as a window to specialisation. 3. Link concepts of different hypotheses about self-consciousness to each other and to mechanisms at the cellular, molecular and genetic levels.	1. Link advanced digital brain models to spinal cord models based on multilevel atlases. 2. Model sensorimotor integration and coordination for interaction, task performance and navigation. 3. Integrate somatic and autonomic regulation in combined, multi-organ models to construct Patient Twins, which reflect nervous system, organ and body regulatory functions. Develop and apply cellular level body twins which model nervous system, endocrine/hormone, immune regulatory and homeostatic mechanisms.
DIGITAL BRAIN MEDICINE	**BRIDGING THE GAP BETWEEN HUMAN AND MACHINE INTELLIGENCE**
1. Develop and apply personalised models, informed by brain atlas and individual patient data, for diagnosis and treatment of a broad range of brain disorders (e.g., epilepsy, tumours, movement disorders, psychiatric disorders). 2. Construct and apply data-driven models of development and aging, to brain medicine in different age groups (from children to elderly). 3. Develop and apply digital body twins, continually amenable to new real-life sensor data, to brain medicine (e.g., diagnostics, rehabilitation, intensive care and surgery).	1. Simulate complex behaviour using robots interacting with rich environments. Promote convergence of deep learning A.I. and event-based (spiking) neural networks facilitated by neuromorphic technology. Democratise and develop complex (brain-inspired) A.I. models, including large language models, in an open and transparent approach. 2. Apply insights into brain mechanisms behind cognitive functions, such as perception and decision-making, to emulate learning and developmental processes in the fields of A.I. and neuromorphic technology, and test the potential role of organoids and organoid intelligence. 3. Apply fundamentally new concepts and algorithms to machine learning and novel engineering applications (e.g., new materials, artificial life, replacing and enhancing brain function).

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