EPFL

# Blue Brain Project

Digitally reconstructing and simulating the mouse brain
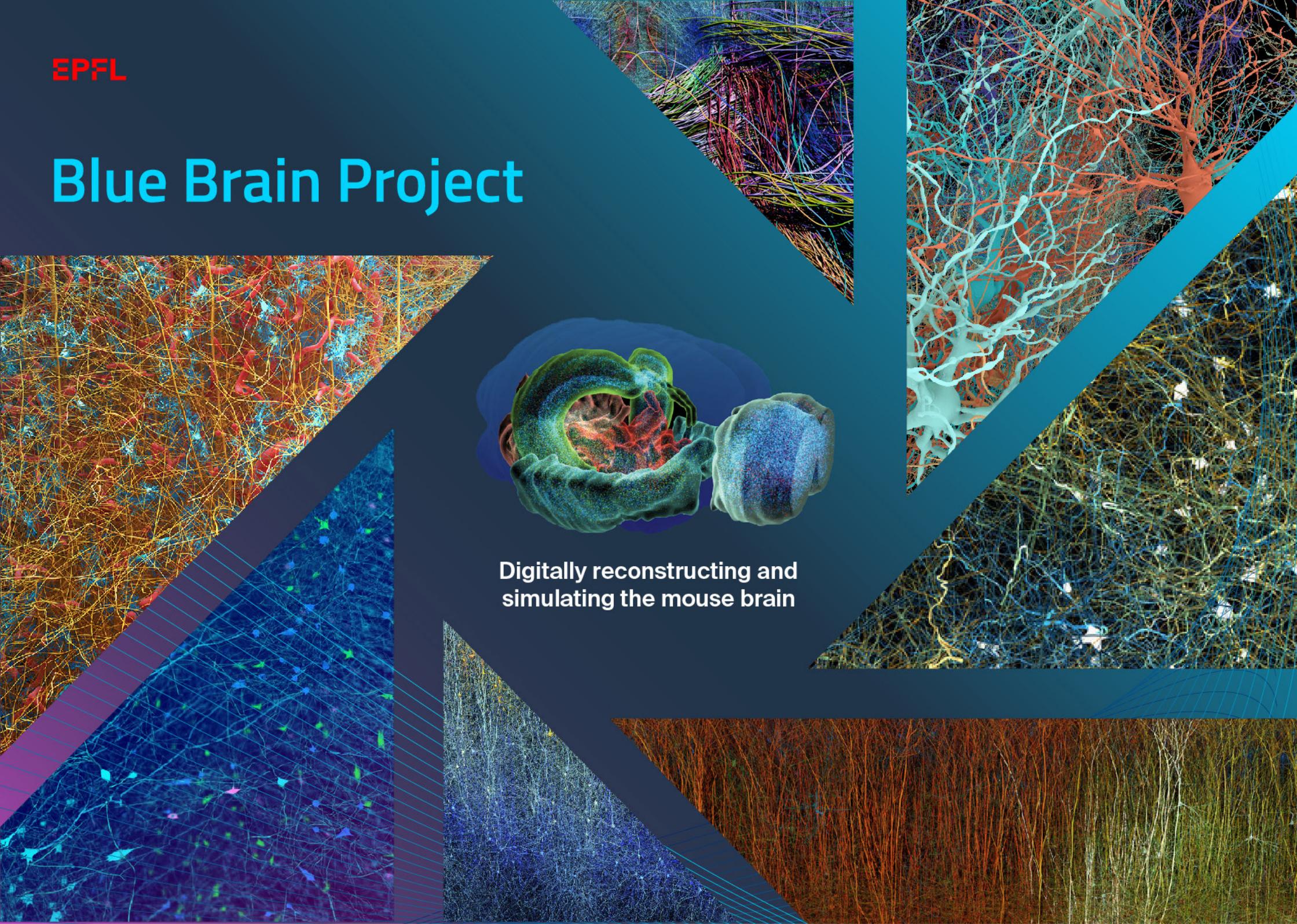
What is the Blue Brain Project?

EPFL's Blue Brain Project is a Swiss brain research Initiative led by Founder and Director Professor Henry Markram.

The aim of Blue Brain is to establish simulation neuroscience as a complementary approach alongside experimental, theoretical and clinical neuroscience to understanding the brain by building the world's first biologically detailed digital reconstructions and simulations of the mouse brain.

Why is the Blue Brain Project so important?

Understanding the brain is one of the largest Big Data challenges we have today. After years of theory and experimentation, simulation is the evolved phase of many of the sciences and engineering fields. Simulation neuroscience is fundamental to understanding the brain as a complex multi-scale system.

Therefore, the supercomputer-based simulations and reconstructions built by Blue Brain offer a radically new approach for understanding the multi-level structure and function of the brain.

Did you know?

There are more than 600 brain diseases
Understanding the brain is essential to diagnosing and treating neurological disorders (such as Alzheimer's disease) that are imposing a rapidly increasing burden on the world's ageing populations.

Facts about the Human Brain

- Around **100 billion** neurons
- **1,000 trillion** synapses
- **More than one billion** molecules in a single cell
- **20,000** genes
- **Over 800** different brain regions
- **More than 200,000** different proteins

Blue Brain has published over 230 papers and pre-prints in international journals.

10M
Neurons modelled

88B
Synapses modelled

1M+
Open access shared – million-plus Kv channel recordings from over 18,000 cells
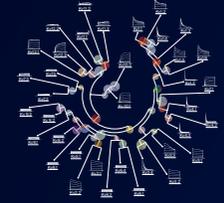
737
First digital 3D atlas of every cell in the 737 regions in the mouse brain
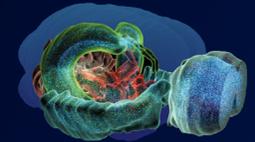
120+
Open source repositories and nine major libraries

230+
Papers and pre-prints in international journals

150
Employees from around the world

35
Nationalities

18K
Registrations for BBP Massive Open Online Courses

How does the Blue Brain Project work?

1. Blue Brain's data-driven approach

In pursuit of our goal, we have a data-driven modelling process with five main stages and many elements feeding in. These inter-disciplinary stages begin with the gathering and organizing of data through to the refinement of the models and experiments.

Read more

2. Blue Brain's Scientific Milestones

Blue Brain follows a four-year roadmap with specific scientific milestones to achieve during this period as we work towards our ultimate goal of digitally reconstructing the entire mouse brain.

The scientific milestones, which are verified by independent scientists, guide us in our day-to-day science but when achieved and shared, help other brain initiatives and the wider scientific communities achieve their goals.

Read more

3. Team Science

Blue Brain's team science approach with scientists working alongside engineers, mathematicians and HPC experts supported by BBP's architecture of software, tools and visualization abilities is applied to a vast range of *in silico* (simulation) predictions made with unique *in silico* experiments which would be infeasible or impossible *in vitro* or *in vivo*.
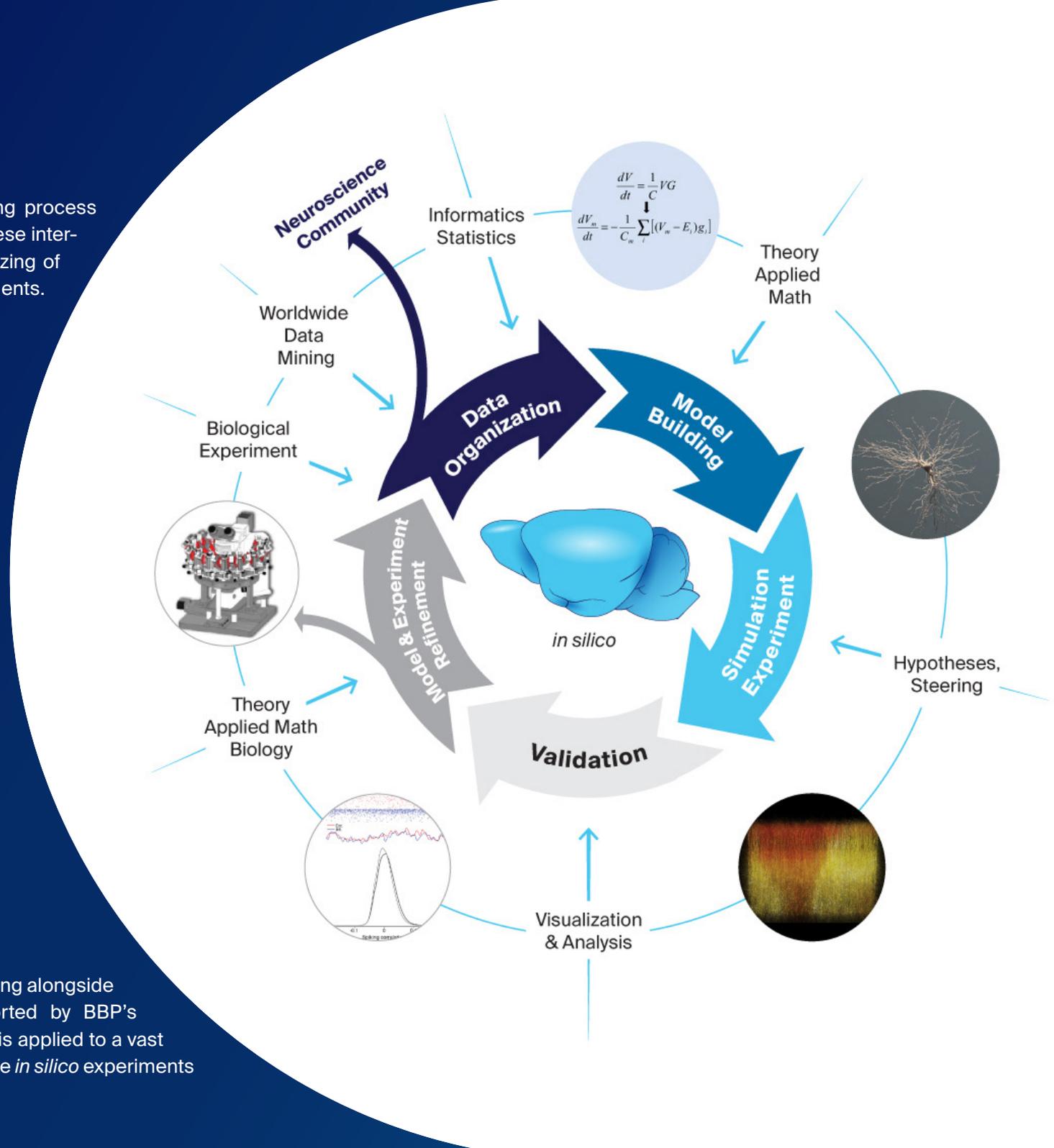
Blue Brain's major findings

In 2015, Blue Brain reached a major milestone with the publication of a first draft of the digital reconstruction of neocortical microcircuitry (Markram et al, 2015). The study confirmed the feasibility of building and simulating a digital copy of a part of the brain and demonstrated that multidisciplinary Big Science in the field of neuroscience yields favorable results (82 scientists contributed to the study).

The paper, which appeared in the journal Cell, represents the most complete description of any neural microcircuit to date. It provides a complete digital map of all the cells and synapses in a block of neural tissue and describes simulation experiments replicating a range of previous *in vivo* experiments. In other words, Blue Brain's digital copy of a part of the brain behaves like a real part of the brain.

Most significantly, this study advances the case for simulation as a useful new method in neuroscience. It proves that we understand the basic properties of the components and interconnections of the brain well enough to be able to reconstruct and simulate certain physiological functions.

## Consequently, Blue Brain has now:

- **Produced** the first draft model of the rules guiding neuron-to-neuron connectivity of a whole mouse neocortex. Based on these rules, the team has generated statistical instances of the micro-connectome of 10 million neurons, a model spanning five orders of magnitude and containing 88 billion synaptic connections that will serve as the basis of the world's largest-scale simulations of detailed neural circuits.

- **Released** the Blue Brain Cell Atlas - the first digital 3D atlas of every cell in the mouse brain. This provides neuroscientists with previously unavailable information on major cell types, numbers and positions in all 737 brain regions.

- **Built** a digital copy of the whole somatosensory cortex with around four million neurons, a part of the hippocampus (a brain region that serves as our GPS system in the brain) and a microcircuit of the thalamus (a part of the brain that organizes all the information that goes to and from the neocortex).

- **Helped** other groups to build digital copies of other brain regions.

- **Mapped** the kinetic behavior of the largest family of ion channels: Kv channels and provided open access to the million-plus Kv channel recordings from over 18,000 cells, and a growing dataset for other channels. These are publicly available for download on the dedicated, wiki-like platform Channelpedia. **channelpedia.epfl.ch**.

- **Performed** an extensive meta-analysis to integrate protein and metabolite quantitative data from publicly available resources and created a simulation-ready database to support more standardized and comparable molecular and systems biology studies – the Brain Molecular Atlas.

- **Digitally reconstructed** the architecture of the Neuro-Glia-Vascular system. The experimental data, models and tools used to reconstruct brain tissue at this resolution are open source in the Blue Brain NGV web portal.

- **Contributed** to the fight against COVID-19 through translational knowledge and expertise and the development and open sourcing of new software and tools.

The neocortical circuitry

Neurons in the mouse neocortex form billions of synaptic connections

First digital reconstruction of the Neuro-Glia-Vascular Architecture

Blue Brain Cell Atlas

Mapping the kinetic behavior of Kv channels
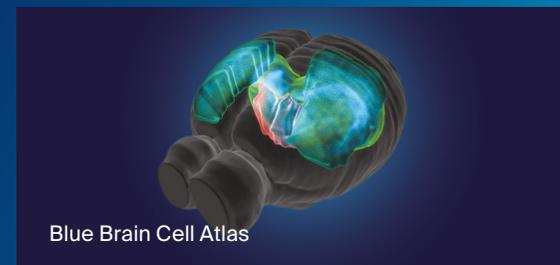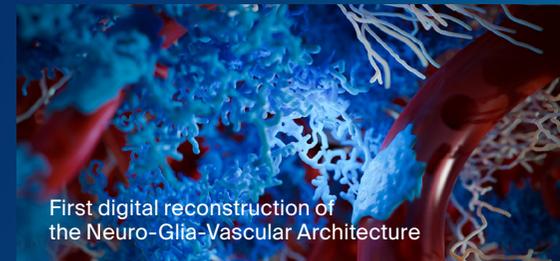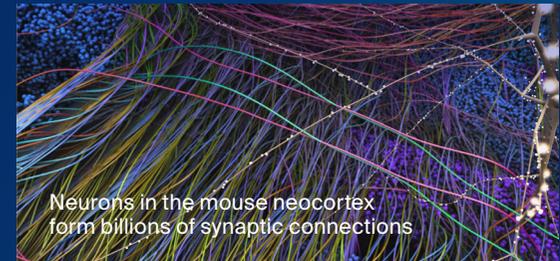
What next?

So far, Blue Brain has established a solid approach to feasibly reconstruct, simulate, visualize and analyze a digital copy of mouse brain tissue and the whole mouse brain. We are now at the stage where we are building larger mouse brain regions and integrating more biological detail. Furthermore, we can use the modelled circuit for gaining new insights into the operation of large-scale circuits, connecting the micro-scale cellular level (e.g., membrane ion channels, synaptic and spike dynamics) to the macroscale level (the emergence of behavioural-related brain states) – e.g., the work by Reimann et al. (2013) and Newton et al. (2021) or the recent works released as preprints by Amsalem et al. and Chindemi et al.

Science

Building more and more multiple-regions of the mouse brain with the target of the whole mouse brain by 2024.

Translational research

Responding to future global needs such as the COVID-19 pandemic whereby our tools and research can accelerate both solutions and collaboration.

Dissemination

Continuing to provide data, models, open source software and online tools to the scientific community through the Blue Brain Portal and as a collaborator on the platforms of the European Human Brain Project. Blue Brain is catalyzing community collaboration on reconstructing and simulating biologically detailed models of the brain.
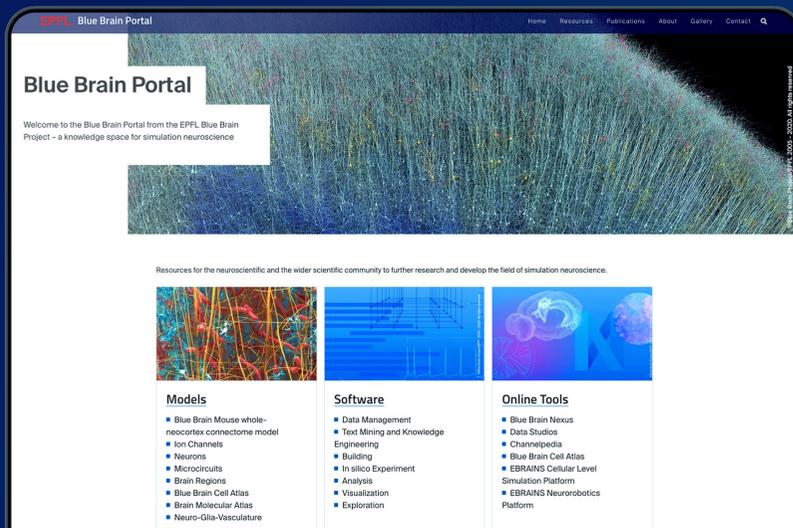
Promoting open science and collaboration

Blue Brain models, data, online tools and software are available to the neuroscience and broader scientific community through the Blue Brain Portal.

As a research center at École polytechnique fédérale de Lausanne (EPFL), Blue Brain advocates EPFL's open science initiative, which seeks to maximize the reach and impact of research conducted at the school.

Visit the Blue Brain Portal
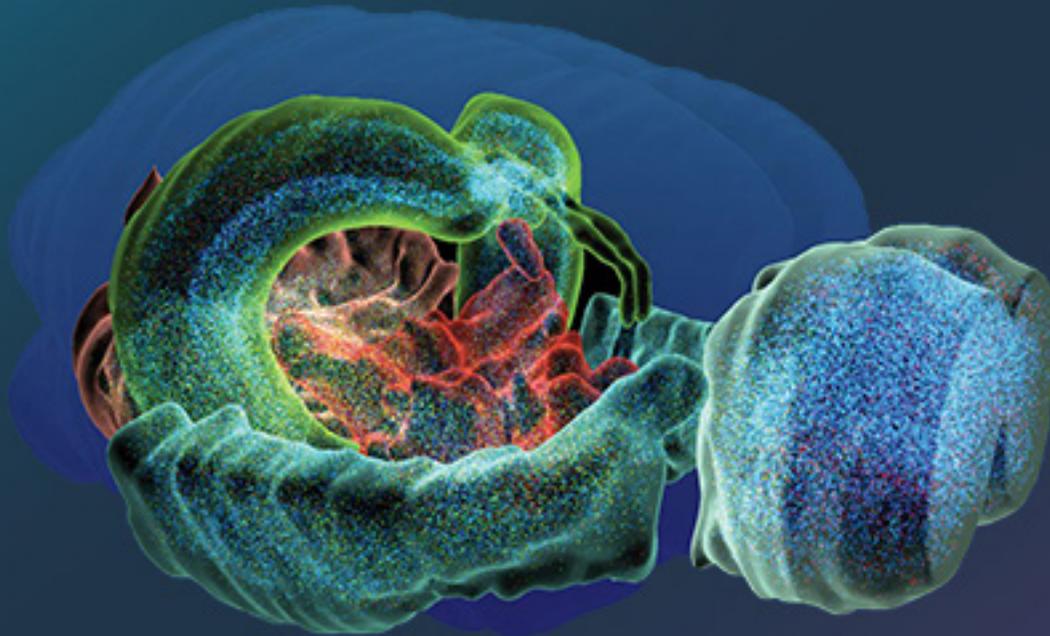
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Follow our progress at:

https://www.epfl.ch/research/domains/bluebrain/

portal.bluebrain.epfl.ch