The Human Brain Project

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Upon this gifted age, in its dark hour,
Rains from the sky a meteoric shower
Of facts . . . they lie unquestioned, uncombined.
Wisdom enough to leech us of our ill
Is daily spun; but there exists no loom
To weave it into fabric;

Edna St. Vincent Millay, 1939
Developmental Disorders
- Autism spectrum disorders
- ADHD
- Learning disorders, conduct disorders
- Strong genetic disorders (Fragile X, Down’s etc)

Adolescent Disorders
- Depression, Suicide
- Eating disorders
- Bipolar disorder
- Conduct disorders and violence
- Borderline syndrome
- Adjustment disorders
- Anxiety, phobias, suicide
- Tourette’s syndrome
- Epilepsy

Adult Disorders
- Schizophrenia
- Epilepsy
- Mood disorders, hysteries, anxieties and phobias
- Obsessive compulsive disorders
- Eating disorders, sexual disorders
- Sleep disorders, stress disorders
- Impulse control disorders
- Substance abuse disorders
- PTSD/TBI

Aging Disorders
- Depression
- Dementia
- Neurodegenerative disorders
  - Alzheimer’s
  - Parkinson’s
  - Huntington’s
- Memory disorders

Glutamate
Nutrition
Dopamine
Genes
Sugar
GABA
Myelin
Serotonin
Metals
Dopamine
Toxins
Acetylcholine
Protein misfolding
What is the Human Brain Project?

A 10-year European initiative to launch a global, collaborative effort to understand the human brain, enabling advances in neuroscience, medicine and future computing.

One of the two final projects selected for funding as a FET Flagship from 2013.

A consortium of 256 researchers from 146 institutions, in 24 countries across Europe, in the US, Japan and China.

Will receive funding of €1 billion over 10 years - half provided by the European Commission. Funding provided in phases with regular reviews.
What is a FET Flagship?

Future and Emerging Technologies (FET) Flagships are ambitious large-scale, science-driven, research initiatives that aim to achieve a visionary goal.

The scientific advance should provide a strong and broad basis for future technological innovation and economic exploitation in a variety of areas, as well as novel benefits for society.

Objective is to keep Europe competitive and drive technological innovation.
The Human Brain Project should:

- Lay the technical foundations for a new model of ICT-based brain research
- Drive integration between data and knowledge from different disciplines
- Catalyze a community effort to achieve a new understanding of the brain, new treatments for brain disease and new brain-like computing technologies.
**Neuroscience**

**Integrate** everything we know about the brain into computer models and simulations

**Medicine**

Contribute to **understanding, diagnosing and treating** diseases of the brain

**Future Computing**

**Learn from the brain** to build the supercomputers of tomorrow
## Scientific organization

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<th>Organisation of HBP Scientific &amp; Technological Work</th>
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Data

Platform building

Platform use
Generate and interpret strategically selected data needed to build multilevel atlases and unifying models of the brain.
The Data Ladder to the Human Brain

- **Mouse brain data**
  - Behavioural profiling
  - Dimensions and volumes of brain regions, areas, nuclei, layers, white matter, ventricles
  - Map of targets for each brain region
  - Number and type of projecting cells
  - Axon diameters, lengths
  - Neuroglial numbers and general density distributions
  - Architecture of neuroglial-vascular system
  - Proteins in neurons and glia
  - Proteins and numbers and distributions
  - Protein-protein interactions, reaction kinetics, drug binding
  - Cell-type transcriptomes
  - Activity dependent gene expression
  - Genetic variations and phenotypic correlations

- **Human brain data**
  - Cognitive architectures
  - Dimensions and volumes of brain regions, areas, nuclei, layers, white matter, ventricles
  - Map of targets for each brain region
  - Number and type of projecting cells
  - Axon diameters, lengths
  - Number of projections per neuron
  - Neuroglial numbers and general density distributions
  - Neuronal and glial morphologies
  - Proteins in mouse synapses
  - Structural properties of mouse synapses
  - Architecture of neuroglial-vascular system
  - Proteins in neurons and glia
  - Receptor distributions
  - Protein-protein interactions, reaction kinetics, drug binding
  - Cell-type transcriptomes
  - Activity dependent gene expression
  - Genetic variations and phenotypic correlations
However,

HBP is **NOT** primarily a data generation project

It **IS** a data integration project.
The Human Brain Project

Build, Simulate and Validate Unifying Brain Models

Experimental Data Gathering

Worldwide Published Data, Models and Literature

Refinement of Models and Experiments

Model Building

Simulation

Supercomputing

Model Validation

Analysis and Visualization

Worldwide Published Data, Models and Literature

10 ms
50 mV
V
I
stim
4 nA

Stimulation Site
Firing Cell Count

Experimental Data Gathering

Supercomputing
Six new ICT platforms:

1. Neuroinformatics
2. Brain Simulation
3. Medical Informatics
4. High Performance Computing
5. Neuromorphic Computing
6. Neurorobotics

For the entire research community.
Neuroinformatics Platform

Provide technical capabilities to federate neuroscience data, analyze structural and functional brain data and to build and navigate multi-level brain atlases. This involves:

- spatial and temporal data registration
- ontology development and semantic annotation
- predictive neuroscience
- machine learning, data mining
- track provenance, build workflows.

Goal: enable an integrated view of the neuroscience data. Prepare data for modeling pipelines
Data management strategy

DATASPACE

- Don’t centralize - federate
- INCF Global datasharing infrastructure
- Federated data management
- Dropbox-like Ease of Use
- Big Data Capabilities
- Robust Infrastructure
- Data Replication Services
- Persistent Identifier Services
- Semantic & Linked Data Annotation Services
Knowledge integration strategy

Knowledge SPACE

- INCF Community encyclopedia
- Living review articles
- Build and maintain working ontologies
- Links to data, models and literature
- Define all vocabulary, terms, protocols, brain structures, diseases, etc
- Semantic organization, search, analysis and integration
- Global directory of all shared vocabularies, CDEs, etc

neurolex.org
Multiscale and Multimodal Brain Atlases

Atlases - collections of spatially and semantically registered and searchable data, models and literature

Highly controlled data for building models

Other data for validations
Brain Simulation Platform

Provide technical capabilities to build and simulate multi-scale brain models at different levels of detail.

- internet portal for neuroscientists
- modeling tools
- workflows
- simulation
- virtual instruments (EM, LFP, fMRI, etc)
- link to virtual body and environment
- in silico experiments

Goal: Integrate large volumes of heterogeneous data in multi-scale models of the mouse and human brains, and to simulate their dynamics.

Enable neuroscientists to ask new questions and prioritize experiments.
Brain Simulation Platform: Multiscale representations

Electrodynamics and Phenomenological Descriptions

- Surface Mesh
- Dendrogram
- 3D Points
- Microcircuit

Physical Chemistry
- Volume Mesh

Field Physics and Fluid Dynamics
- Particle Tracking
- Volume
- Region Geometry

Ontology and Index
Multi-scale

Point neuron, e.g. Izhikevich

\[ v = 0.04v^2 + 5v + 140 - u + l \]
\[ u' = a(bv - u) \]

If \( v = 30 \text{ mV} \), then \( v - c, u - u + d \)

Single Compartment HH model

\[
\frac{C_m dV_m}{dt} = \frac{E_m - V_m}{R_m} + I_{channels}
\]
\[
\frac{dm}{dt} = \alpha_m(V_m)(1 - m) - \beta_m(V_m)m
\]
\[
\frac{dh}{dt} = \alpha_h(V_m)(1 - h) - \beta_h(V_m)h
\]
\[
I_{channel} = m^n h^g_{channel}(V_m - E_{channel})
\]

Multi Compartment HH model

\[
\frac{C_m dV_m}{dt} = \frac{E_m - V_m}{R_m} + I_{channels}
\]
\[
2\left(\frac{V_{m_{i+1}} - V_{m_i}}{R_{i+1}}\right) + \frac{2\left(V_{m_{i-1}} - V_{m_i}\right)}{R_{i-1} + R_i}
\]

Reaction-Diffusion model

\[
p(x; t) = -p(x; t) \sum_{\mu=1}^{M} a_{\mu}(x) + \sum_{\mu=1}^{M} p(x-s_{\mu}; t)a_{\mu}(x-s_{\mu})
\]

Brain Simulation Platform: Multiscale solvers

Coarse-Graining/MD
Integration of laboratory data

S1L1 Neocortical Microcircuit
30’000 neurons

Gene profiles
Protein profiles
Electrical profiles
Morphology profiles
Synaptic profiles
Connectivity profiles
Circuit profiles
Automatically building neuron models

\[ g = g_k n^4 \]

Non Inactivating K Channel

\[ g = g_{Na} m^3 h \]

Inactivating Na Channel

Ion Channels
1. \( Na_{pu} \), Fast Na⁺
2. \( Nat \), Persistent Na⁺
3. \( K_{fast} \), Delayed Rectifier K⁺
4. \( K_{slow} \), Slow K⁺
5. \( K \), Transient K⁺
6. LVA Ca²⁺
7. HVA Ca²⁺
8. \( I_h \), H-Current
9. \( I_m \), M-Current
10. BK, Large g, Ca²⁺ activated K⁺
11. SK, Small g, Ca²⁺ activated K⁺
12. Leak Current

Relative Density
- Data constrained
- Generic algorithm

Composition
- Single cell RT-PCR
- ISH expression distribution
- Literature

Distribution
- Staining, Literature, Assumed
- Given Somatic Distance Function
- Fitted within given tolerance

~400 compartments
~8000 segments

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Ion Channels

- \( Na_{pu} \), Fast Na⁺
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Composition

- Single cell RT-PCR
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Distribution

- Staining, Literature, Assumed
- Given Somatic Distance Function
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Brain Simulation Platform

Data-driven biophysical single cell models

Hay et al., PLOS Comp. Biology, 2012
Building a cortical microcircuit
Predictive Neuroscience: One example

2,970 possible synaptic pathways in a cortical microcircuit alone.

22 have been characterized.

Can we identify principles to predict the rest?

Hill et al. PNAS 2012
Cortical microcircuitry
Brain Simulation Platform

Cortical microcircuitry and local field potential

Reimann et al., Neuron, 2013 in collaboration with the Allen Institute, Seattle, WA
Simulated in vitro cortical slice preparations
High Performance Computing Platform

Provide the project and the community with:
• The computing power necessary to build and simulate models of the brain.
• Develop new supercomputing technology, up to the exascale
• Drive new capabilities for interactive computing and visualization.
High Performance Computing Challenges

- **Memory Requirements**
  - O(1 MB)
  - O(10 GB)
  - O(1 TB)
  - O(10 TB)
  - O(100 TB)
  - O(100 PB)

- **Computational Complexity**
  - O(GigaFlops)
  - O(10 TeraFlops)
  - O(100 TeraFlops)
  - O(1 PetaFlops)
  - O(1 Exaflops)

- **Models**
  - **Single Cell Model**
    - Reaction-Diffusion: O(1,000x memory)
  - **Cellular Neocortical Column**
    - O(10,000x cell)
    - Reaction-Diffusion: O(1,000x memory)
  - **Cellular Mesocircuit**
    - O(100x NCC)
  - **Cellular Human Brain**
    - O(1,000x Rat Brain)
  - **Cellular Rat Brain**
    - O(100x Mesocircuit)
  - **CADMOS 4-rack BlueGene/P**
  - **EPFL 4-rack BlueGene/L**
  - **Reac. Diffusion**
    - O(1,000x memory)
  - **Glia-Cell Integration**
    - O(10x memory)
    - Reaction-Diffusion: O(1,000x memory)
  - **Vasculature**
    - O(1x memory)
  - **Plas. city**
    - O(1-10x performance)
  - **Electric Field Interaction**
    - O(1-10x performance)
  - **Plas. city**
    - O(1-10x performance)
  - **Behavior**
    - O(10-100x performance)
  - **Local Field Potentials**
    - O(1x performance)
  - **Plas. city**
    - O(1-10x performance)
  - **Behavior**
    - O(10-100x performance)
  - **Glia-Cell Integration**
    - O(10x memory)
  - **Vasculature**
    - O(1x memory)
  - **Reac. Diffusion**
    - O(100-1,000x performance)
  - **Glia-Cell Integration**
    - O(1-10x performance)
  - **Vasculature**
    - O(1x performance)
  - **Behavior**
    - O(10-100x performance)
  - **EEG**
    - O(1-10x performance)

- **Computational Challenges**
  - **Particles**
    - O(10-100x memory)
  - **Reaction-Diffusion**
    - O(1,000x memory)
  - **Glia-Cell Integration**
    - O(10x memory)
  - **Vasculature**
    - O(1x memory)
• Federate clinical data from hospital archives and proprietary databases, while providing strong protection for patient data.

• Enable researchers to identify “biological signatures” of diseases.

• Develop new approaches to understanding the causes of disease and identifying effective treatments.
Simulate models on low power chips. Build off of BrainScaleS and Spinnaker projects to provide ability to run large-scale simulations at or beyond real time with low power consumption.
Neurorobotics Platform

Virtual bodies, sensory input and environments to couple with the simulations. This platform is key to providing sensory input to the simulations and depicting the motor outputs.
Use Case 1: Tracing causal mechanisms of cognition

Applications: Understanding principles of cognition
Use Case 2: Developing new drugs for brain disorders

Multi-level biological signature of disease

Model of healthy brain

Model of diseased brain

Target identification

In silico search for treatments

Binding kinetics

Side effects

Target identification

Clinical trials

Preclinical trials

New drug

Computational chemistry & Molecular Dynamics simulations
Use Case 3: Developing neuromorphic controllers for car engines

Figure 30: Use of the HBP platforms to accelerate the development of future computing technologies. Four steps: brain simulation; simplification; rapid prototyping; low-cost, low-power chips

Biologically detailed brain model

SELECT the most suitable models of cognitive circuitry

Simplified brain model

EXPORT simplified brain model and learning rules to generic neuromorphic system

TRAIN neuromorphic circuit rapidly in closed loop with simulated robot in simulated environment

EXTRACT custom, compact, low-power, low-cost neuromorphic designs

Applications: Developing neuromorphic controllers
Theory enables effective application of knowledge about the brain to medicine or computing.
“A far-reaching Society and Ethics program, funding academic research into the potential social and economic impact of HBP research, and its ethical and conceptual implications…

…managing programs to raise ethical and social awareness among HBP researchers, and, above all, encouraging an intense dialog with stakeholders and with civil society.”
Figure 38: Scientists identified to participate in the HBP. The scientists listed have agreed to participate in the HBP, if it is approved as a FET Flagship.
~20% of funding (~200M€) allocated to open calls

**HBP open calls**
- Point of entry for individual researchers
- **HBP Advanced Research Grants** for internationally recognised senior researchers
- **HBP Young Investigator Grants** for advanced postdoctoral researchers
- **HBP Post-Doctoral Fellowships** for entry into independent research
- **HBP Studentships** for mobility, exchange and interdisciplinary training

**ERANET+**
- Point of entry for European research groups
- Three-year research grants jointly financed by the EU and the Member States awarded to research groups with proven competence to contribute to:
  - data generation
  - platform building
  - research using the platforms

in the areas of expertise covered by HBP divisions
The Initial HBP Consortium

For more information and a full list of leaders, partners and collaborators please visit:

www.humanbrainproject.eu