

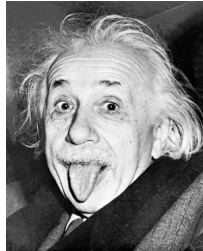
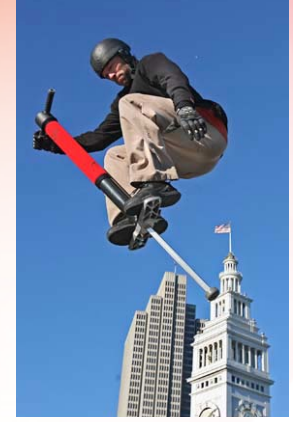


Human Brain Project
Unifying our understanding of the human brain.



BoF on Advancing data-driven research through the Data Commons

**Sean Hill
co-Director, Neuroinformatics
Human Brain Project**



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, hysterias, anxieties and phobias
- Obsessive compulsive disorders
- Eating disorders, sexual disorders
- Sleep disorders, stress disorders
- Impulse control disorders
- Substance abuse disorders
- PTSD/TBI

The Worldwide Cost

Disability-adjusted life years (DALY) is a commonly used public-health metric meant to express the number of years lost as a result of bad health, disability, or premature death.

Disorder	DALYs
Unipolar depressive disorders	65,000,000
Bipolar affective disorder	14,000,000
Schizophrenia	17,000,000
Epilepsy	8,000,000
Alcohol use disorders	24,000,000
Alzheimer's and other dementias	11,000,000
Drug use disorders	8,000,000
Post-traumatic stress disorder	3,000,000
Obsessive-compulsive disorder	5,000,000

Sources: Harvard School of Public Health and the World Economic Forum (2011)

MIT Technology Review

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. Technology program funding.

Officially launched October 1, 2013.

A consortium of **256 researchers** from **135 research groups**, **81 partner institutions** in **22 countries** across Europe, America and Asia.



Figure 1: The Human Brain - one of the greatest challenges for 21st century science

The Human Brain Project

Neuroscience
Unifying our understanding of the human brain

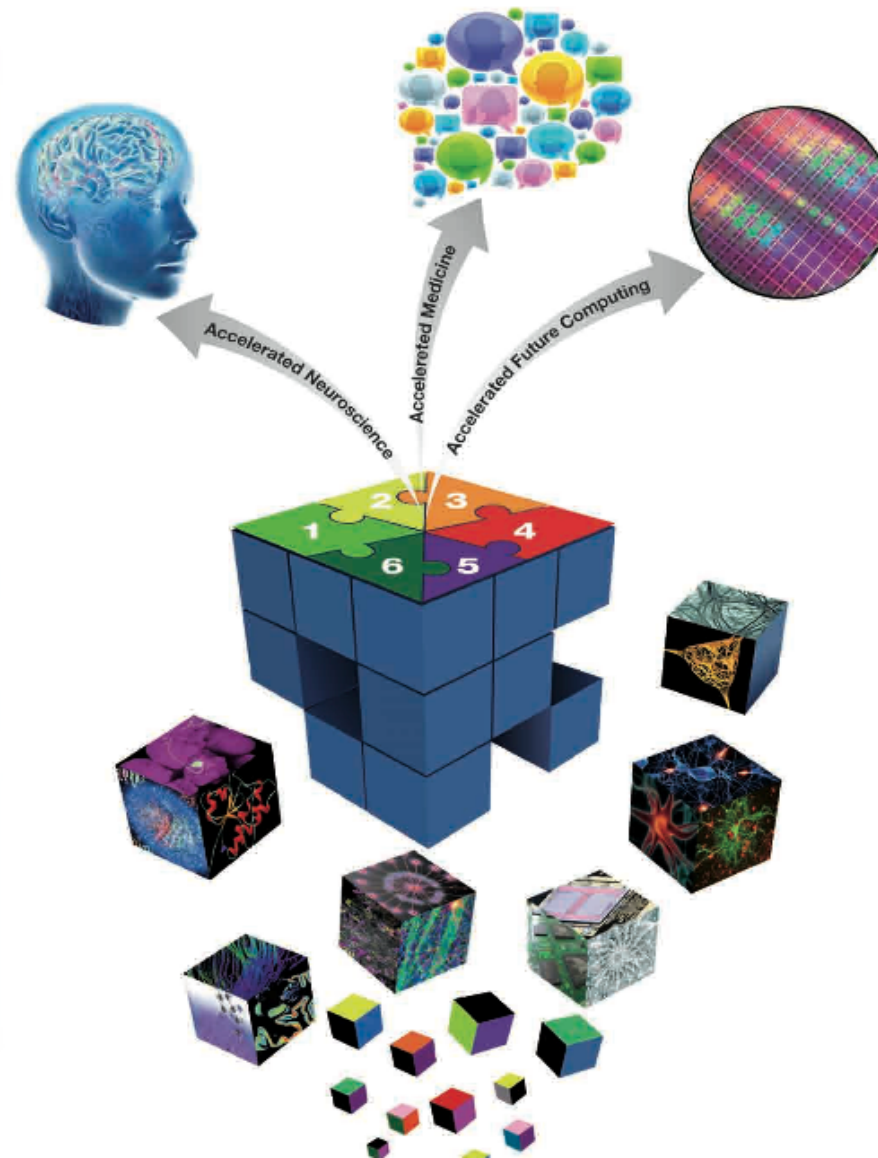
Medicine
Defining and diagnosing brain diseases and disorders

Computing
Advancing the frontiers of brain-inspired technology

Collaboration
Catalysing open science and global collaboration

Education
Training the next generation of scientists

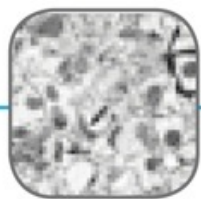
Ethics
Responsible Research and Innovation



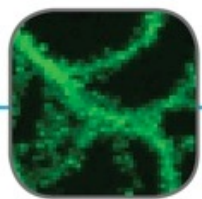
↑
subcellular
resolution



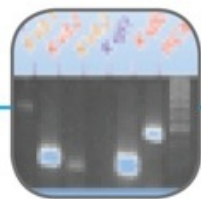
Microarrays



Electron
Microscopy



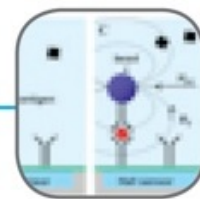
Confocal
Microscopy



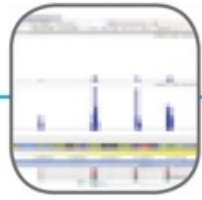
Single Cell PCR



Protein
quantification



Magnetic bead



Gene sequencing



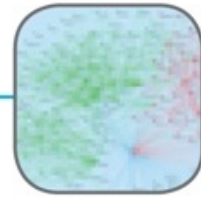
Gene silencing



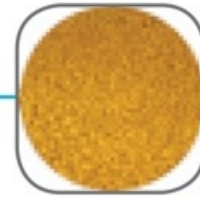
Gene over-
expression



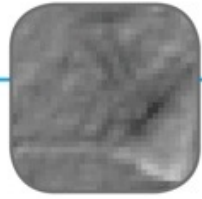
Genetic vectors



Two-hybrid
system



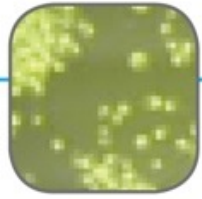
Protein separation



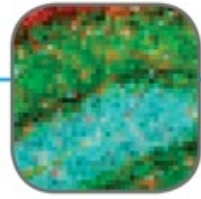
Wholecell &
Inside-Out Patch



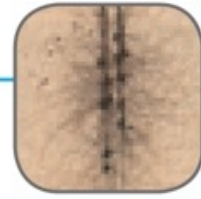
Laser micro-
dissection



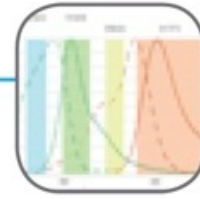
Cell culture



Fluorescence
microscopy



Cellular
tracing



Cell sorting



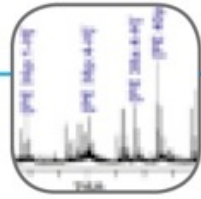
In situ
hybridization



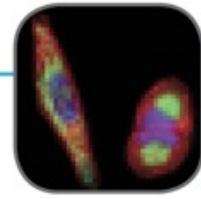
Rhodopsin
vectors



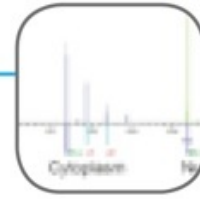
Immuno-detection
amplified by T7



Mass-spectrometry

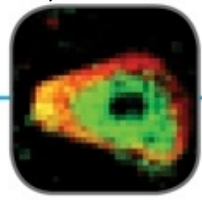


Organelle
transfection

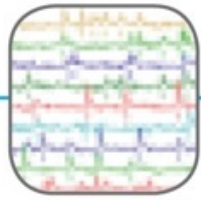


Spatial
Proteomics

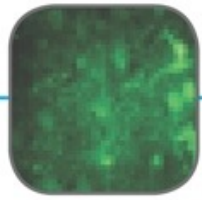
tissue
resolution



Immuno-staining



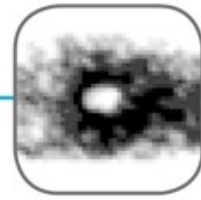
Multi Electrode Array
Extracellular Recording



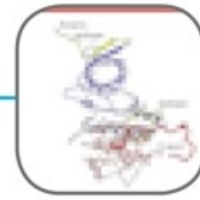
Dye Imaging



2DE proteomics



Tissue transfection



Enzymatic-activity measurement

whole brain
scale



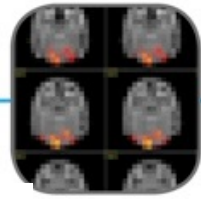
Behavioral Studies



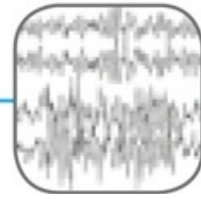
Ultramicroscopy



Magnet Resonance
Diffusion Imaging



fMRI

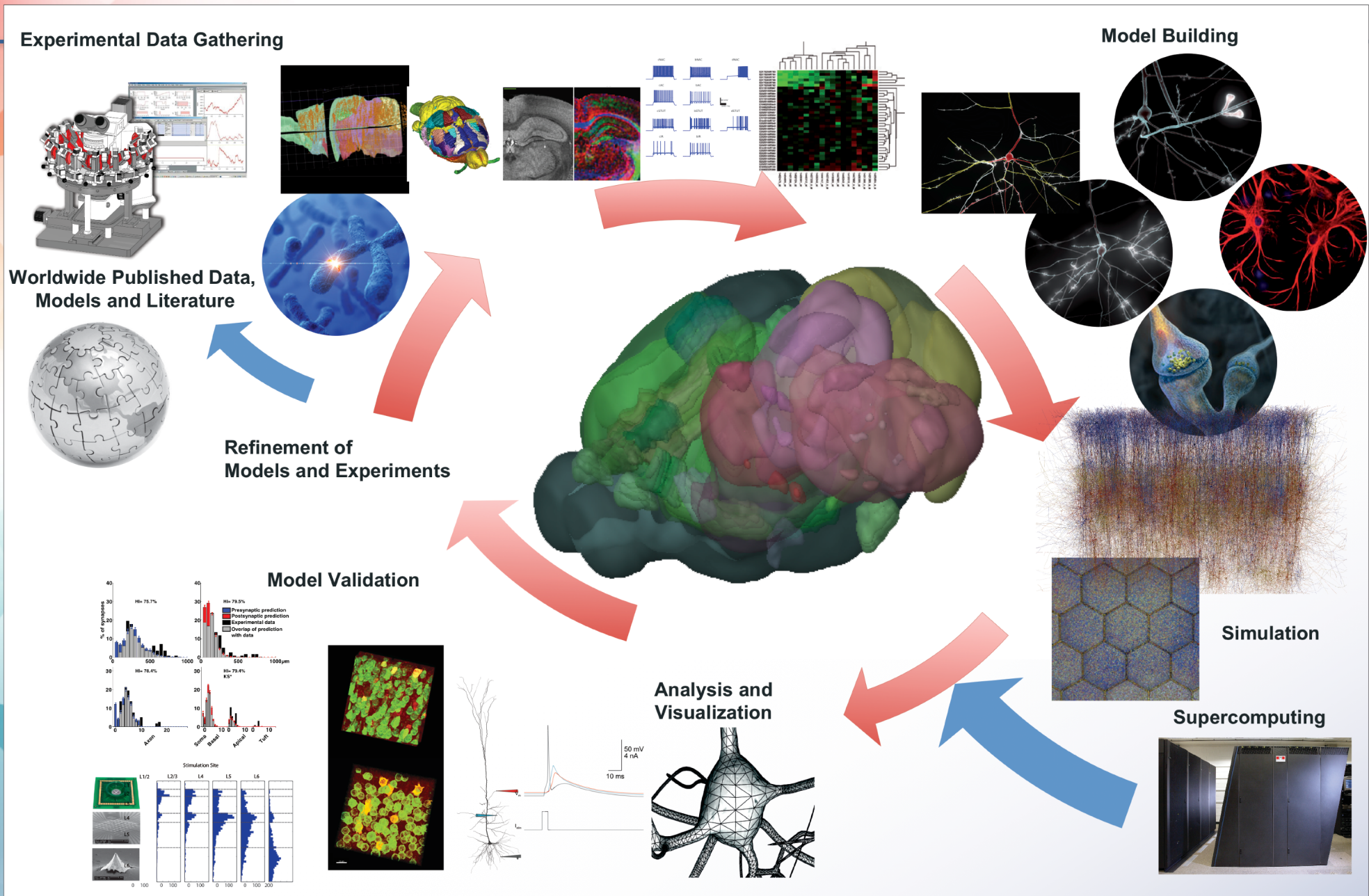


EEG



Transgenic lines

Build, Simulate and Validate Unifying Brain Models





Open Science Infrastructure

Neuroinformatics Platform

Organize, search and access the massive volumes of heterogeneous brain research data, knowledge and tools.

Brain Simulation Platform

A suite of software tools and workflows enabling researchers to model brain circuitry at different levels of biological detail, and to simulate them on supercomputers.

High Performance Computing Platform

Supercomputing, data and visualization hardware and software capabilities required for multi-scale brain modelling, simulation and data analyses.

Medical Informatics Platform

Access and analyse large amounts of patient and research data using data mining and machine learning to develop new classifications of brain disorders.

Neuromorphic Computing Platform

Provide access to two complementary kinds of neuromorphic systems:

1. Large-scale analog VLSI
2. Millions of digital computing cores with a low-power interconnect

Neurorobotics Platform

Provide brain models with a body, designing “closed loop” systems in which brain models are connected to simulated robots operating in a simulated physical environment.



Open Science Infrastructure: Science as a Service

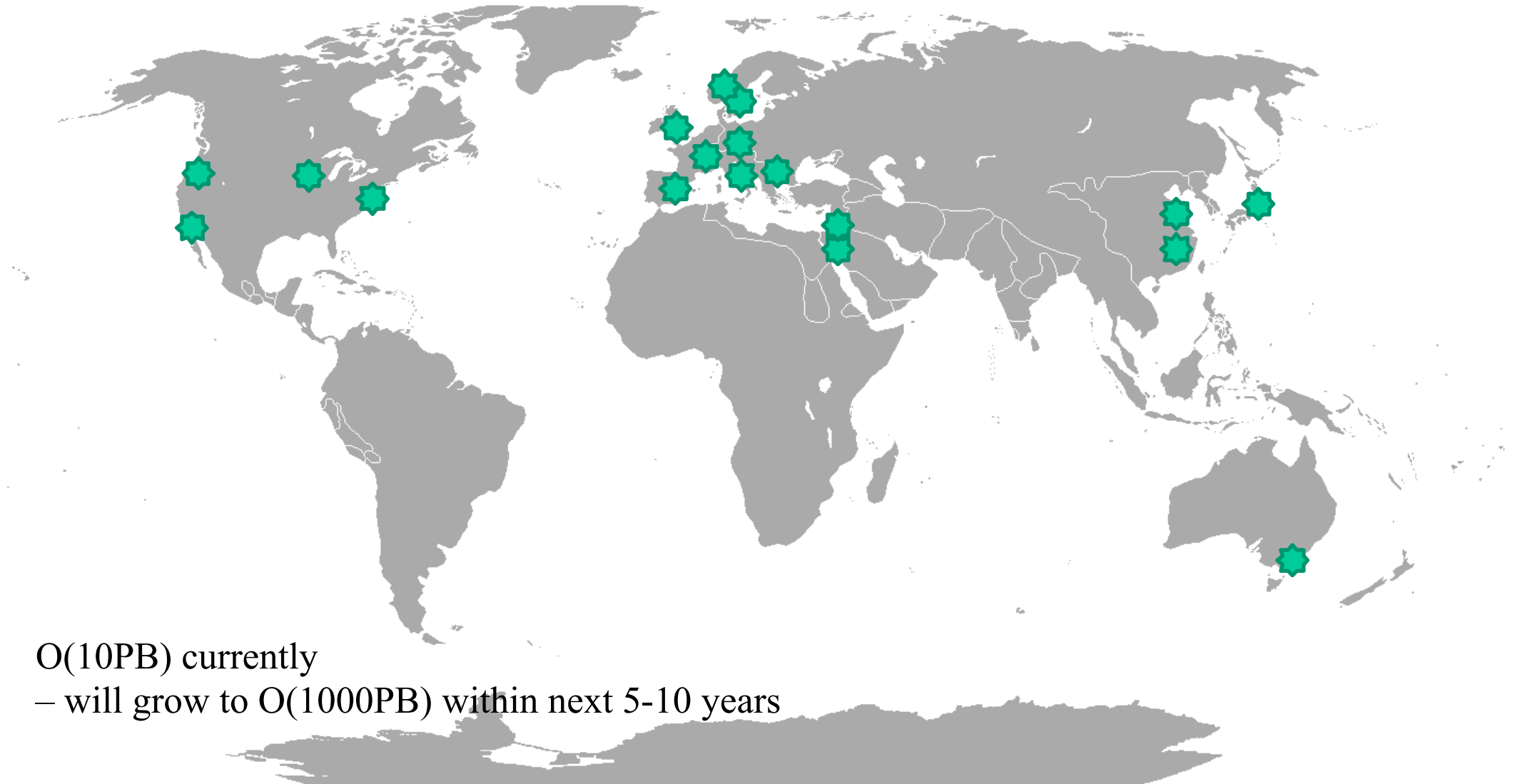
	HBP Collaboratory			
Web portal				
Software as a Service (SaaS)	Neuroinformatics	Brain Simulation	Neurorobotics	Medical Informatics
Data as a Service (DaaS)	Neuroinformatics		Medical Informatics	
Platform as a Service (PaaS)	HPC platform (e.g. Interactive Supercomputing)		Neuromorphic tools/platform	
Infrastructure as a Service (IaaS)	HPC & Non-HPC Infrastructure Services		Neuromorphic infrastructure service	
Bare Infrastructure (Compute, storage, network)	JSC / CSCS / CINECA / BSC / KIT / Manchester & Heidelberg			



Human Brain Project

Unifying our understanding of the human brain.

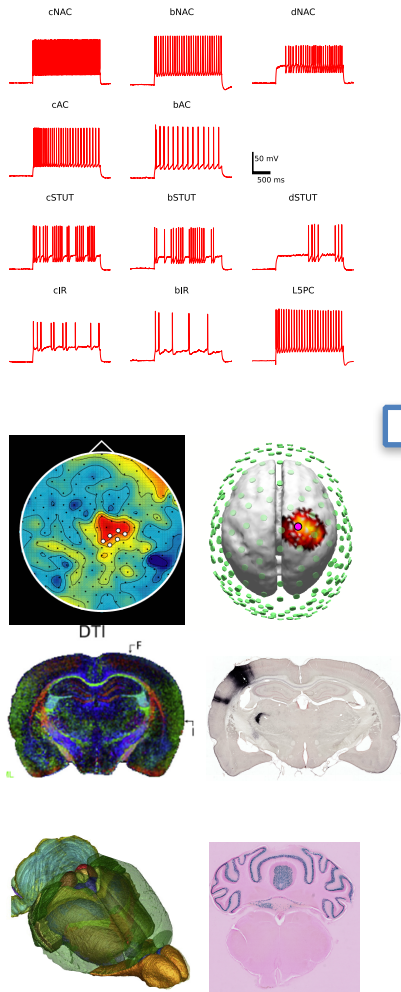
Neuroinformatics platform:
Publicise, discover and access globally distributed
heterogeneous neuroscience data



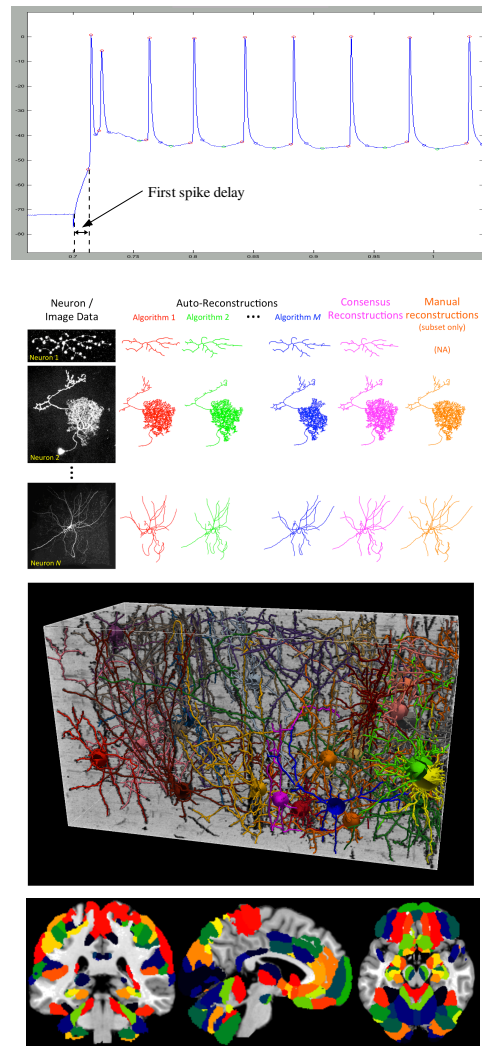
O(10PB) currently
– will grow to O(1000PB) within next 5-10 years

Data Driven Knowledge Discovery

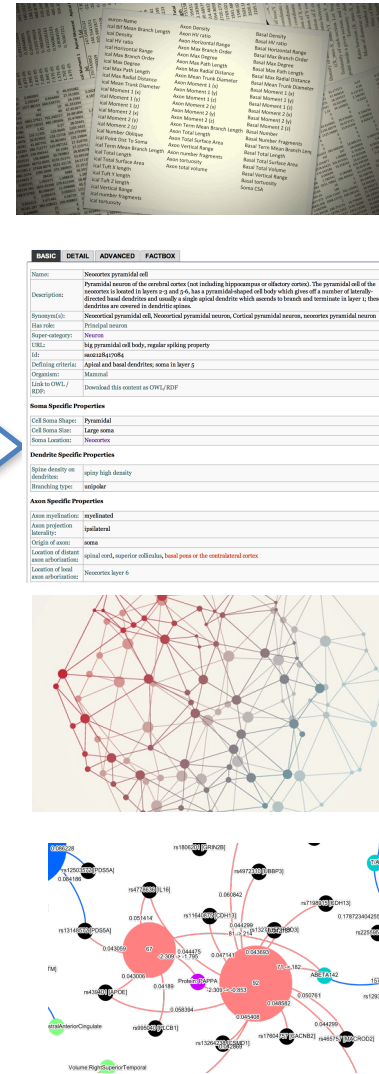
Active Data Repositories



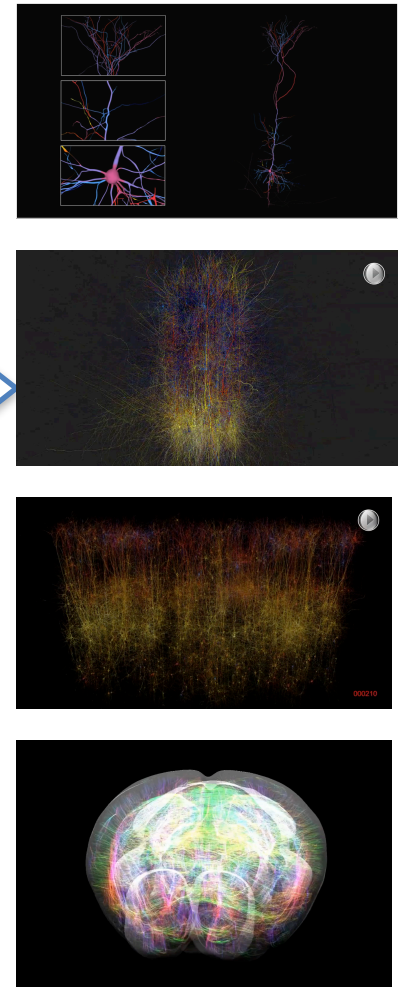
Federated Datamining



Knowledge Management and Search



Collaborative Platforms for analysis and data-driven modelling



Neuroinformatics Platform

Application layer

Neuroinformatics Portal, Unified Portal, Applications

Curation layer

Data Registration

Private LabSpace

Public KnowledgeSpace

Service layer

Ontology
Service

Document
Service
(Unified
Portal)

Knowledge
Graph

Search
Services

Atlasing
Services

Analysis and
Mining
Services

Data access layer

Data federations and repositories (INCF DataSpace, EUDAT, Figshare, Dryad, etc)

All services available via REST APIs

HBP Knowledge Graph

Publicise

Discover

Biological or In silico
Data

Access & Use

HBP Core Data Model

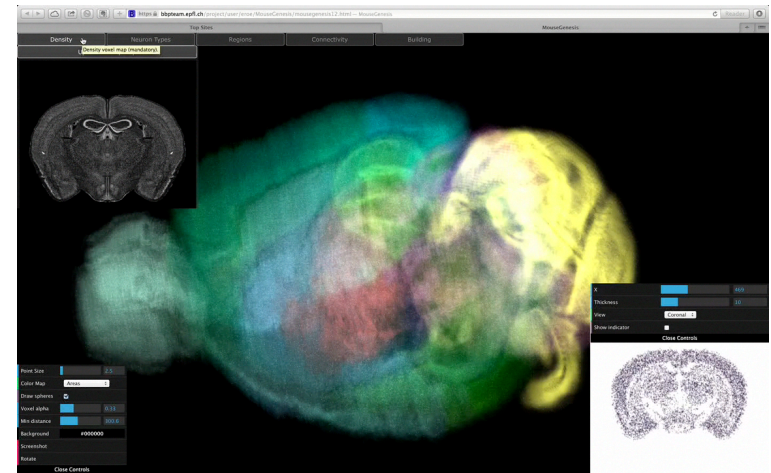
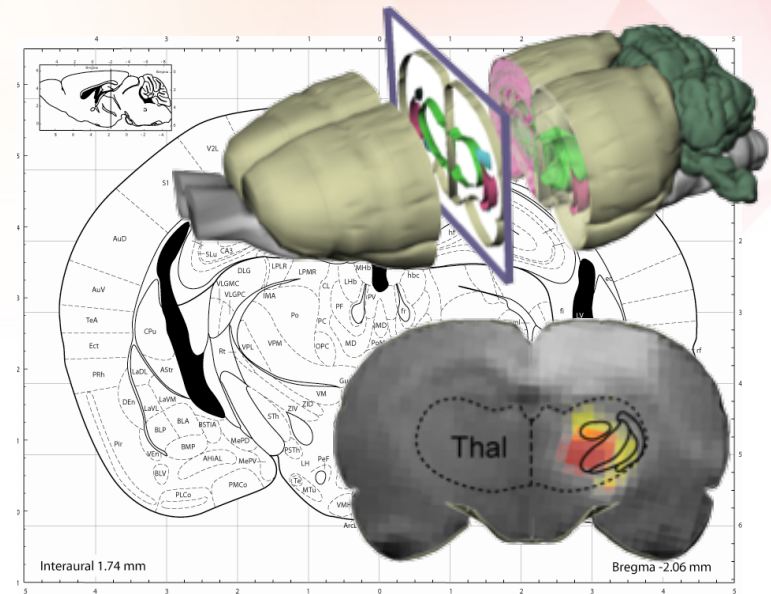
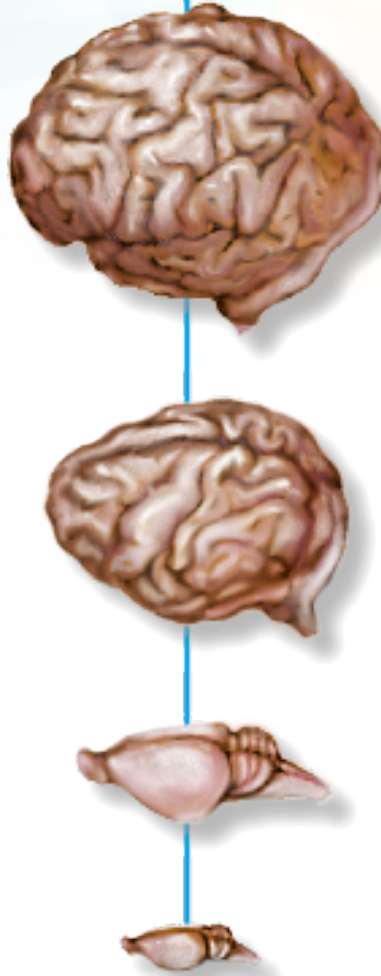
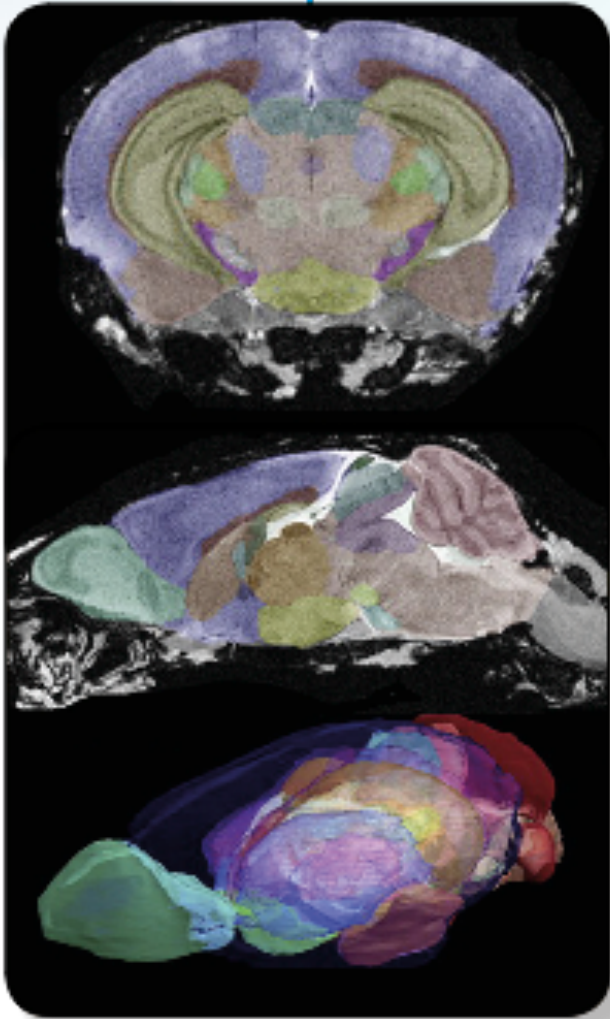
- Built on W3C PROV-O
- Represents biological or simulated **entities**
- Represents **observations**
- Describes properties using **ontologies**
- Records **where** an entity or observation is located
- Tracks **how** data is produced
- Tracks **who** performed experiments/manipulations
- Provides **URI** (including PIDs) access to data



Multilevel and Multimodal Brain Atlases

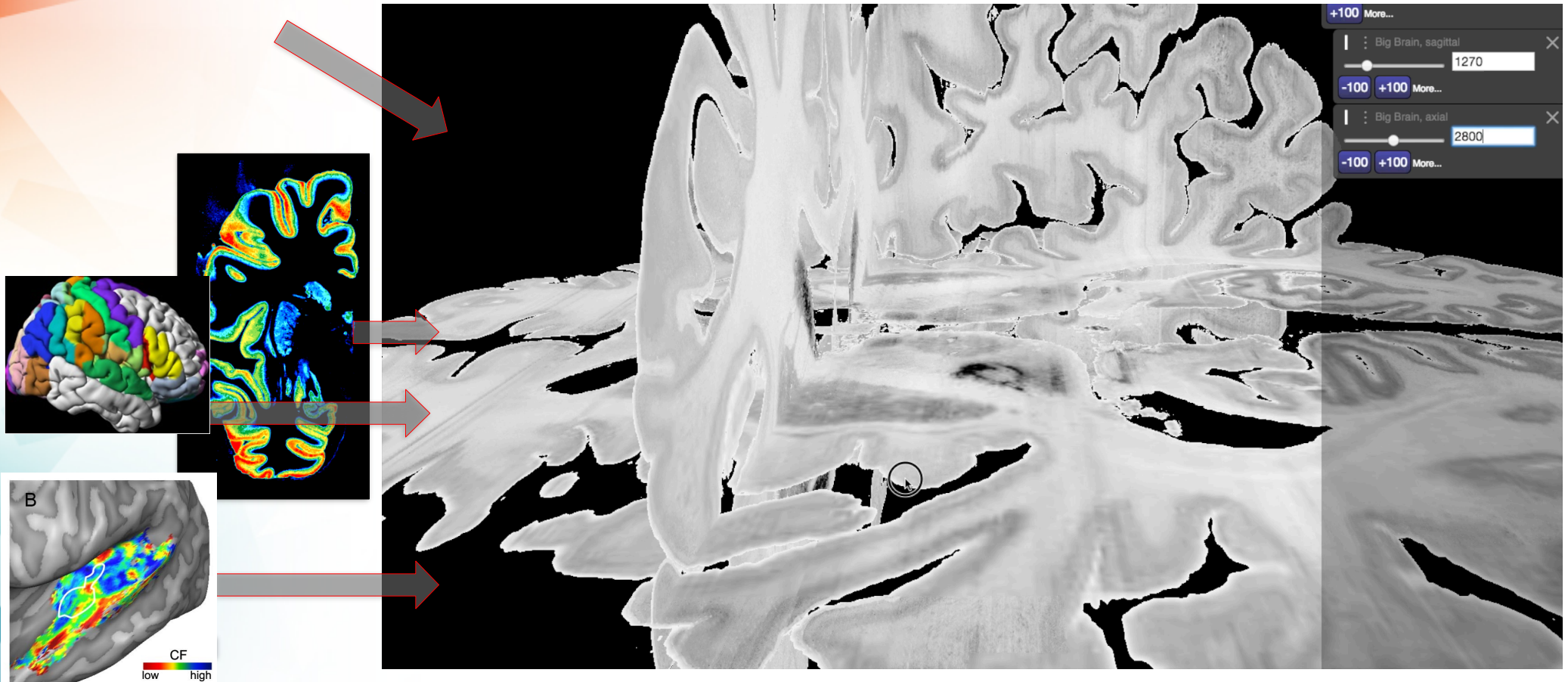
Anchor data to standard coordinate spaces:

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



BigBrain(s): cellular architecture

In the HBP Collaboratory



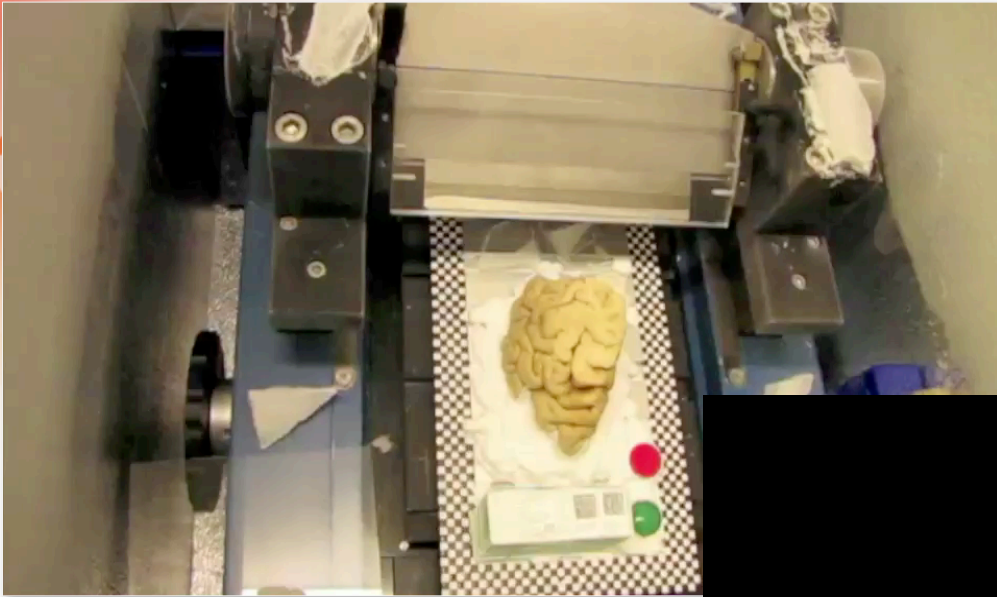
MIT
Technology
Review
10
Breakthrough
Technologies
2014

Amunts et al., in *Brain Inspired Computing*, Grandinetti, Lippert, Petkov, (Ed.), 2014, *Lecture Notes in Computer Science* 8603: 3-14, Springer.

BigBrain(s): fiber architecture

3D-PLI

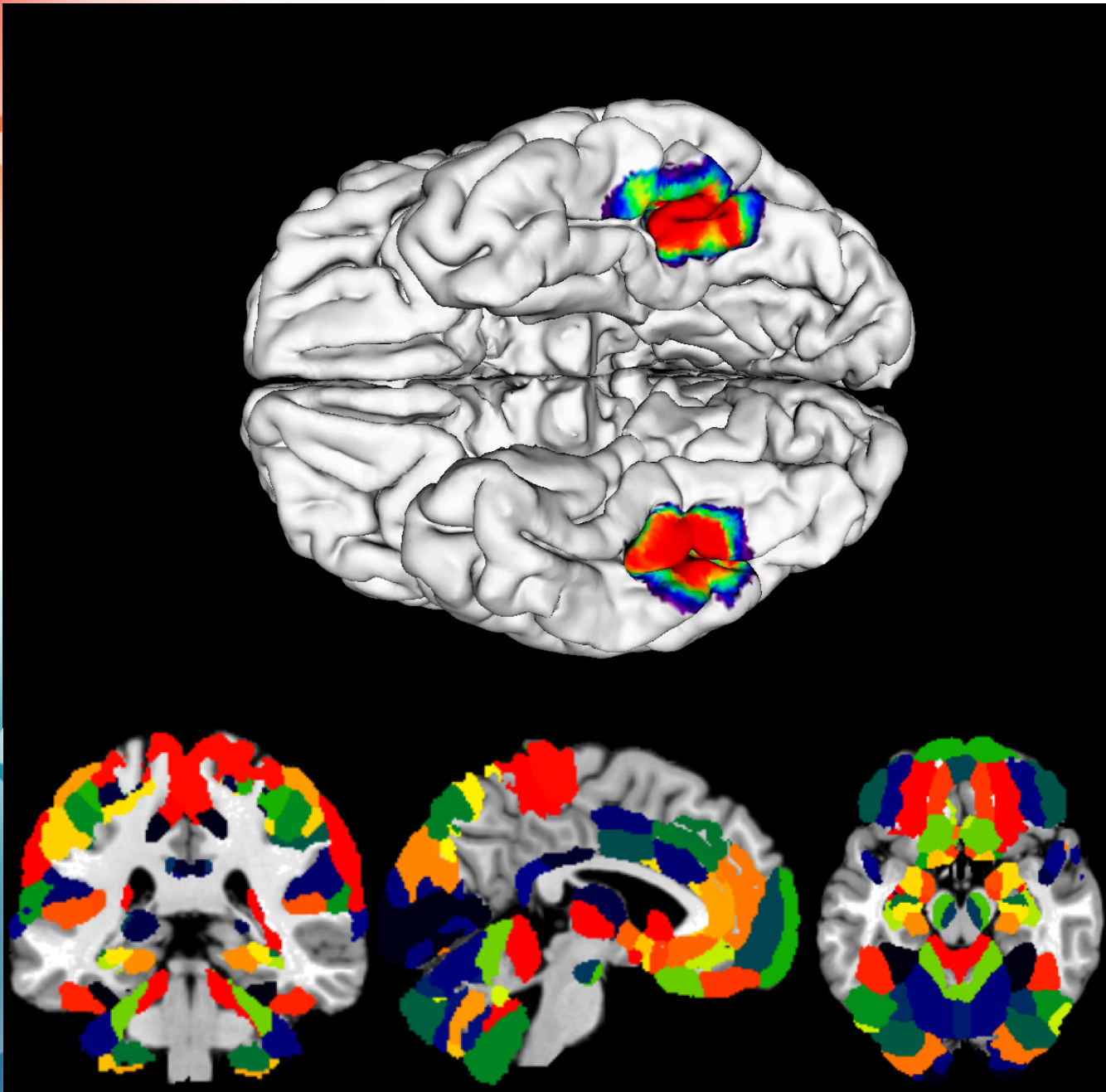
Polarized Light Imaging as a tool to analyze the fibres at microscopical resolution in 3D



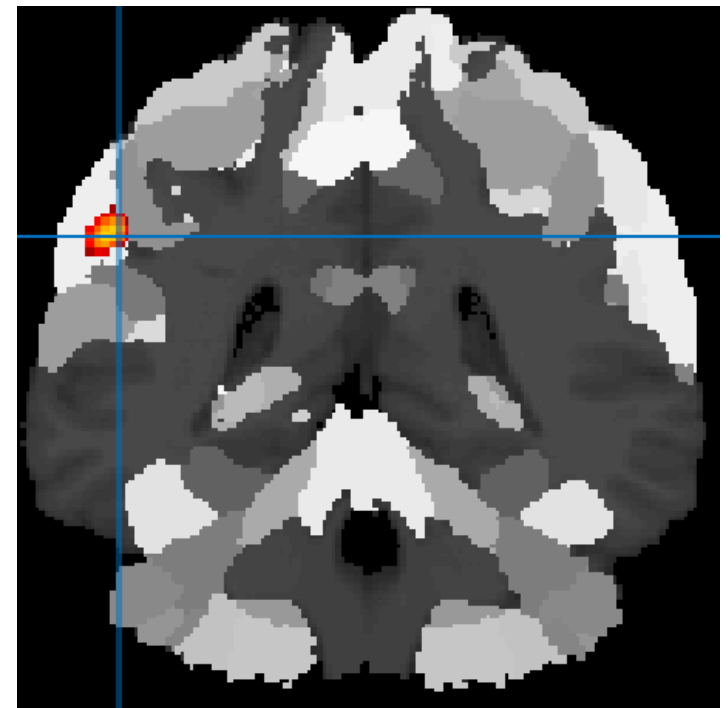
N: 1.500 – 3.000 per brain
Thickness: 100 – 50 μm
Resolution: 1.3 μm in-plane



The MNI space as a common template for different data modalities

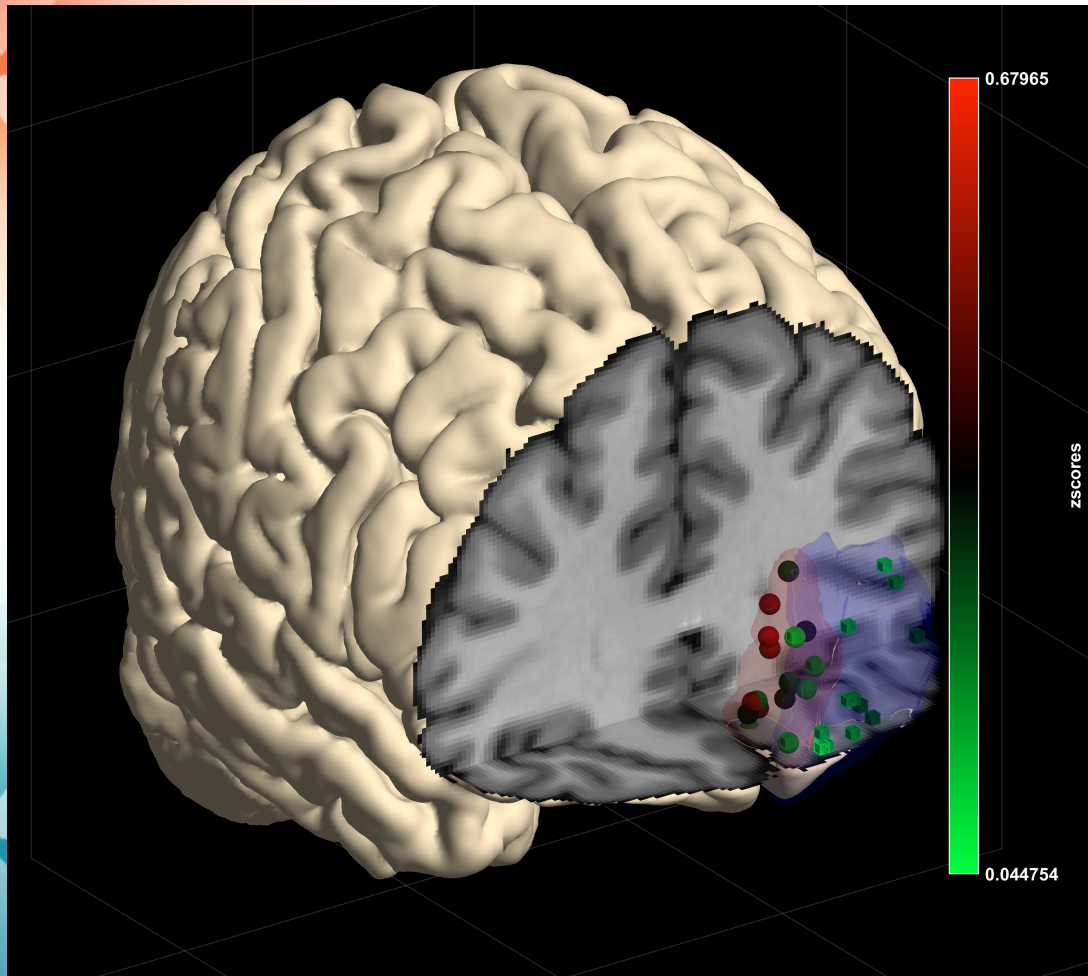


JuBrain atlas for interpreting fMRI data on visuo-motor coordination

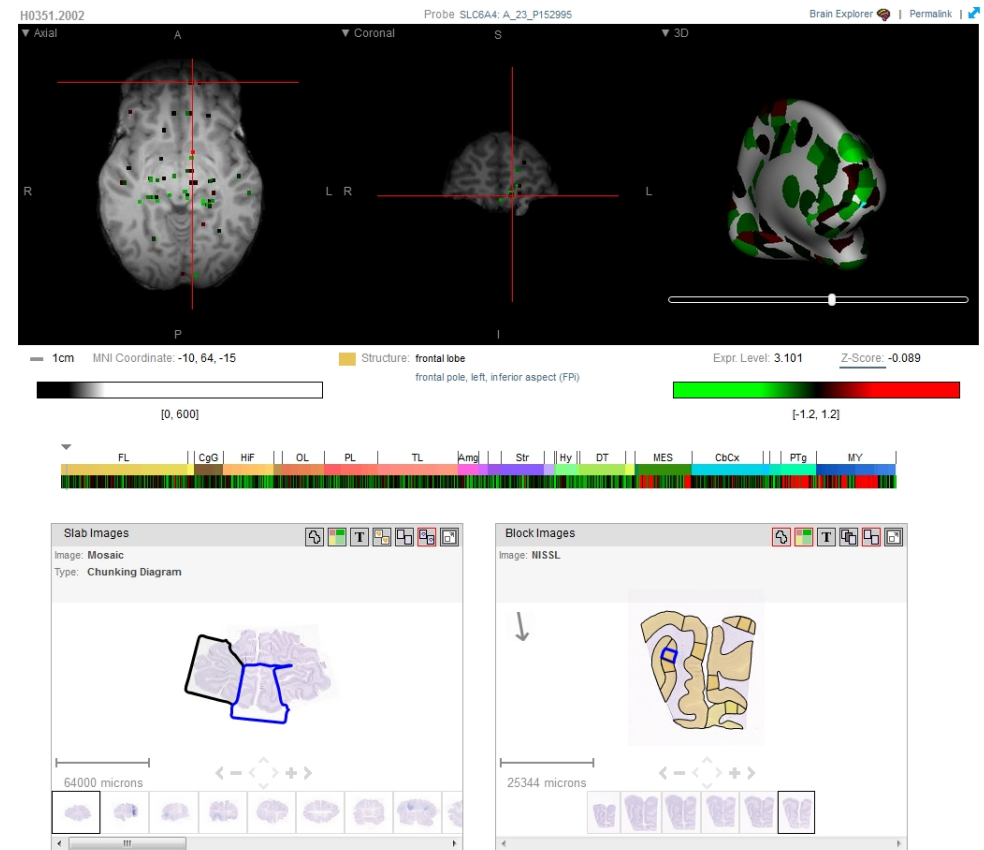


80.5% in left Area PF (IPL) (11.7% activated)
14.9% in left Area PFT (IPL) (1.7% activated)
3.5% in left Area hIP2 (IPS) (1.0% activated)

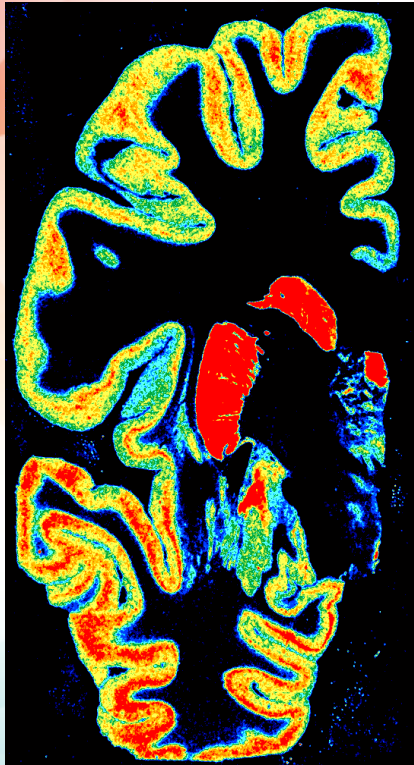
JuBrain connects to Allen Brain



ALLEN BRAIN ATLAS DATA PORTAL

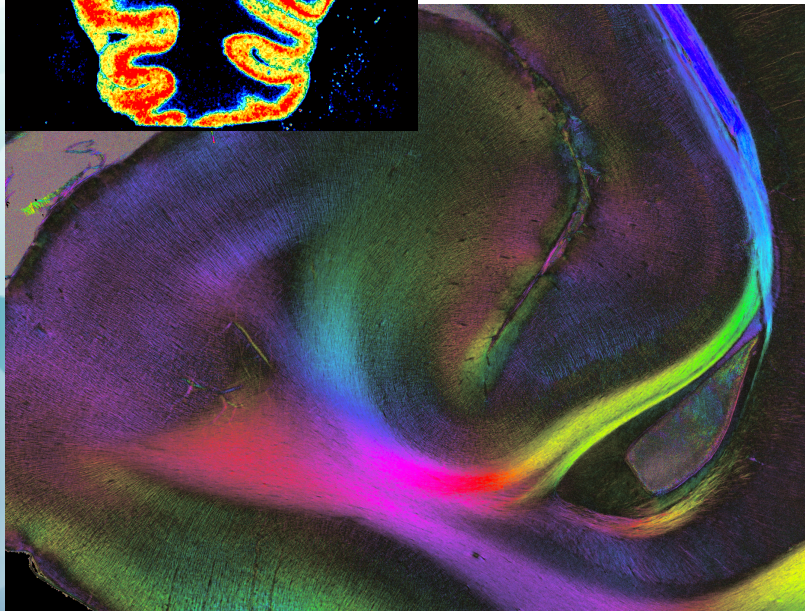


Human and rodent brain atlases



Muscarinic M2-receptor in the human brain

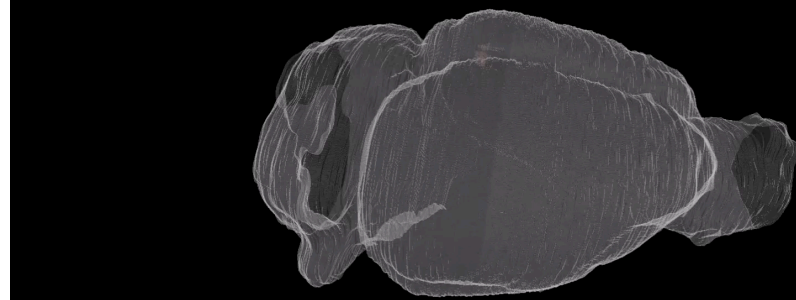
3D-reconstruction of nerve fibres (3D-PLI)



Muscarinic M2-receptor in the rat brain



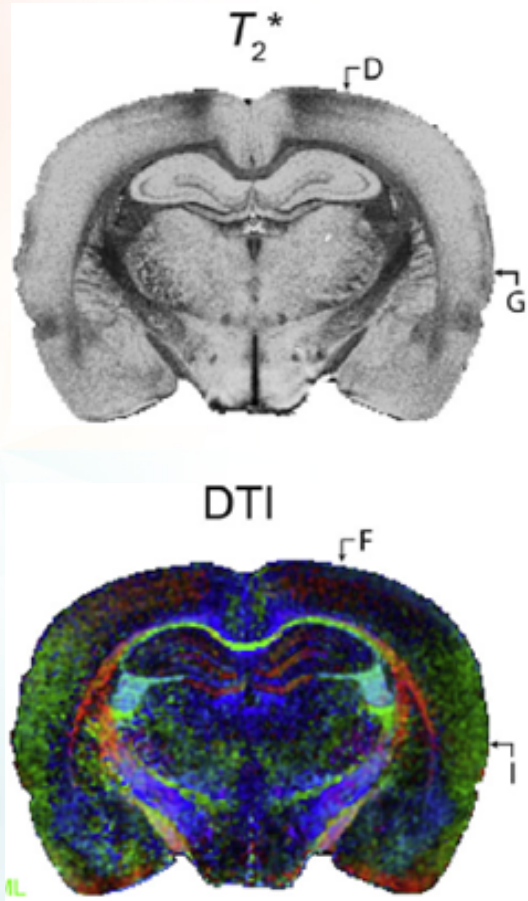
Schubert, Axer, Amunts, Zilles (Jülich)



3D-reconstruction of nerve fibres (3D-PLI)

Rodent brain atlases

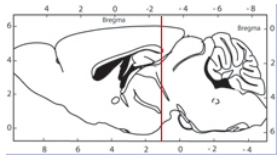
HBP Waxholm Space rat brain atlas



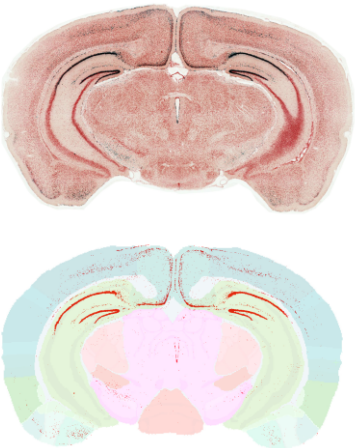
Papp et al., Neuroimage, 2014
Kjonigsen et al., Neuroimage, 2015
Boccaro et al., Hippocampus, 2015, in press

Waxholm Space rat brain atlas v2.0: updated and detailed delineations of the hippocampus

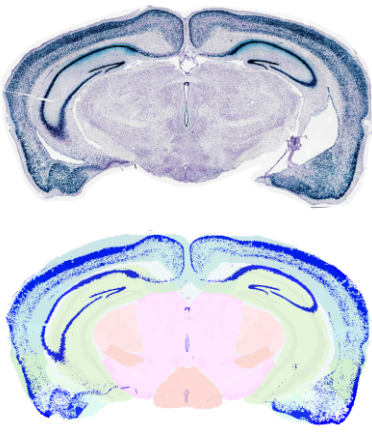
Data integration in atlas space



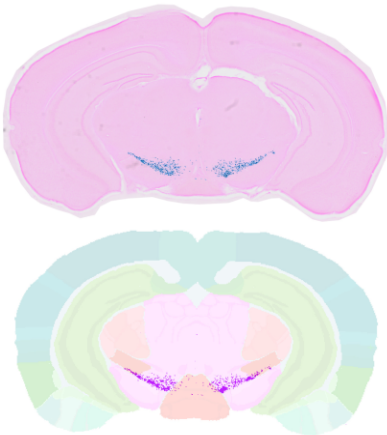
PrP-tTA



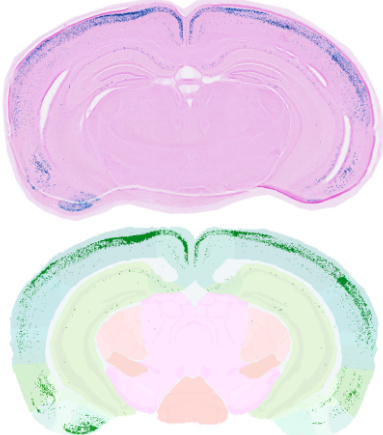
CamKII-tTA



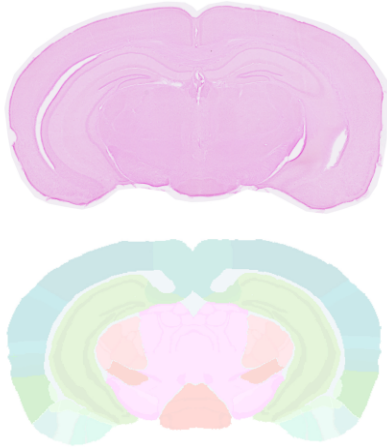
PitX3-tTA



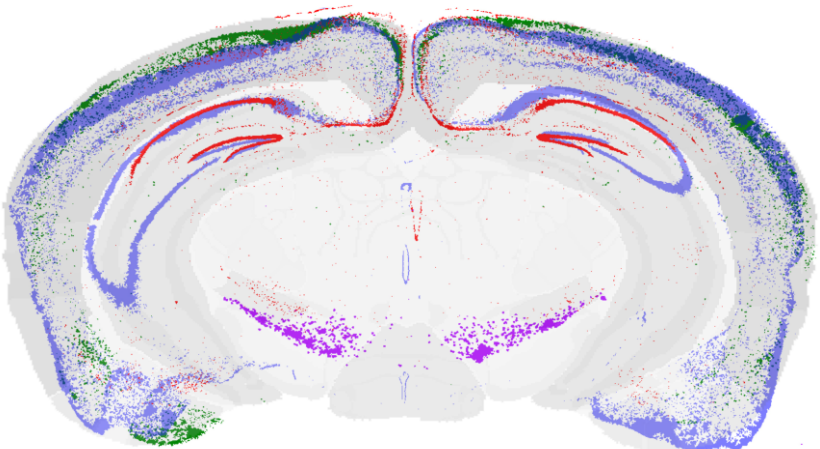
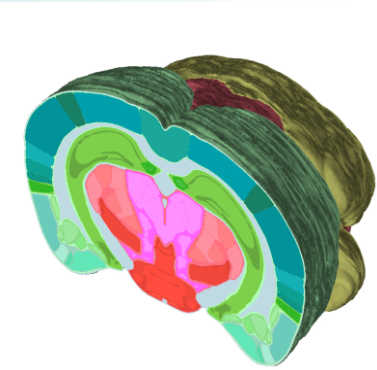
NOP(EC)-tTA



PcP2-tTA



3D Allen Mouse Brain Atlas



- PrP
- CamKII
- PitX3
- NOP
- PcP2

Transgene expression in five tTA driver mouse lines integrated in Allen mouse brain atlas space

