BRAIN MIND INSTITUTE BMI

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Blue Brain Project

Human Brain Project resources for the integrative modeling community

Human Brain Project

Eilif Muller
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http://bluebrain.epfl.ch

"At any large neuro-science meeting, one is struck by the pace of discovery, with **50,000 or more practitioners heading away from each other in all directions, in a sort of scientific Big Bang**. Although this independence is necessary, it has prevented neuroscience from entering a more mature phase, which would involve developing common standards and collaborative projects. **Neurophysiologists are more likely to use each other's toothbrushes than each other's data and software** [**and models**].

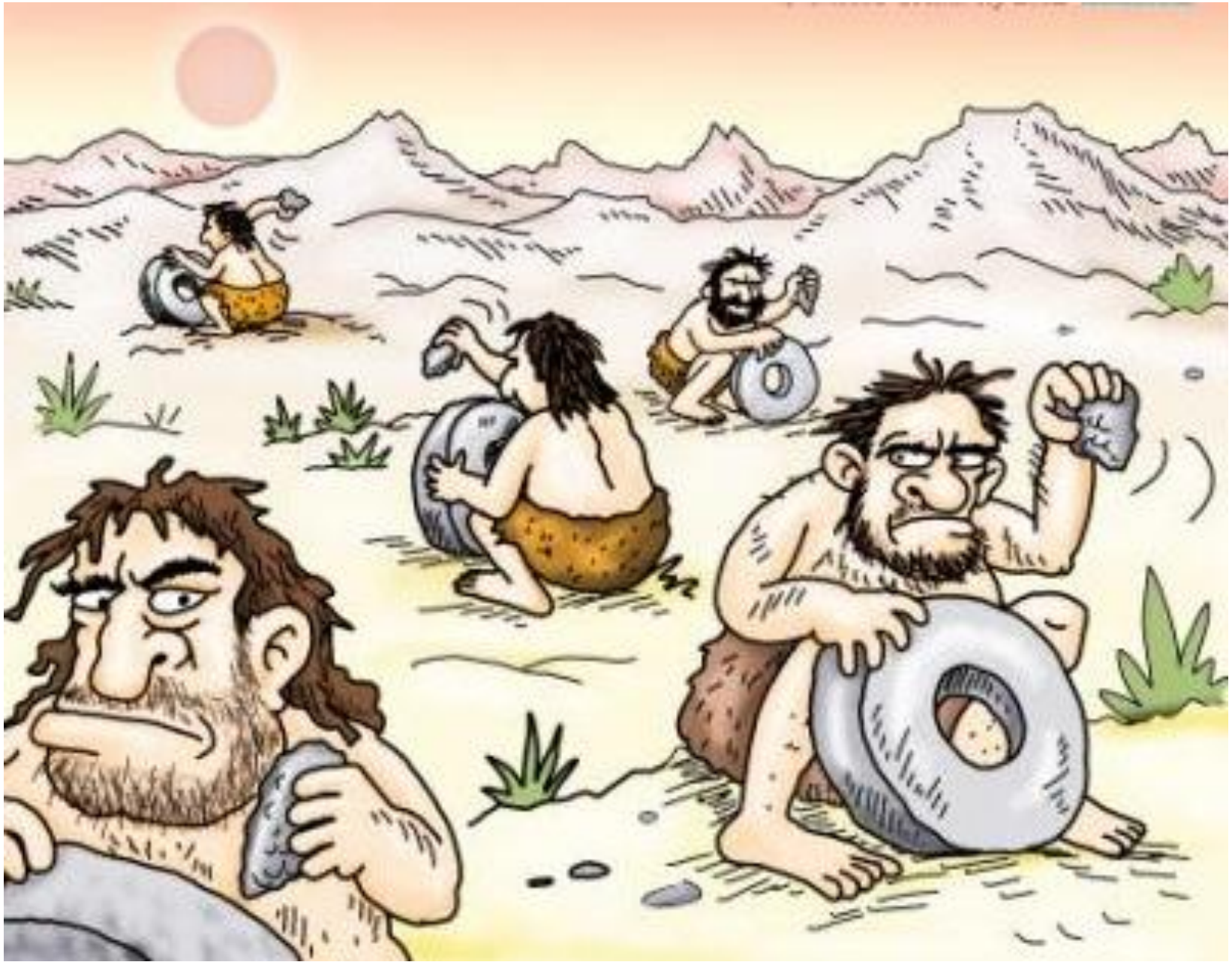
Koch and Reid, 2012

“We find that the major obstacle that hinders our understanding the brain is the fragmentation of brain research and the data it produces.

Our most urgent need is thus a concerted international effort that can integrate this data in a unified picture of the brain as a single multi-level system...”

The HBP-PS Consortium Report 2012:8
https://goo.gl/xjjoSB

Human Brain Project

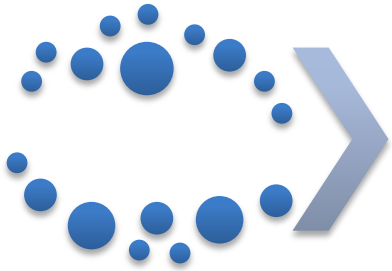


A Whole Community Approach

- **Challenge is to bring experimental and theoretical & computational neuroscience closer.**
- While the latter seek minimal models, the former want hard earned experimental facts not to be ignored adhoc.
- Adhoc simplification is a matter of taste.

> ***" New databases can be used to study biologically realistic circuit models and test the relevance of the microscopic complexity to computations at the level of local circuits. These studies might demonstrate that the molecular specificity of cell and synaptic types with their complex biophysics plays a major role in neuronal computations"***
>
> Sompolinksy, 2014

Microcircuit – Somatosensory Cortex

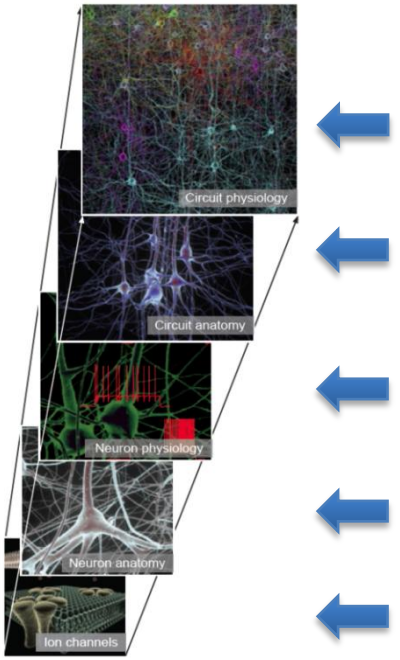


Sparse Data

Inductive Principles Algorithms

Models

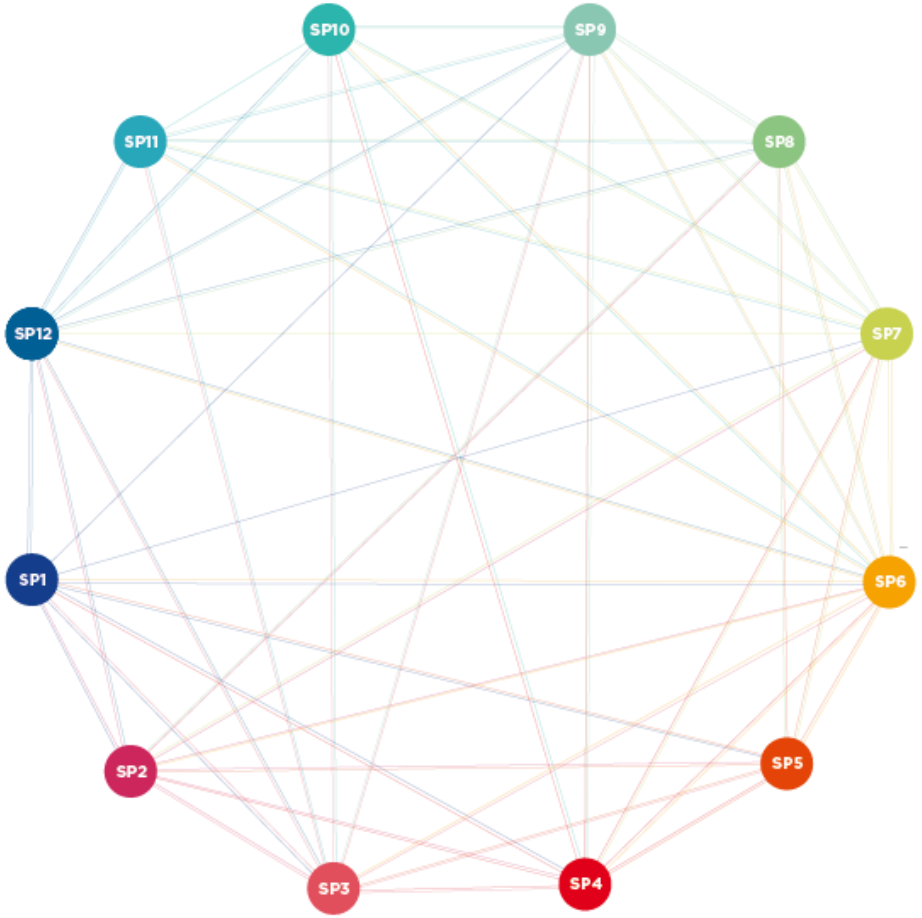
"Massively Collaborative Modeling"



2nd round review: *Markram et. al., "Reconstruction and simulation of neocortical microcircuitry";* Collaborative science: 78 authors.

HBP Overview

The HBP is organized in twelve subprojects, spanning the development of six new informatics-based platforms, plus brain organisation, cognitive neuroscience, theory, ethics and society and management



The informatics-based platforms

Neuroinformatics

searchable atlases and analysis of brain data

Brain Simulation

building and simulating multi-level models of brain circuits and functions

Medical Informatics

analyzing clinical data to better understand brain diseases

Neuromorphic Computing

brain-like functions implemented in hardware

Neurorobotics

testing brain models and simulations in virtual environments

High Performance Computing

providing the necessary computing power

SP6 Members (WP and Task Leaders)

Data-driven reconstruction of brain models

Henry Markram
Idan Segev
Marc-Oliver Gewaltig
Felix Schürmann

Brain Simulation Platform: integration and operations

Henry Markram
Jeffrey Muller

Brain Simulation Platform: user support and community building

Felix Schürmann

WP6.1
WP6.2
WP6.5
WP6.7
WP6.6

Brain simulation engines

Felix Schürmann
Erik De Schutter
Julian Shillcock
Michael Hines
Markus Diesmann
Fabien Delalondre

Brain Simulation Platform: scientific coordination

Felix Schürmann

Molecular dynamics simulation

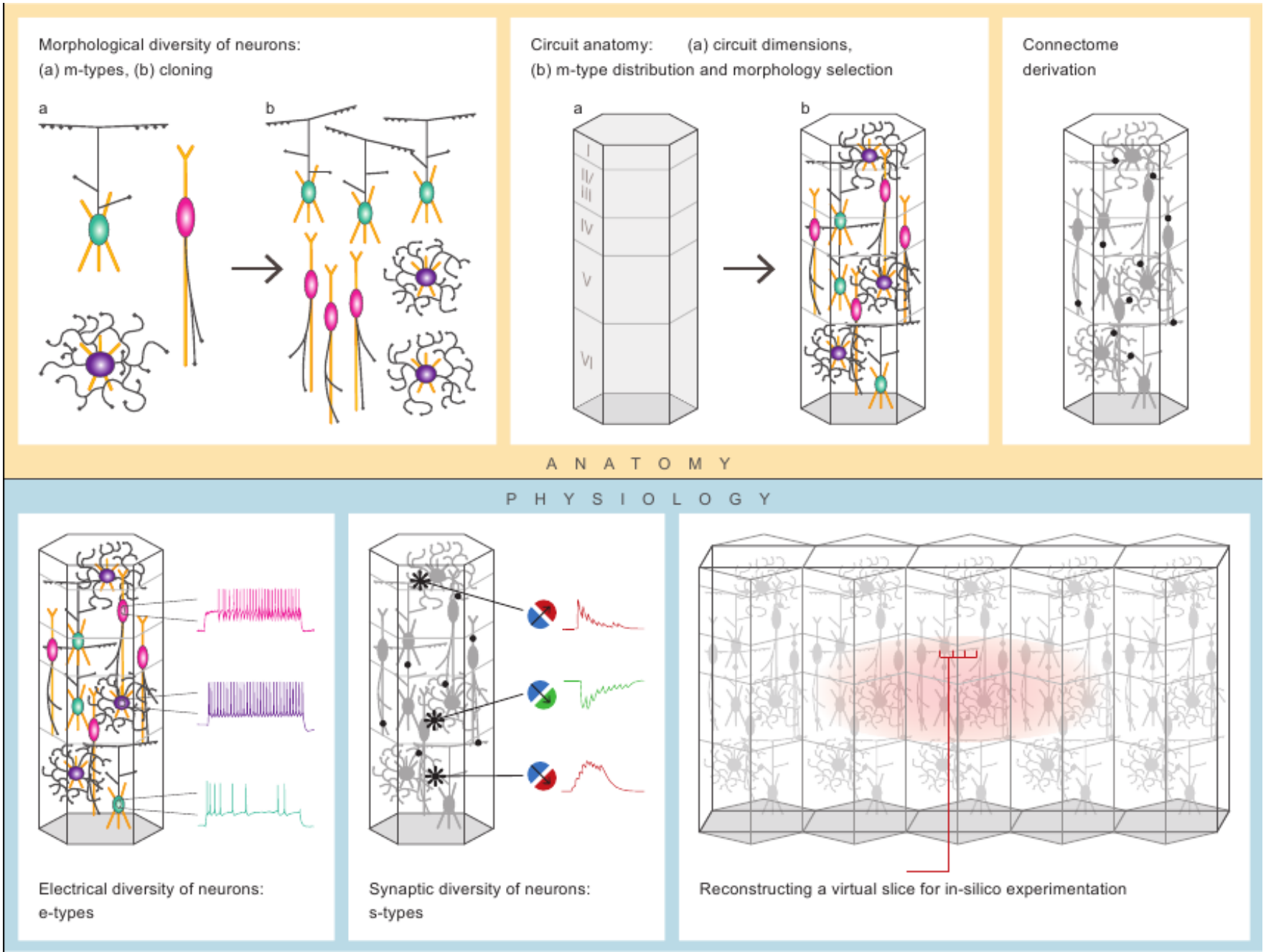
Paolo Carloni
Richard Lavery
Rebecca Wade

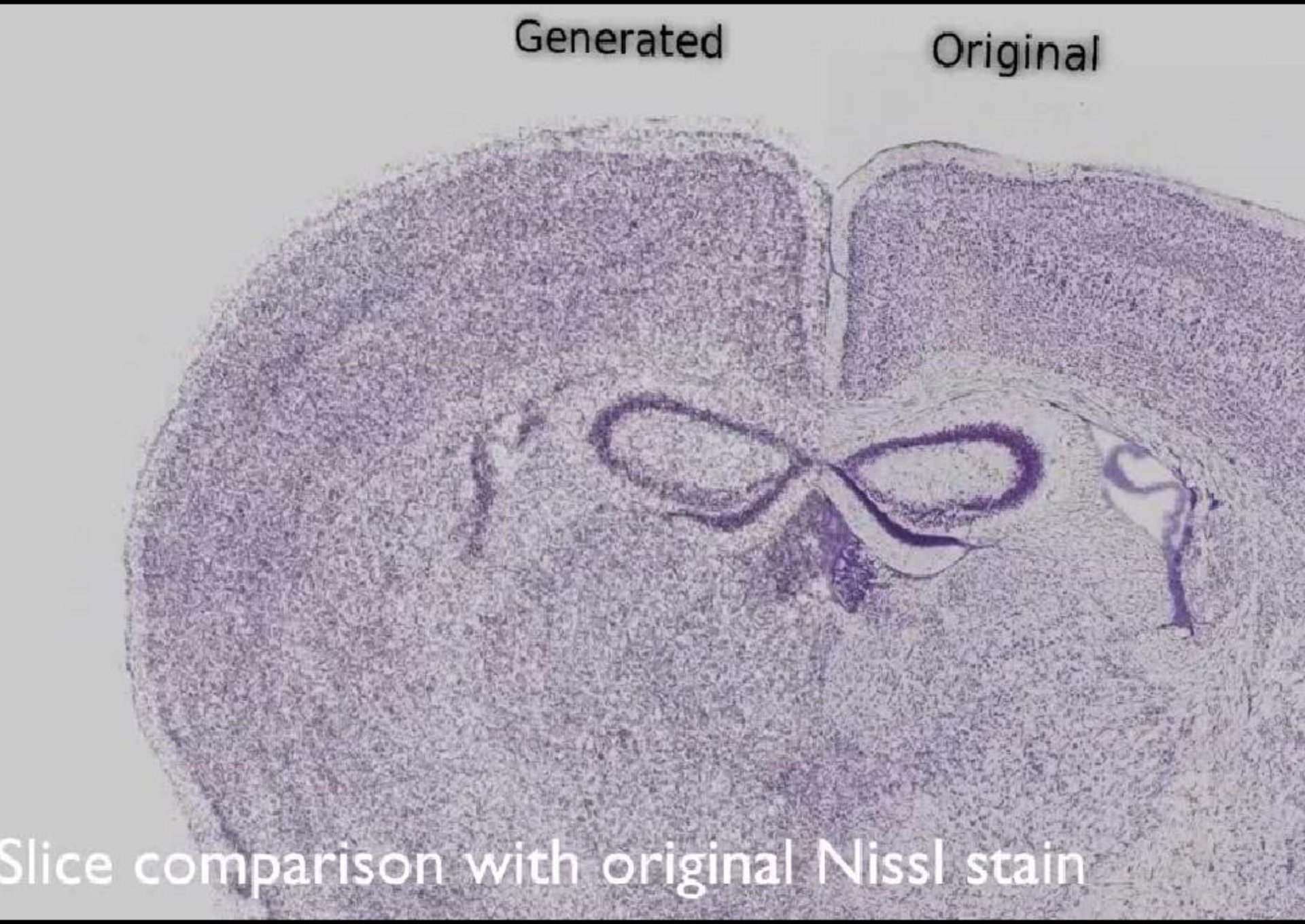
WP6.3
WP6.4

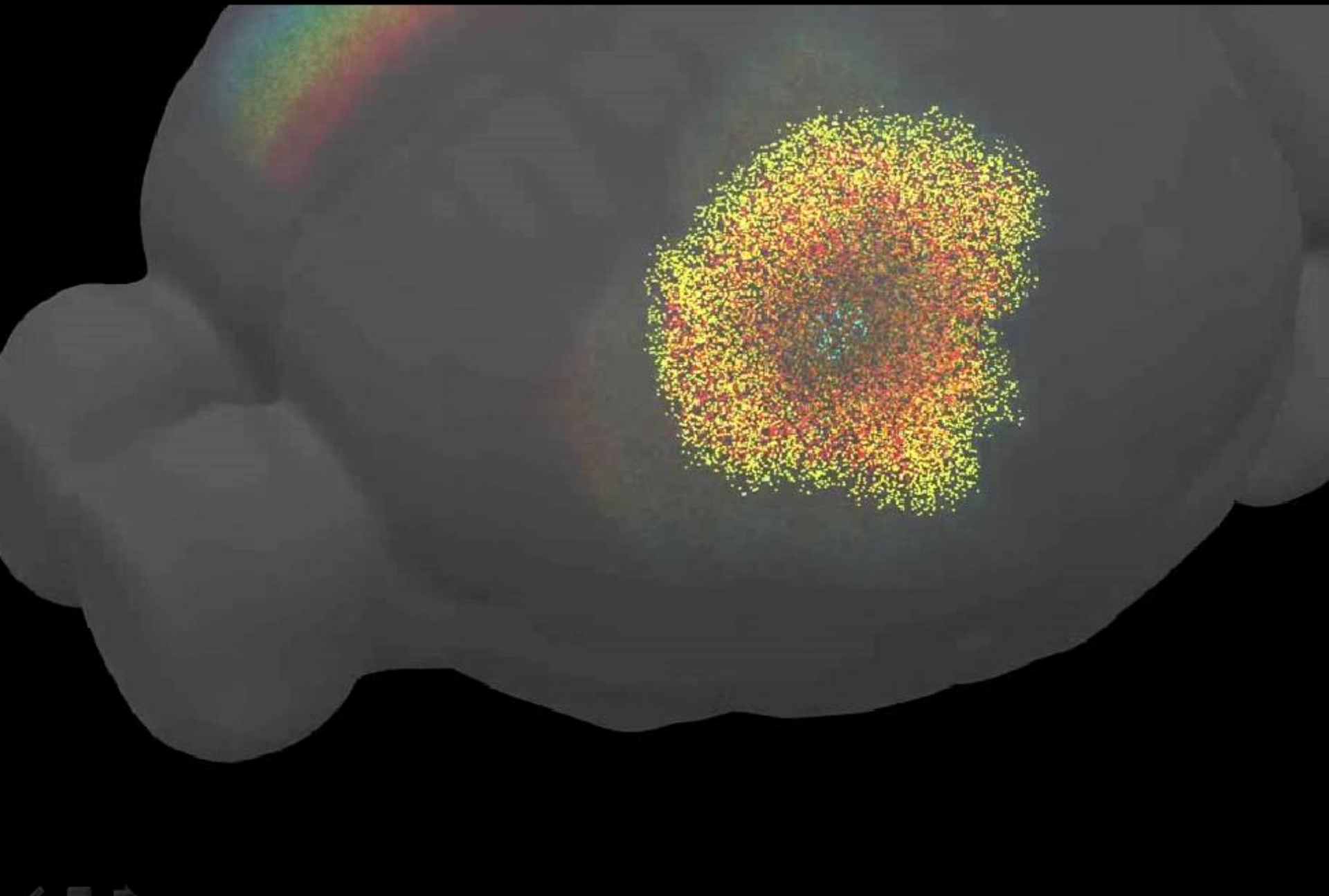
Initial brain models

Jeanette Hellgren Kotaleski
Antoine Triller
Pierre Magistretti
Alex Thomson
Eilif Muller
Egidio D'Angelo
Sten Grillner

Biological Microcircuit Reconstruction Workflow




Generated
Original
Slice comparison with original Nissl stain



Brain Simulation Platform

- The BSP is a collaborative internet-accessible user interface for brain reconstruction and simulation
- High-level Ramp-up Goals:
  - Allow multiple users to collaborate on brain reconstruction and simulation
  - Expose brain building tools and workflows to users
  - Drive user engagement (M18 for HBP members and M30 for community)

WP6.4 Initial Brain Models

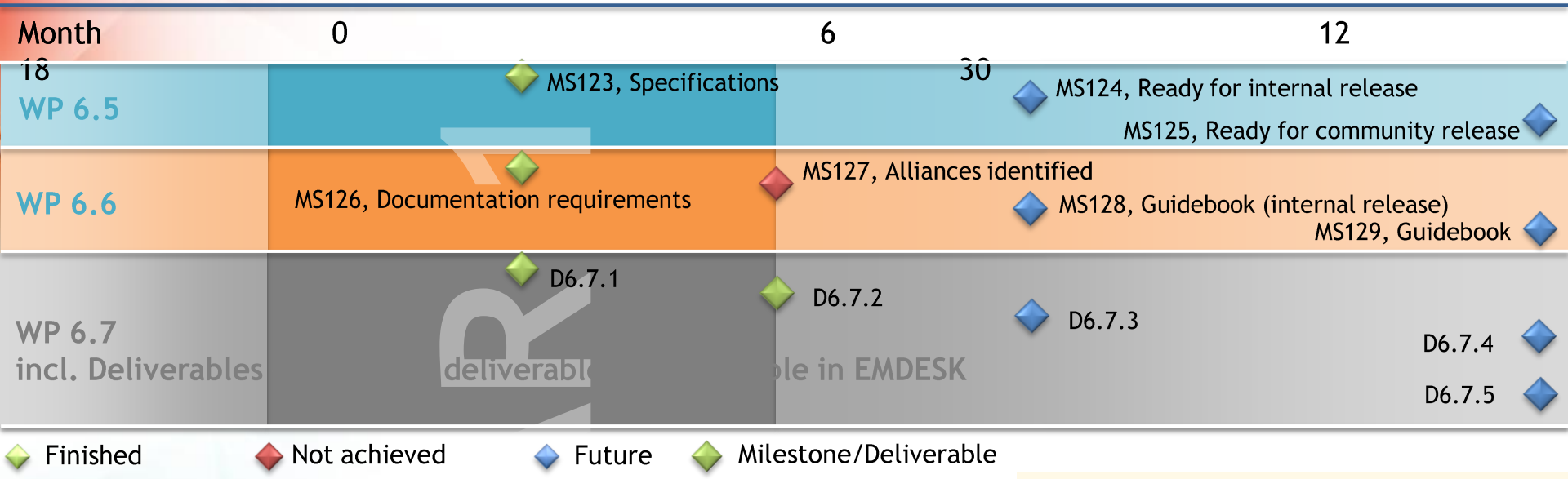
Develop initial models across the scales:

- Macro (whole-brain)
- Meso (brain regions)
- Microcircuits (unitary networks)
- Cells (neurons and glia)
- Sub-cellular (neurons, glia, synapses, vasculature)

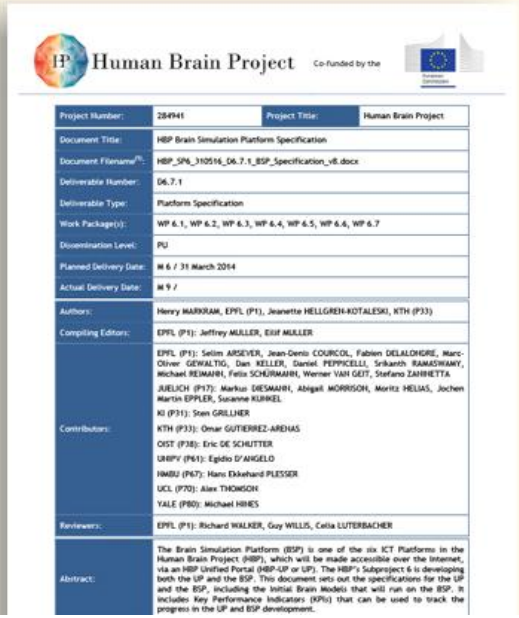
to …

- Exercise the building workflows
- Guide platform development
- Be made available for the community to build-on

Summary to M12



- D6.7.1 – Platform Specification – M6 (June 2014)
- D6.7.2 – Platform Setup Document – M12 (Dec 2014)
- Documentation Requirements
- First developer seminar (Summit 2014)
- To be released to HBP on M18
- To be released to the public in M30


Human Brain Project

Co-funded by the

Project Number:	284941
Project Title:	Human Brain Project
Document Title:	HBP Brain Simulation Platform Specification
Document Filename[1]:	HBP_SP6_310516_D6.7.1_BSP_Specification_v8.docx
Deliverable Number:	D6.7.1
Deliverable Type:	Platform Specification
Work Package(s):	WP 6.1, WP 6.2, WP 6.3, WP 6.4, WP 6.5, WP 6.6, WP 6.7
Dissemination Level:	PU
Planned Delivery Date:	M 6 / 31 March 2014
Actual Delivery Date:	M 9 /
Authors:	Henry MARKRAM, EPFL (P1), Jeanette HELLGREH-KOTALESKI, KTH (P33)
Compiling Editors:	EPFL (P1): Jeffrey MULLER, Eilif MULLER
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Reviewers:	EPFL (P1): Richard WALKER, Guy WILLIS, Celia LUTERBACHER
Abstract:	The Brain Simulation Platform (BSP) is one of the six ICT Platforms in the Human Brain Project (HBP), which will be made accessible over the Internet, via an HBP Unified Portal (HBP-UP or UP). The HBP's Subproject 6 is developing both the UP and the BSP. This document sets out the specifications for the UP and the BSP, including the Initial Brain Models that will run on the BSP. It includes Key Performance Indicators (KPIs) that can be used to track the progress in the UP and BSP development.

Public Deliverables

https://www.humanbrainproject.eu/en_GB/ec-deliverables

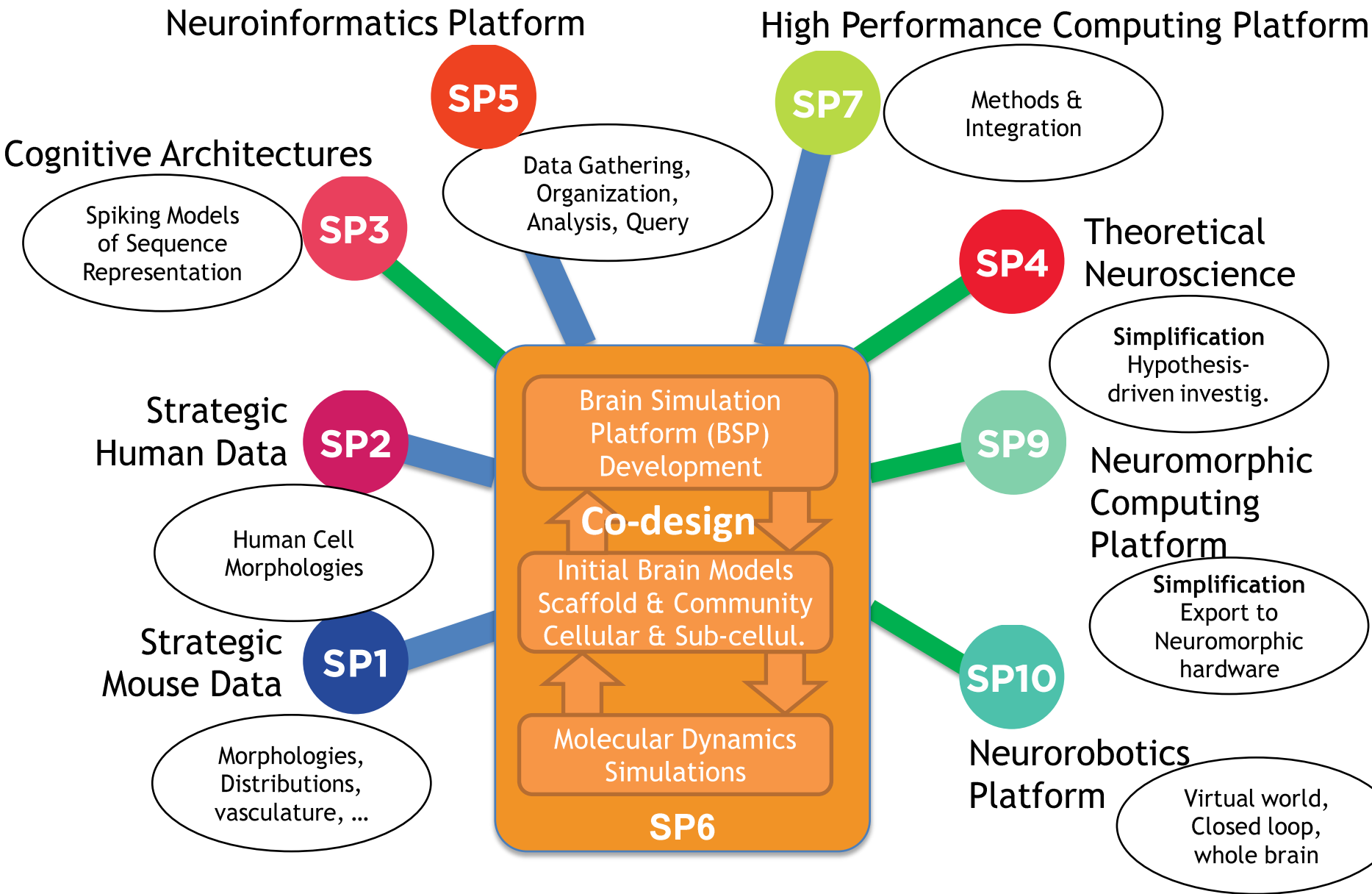
SP6 - Brain Simulation Platform

D6.7.1: Brain Simulation Platform v1 - specification document (report).

D6.7.2: Brain Simulation Platform v1 - set-up document (report).

And others from other SPs …

SP6 - Brain Simulation Platform Interactions within HBP



1st HBP release of network simulator

frontiers in
NEUROINFORMATICS

ORIGINAL RESEARCH ARTICLE
published: 10 October 2014
doi: 10.3389/fninf.2014.00078

Spiking network simulation code for petascale computers

Susanne Kunkel[1,2]*, Maximilian Schmidt[3], Jochen M. Eppler[3], Hans E. Plesser[3,4], Gen Masumoto[5], Jun Igarashi[6,7], Shin Ishii[8], Tomoki Fukai[7], Abigail Morrison[1,3,9], Markus Diesmann[3,7,10] and Moritz Helias[2,3]

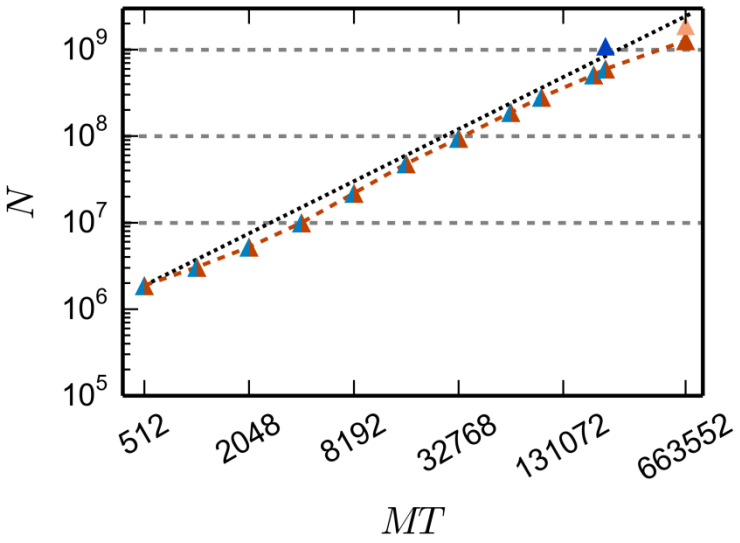
[1] *Simulation Laboratory Neuroscience – Bernstein Facility for Simulation and Database Technology, Institute for Advanced Simulation, Jülich Aachen Research Alliance, Jülich Research Centre, Jülich, Germany*
[2] *Programming Environment Research Team, RIKEN Advanced Institute for Computational Science, Kobe, Japan*
[3] *Institute of Neuroscience and Medicine (INM-6), Institute for Advanced Simulation (IAS-6), Jülich Research Centre and JARA, Jülich, Germany*
[4] *Department of Mathematical Sciences and Technology, Norwegian University of Life Sciences, Aas, Norway*

- scale 100,000 compute nodes
- public open source release Dec 23rd 2014, NEST 2.6.0
- demonstrates that neuroscience can exploit petascale systems

Slide credit: M. Diesmann

HBP Year 1: NEST - Maximum network size

- using 663,552 cores of “K computer”
- using 229,376 cores of JUQUEEN
- worst case: random network
- exc-exc STDP

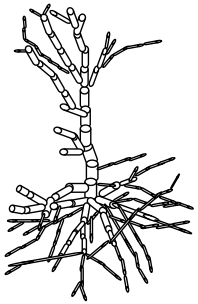


- largest general network simulation performed to date:
- 1.86x10^9 neurons, 6000 synapses per neuron
- 1.08x10^9 neurons, 6000 synapses per neuron

Slide credit: M. Diesmann

HBP Year 1: NEURON Refactoring for HPC

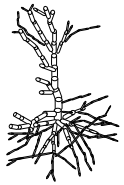
NEURON (300k Lines of Code)



18MB (w/ introspection)

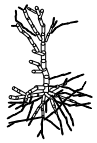
MS113
(Month 12)

coreNeuron (15k LoC)



2.2MB (w/o introspection)

Optimized coreNeuron

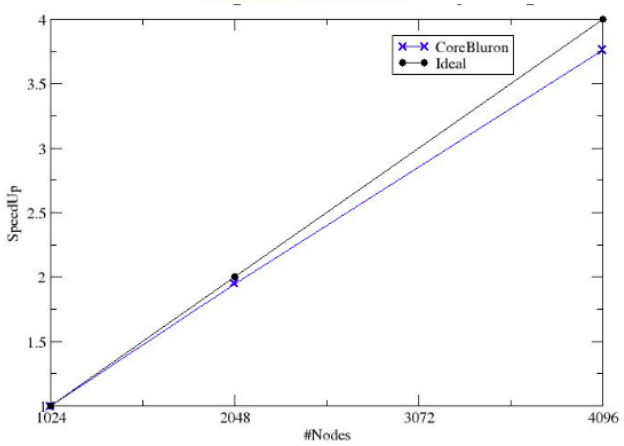


1MB (w/o introspection)

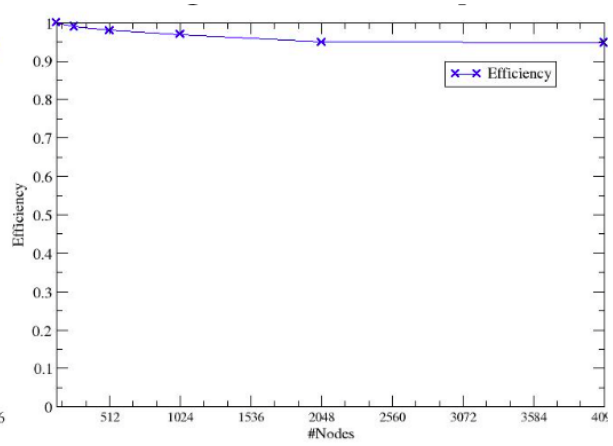
Slide credit: F. Schuermann

HBP Year 1: NEURON Scaling

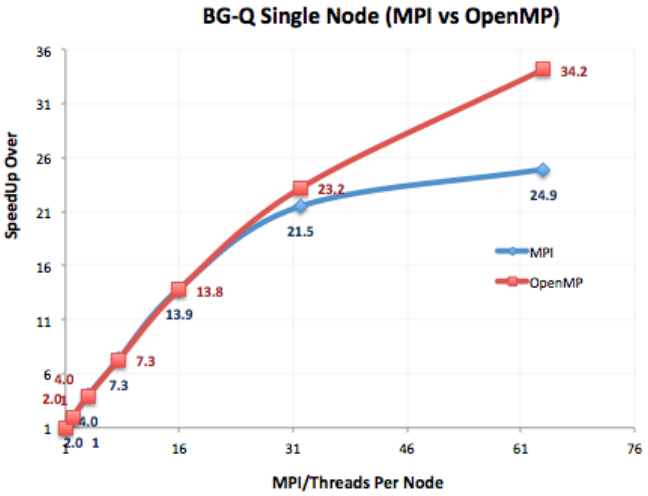
- Largest simulated cellular network to date
  - ~25 Million neurons, ~76 Billion synapses
  - HBP Development Computer (4 rack BGQ) @ CSCS
  - Filling ~61TB (of 64TB total) memory; ~370 neurons/core, ~2.5MB/neuron
- Scaling



a) Strong Scaling

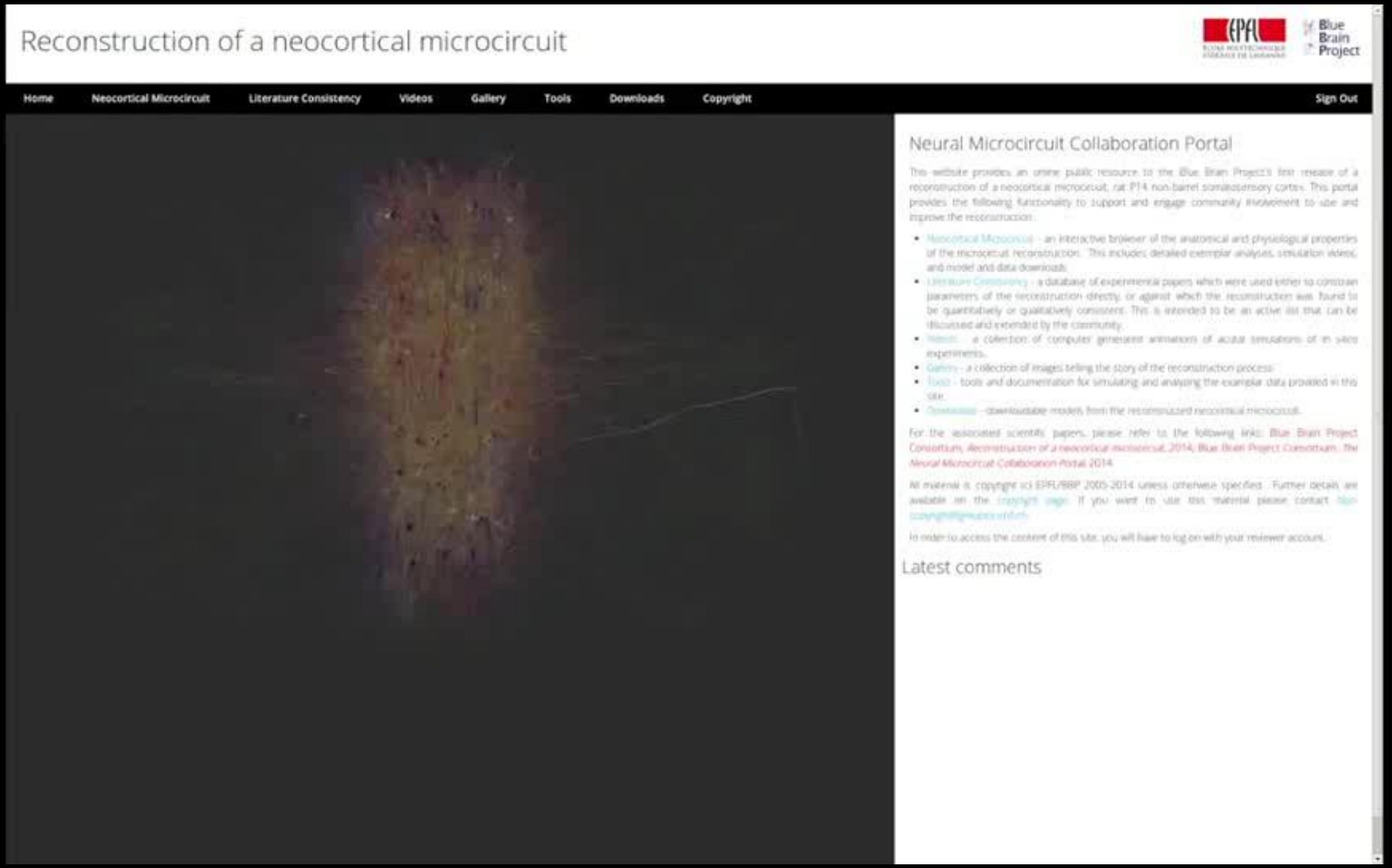


b) Weak Scaling



- Scaling to full JUQUEEN (28-racks) achieved
- Planned for Open-source release before FENS 2016

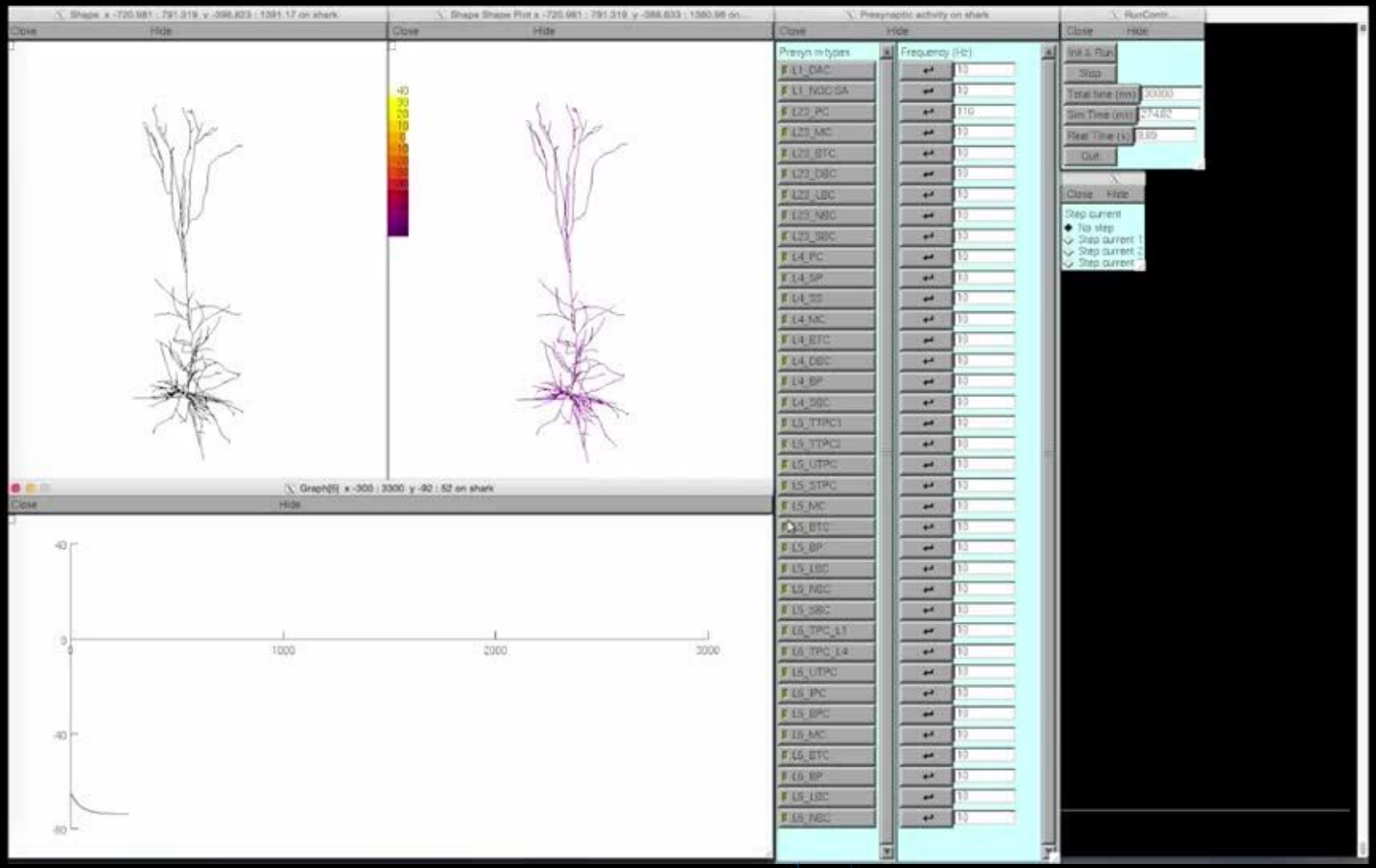
Slide credit: F. Schuermann



Public BETA: https://bbp.epfl.ch/nmc-portal

Slide credit: J.-D. Courcol, S. Ramaswamy

>1000 Neuron models of 55 excitatory and inhibitory neuron types and incoming synapses released in compact self-contained open-source bundles for NEURON



Working with NeuroML devs to allow export of models to NeuroML 2.0 , OSB

NeuroML

Slide credit: Werner Van Geit

Open Software Repositories

Blue Brain Project

The Blue Brain Project

Lausanne, Switzerland http://bluebrain.epfl.ch/ bbp-open-source@googl...

https://github.com/BlueBrain

Human Brain Project

Human Brain Project

https://www.humanbrainproject.eu/

https://github.com/HumanBrainProject

Blue Brain Project

Electrophys Feature Extraction Library

The Electrophys Feature Extract Library (eFEL) allows neuroscientists to automatically extract eFeatures from time series data recorded from neurons (both in vitro and in silico). Examples are the action potential width and amplitude in voltage traces recorded during whole-cell patch clamp experiments. The user of the library provides a set of traces and selects the eFeatures to be calculated. The library will then extract the requested eFeatures and return the values to the user.

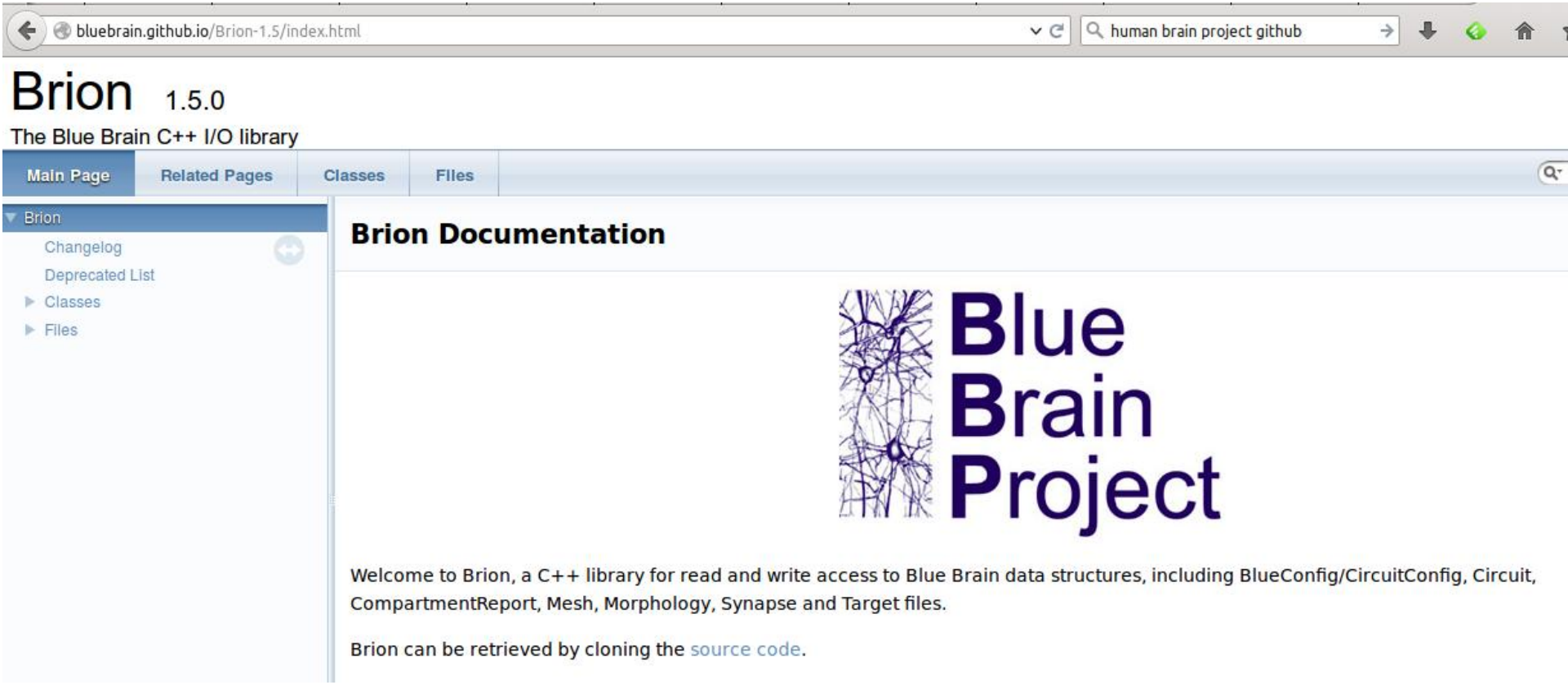
The core of the library is written in C++, and a Python wrapper is included. At the moment we provide a way to automatically compile and install the library as a Python module. Soon instructions will be added on how to link C++ code directly with the eFEL.

The source code of the eFEL is located on github: **BlueBrain/eFEL**

Using the eFEL, pyNeuron and the DEAP optimisation library one can very easily set up a genetic algorithm to fit parameters of a neuron model.

http://bluebrain.github.io/eFEL/deap_optimisation.html

Circuit and Simulation I/O



A Python API is also coming in next months …

More software developed in part by HBP members

neural ensemble .org

NeuralEnsemble

http://neuralensemble.org

https://github.com/NeuralEnsemble

PyNN Python ★53 ⑂35

A Python package for simulator-independent specification of neuronal network models.

Updated 22 days ago

python-neo Python ★41 ⑂55

Neo is a package for representing electrophysiology data in Python, together with support for reading a wide range of neurophysiology file formats

Updated 13 days ago

libNeuroML Python ★21 ⑂13

This package provides Python libNeuroML, for working with neuronal models specified in NeuroML

Updated on Jun 26

elephant Python ★11 ⑂32

ElePhAnT is the ElectroPhysiology Analysis Toolkit

Updated 6 days ago

This is not an exhaustive list …

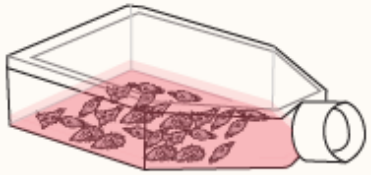
Channelpedia: Ion Channels

Channelome

Stable cell line library

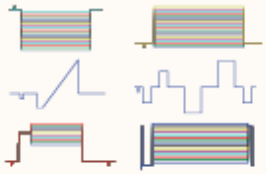
CHO Cells

Stable transfection (cDNA)

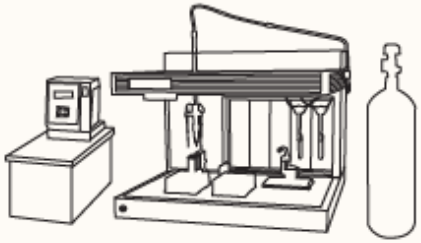


Stable cell line maintenance

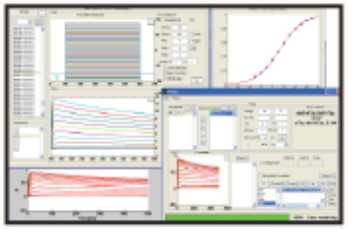
Automated biophysics characterization



Biophysical assay

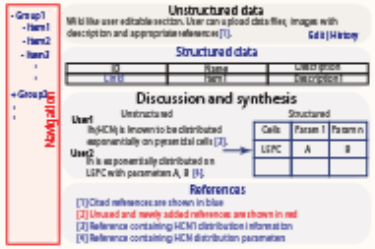


Automated patch setup

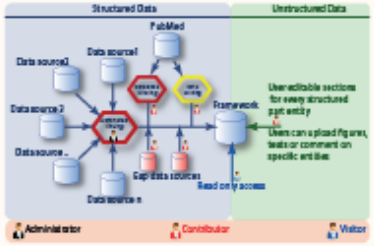


Automated model fitting

Channelpedia



Framework



Data sources

Channelpedia

[NeuroML]

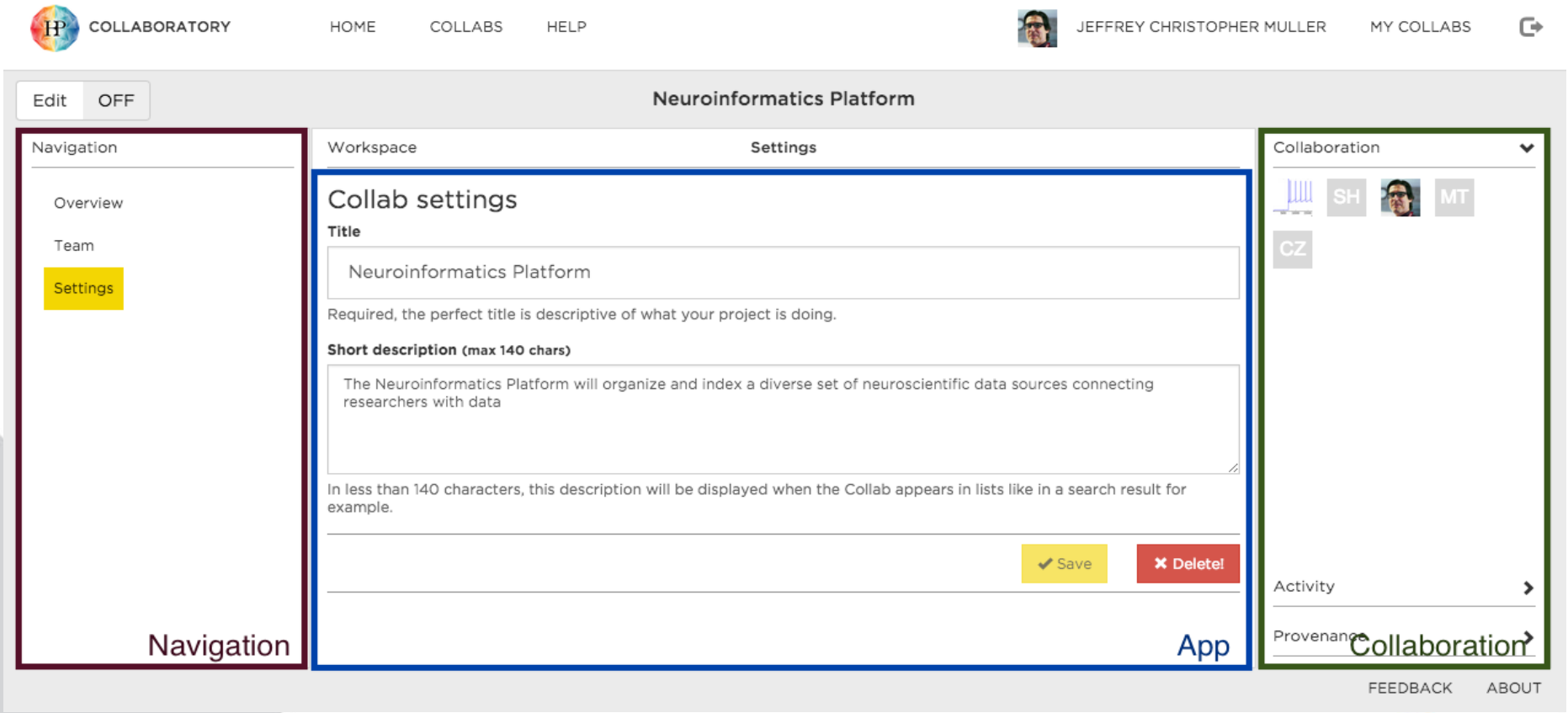
Contact: ranjan.rajnish@epfl.ch, emmanuelle.logette@epfl.ch, severine.petitprez@epfl.ch, mirjia.herzog@epfl.ch

URL: http://channelpedia.epfl.ch

Slide credit: Rajnish Ranjan

HBP Collaboratory

"A 'dating' site for [scientific collaboration]"
– Dr. Christine Aicardi



To be released @ FENS 2016 …

Slide credit: Jeff Muller

European Commission

Human Brain Project

10th FENS Forum of Neuroscience

July 2-6, 2016 | Copenhagen, Denmark

TECHNICAL WORKSHOPS

Saturday, July 2, 2016, 10:30 - 13:30

W04 - Introduction to the Human Brain Project Collaboratory.

Chaired by: E. Muller (Geneva, Switzerland); A. Davison (Gif sur Yvette, France)

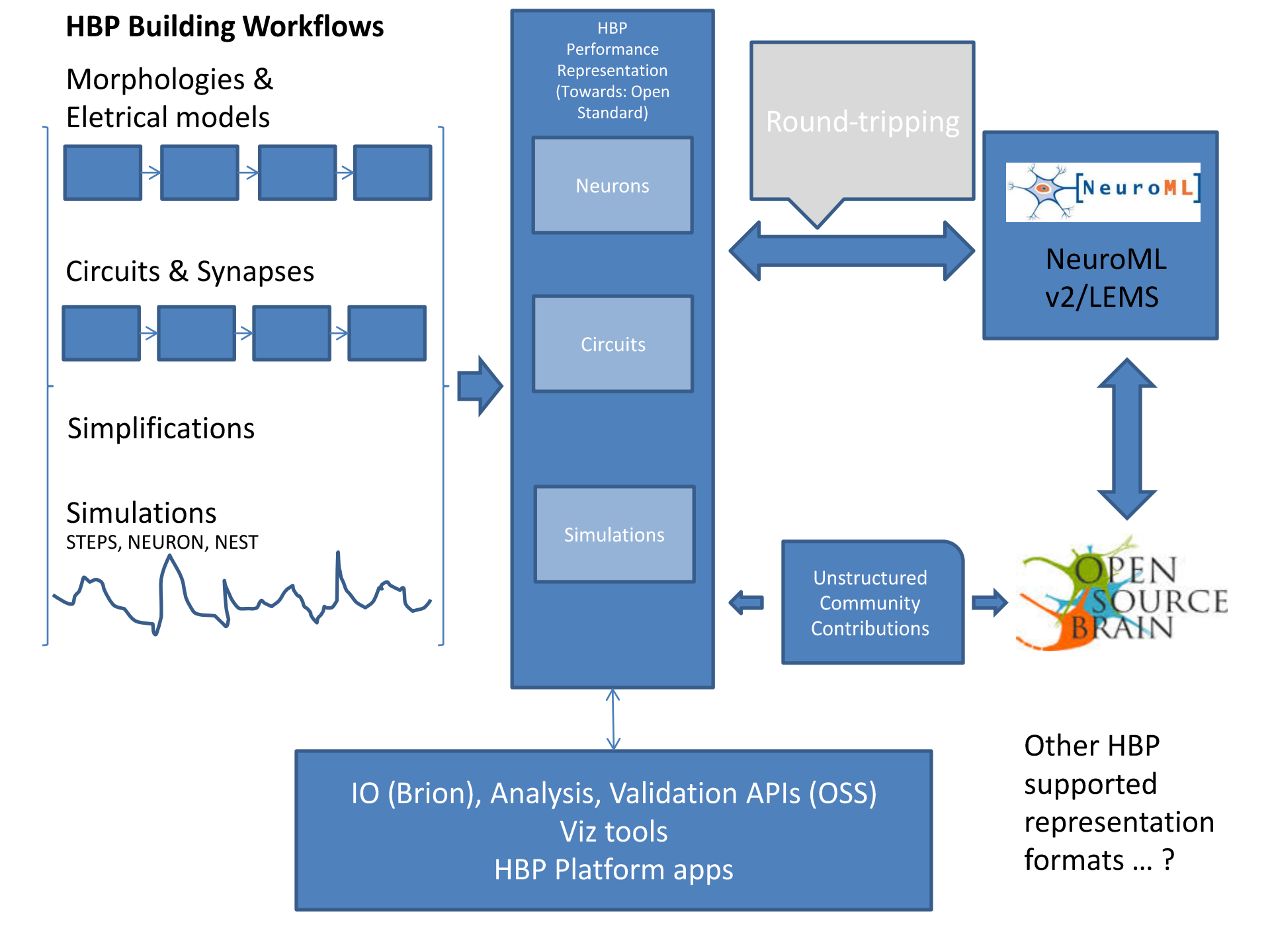
"This workshop will provide an introduction to the Human Brain Project web-based platforms, ""The HBP Collaboratory"", with a focus on neuroscientific use-cases available as of the initial public release of spring 2016, and first success stories. These include neuroinformatics and data integration, single neuron and neural tissue modelling and analysis, integration with 3D brain atlases, and the joint Allen Institute for Brain Science and HBP community data and model release of March 2016."

Muller J. (Geneva, Switzerland)
The HBP "Collaboratory".
Zwahlen C. (Geneva, Switzerland)
The Neuroinformatics platform: Contributing and querying data.
Ramaswamy S. (Geneva, Switzerland)
Interactive resources for e-Neuroscience.
Grün S. (Juelich, Germany)
Analysis of large-scale recordings of neural activity in vivo and in silico.
D'Angelo E. (Pavia, Italy)
Modeling cerebellar neurons and microcircuits using the HBP Collaboratory.
Anastassiou C. (Seattle, USA)
Collaborative transatlantic efforts to create faithful single-neuron representations for the community.

HBP – Brain Simulation Platform - Relationship to other initiatives

- Focused on platforms
- Model building pipelines and workflows from Experimental data -> Neuroinformatics -> data-driven models
- Model validation suites bound to Neuroinformatics platform
- Not a data-generation project
    - Strategic data for atlas-based brain building in mouse and human
- Simplification strategies to engage users (mostly hypothesis-driven)
- Foundation software
    - large-scale simulation, analysis and visualization using supercomputers
- Closed-loop (with Neuromorphic , SpiNNaker) and Neurorobotics
- Will leverage/integrate/federate/develop many community developed tools
- Round-tripping with OSB via NeuroML
- Transitioning from Cathedral to Bazaar model

OSB
OpenWorm (Bazaar)
Geppetto (Bazaar)
Allen Brain Institute - Mind Scope


HBP Building Workflows
Morphologies & Eletrical models
Circuits & Synapses
Simplifications
Simulations
STEPS, NEURON, NEST
HBP Performance Representation (Towards: Open Standard)
Neurons
Circuits
Simulations
Round-tripping
NeuroML
NeuroML v2/LEMS
Unstructured Community Contributions
OPEN SOURCE BRAIN
IO (Brion), Analysis, Validation APIs (OSS)
Viz tools
HBP Platform apps
Other HBP supported representation formats … ?

Old argument

We can’t collaborate because we don’t have the tools!


SO WHAT HELPS PEOPLE COLLABORATE?
Believing ANY idea COULD BE THE idea
GIVING EVERYONE
NO TOOLS
REQUIRED
Demonstrate AND Celebrate THE RESULTS OF TEAMWORK
GOOD SEARCHABLE KNOWLEDGE
at your FINGERTIPS
2 Minds ARE ALWAYS BETTER
SHOW how IT SAVES
and
STAND-ARDI-SATION
Mutual Respect

HBP Hippocamp CA1: Collaborative and Integrative Modeling of Hippocampal Area CA1

31st March-1st April 2015, London, United Kingdom

Aim #1

- Engage community
- Highlight existing:
  - modeling efforts
  - strategic datasets

Aim #2

- Define and bootstrap an inclusive community-driven model and data-integration process
- Open pre-competitive reference models of hippocampus CA1
- Documented, validated, and alive

http://neuralensemble.org/meetings/HippocampCA1

Why now?

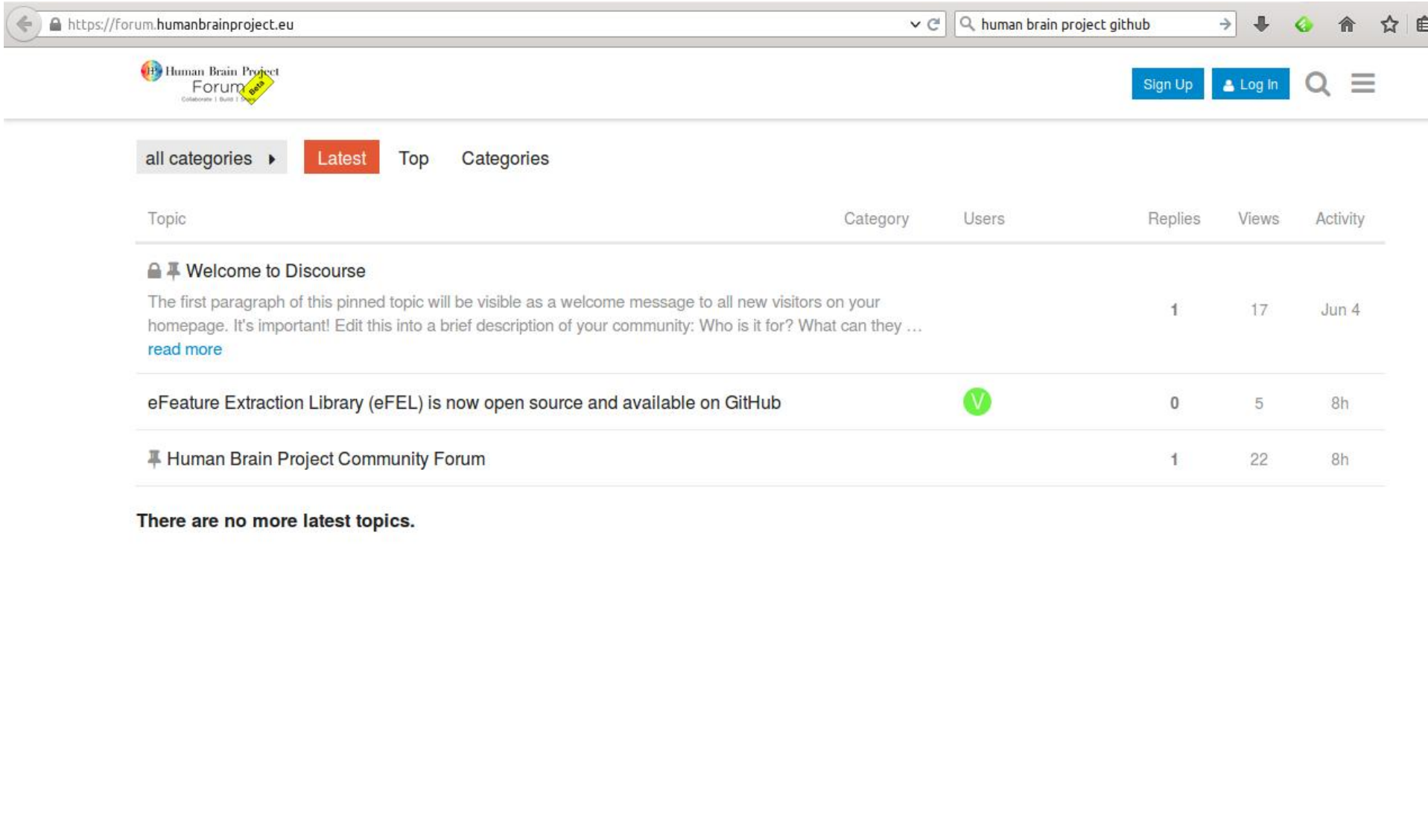
- HBP roadmap to deliver models of neocortex, hippocampus, cerebellum of similar detail to BBP cortical column model (April 2016)
- CA1 Model by Sept 2015
- **HBP mandate for open, collaborative modeling**
- **Be inclusive, non-competitive with work of community of experts**
- **Avoid yet another model**
- **Models by community for community**

Next steps

- Openness consensus ✓
- Discuss relationship between HBP collaboratory and OSB
- Public Discussion Forum (June 1st) ✓
- **Hippocamp opinion paper**
  - Sources of fragmentation
  - Possible solutions
  - Review state-of-the-art
  - Community roadmap
- **Form CA1 Neuron Models Sub-group**
  - eFEL https://github.com/BlueBrain/eFEL ✓
  - http://bluebrain.github.io/eFEL/deap_optimisation.html ✓
- First release CA1
- Demonstrate: Simplification and hypothesis-driven use cases
- **FENS 2016 – Technical workshop - Copenhagen**

  "Introduction to HBP Collaboratory"

https://forum.humanbrainproject.eu/



What is a community model?

HBP Collaboratory: Whole Community Modeling

An end-to-end approach which integrates the whole community, and will have a lasting impact on addressing fragmentation

Driving use case:

Experimentalists -> Neuroinformatics ->
Data-driven models -> Extensive validation ->
Principled simplification & validation ->
Hypothesis-driven science ->
Neuromorphic application

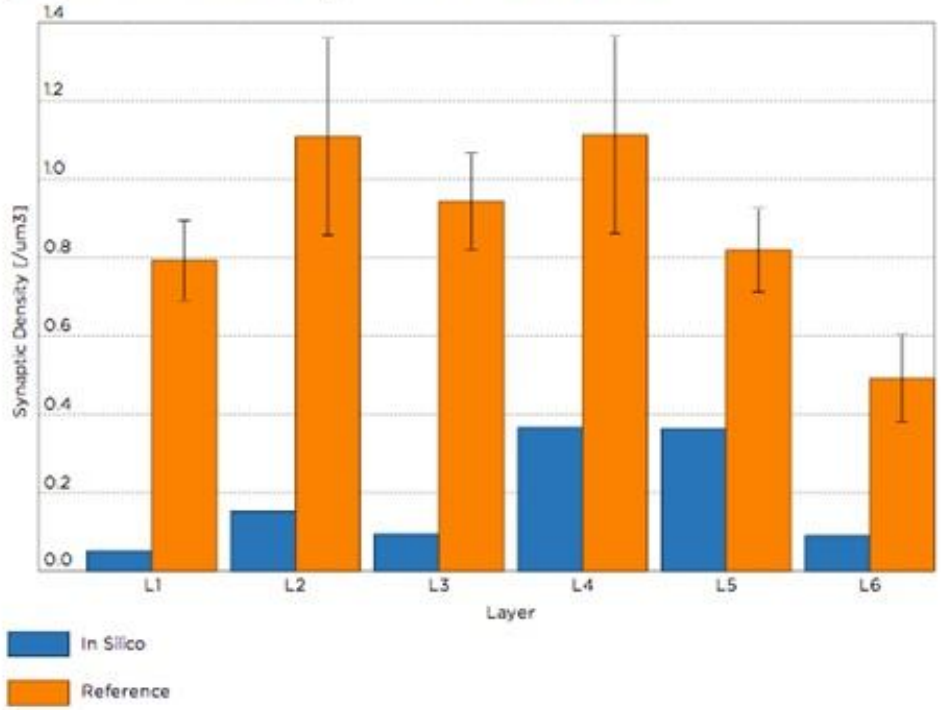
Contrast: Whole community building models

HBP Collaboratory: Whole Community Modeling

- Open data-driven model building tools beyond BBP
- Parameterization and validation data registered in (community or HBP) Neuroinf. platforms
- Transparency of model parameterization
  - Integration with Neuroinformatics
  - Provenance: Auditable by 3rd party
- Automated anatomy and physiology validation suite ala Test-Driven-Development (TDD)
  - User contributed validations
  - against data pulled from Neuroinformatics
  - Whole suite click button runnable by everyone
  - Produces human readible report, statistical tests against data, pass-fail
  - History tracked across releases

“Continuous Integration” for models

Validation Preview



Validation of average synapses density per layer. This validation samples a 50x50x50 um3 cube centered at the center of the central hypercolumn and at the center of each layer. With the help of Farhan's spatial indexer, we can query all the synapses which are located inside the samples. The synapse density of each sample is then compared to data originating from 180 um3 EM reconstructions from DeFelipe's lab. In this biological dataset, the animal model was chosen to be as consistent with the simulated bbp column as possible, i.e. P14 to P16 Wistar rat, primary somatosensory area, hindlimb.

System Properties

name validation_
content
description
created by
created on 2014-10-3
show more

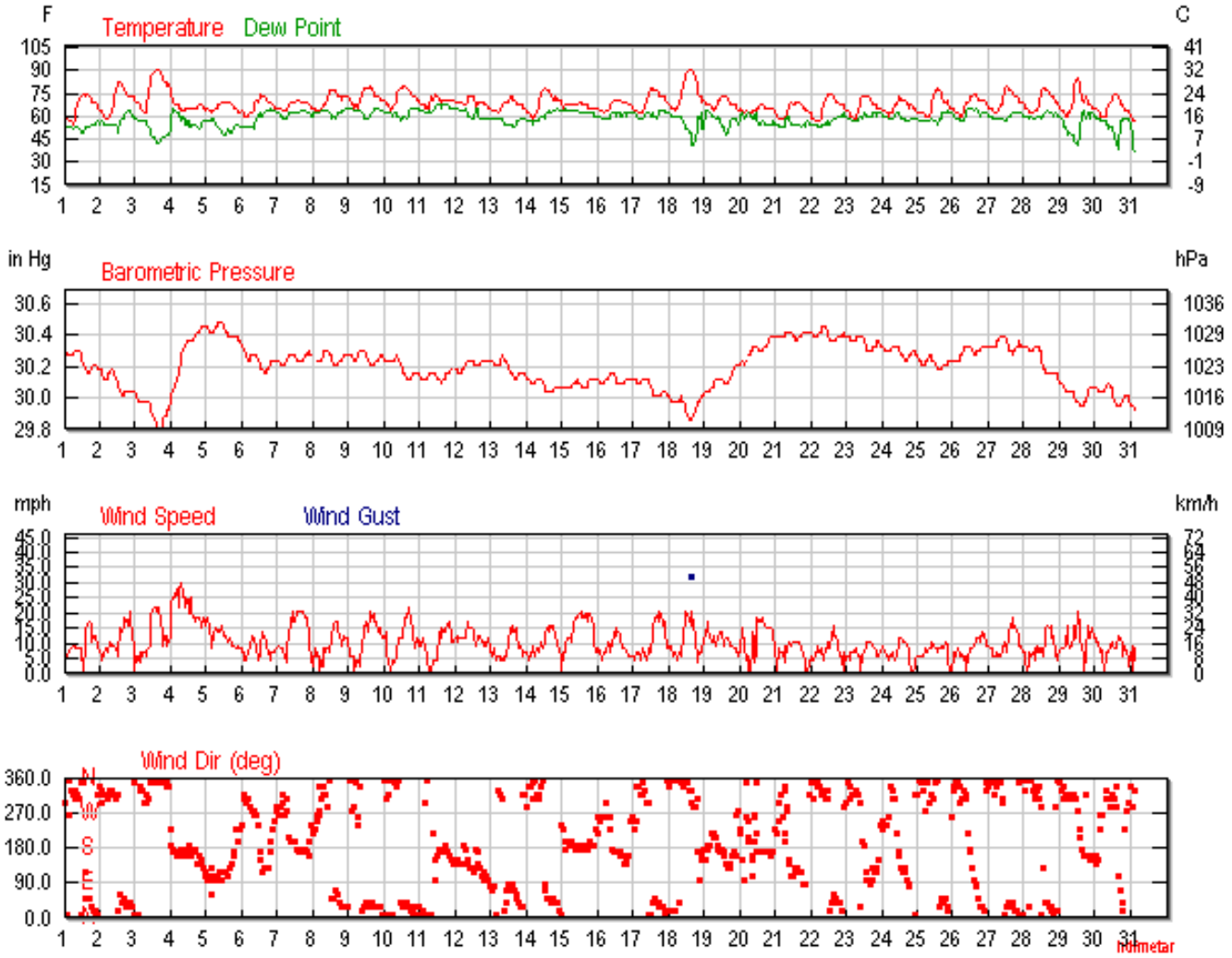
Actions

Validations

Analyses

History tracking of validations …

Models are finicky like the weather …



~6 month release cycle?

- Freeze and release e.g. every 6 months
  - "It's ready" ☞ archival checkpoint
  - End-to-end publication quality build
  - Achievable refinement "chunks"
  - Resource for hypothesis-driven science
  - Automatically generated simplifications
- Cost of release growing
  - As more data is integrated
  - Library of simplifications (and their validations)
  - Growing community contributed validation suite
  - Simulations as validations …

HBP Collaboratory: Whole Community Modeling

- Functionality for regular releases
  - History of validations to track regression
- Community facilities to discuss and plan refinement roadmaps
  - ticket/task system, wikis, agile estimation tools, a discussion forum, comment streams
- Principle-based simplification
  - >same quality metrics as reference model
  - assess impact of simplification.
- Loss-less export of simplified models to neuromorphic
  - Compatible representation, e.g. PyNN.

Level of detail: A rift in neuroscience

1. Simplify the details
   - minimal model for hypothesis-driven science
   - Adhoc simplification
   - Minimal for which question?

vs

2. Consider all known
   - data-driven is data-ready
   - Hypothesis-free integration of facts
   - Algorithms fill in gaps from sparse data
   - Fewer **free** parameters!
   - Avoid wasting time hand tuning parameters for a given model “island”

Level of detail - False Dichotomy

- Integrate new data in models @ level of data
  - *Data-driven is data-ready*
  - Algorithms fill in gaps from sparse data
  - Fewer **free** parameters!
  - Avoid wasting time hand tuning parameters for a given "hypothesis island"
- Necessary but not sufficient:
  - Automated & principled & repeatable & quantifiable simplification
  - … of data-driven reference
  - … to minimal model for given hypothesis

$$f(x) = f(a) + f'(a)(x-a) + \frac{f''(a)}{2!}(x-a)^2 + \frac{f^{(3)}(a)}{3!}(x-a)^3 + \ldots + \frac{f^{(n)}(a)}{n!}(x-a)^n + \ldots.$$

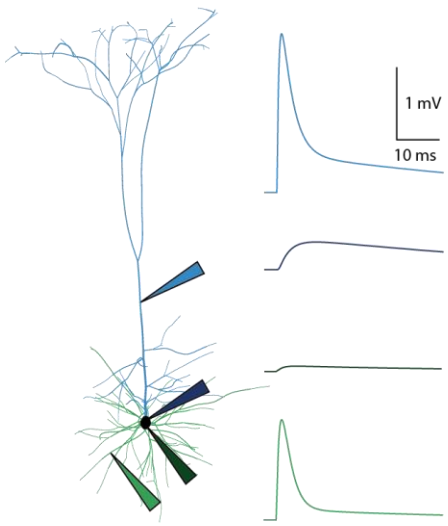
We know alot, but understand very little …

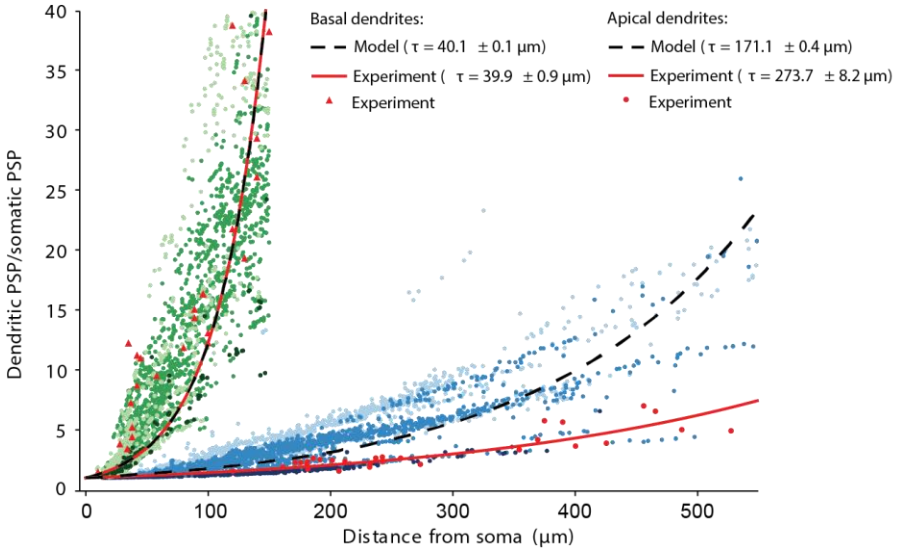
Take best of both worlds …

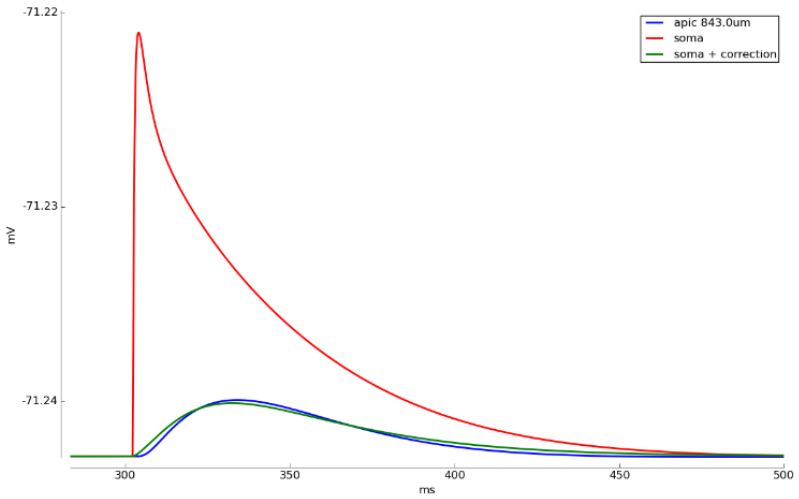
Road to achieve community convergence?

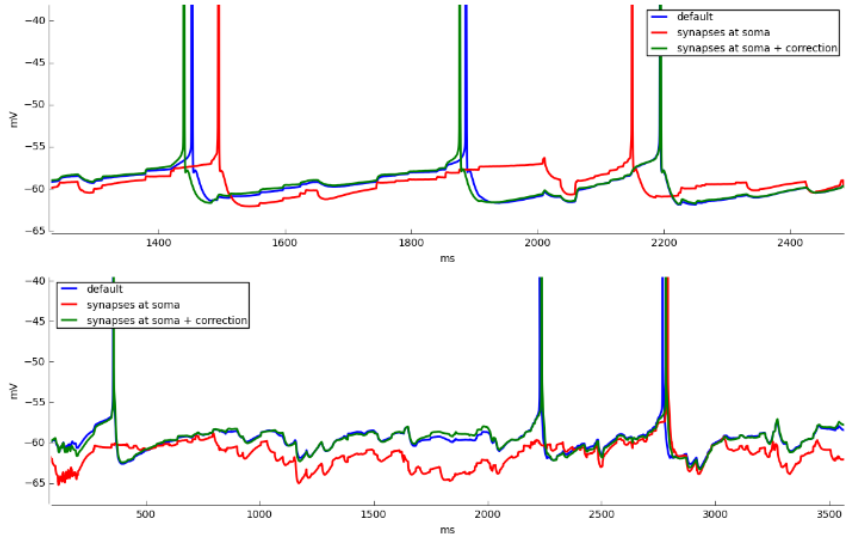
- **Data-driven is data-ready -> resource**
- Latest biological facts taken into account at regular release intervals
- Growing automated validation test suite
- Hypothesis-driven **quantitative automated reproducible simplification**
- Families of simplified models (I&F, mean-field, simplified morphology, …) are generated automatically from release

Simplification example: Collapsing synapses onto the soma (C. Roessert)







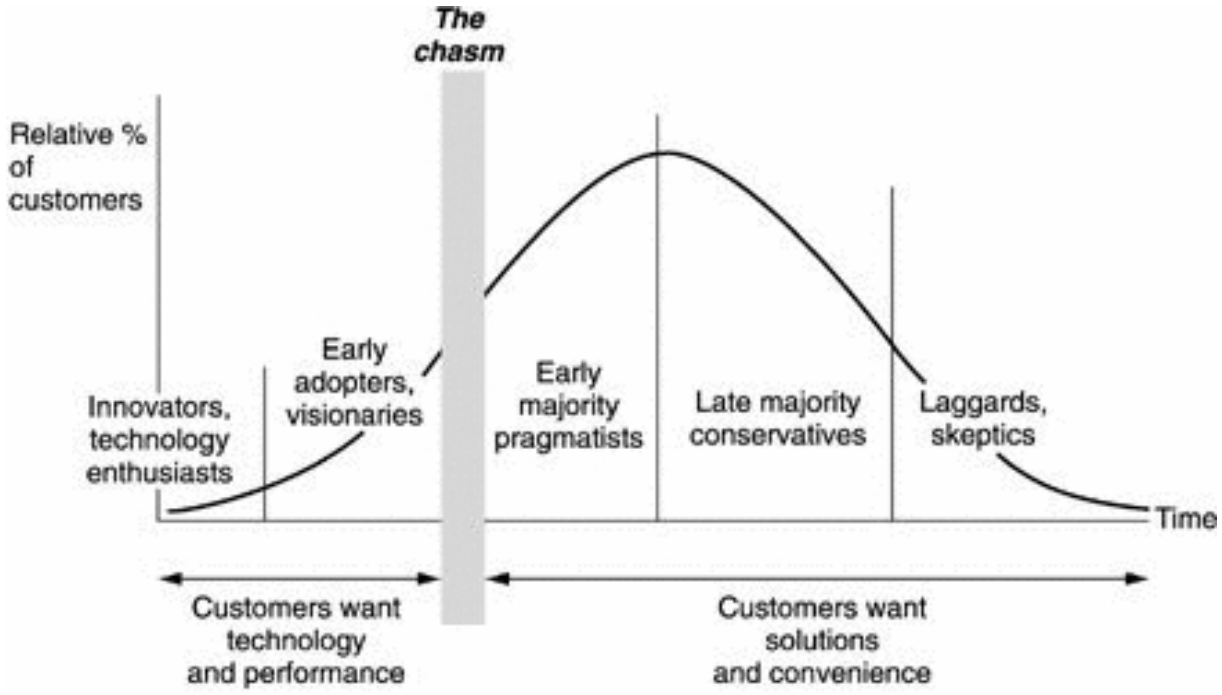


Working with HBP partners to fit point-neuron models suitable for NEST

(Circuit -> NMC portal; example simplification -> github)

Slide credit: Christian Roessert

Community vs Scaffold: The adoption curve



- **We seek early adopters! Establish a badwagon**
- **Work out key problems**
- **Target capabilities towards value proposition**
  - **Prioritize implementing success stories**
  - **Don't focus on convenience now**
- **Early adoptors: Scaffold models … need to be on HBP payroll**
  - **Co-designers of the pipeline: Experimental data -> Neuroninf -> Validated data-driven model**
- **Early majority: Community models … can't be on HBP payroll**
  - **Key use case is: Whole-Community "Experiment to Neuromorphic"**

Summary
HBP Collaboratory: Whole Community Modeling

An end-to-end approach which integrates the whole community, and will have a lasting impact on addressing fragmentation

Driving use case:

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Neuromorphic application

Contrast: Whole community building models

Early adoptors: Scaffold models

- Co-designers of the pipeline: Experimental data -> Neuroninf -> Validated data-driven model
- For specific domains of expertise (Hippocampus, Cerebellum, …)
- On HBP payroll to trail blaze key problems
- **Establish a badwagon to jump on.**
- **Second phase: Drive boot-strapping community process**

Early majority: Community models

- **Leverage Scaffold model workflows & pipelines**
  - Parameterization and validation data registered in (community or HBP) Neuroinf. platforms
  - **Transparency of model parameterization**
- **Benchmark/validation suite with community contribution**
  - Quantitative history
  - **Feedback on regression due to refinement**
  - **Low-barrier for community to become stakeholder**
- Community facilities to coordinate roadmaps
- **Support community use-cases:**
  - Portal: Simulation launch to HPC infra, collab. Analysis
  - **Simplification & export**
  - **Success stories drive adoption**

Acknowledgments

The BBP team

Human Brain Project

FET FLAGSHIPS

European Commission

Hippocamp Participants

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Blue Brain Project

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Data-driven reconstruction of brain models

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Felix Schürmann

Brain Simulation Platform: integration and operations

Henry Markram
Jeffrey Muller

Brain Simulation Platform: user support and community building

Felix Schürmann

WP6.1
WP6.2
WP6.5
WP6.7
WP6.6

Brain simulation engines

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Brain Simulation Platform: scientific coordination

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Molecular dynamics simulation

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WP6.3
WP6.4

Initial brain models

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Eilif Muller
Egidio D'Angelo
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BBP Platform Team









European Commission

Human Brain Project

HBP Platform Teams

- SP5 – Neuroinformatics
- SP6 – Brain Simulation
- SP7 – HPC
- SP8 - Medical Informatics
- SP9 – Neuromorphic
- SP10 - Neurorobotics