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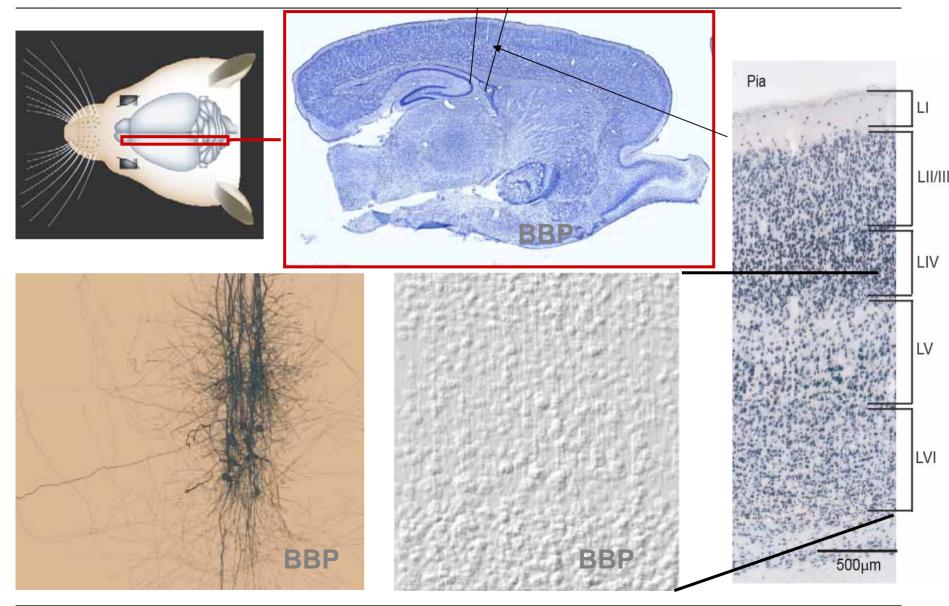


Reverse-Engineering the Brain



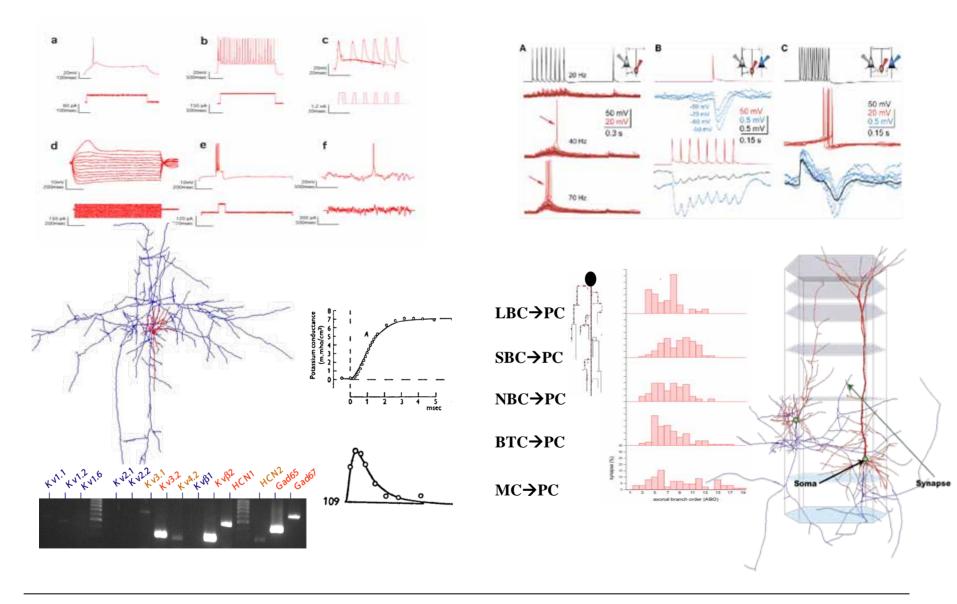


The Electrophysiologist's View



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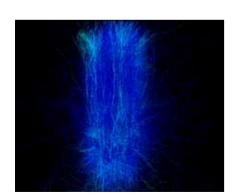




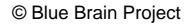
Create a faithful "in silico" replica at cellular level of a neocortical column of a young rat by the means of:

- reverse engineering the biology components
- forward constructing functional mathematical models





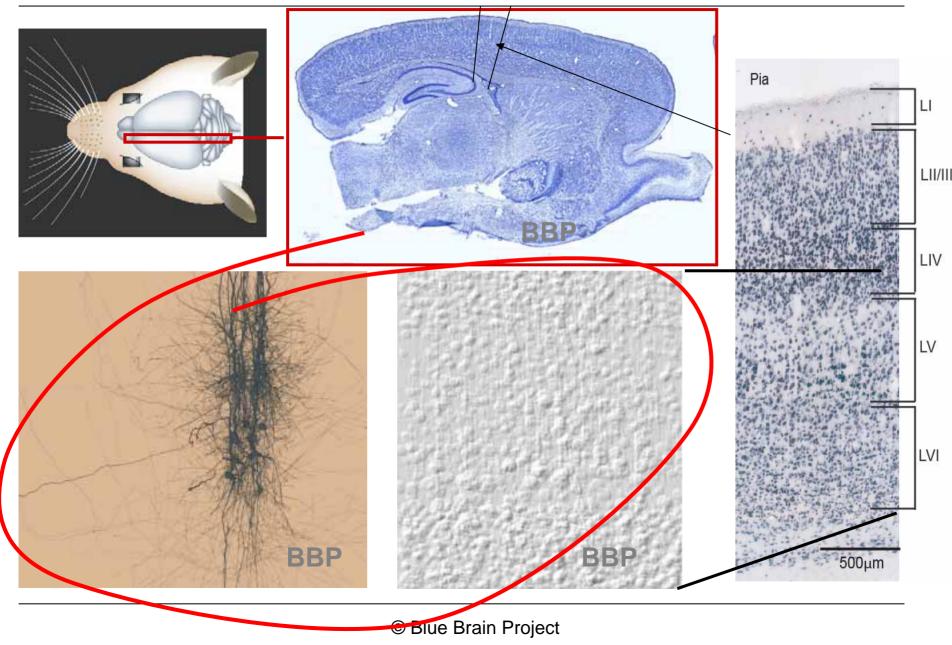
- Building 10,000 morphologically complex neurons
- **Constructing** a circuit with 30,000,000 dynamic synapses
- Simulating the column close to real-time





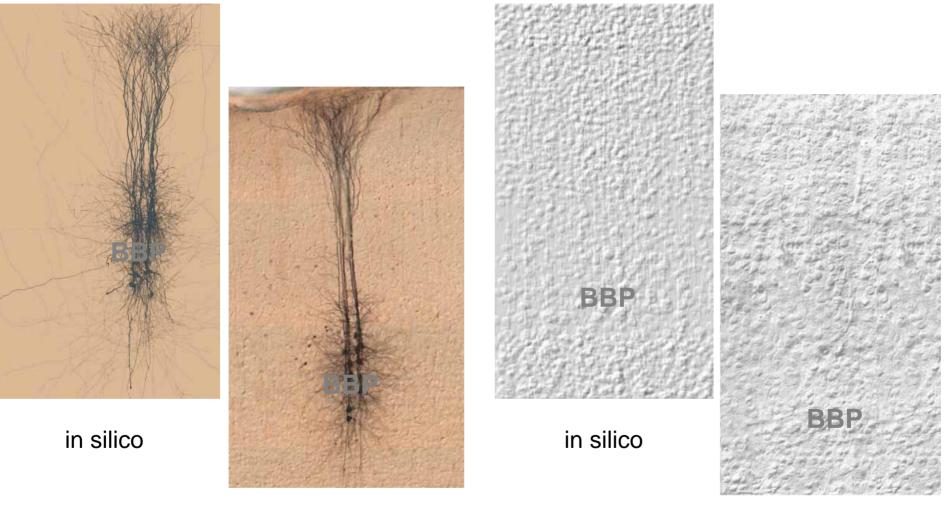


The Electrocphysiologist's View - Revisited





BBP Phase I: « in vitro » vs. « in silico »

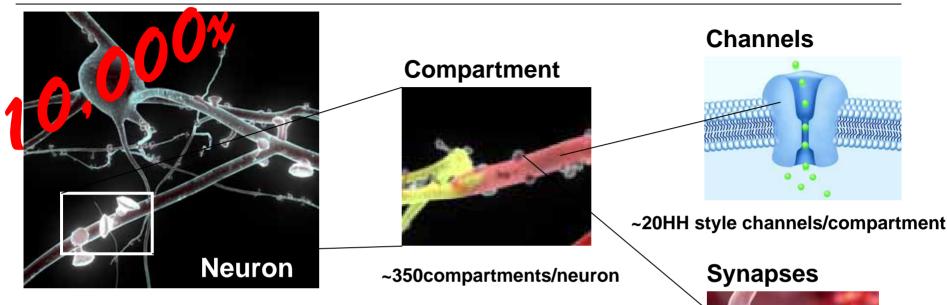


in vitro

in vitro



Level of Detail



A Rat's Neocortical Column:

- ~1mm^3
- 6 layers
- > 50 morphological classes
- ~340 morpho-electrical types
- ~200 types of ion channels
- 10,000 neurons
- 18 types of synapses
- 30,000,000 synapses

IT Challenge:

- 3,500,000 compartments
 - passive (cable, Gauss Elimination)
 - active HH style channels
- 30,000,000 synapses dynamic

- 2
- ~3,000/neuron
- \rightarrow reporting 1 value/compartment \rightarrow 140GB/biol sec



Usage of BG/L in the BBP



Dedicated 4 rack BG/L @ EPFL with 8192 processors, 2TB of distributed memory, 22.4 TFlop (peak)

 \rightarrow Used throughout all parts of the project

 \rightarrow Allows iteration of complete process within a week

- Building: Run evolutionary algorithms for fitting of thousands of single cell models to data

typical job size: 2048 procs

S. Druckmann et al., A Novel Multiple Objective Optimization Framework for Constraining Conductance-Based Neuron Models by Experimental Data, Frontiers in Neuroscience 2007

 Constructing: Run dedicated algorithm to establish connectivity between cells

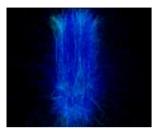
typical job size: 8000 procs

J. Kozloski et al., *Identifying, tabulating, and analyzing contacts between branched neuron morphologies,* IBM Journal for Research and Development, Issue 52, Number 1/2, 2008

• Simulating: Run simulation of cell networks typical job size: 8192 procs

M. Hines et al., *Fully Implicit Parallel Simulations of Single Neurons*. Journal of Computational Neuroscience, accepted





20,000X

A Rat's Neocortical Column

10,000 (10^4) neurons 30,000,000 (10^7) synapses

~1 neuron/core \rightarrow 1:10-100 time penalty



~10^4 cores

~10^13 Flops (~10TeraFlops)

~10^12 Bytes RAM (TeraBytes)



A Rat's Brain

200,000,000 (10^8) neurons 10^11 synapses

PetaScale HPC

~10^5-10^6 cores ~10^15 Flops (PetaFlops) ~10^14 Bytes RAM (~100TB)



~500 neurons/core \rightarrow 1:5,000 - 50,000 time penalty



A Human's Brain

10^11 neurons 10^14-10^15 synapses **ExaScale HPC**

~10^18 Flops (ExaFlops) ~10^17 Bytes RAM (~100PB)



10^18 = ExaFlops	1 sec biological time = 1/2 day computation → unique brain research facility
10^21 = ZettaFlops	1 sec biological time = few seconds computation → brain-scale plasticity simulations → desk-side brain simulations
10^23 = 100 ZettaFlops	1 year biological time = 1 day computation → brain-scale developmental simulations → personalized models

But all this scaling is based on electrical models...

- Glial cells
- Vasculature
- Ligand-gated ion channels
- Second-messengers
- Receptors

- Organelles
- Bio-chemical pathways/cascades
- Proteins, Protein-interactions
- Genes

Hodgkin-Huxley \rightarrow Langevin Description \rightarrow Fokker-Planck \rightarrow Master Equation \rightarrow Ensembles of stochastic channels \rightarrow Reaction/Diffusion Models \rightarrow ...

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- The general recommendations from biology are clear
 - \rightarrow go analog (energy)
 - \rightarrow go local persistent memory (energy)
 - \rightarrow go sparse activity (energy density)
 - \rightarrow go 3D (integration, connectivity)
 - \rightarrow go distributed encoding (robustness)
- Along the way we will be able to extract principles for specific applications

→generic building principles (structure, composition, connectivity)

 \rightarrow specialization rules (circuit rewiring)

→learning rules (local learning, homeostatic principles)

 We will have to go quite some way with computers that at least *look* like digital Von-Neumann machines to reverseengineer biology and consolidate our knowledge in a model

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