Simulation Codes in the Human Brain Project

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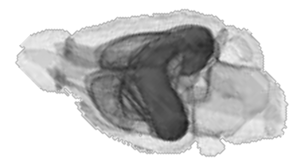
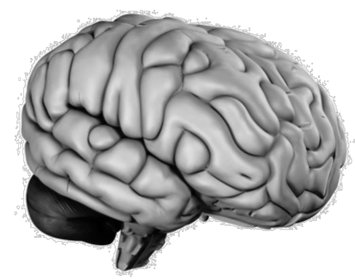
Some Numbers on the Brain

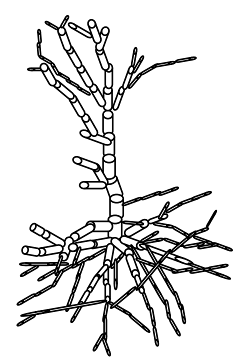
- Rat brain*
  - ~200M ($2x10^8$) nerve cells
  - ~130M glial cells
  - ~O(10^{12}) synapses



- Human brain**
  - ~90B (10^{11}) nerve cells
  - ~90B glial cells
  - ~O(10^{15}) synapses

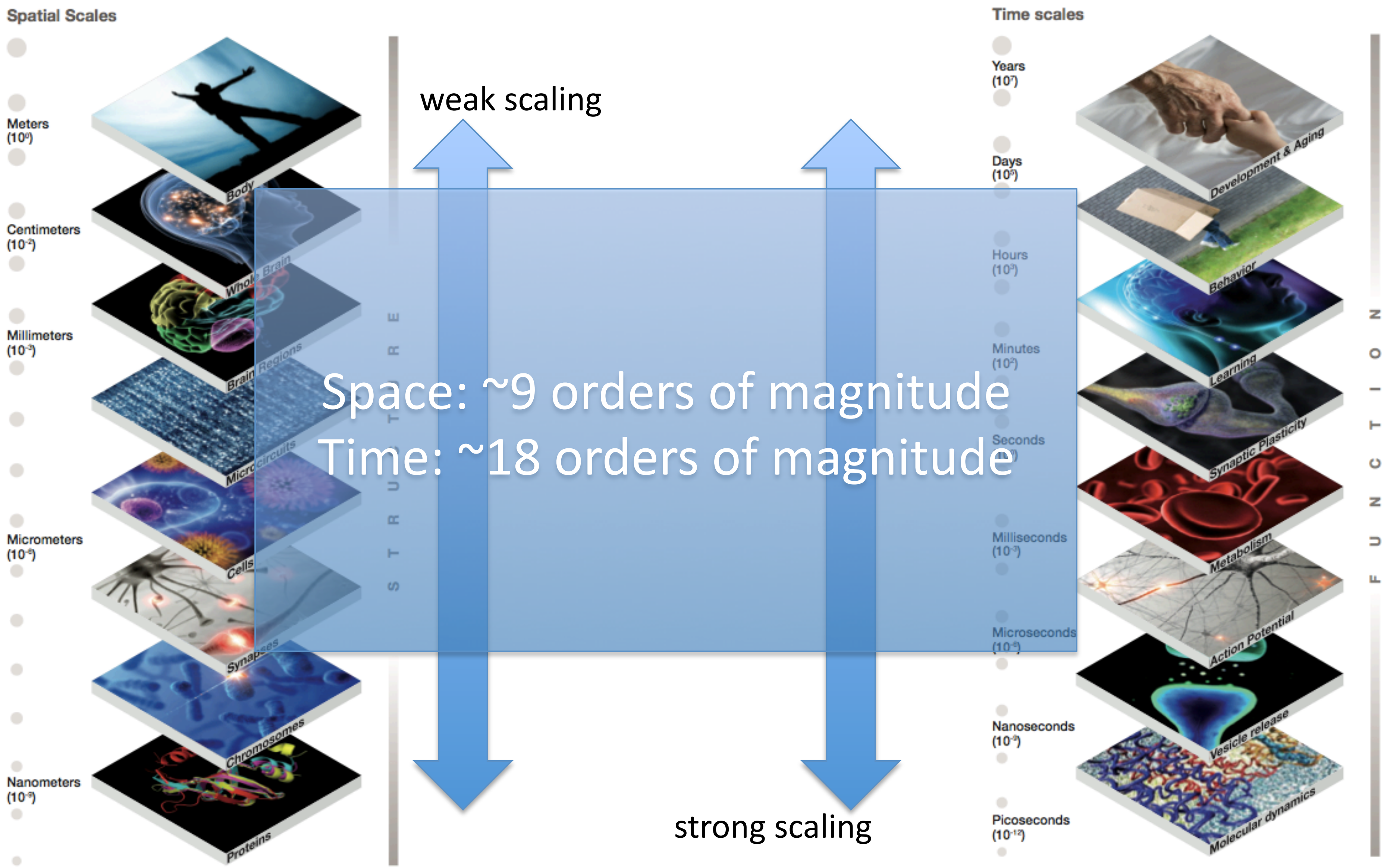


- Each cell – a universe***
  - ~O(10B) proteins/nerve cell

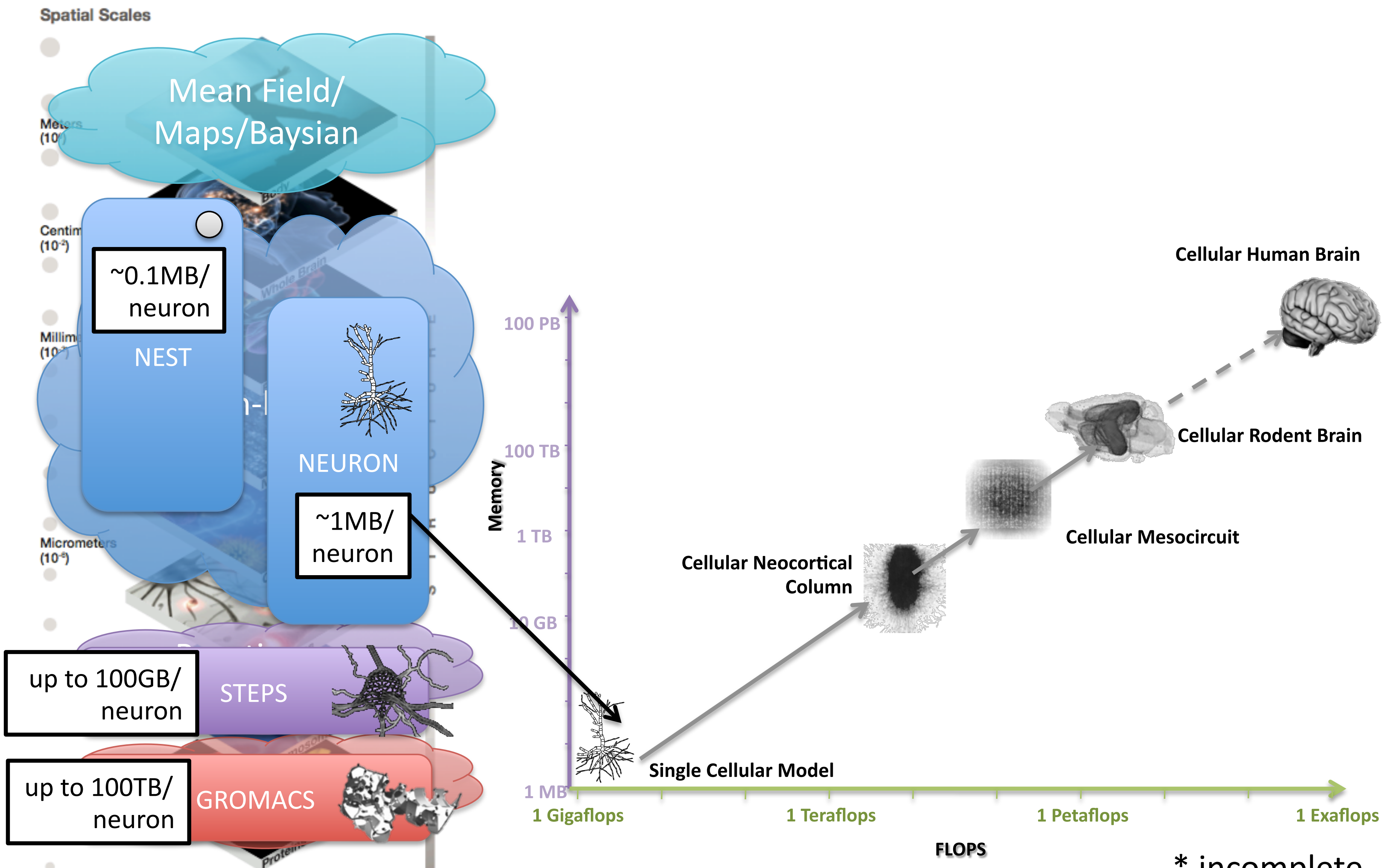


* Herculano-Houzel et al. 2006; **Herculano-Houzel 2009; *** Sims et al. 2007

Relevant Scales



Qualitative Simulator Landscape*



* incomplete

Simulation Codes in the HBP Ramp-up Phase

nest:: simulated()

http://www.nest-initiative.org/
Markus Diesmann, Hans-Ekkehard Plesser, Marc-Oliver Gewaltig
ODEs; loose (global) coupling

NEURON
for empirically-based simulations of neurons and networks of neurons

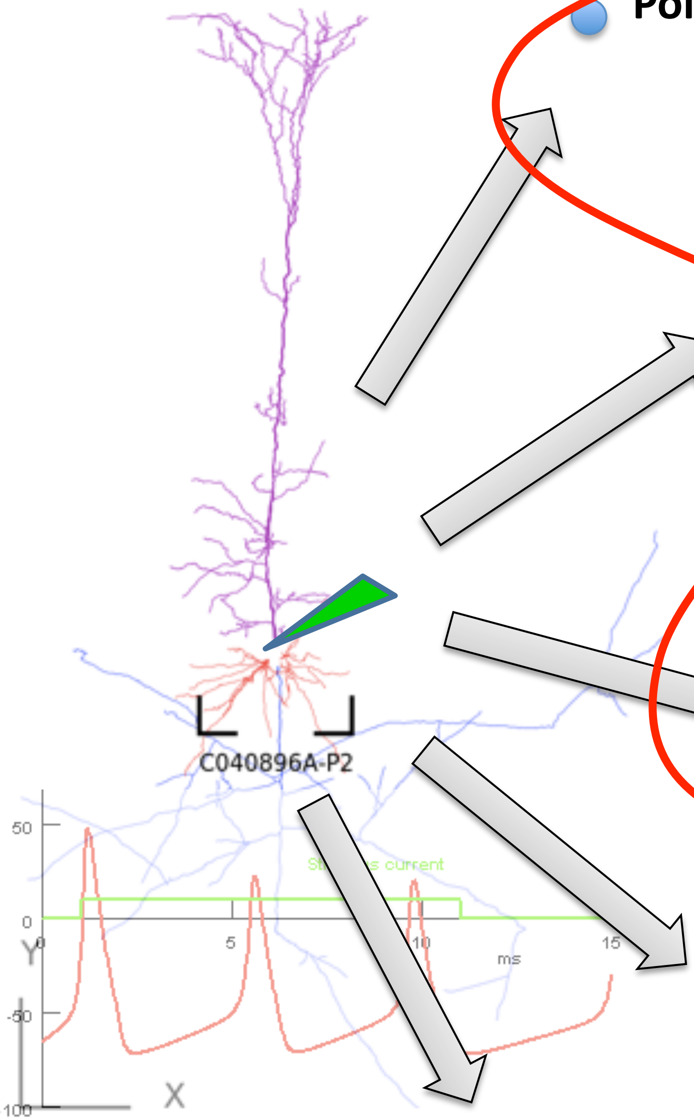
http://www.neuron.yale.edu
Michael Hines
ODEs, LinAlg; loose(global)/tight(specific) coupling
`

STEPS
STochastic Engine for Pathway Simulation

http://www.nest-initiative.org/
Erik De Schutter
Gillespie SSA, diffusion via NN coupling

→ All are open source
→ All have a scripting interface (python) for model setup
→ All have C/C++ compute core
→ All have their community mission and roadmap and HBP complements

In HBP: Anchored to the Neuron

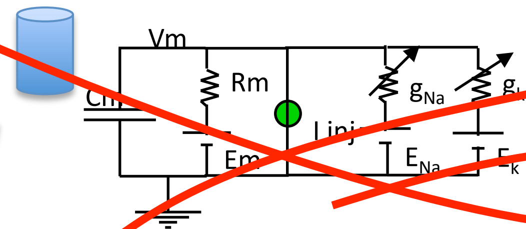


Point neuron, e.g. Izhikevich

$$v' = 0.04v^2 + 5v + 140 - u + I$$
$$u' = a(bv - u)$$

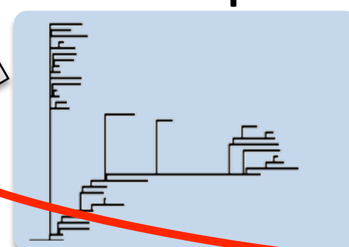
if $v = 30$ mV,
then $v \leftarrow c,\quad u \leftarrow u + d$

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



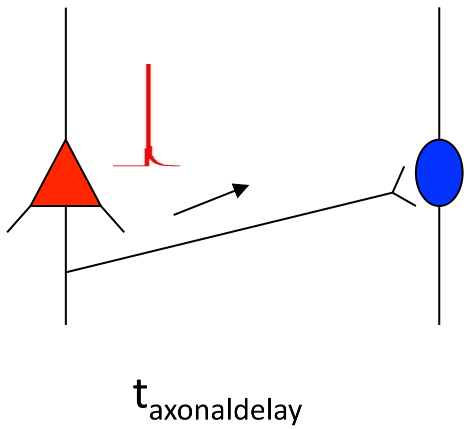
$$\frac{C_m dV_m}{dt} = \frac{E_m - V_m}{R_m} + I_{channels} + \frac{2(V_{m_{i+1}} - V_{m_i})}{R_{a_{i+1}} + R_a} + \frac{2(V_{m_{i-1}} - V_{m_i})}{R_{a_{i-1}} + R_a}$$

Reaction-Diffusion model

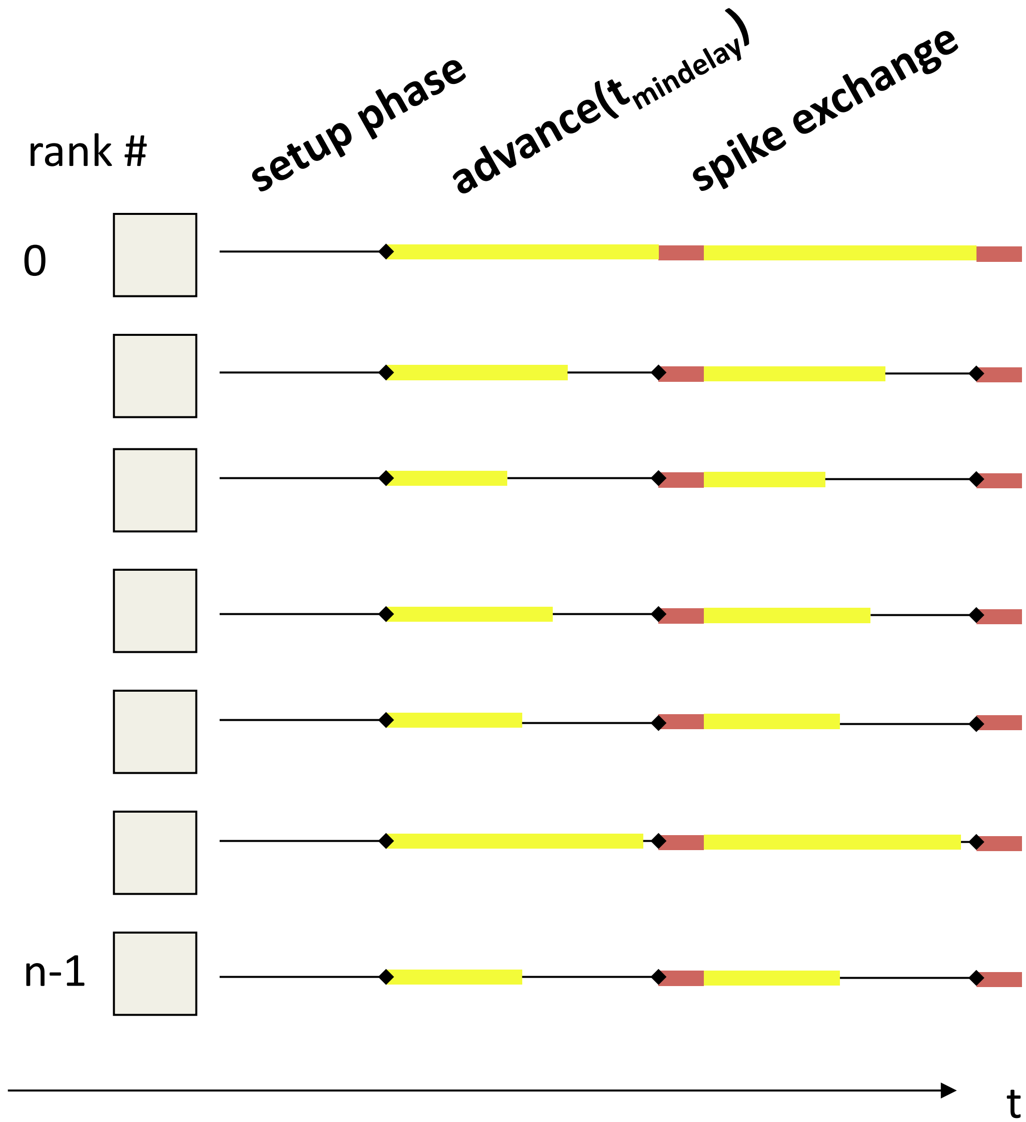
$$\dot{p}(\mathbf{x};t) = -p(\mathbf{x};t)\sum_{\mu=1}^{M} a_\mu(\mathbf{x}) + \sum_{\mu=1}^{M} p(\mathbf{x}-s_\mu;t)\,a_\mu(\mathbf{x}-s_\mu)$$

Coarse-Graining/MD

Useful Properties of Neuron-based Abstraction



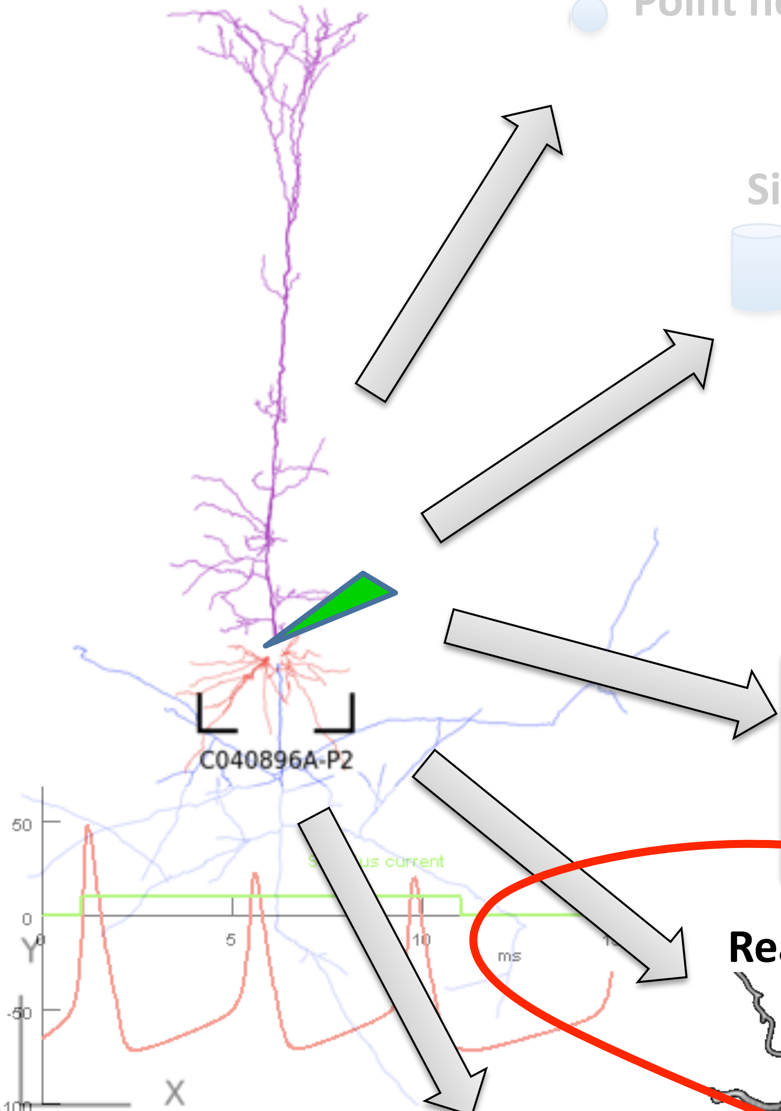
No spike evoked at time *t* can arrive at any postsynaptic cell sooner than $t+\min\{t_{axonaldelay}\}$



Initial Development Goals for NEST, NEURON

- Interactive Supercomputing
  - Use of dense memory; high memory bandwidth
  - Malleability (dynamical runtime)
  - Interaction with analysis and visualization frameworks
- Scalability (Communication, Memory!)
  - To support full brain scale models
  - Reduce memory footprint
- Software Engineering
  - Test driven development; Agile teams
  - Software lifecycle model
    - → NEST has good practice
    - → NEURON has a lot of legacy → coreNEURON
- Efficiency
  - Mini-Apps
  - Accelerator support while maintaining flexibility
    - → Abstraction of SIMD

Subcellular Details



Point neuron, e.g. Izhikevich

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Single Compartment HH model

$$
\begin{aligned}
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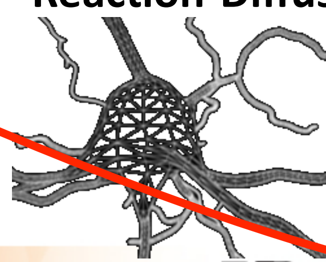
\frac{dh}{dt} &= \alpha_h(V_m)(1-h) - \beta_h(V_m)h \\
I_{channel} &= m^n h g_{channel}(V_m - E_{channel})
\end{aligned}
$$

Multi Compartment HH model

$$
\frac{C_m dV_m}{dt} = \frac{E_m - V_m}{R_m} + I_{channels} + \frac{2(V_{m_{i+1}} - V_{m_i})}{R_{a_{i+1}} + R_a} + \frac{2(V_{m_{i-1}} - V_{m_i})}{R_{a_{i-1}} + R_a}
$$

Reaction-Diffusion model

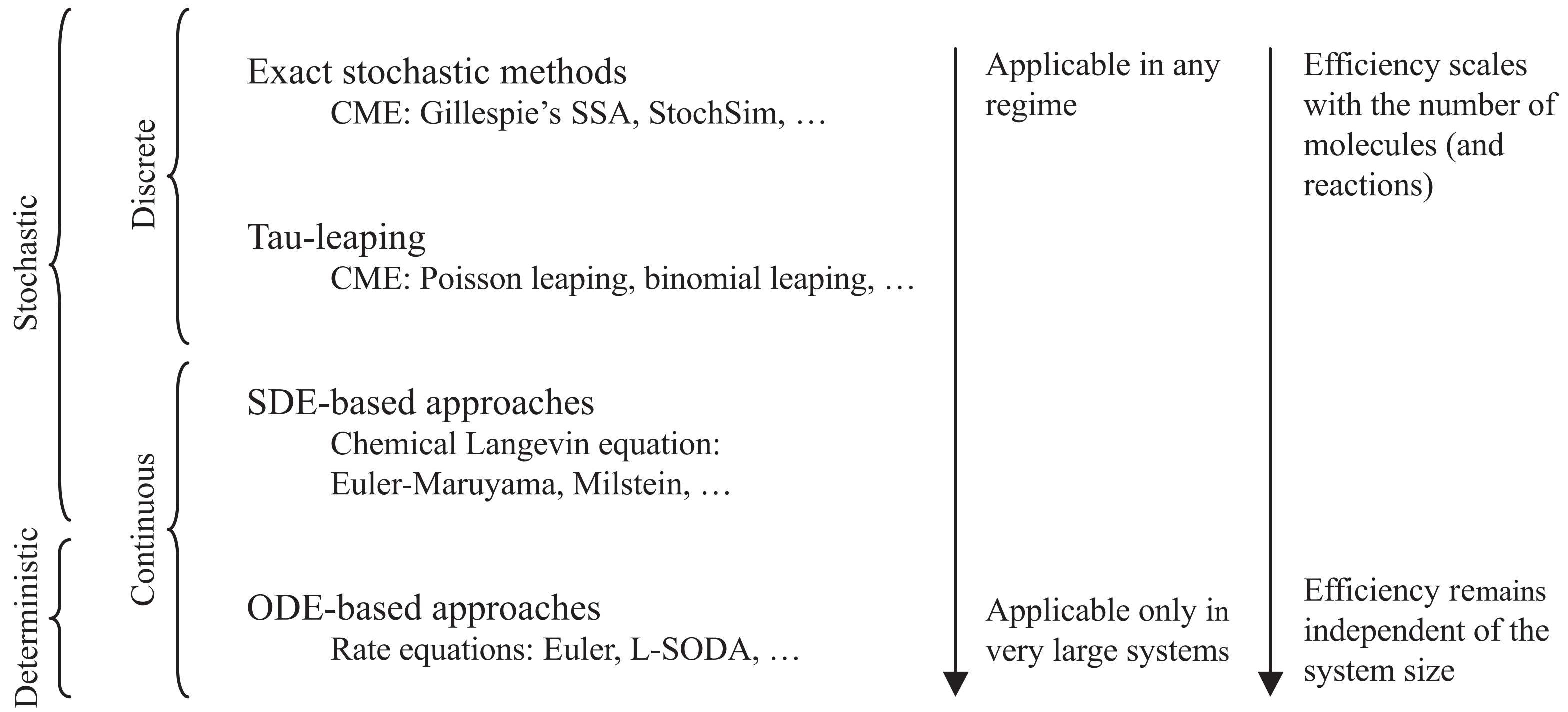


$$
\dot{p}(\mathbf{x};t) = -p(\mathbf{x};t)\sum_{\mu=1}^{M} a_\mu(\mathbf{x}) + \sum_{\mu=1}^{M} p(\mathbf{x}-s_\mu;t)\,a_\mu(\mathbf{x}-s_\mu)
$$

Coarse-Graining/MD

Reaction… and…Diffusion

Reactions



Brownian Motion & Stochastic Diffusion

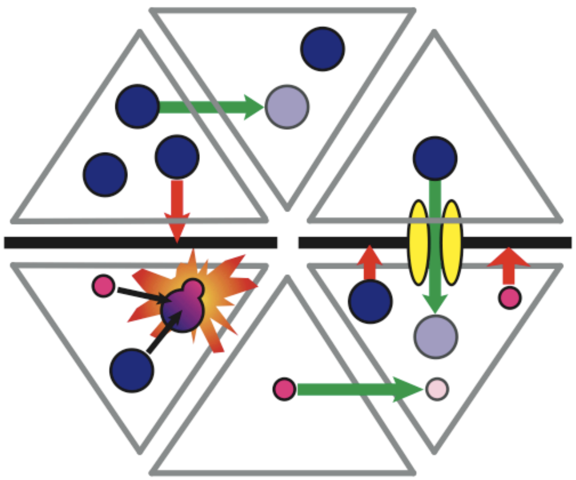
→ General Finite Volume, Finite Element for PDEs
→ Continuous Random Walk (e.g. MCell)
→ Random Walk on discrete lattice
→ Voxel-based methods (e.g. MesoRD, STEPS)

From:
Computational Modeling Methods for Neuroscientists
ed. Erik de Schutter

STEPS Simulator

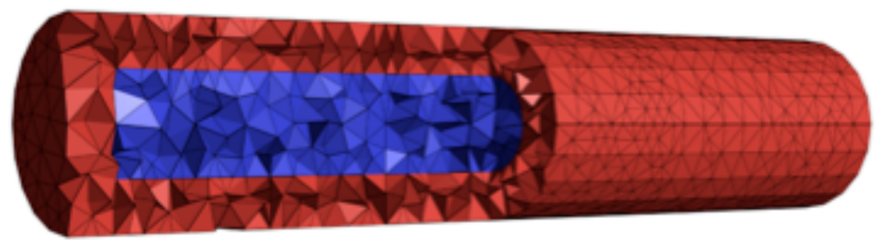
STochastic Engine for Pathway Simulation:

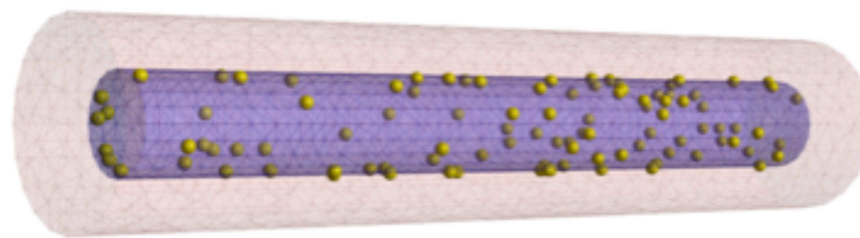
Simulation algorithm



- Each tetrahedron (grey) is a well-mixed volume, in which reactions can occur (Gillespie, 1977).
- Neighbouring tetrahedrons are coupled by diffusive fluxes.
- Triangles (black) act as boundaries and can also embed molecules. These can bind to ligands and transport volume molecules in between tetrahedrons belonging to different compartments.

$$
\begin{aligned}
\frac{d}{dt}\mathrm{Na}_x^+ &= J^x_{\mathrm{leak,Na}} - 3\,J^x_{\mathrm{pump}} + J^x_{\mathrm{stim}}(t)\\
\frac{d}{dt}\mathrm{GLC}_n &= J^{en}_{\mathrm{GLC}} - J^n_{\mathrm{HKPFK}}\\
\frac{d}{dt}\mathrm{GLC}_g &= J^{cg}_{\mathrm{GLC}} + J^{eg}_{\mathrm{GLC}} - J^g_{\mathrm{HKPFK}}\\
\frac{d}{dt}\mathrm{GAP}_x &= 2\,J^x_{\mathrm{HKPFK}} - J^x_{\mathrm{PGK}}\\
\frac{d}{dt}\mathrm{PEP}_x &= J^x_{\mathrm{PGK}} - J^x_{\mathrm{PK}}\\
\frac{d}{dt}\mathrm{PYR}_x &= J^x_{\mathrm{PK}} - J^x_{\mathrm{LDH}} - J^x_{\mathrm{mito,in}}\\
\frac{d}{dt}\mathrm{LAC}_n &= J^n_{\mathrm{LDH}} - J^{ne}_{\mathrm{LAC}}
\end{aligned}
$$





http://steps.sourceforge.net/

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Contacts

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