A Brief Introduction to Computational Neuroscience

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Introduction

- Computational Neuroscience ??
  - What?
  - Why?
- Levels of Modelling
- Single Cell Models
  - Morphologically Detailed Models
  - Abstract Models (Point Neurons)
  - Comparison Between the Modelling Approaches
- Network Models
- Demonstrations: Single Neuron Model, Openworm
- Simulators and Other Resources

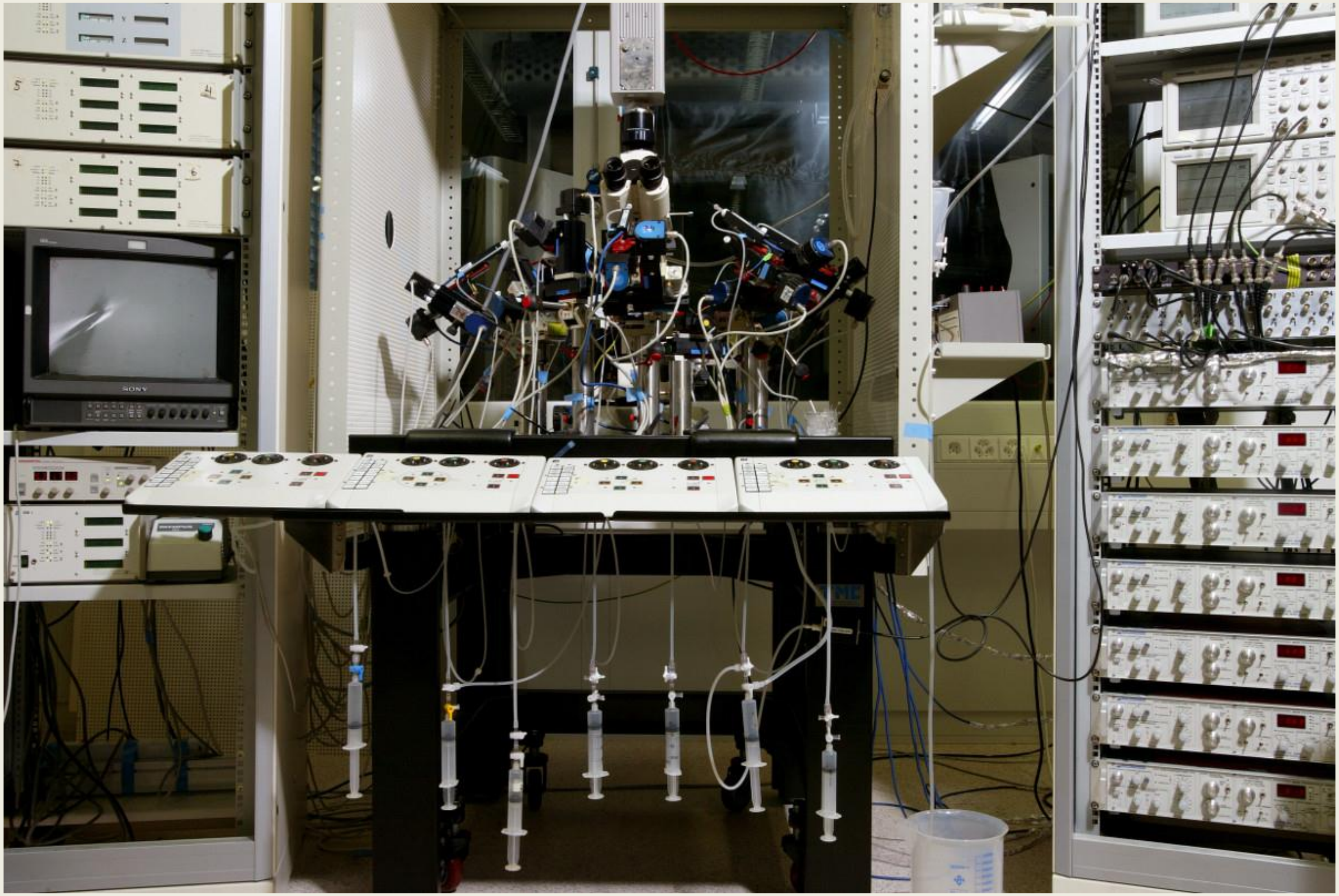
Computational Neuroscience

- Understanding nervous system using computation
- Interdisciplinary field:
  - **Computer Science**: machine learning, neural networks
  - **Neuroscience**: cognitive neuroscience, psychology
  - **Electrical Engineering**
  - **Maths**, **Physics** and more

- How it helps predict things?
  - Understanding common neurological conditions like Addiction, Schizophrenia, etc.
  - Promoting targeted drug development
  - Normal physiology of body

- Other Contributions of the field:
  - Neuromorphic Engineering: SpiNNaker (**Spi**king **N**eural **N**etwork **A**rchitecture) and SyNAPSE (**Sy**stems of **N**euromorphic **A**daptive **P**lastic **S**calable **E**lectronics)
  - Neurorobotics: Simulated neural networks in robots

Experiments are difficult !

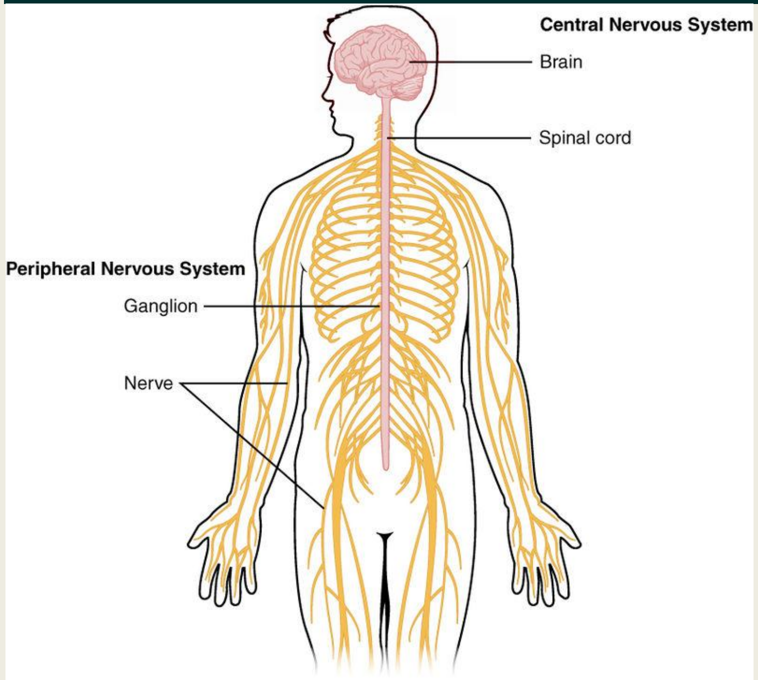


Patch Clamp Apparatus for Recording Single Channel Currents

Source: bbp.epfl.ch

Levels of Modelling

Levels of Modelling

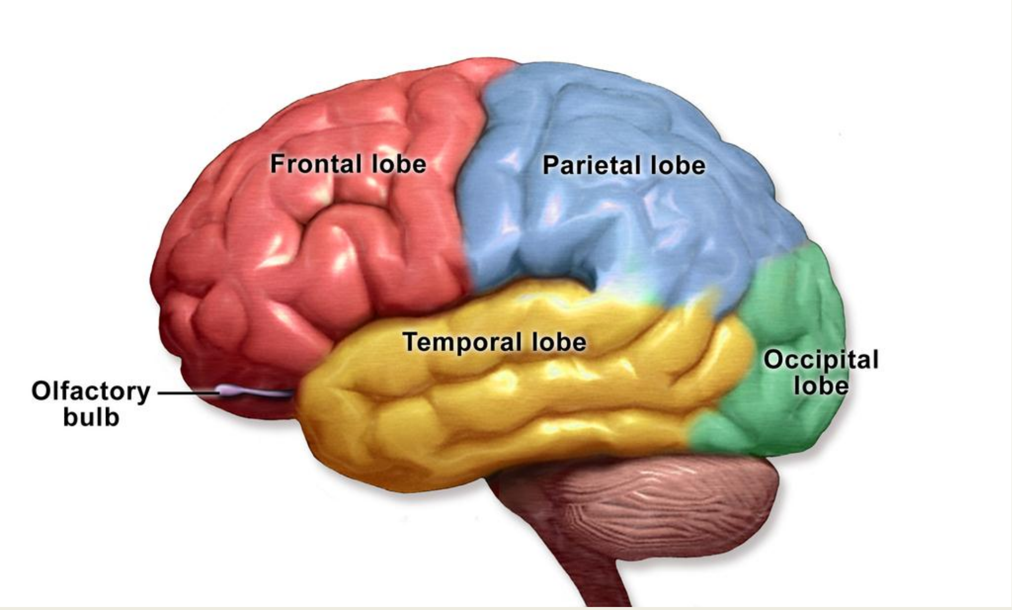


Nervous System

1 m

Brain

10 cm

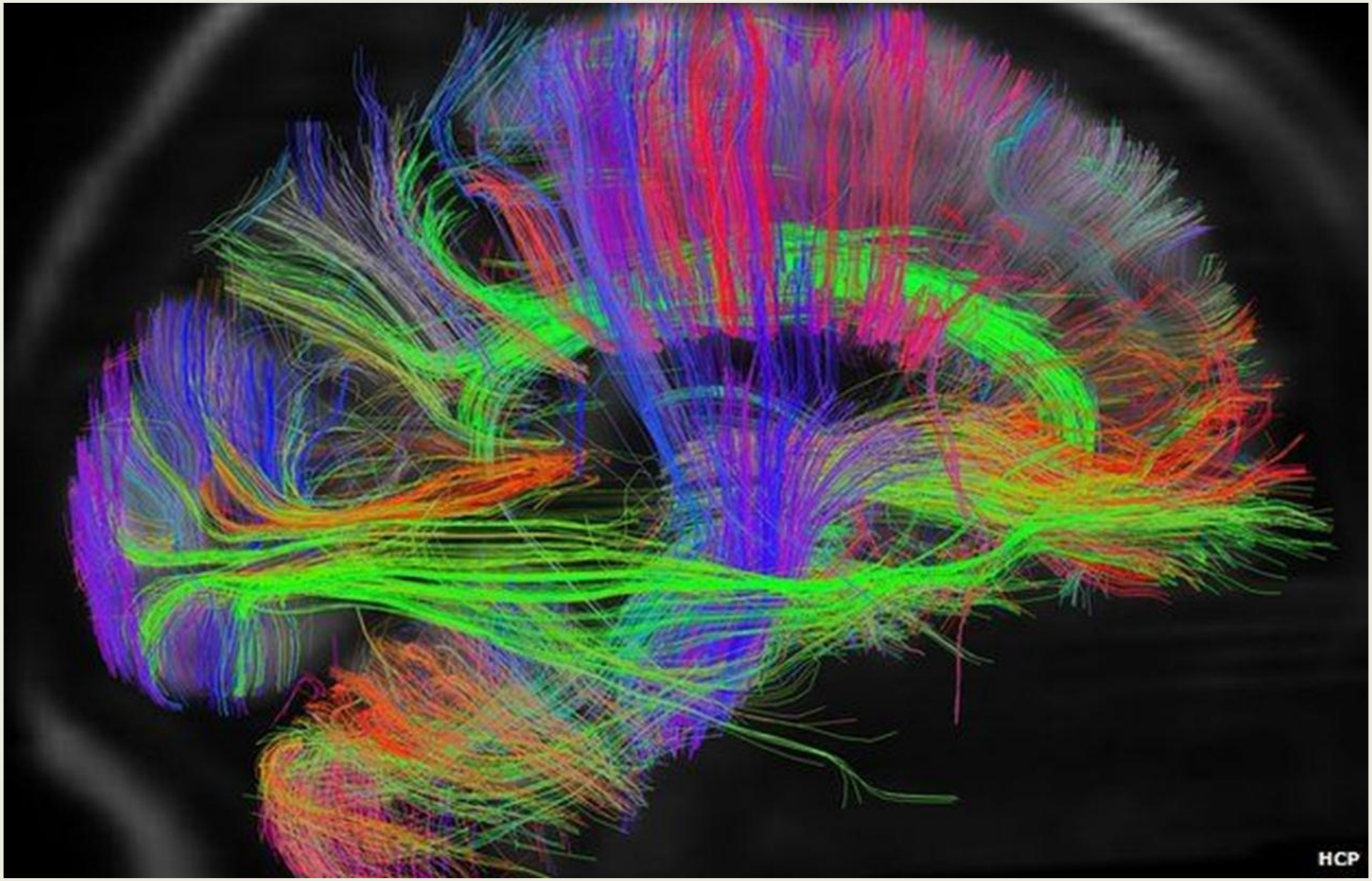


Source: Wikimedia Commons

Levels of Modelling

1 cm

Neural networks



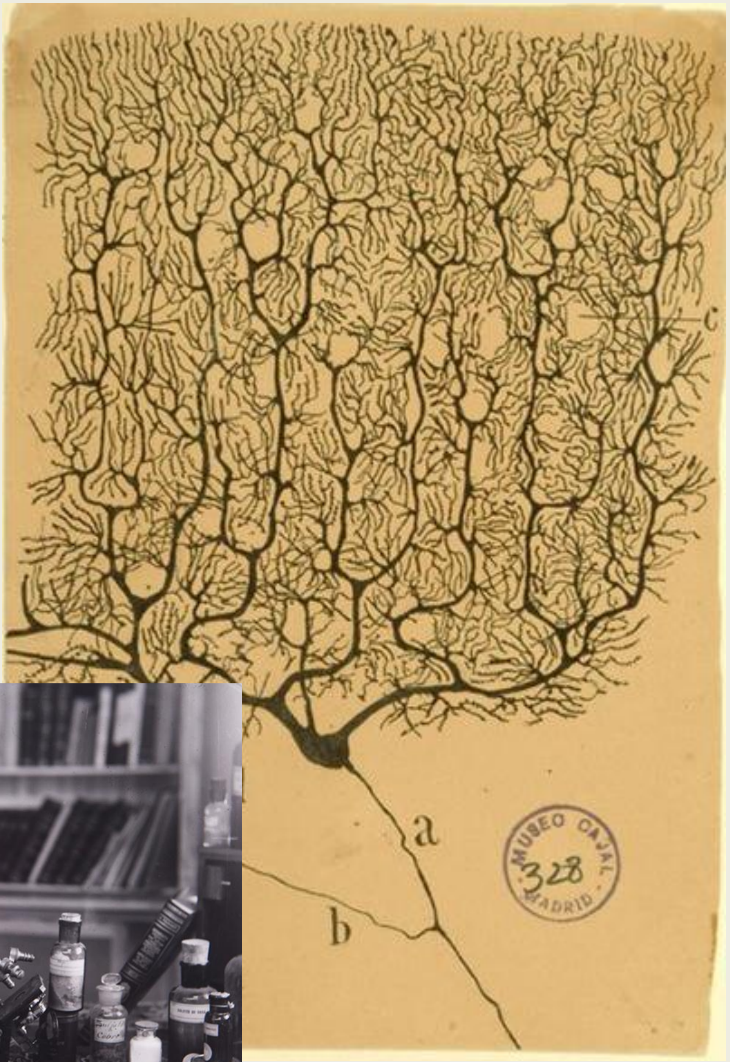
Mapping the human connectome: Human Connectome Project

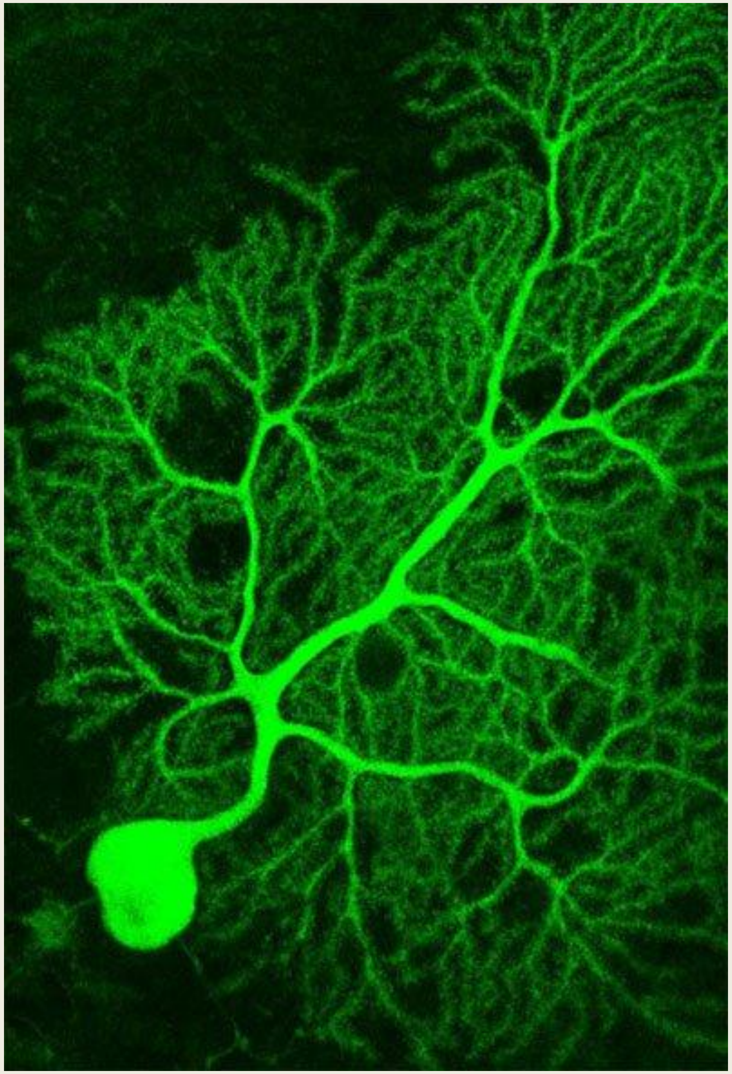
Source: bbc.com/news/science-environment-21487016

Levels of Modelling

100 µm

Neurons



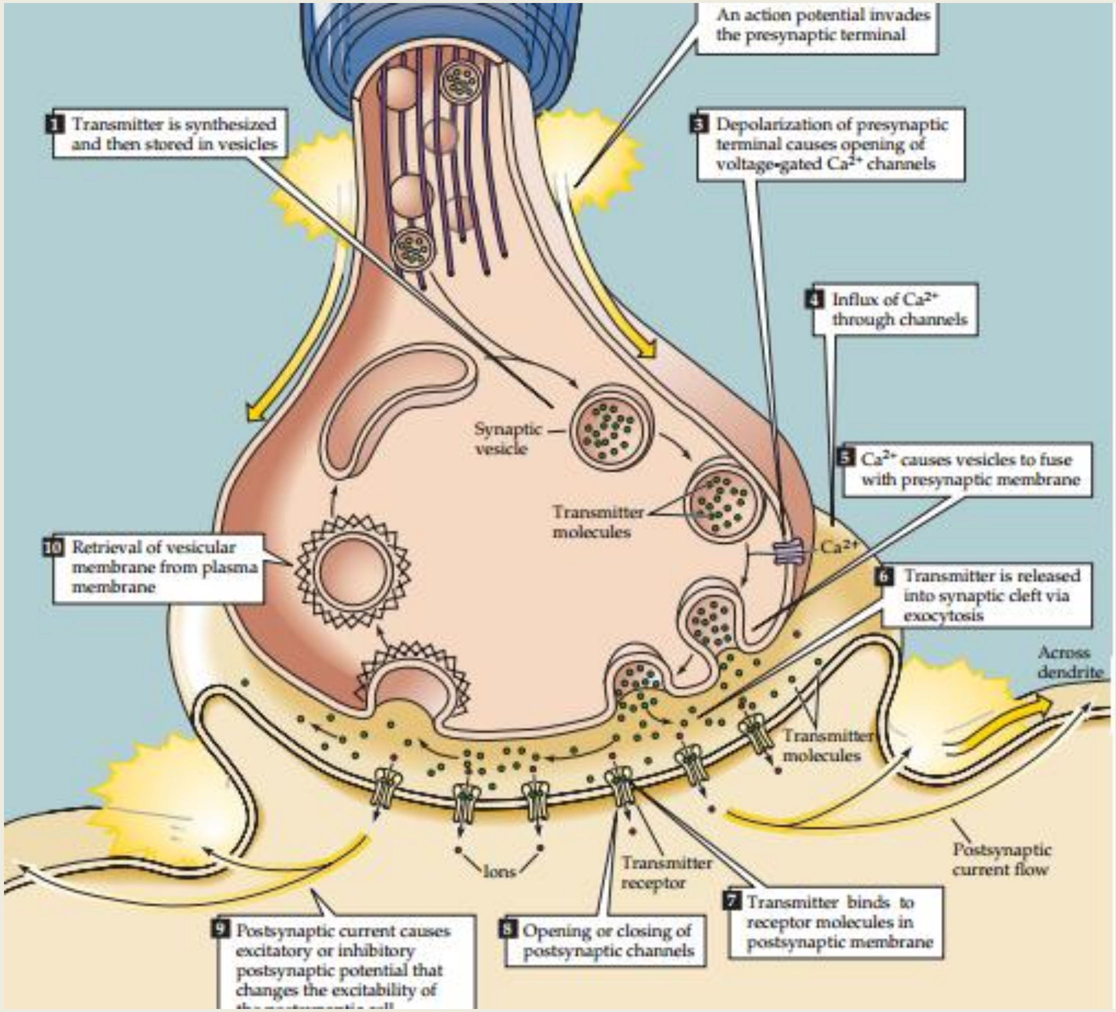


Source: robotspacebrain.com/santiago-ramon-y-cajal/

Levels of Modelling

1 µm

Synapses

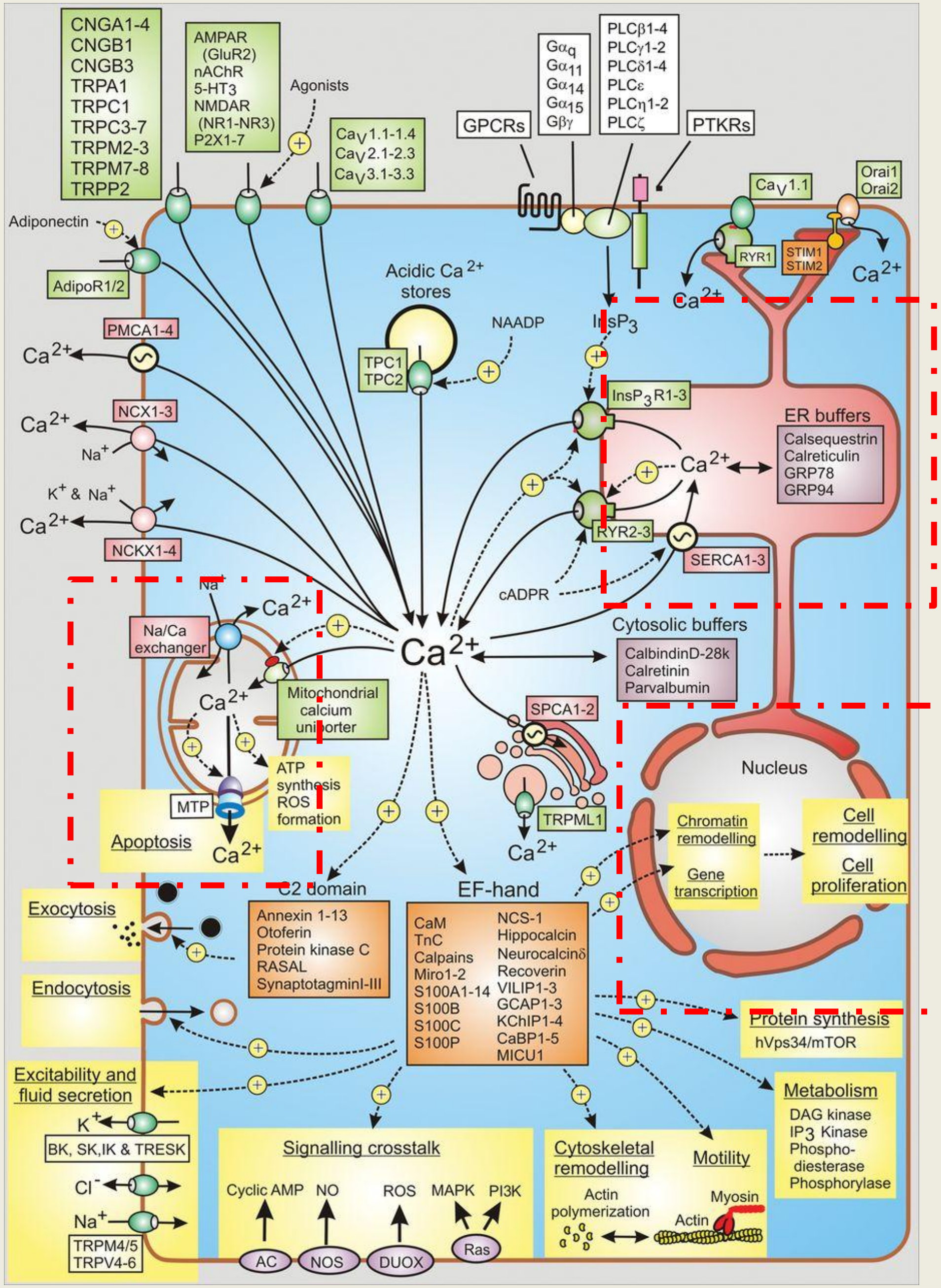


Source: EE 746 Course material

Levels of Modelling

1 nm — Signalling Pathways

1 pm — Ion Channels



Source: Berridge, M.J. (2012)

Levels of Modelling

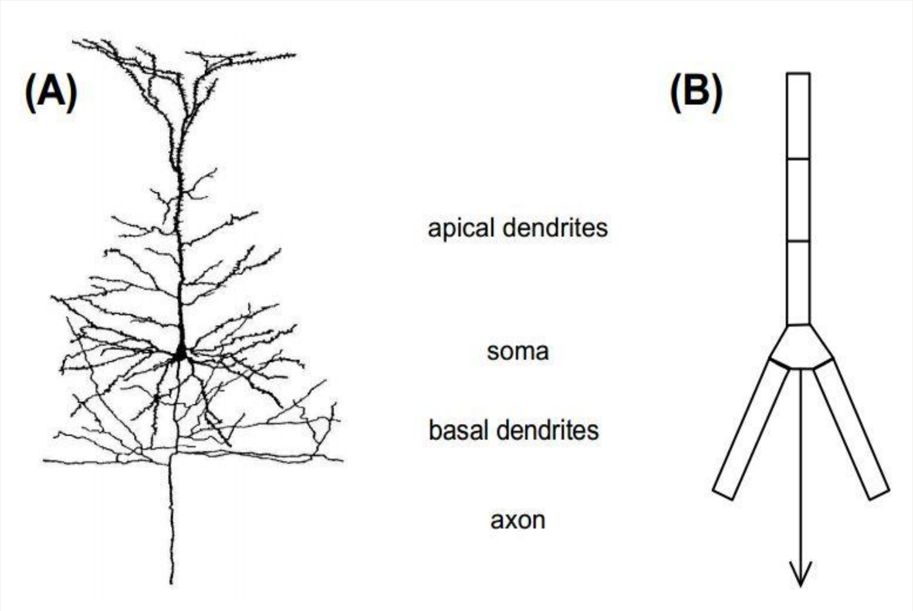
1m	Nervous System
10 cm	Brain
1 cm	Neural networks
100 µm	Neurons
1 µm	Synapses
1 nm	Signalling Pathways
1 pm	Ion Channels

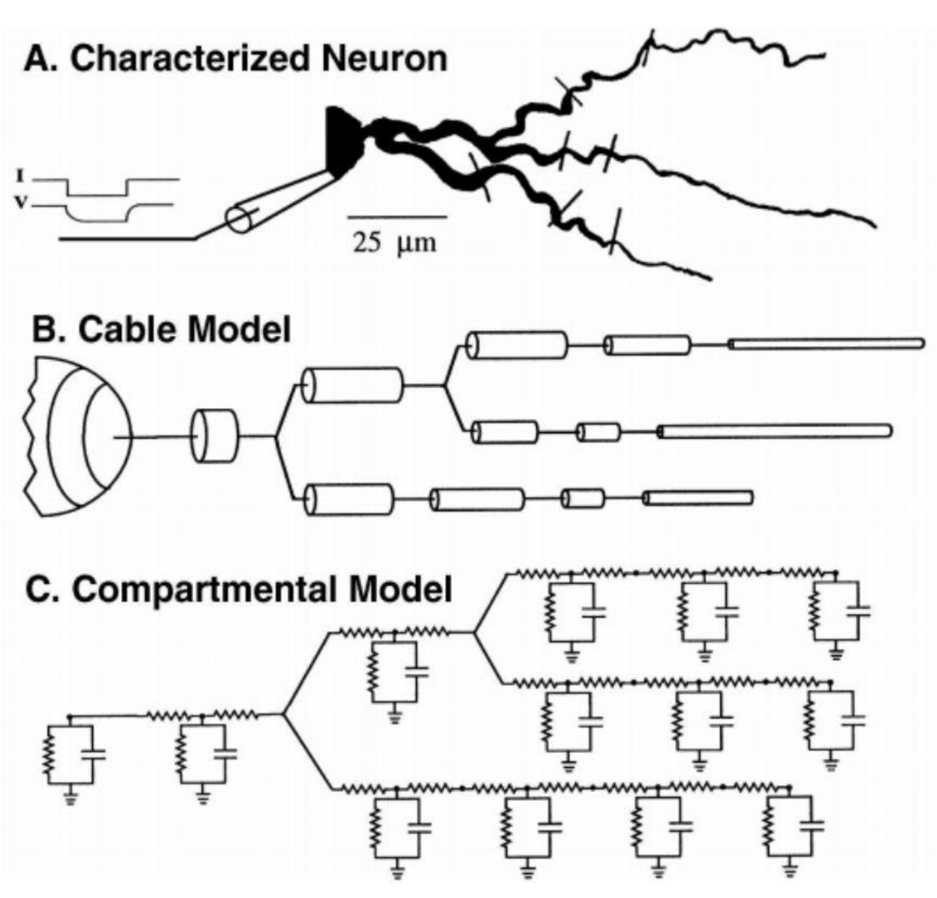
Details in Sterratt et. al., 2011 (1st ed.)

Single Cell Models:
Morphologically Detailed Neurons

Single Cell Models: Detailed

Compartmental Modelling: Simplifying morphology



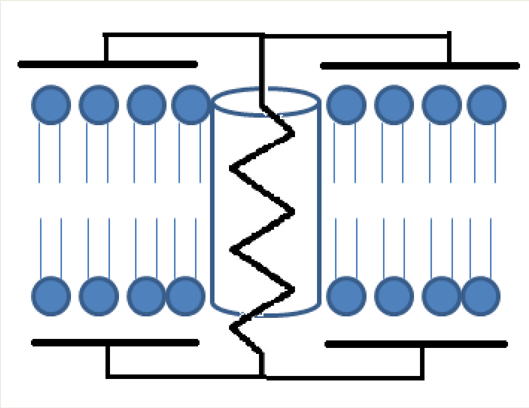


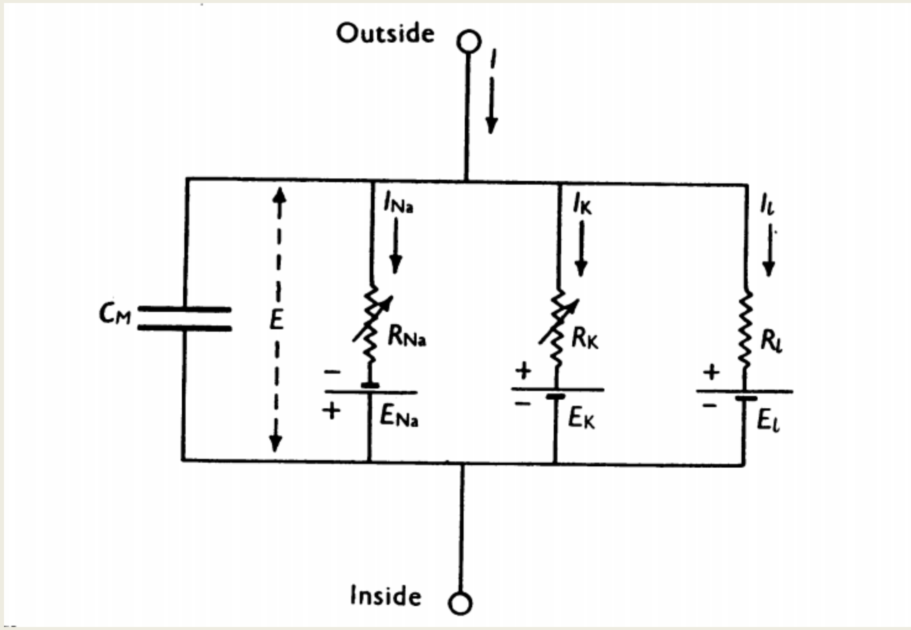
Source: Bower and Beeman, 2003 (Internet ed.)

Single Cell Detailed Models

Membrane Mechanisms

- Ion Channels
  - K^+, Na^+, Ca^{2+}, Cl^-, etc.
- Exchangers
  - Na^+-Ca^{2+} Exchangers
- Pumps
  - Na^+-K^+ Pumps
- Receptors

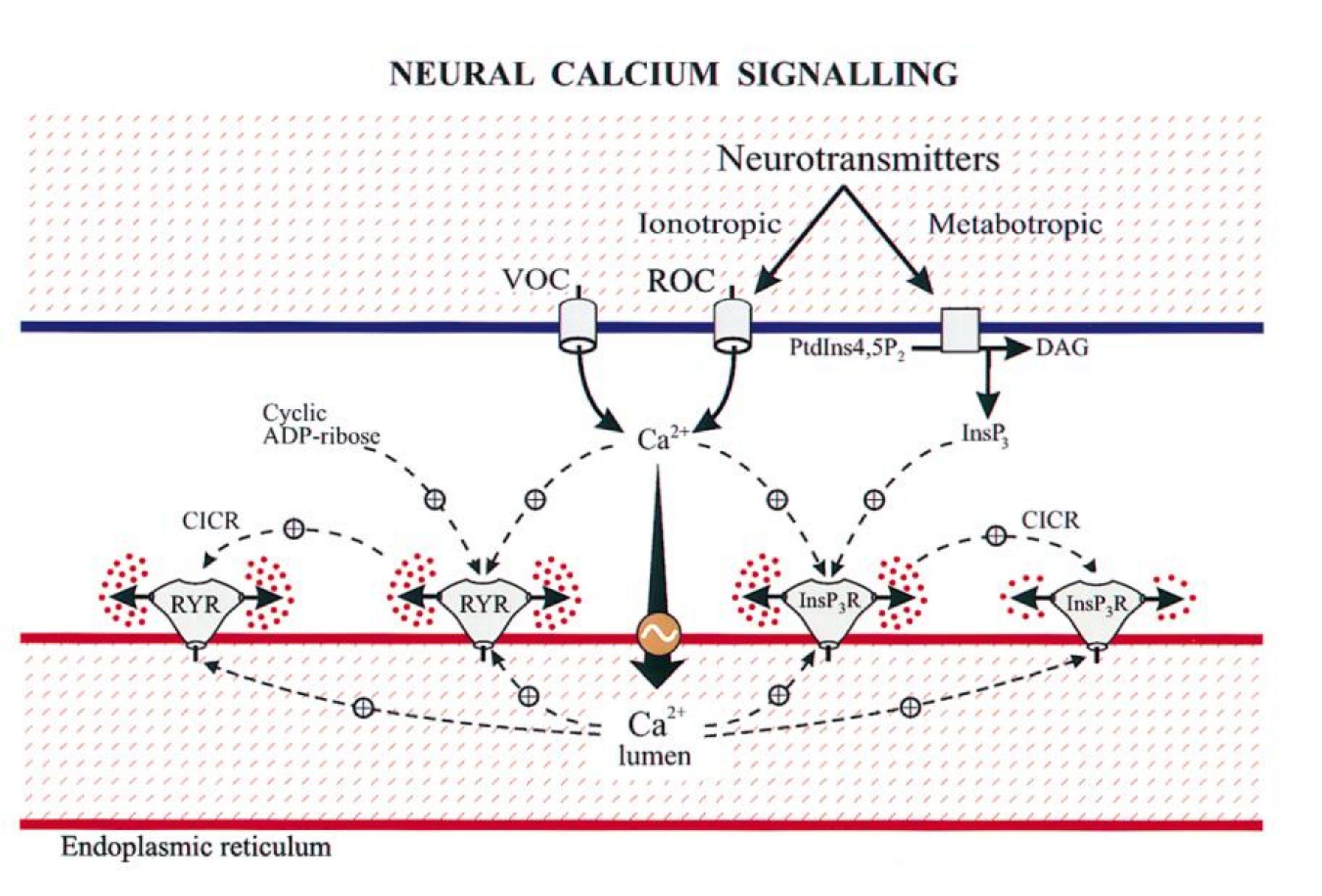




Source: Hodgkin and Huxley, 1952

Single Cell Detailed Models

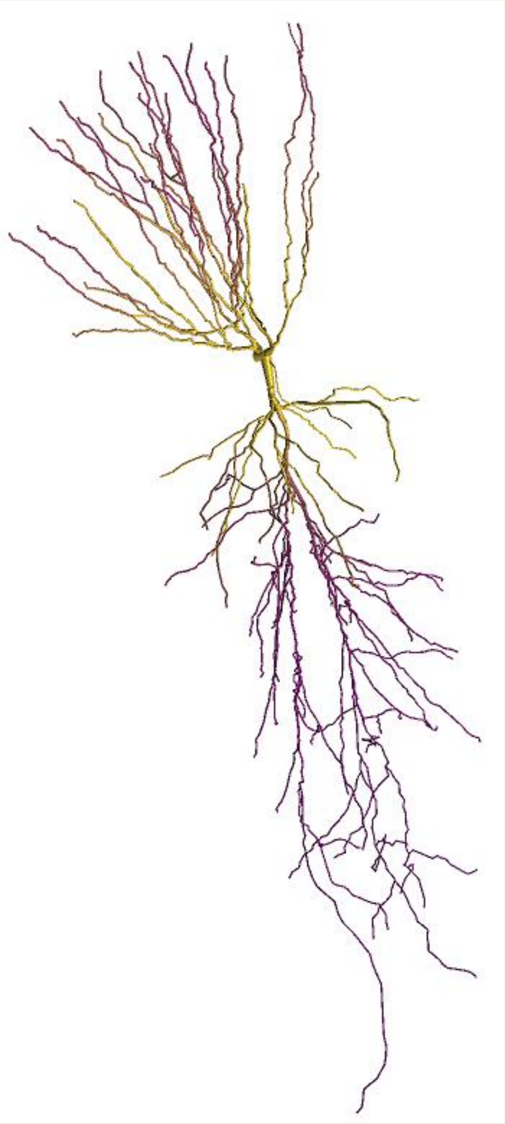
Intracellular Signalling

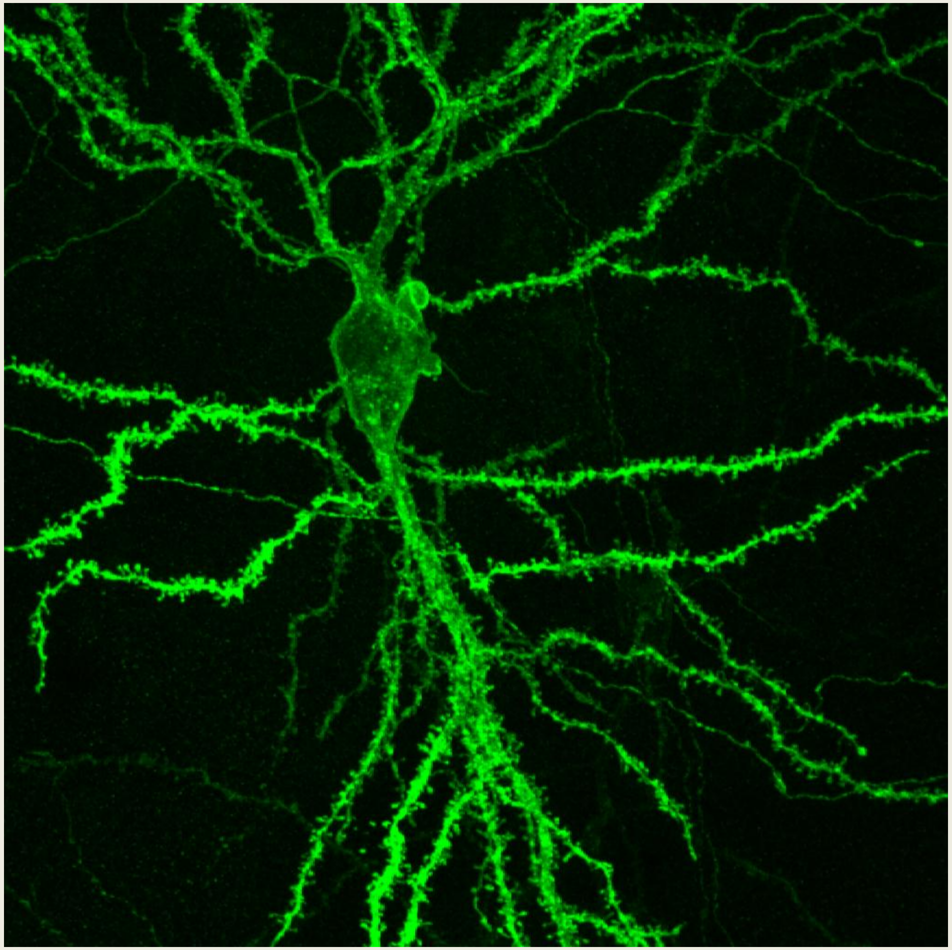


Source: Berridge, 1998

Single Cell Detailed Models

Modelled and Experimental CA 1 Pyramidal Neuron





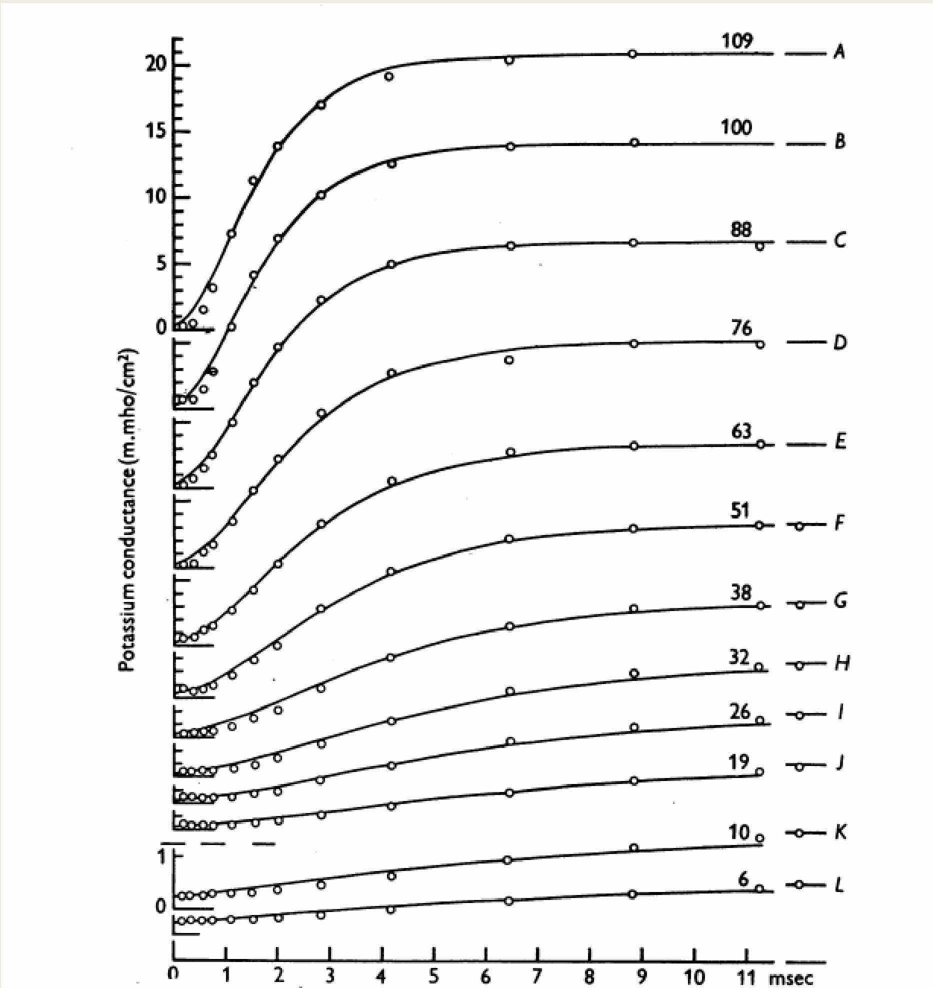
Source: www.opensourcebrain.org, nibr.com

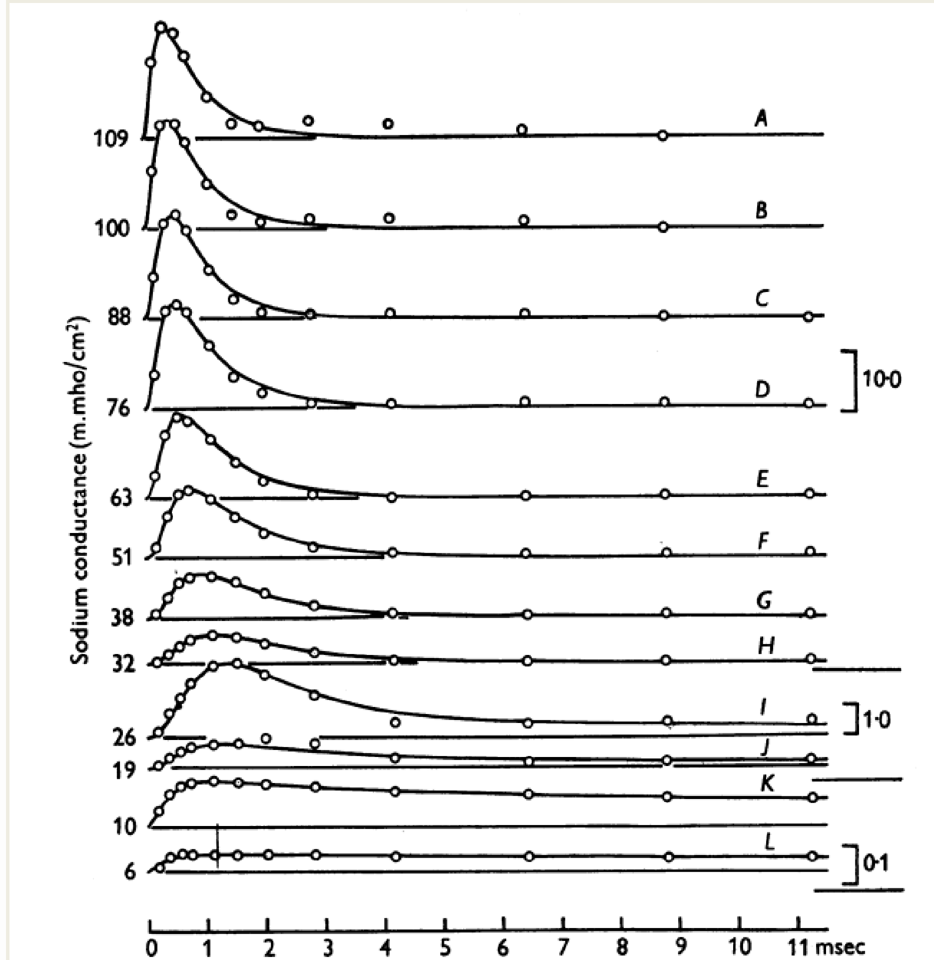
Single Cell Detailed Models

Model Validation

Model

Expt.





Adapted Hodgkin and Huxley, 1952

Single Cell Detailed Models

<u>Demonstration CA1 Neuron and ModelDB</u>

- CA1 pyramidal neuron: Migliore et al 2005

https://senselab.med.yale.edu/ModelDB/ShowModel.cshtml?model=55035

One needs to install NEURON simulator running these simulations.

Once installed, download the model using the "Auto-launch" button on model website and run the simulations.

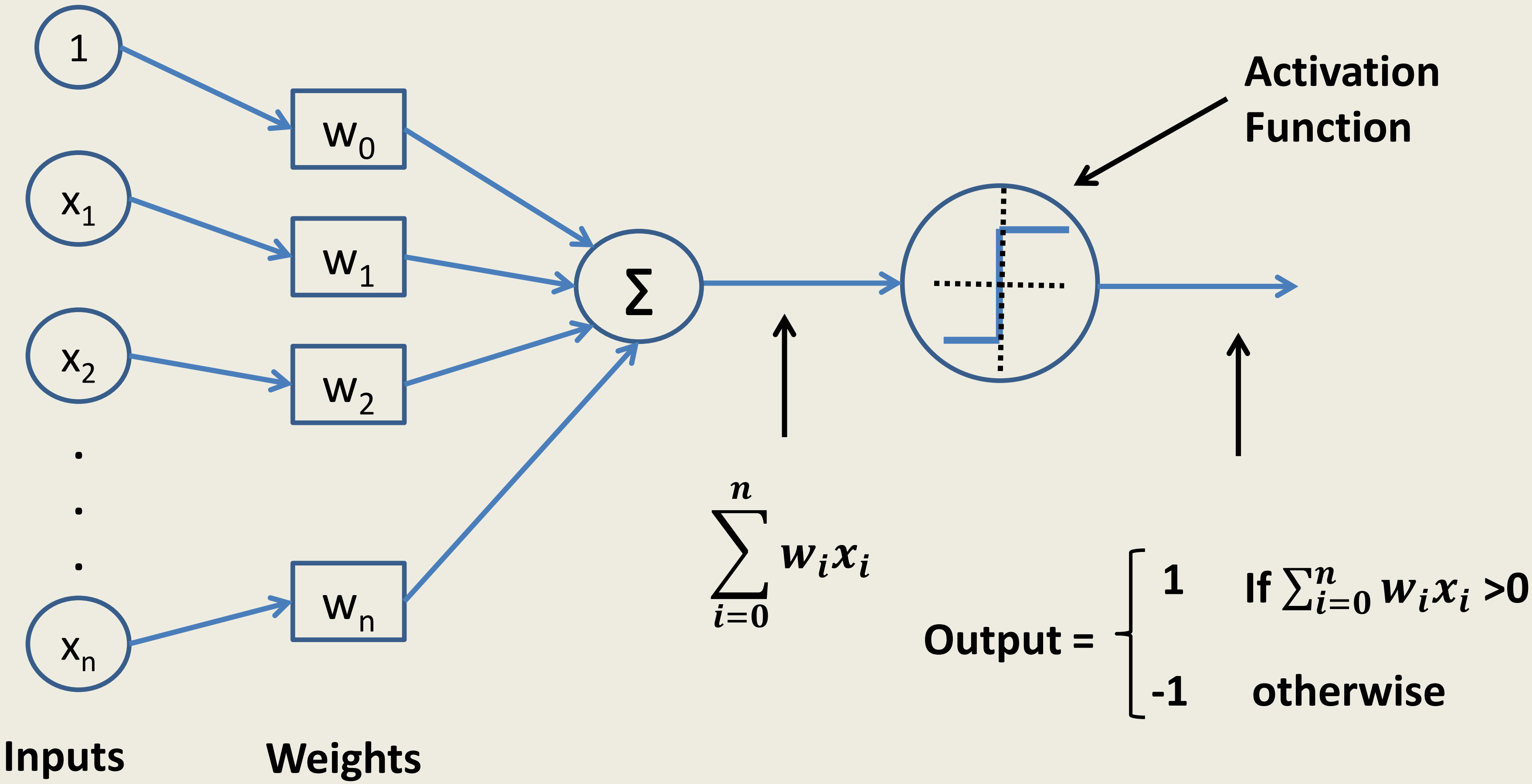
- ModelDB: A database for all types of neuron models (detailed and abstract)

https://senselab.med.yale.edu/ModelDB/default.cshtml

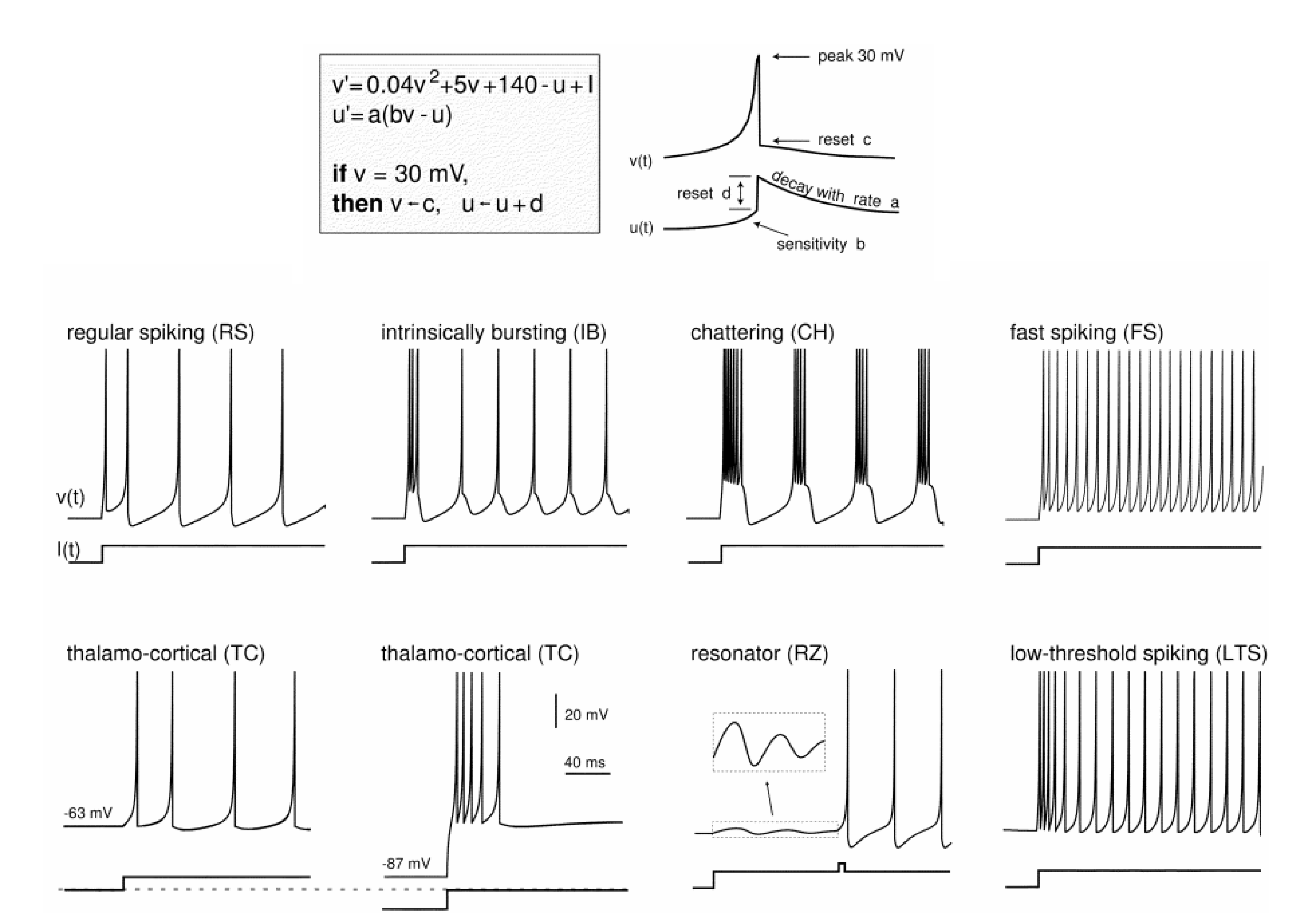
Source: senselab.med.yale.edu/modeldb/

Single Cell Models:
Point Neurons

Single Cell Abstract Models: Artificial Neuron



Single Cell Abstract Models: Izhikevich Neuron



Other point neurons: Integrate and Fire (IF) Neurons, FitzHugh-Nagumo (FHN) Model, Hindmarsh-Rose Models, etc.

Adapted from Izhikevich, 2003

Comparison: Detailed & Point Neuron Models

Morphologically Detailed Models

- **Real neuron morphology and mechanisms**
- Prediction power up to the **molecular** level
  - E.g. we can predict dysfunction of ion channels that control action potential firing rates
- **Structure defines function**: spine density variation (on dentrites) – memory, addiction, etc.
- **Synaptic Plasticity** possible: LTP, LTD, STDP, etc.
- Computationally **expensive**: several highly non-linear partial differential equations

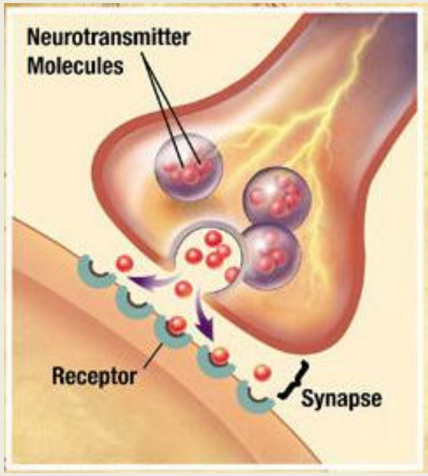
Point Neuron Models

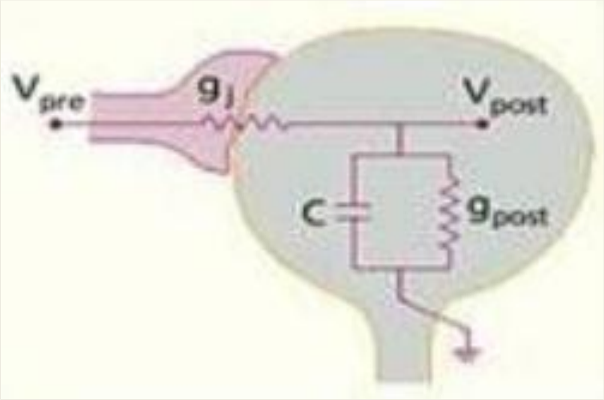
- Models generally **don't represent the underlying biological mechanisms**
- Limited prediction power
  - Can predict at the **neuron** and **syanpse** level
- **No** morphology
- **Synaptic Plasticity** possible
- **Less expensive** computationally
  - Can be used to simulate network with large number of neurons.
  - Few ordinary differential equations

Network Models

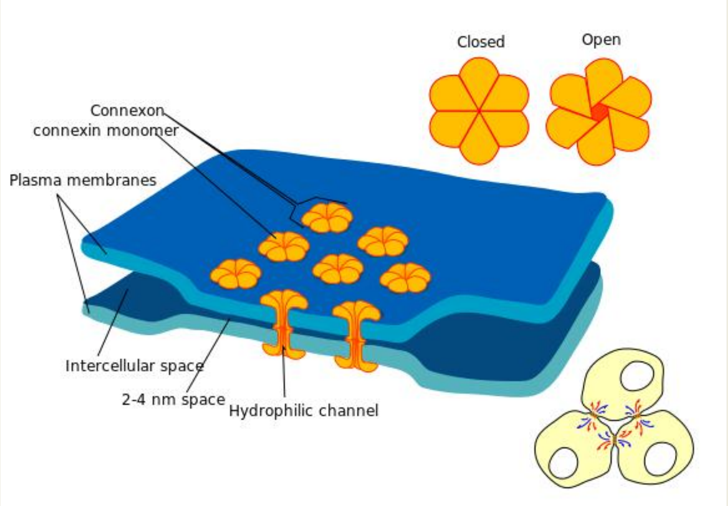
- Neurons connections

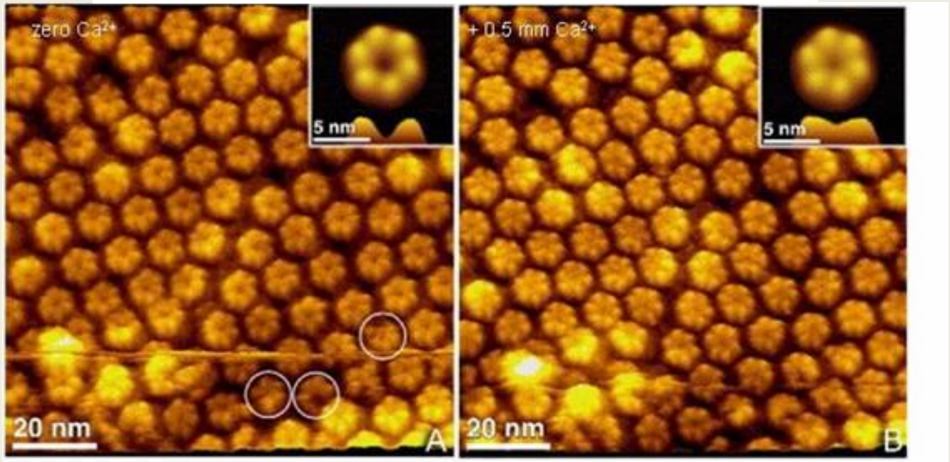
Chemical Synapses





Electrical Synapses: Gap Junctions

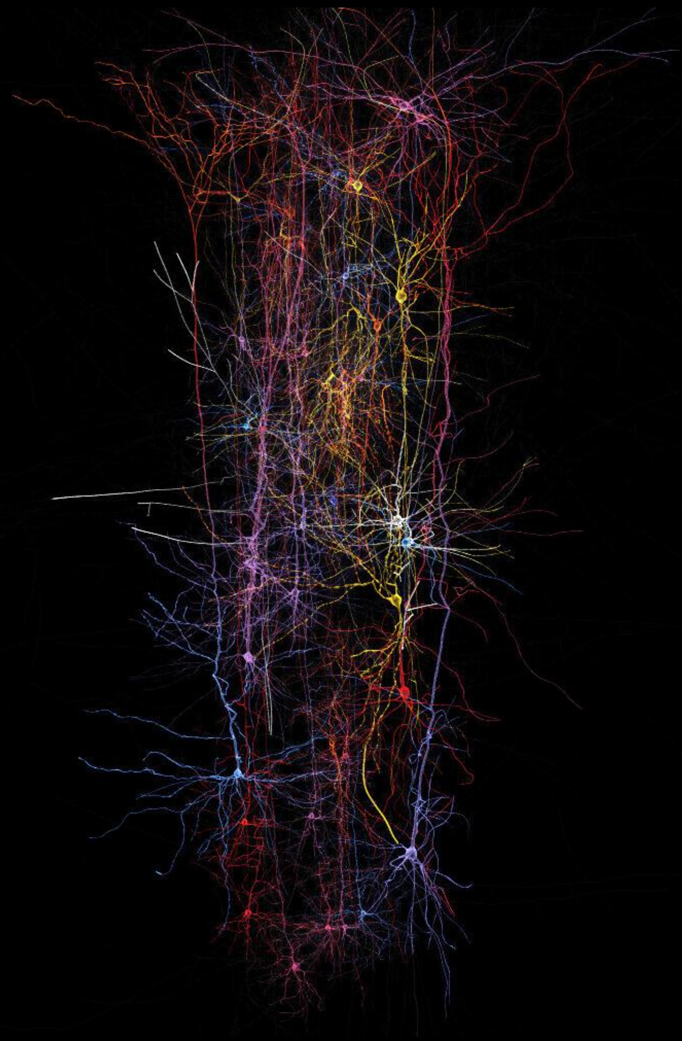


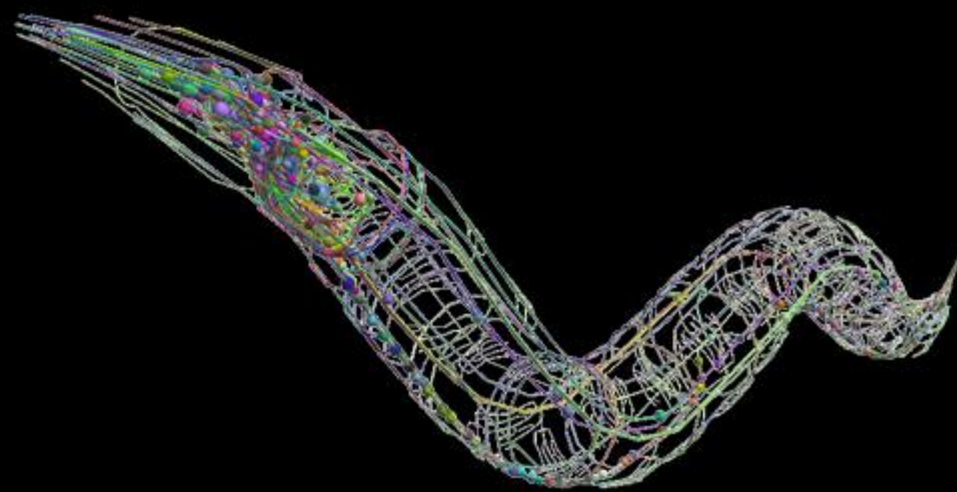


Sosinsky GE, Nicholson BJ. 2005 Structural organization of gap junction channels. Biochim Biophys Acta 1711:99-125

Source: Wikimedia commons, electroneubio.secyt.gov.ar

Network Models





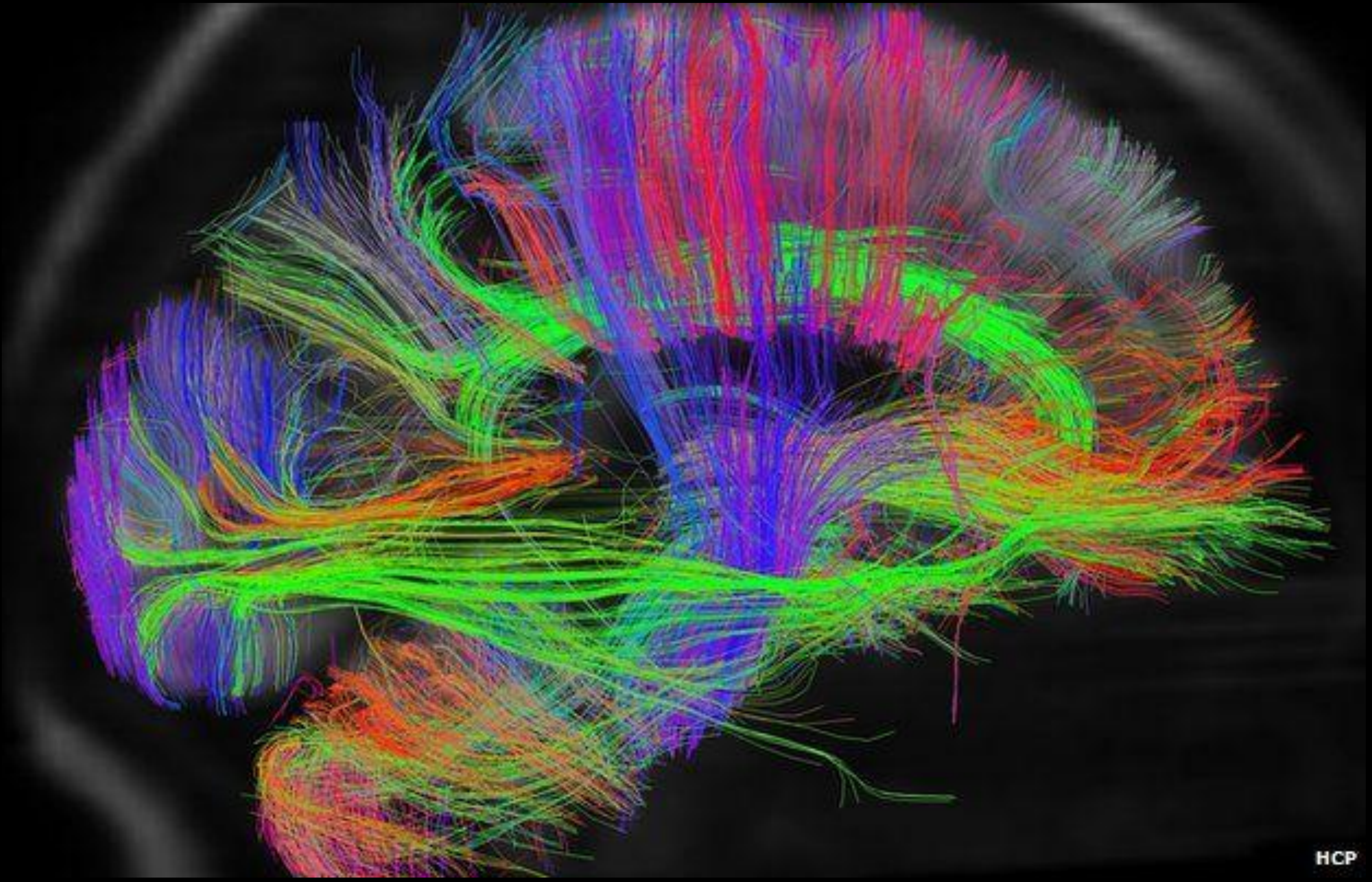
OpenWorm

Mouse Cortical Circuits

Source: http://bluebrain.epfl.ch

C. elegans Neural Network

Human Connectome Project



Source: bbc.com/news/science-environment-21487016

Network Models

Demonstration

- Openworm Code : http://www.openworm.org/downloads.html
- Simulator used for displaying Openworm network: Neuroconstruct

  http://neuroconstruct.org/
- Human Connectome Project Relationship Viewer: shows the connections of different regions of the brain:

  http://www.humanconnectomeproject.org/informatics/relationship-viewer/

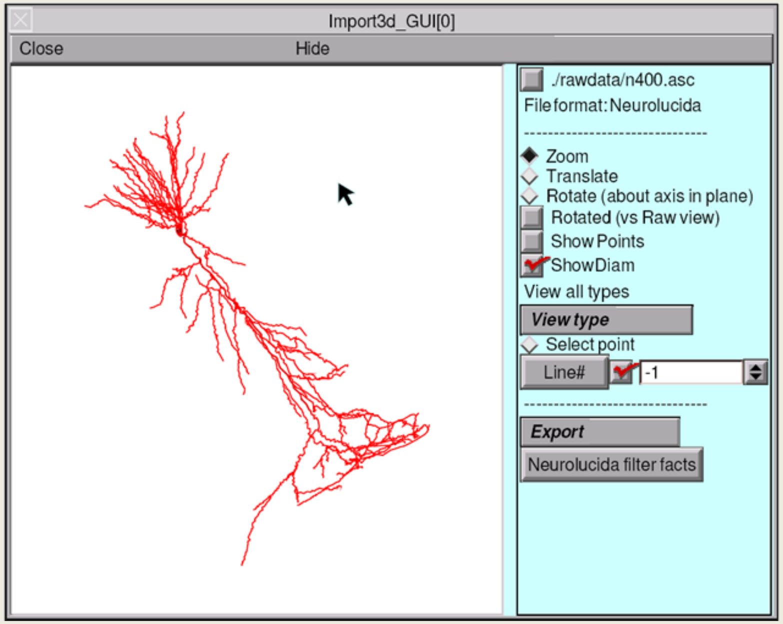
Collaborative Brain Projects

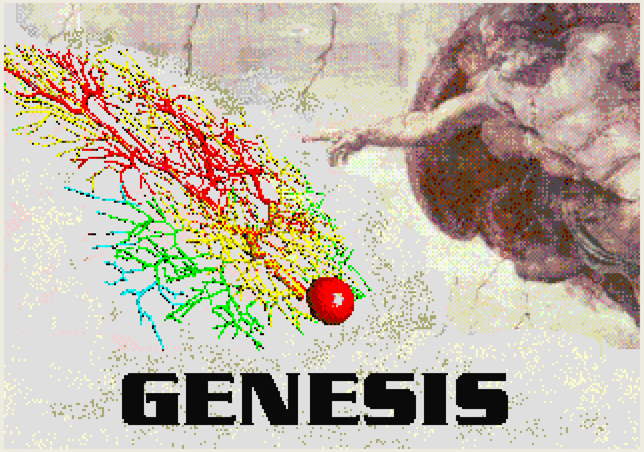
- US BRAIN (Brain Research through Advancing Innovative Neurotechnologies®)Initiative: http://www.braininitiative.nih.gov/

- Human Brain Project (Europe): https://www.humanbrainproject.eu/

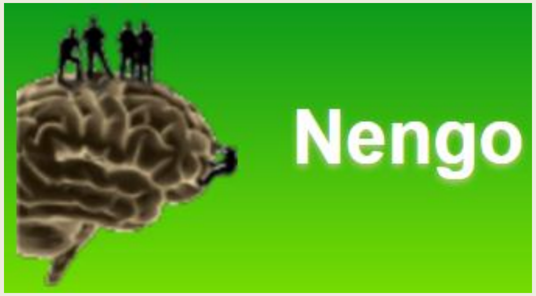
- Other Collaborative brain projects around the world: http://incf.org/activities/projects/collaborative-brain-projects

Simulators





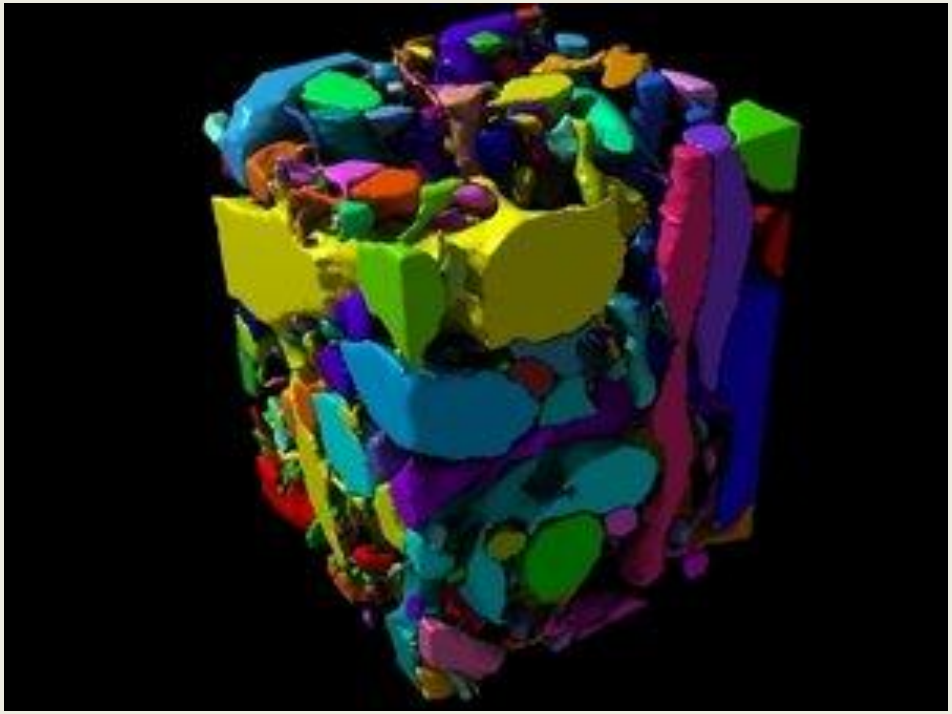
nest:: simulated()



BRIAN

Eyewire

- Game to map the neurons in the mouse retina
- http://eyewire.org/explore
- Cube of stacked retinal imaging slices
- Human participation improve eyewire's AI algorithms.
- Details here.



Courses and Websites

- In IITB:
  - BB661 Biopotentials I: Cellular Signals (Odd Sem.)
  - BB 803 Advanced Cellular Electrophysiology (Odd Sem.)
  - BB 606 Cellular electricity: Physics & modeling (Even Sem.)

- MOOCs:
  - Computational Neuroscience: https://www.coursera.org/course/compneuro
  - Exploring Neural Data:
    https://www.coursera.org/course/neuraldata

- HHsim: Graphical Hodkin Huxley Simulator: http://www.cs.cmu.edu/~dst/HHsim/

- Website for the book -- Principles of Computational Modeling in Neuroscience: http://www.compneuroprinciples.org/

Important References

1. SpiNNaker: http://apt.cs.manchester.ac.uk/projects/SpiNNaker/Publications/
2. DARPA's SyNAPSE Project: http://research.ibm.com/cognitive-computing/neurosynaptic-chips.shtml
3. The Blue Brain Project: http://bluebrain.epfl.ch/
4. Human Connectome Project: http://humanconnectomeproject.org
5. Book: Principles of Computational Modeling in Neuroscience – Steratt et. al., 2011 (1st edition) http://www.cambridge.org/de/academic/subjects/life-sciences/neuroscience/principles-computational-modelling-neuroscience
6. Book: The Book of GENESIS: Exploring Realistic Neural Models with the GEneral NEural SImulation System; James M. Bower and David Beeman http://www.genesis-sim.org/bog/bog.html
7. Hodgkin, Alan L., and Andrew F. Huxley. "A quantitative description of membrane current and its application to conduction and excitation in nerve." The Journal of physiology 117.4 (1952): 500.
8. Berridge, Michael J. "Calcium signalling remodelling and disease." *Biochemical Society Transactions* 40.2 (2012): 297-309.

10. Migliore, Michele, Michele Ferrante, and Giorgio A. Ascoli. "Signal Propagation in Oblique Dendrites of CA1 Pyramidal Cells." *Journal of neurophysiology* 94.6 (2005): 4145–4155.
11. Izhikevich, Eugene M. "Simple model of spiking neurons." IEEE Transactions on neural networks 14.6 (2003): 1569-1572.

Thank You!