Introduction to Systems and Computational Neuroscience

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https://github.com/Wenlab/Computational-Neuroscience-Course/tree/Fall2018

The Magic of Alphago

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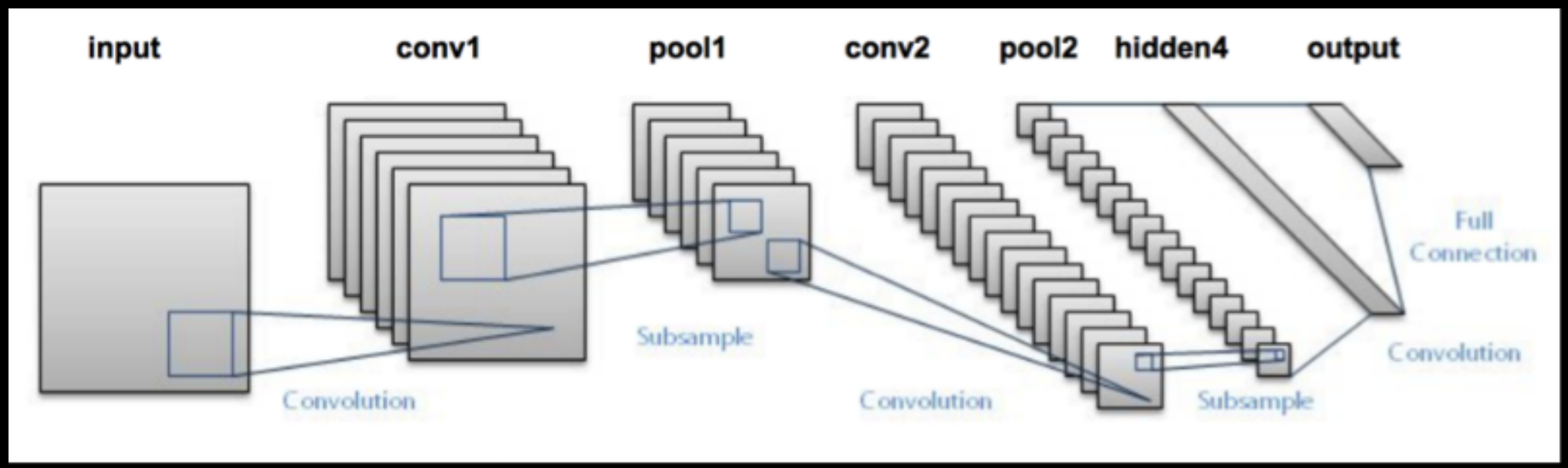
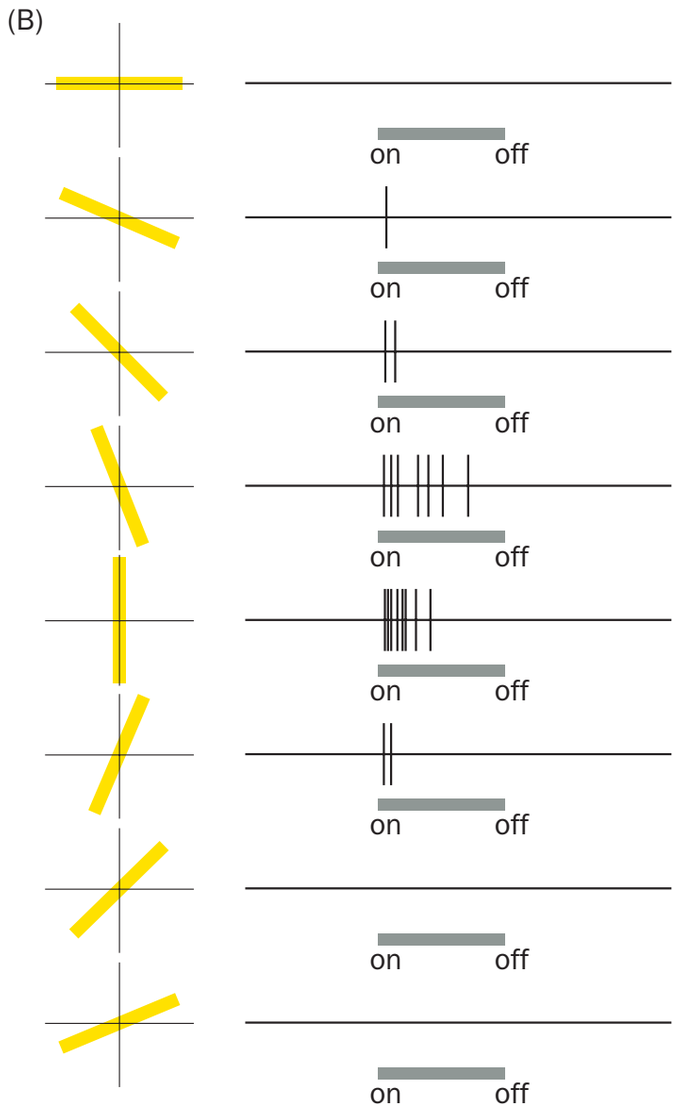
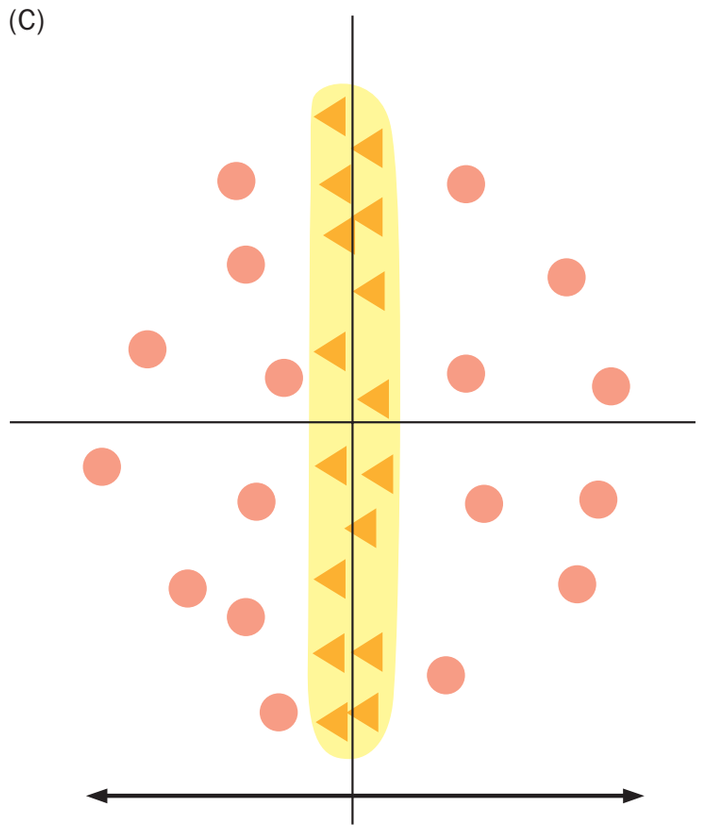


- Deep convolutional neural network
- Reinforcement learning and policy gradient

Convolutional neural net (CNN) was inspired by information processing in mammalian visual pathway

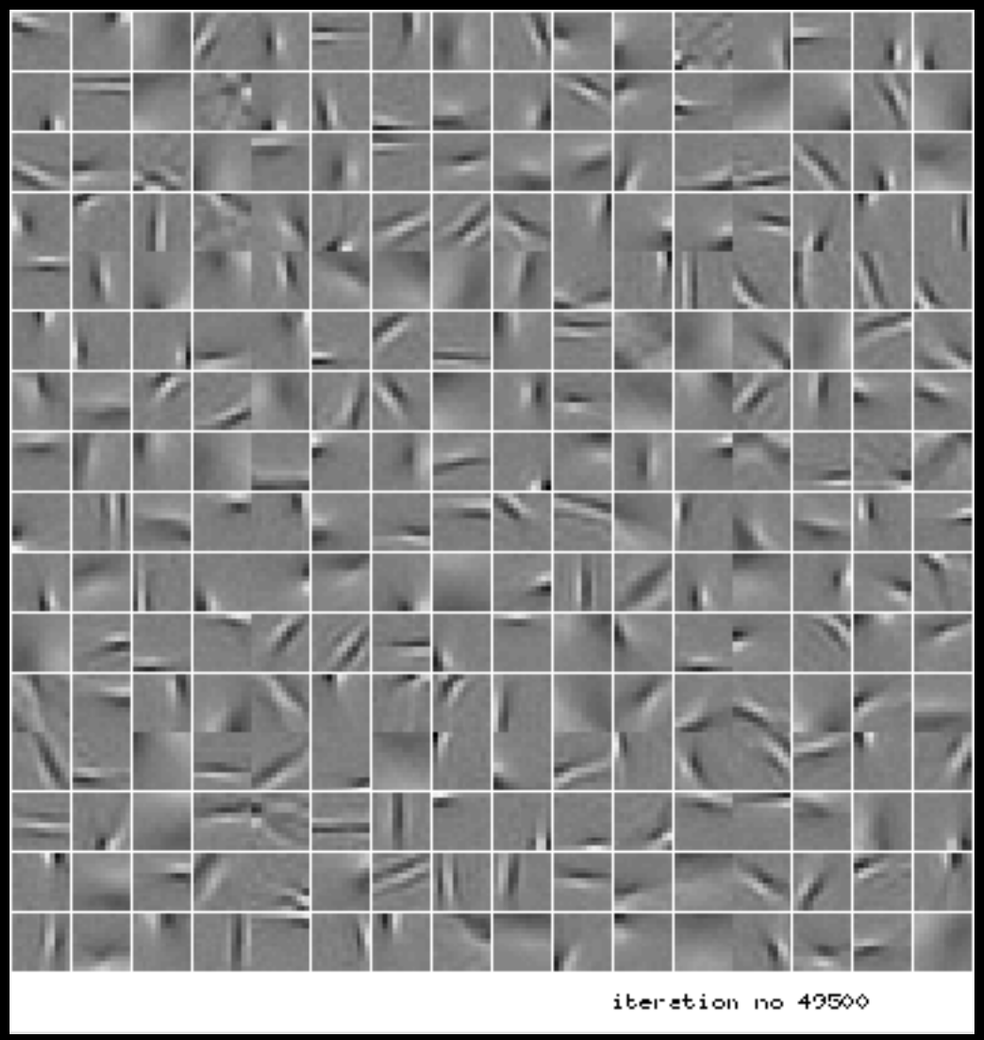




Hubel and Wiesel, 1959 Journal of Physiology

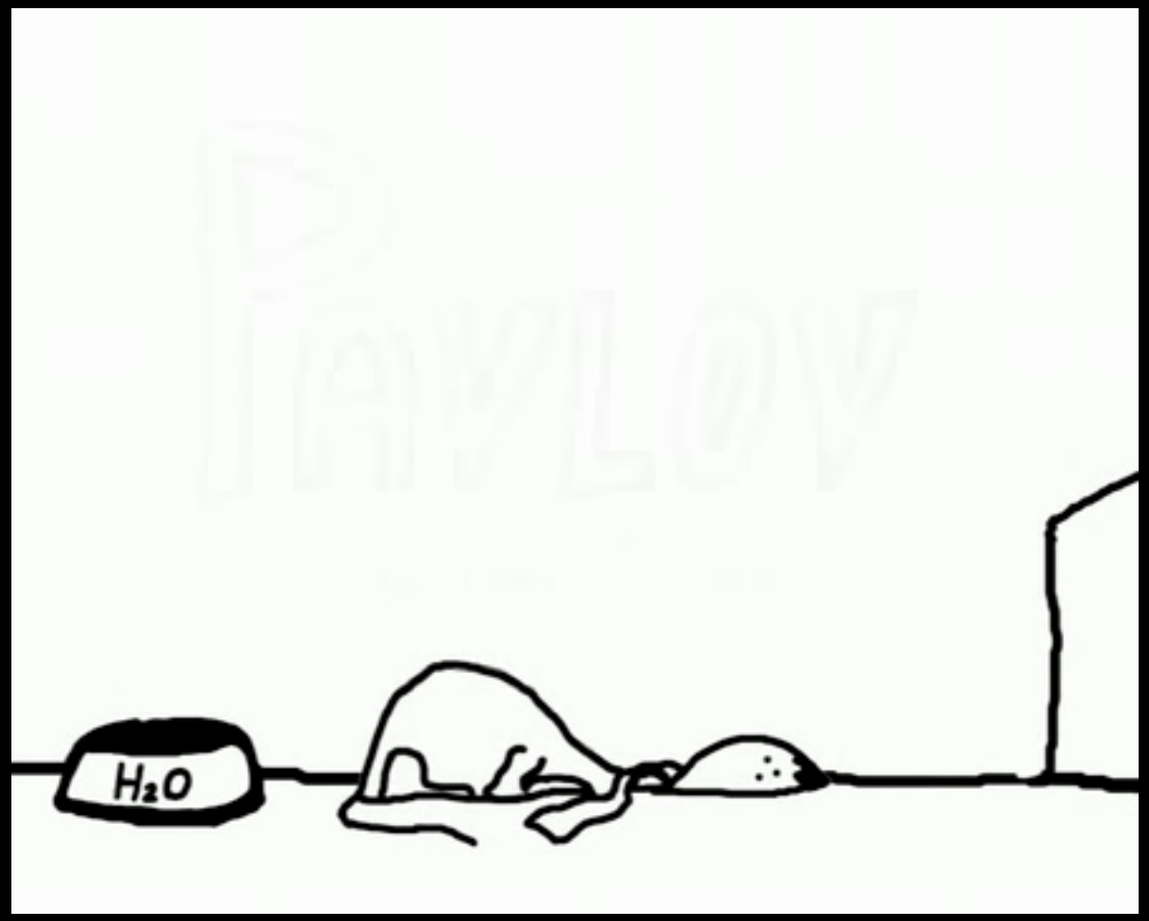
Simple cell receptive field in the cat primary visual cortex

Convolutional neural net (CNN) was inspired by information processing in human visual pathway

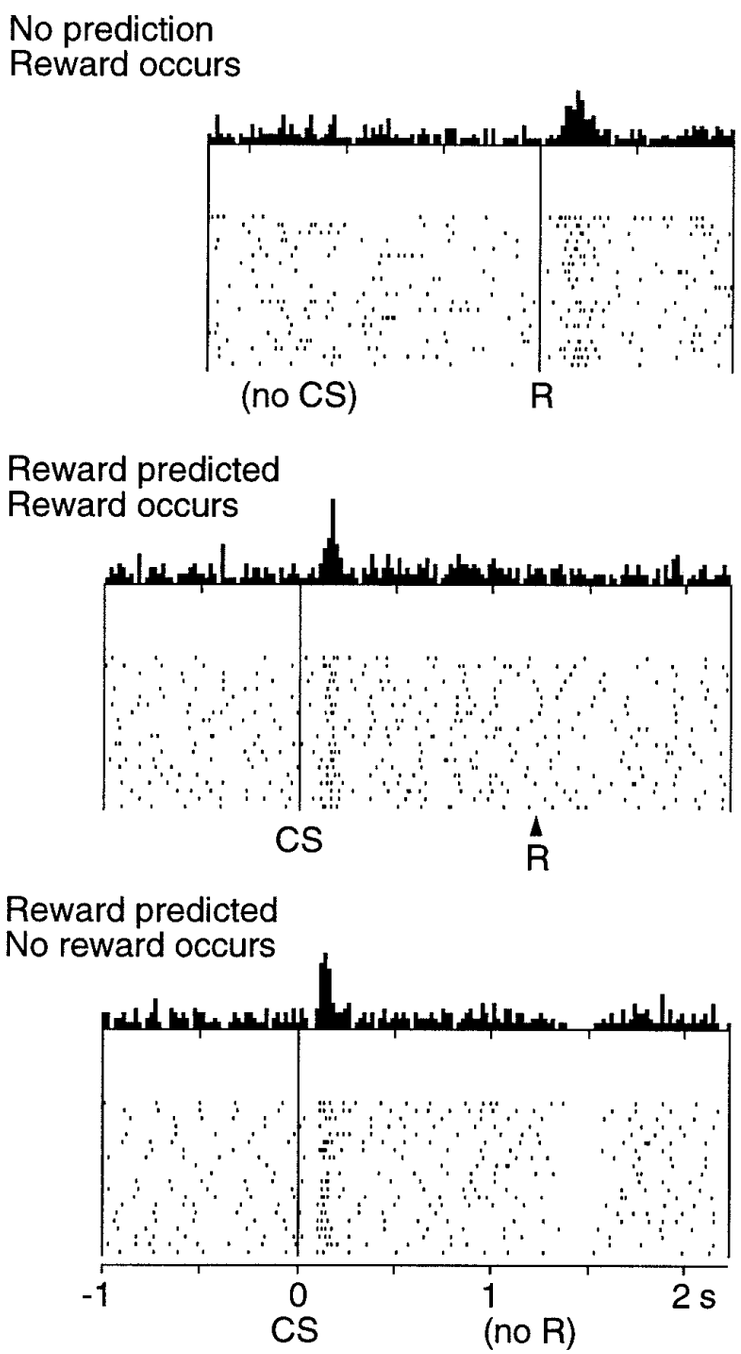


In the first layer of CNN, neurons can generate receptive field just like simple cells in visual cortex

Reinforcement learning in its simplest form
Classical Conditioning

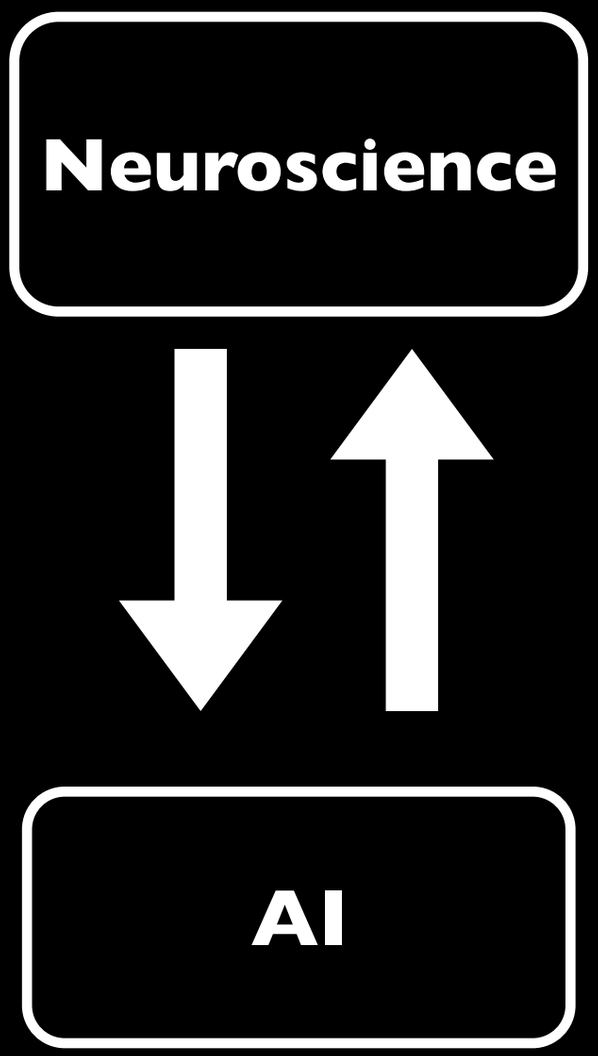


Dopaminergic neurons encode prediction error



Schultz, 1998

What is systems and computational neuroscience?



Our main goal is to use mathematical language to describe how the brain works

"When we discover the laws underlying natural computation …
… we will finally understand the nature of computation itself."

J von Neumann

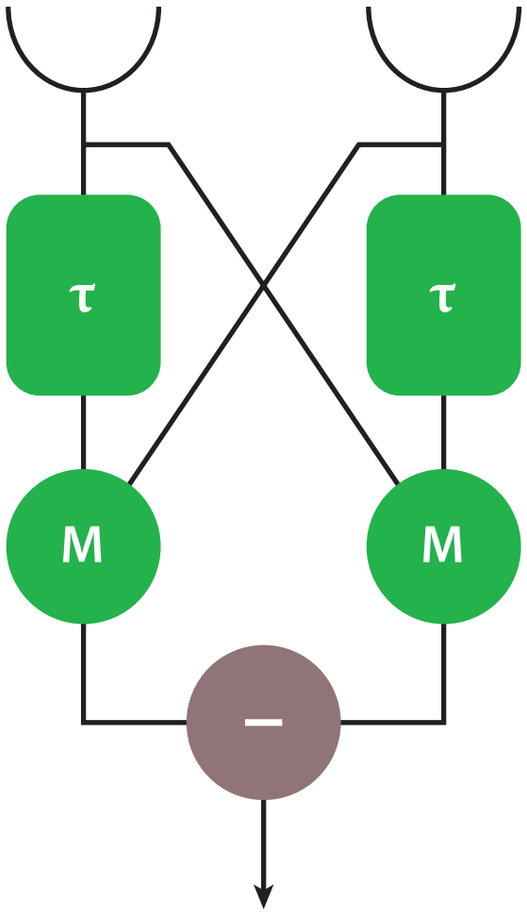
Pioneer in Computational Neuroscience

David Marr 1945-1980

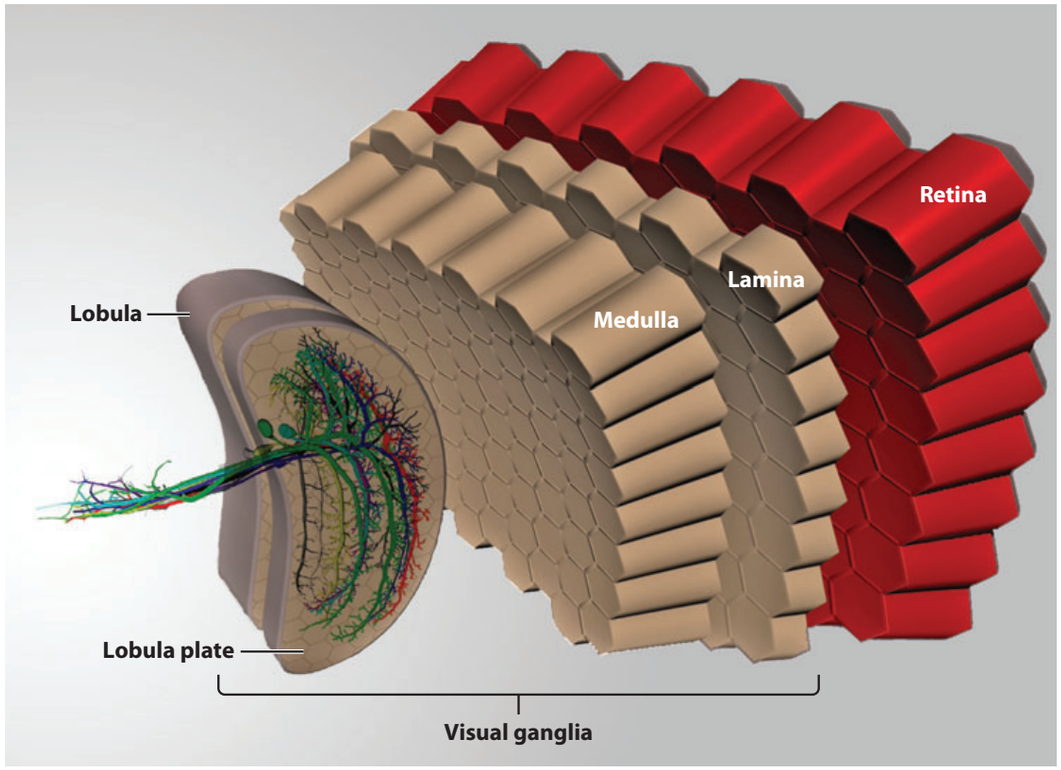
David Marr's legendary 3-level theory of brain computation

- **Computational level**: Identify the computational problem and task that the brain solves.
- **Algorithmic level**: Find the mathematical procedures that solve the problem.
- **Implementation level**: How the algorithms are realized by the nervous system.

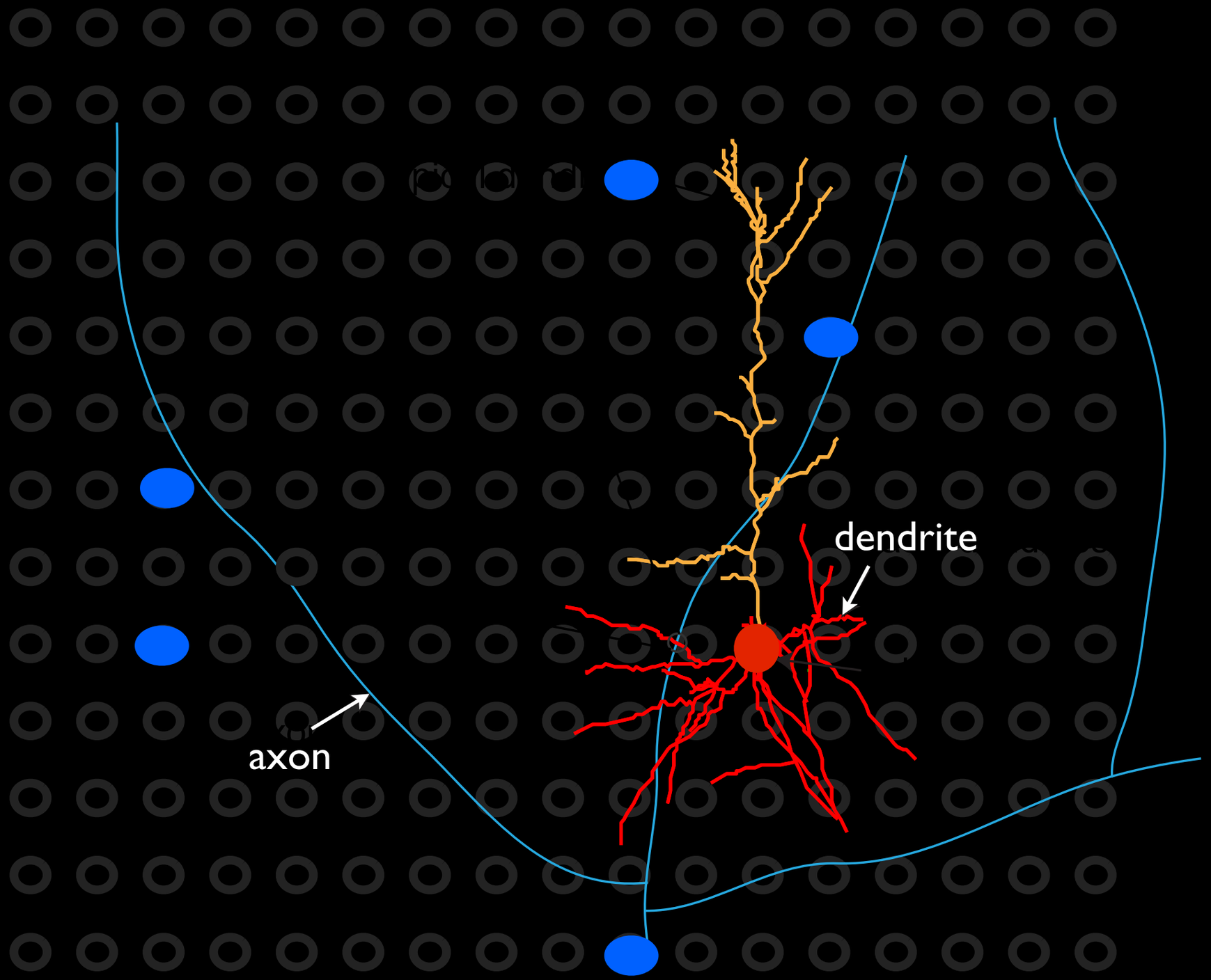
A classic example
motion detection in insect

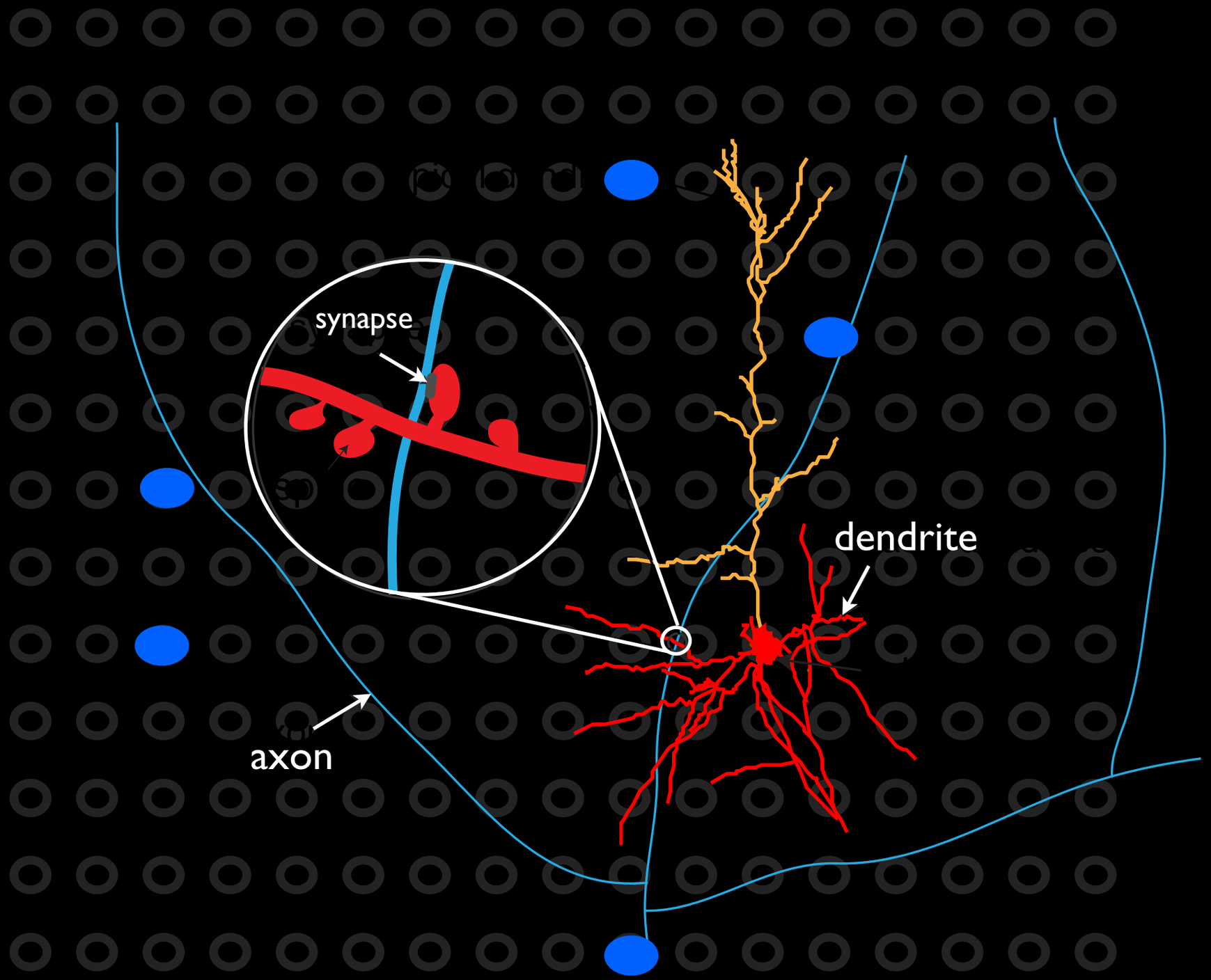


The Fly Visual System

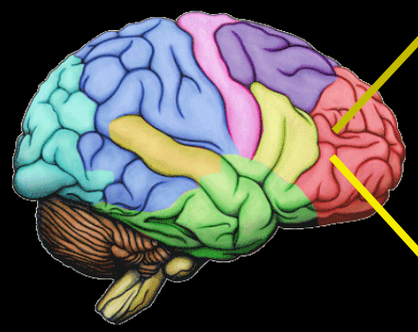


Exploring the brain

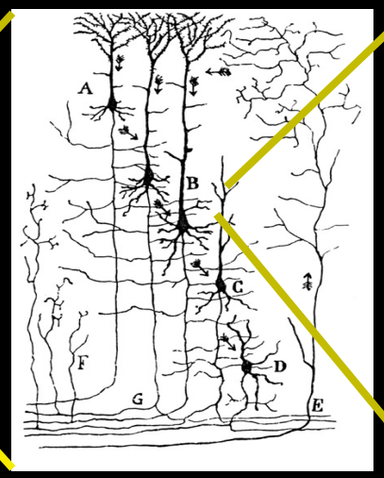

dendrite
axon


synapse
dendrite
axon

Human brain is perhaps the most complex subject in the universe



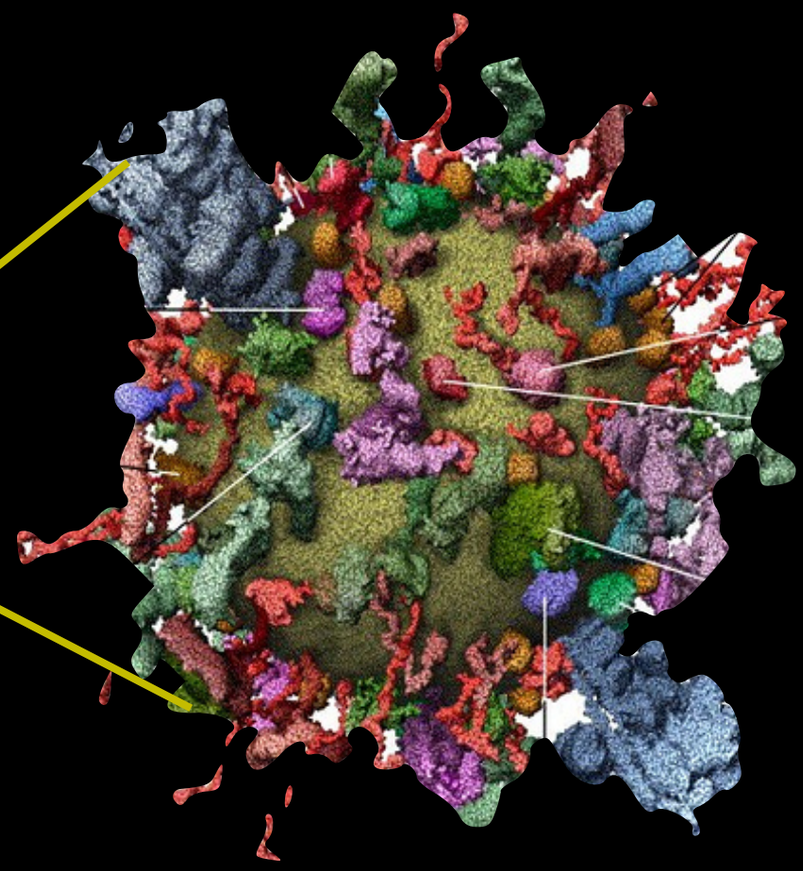
1 kg brain



10^{11} neurons

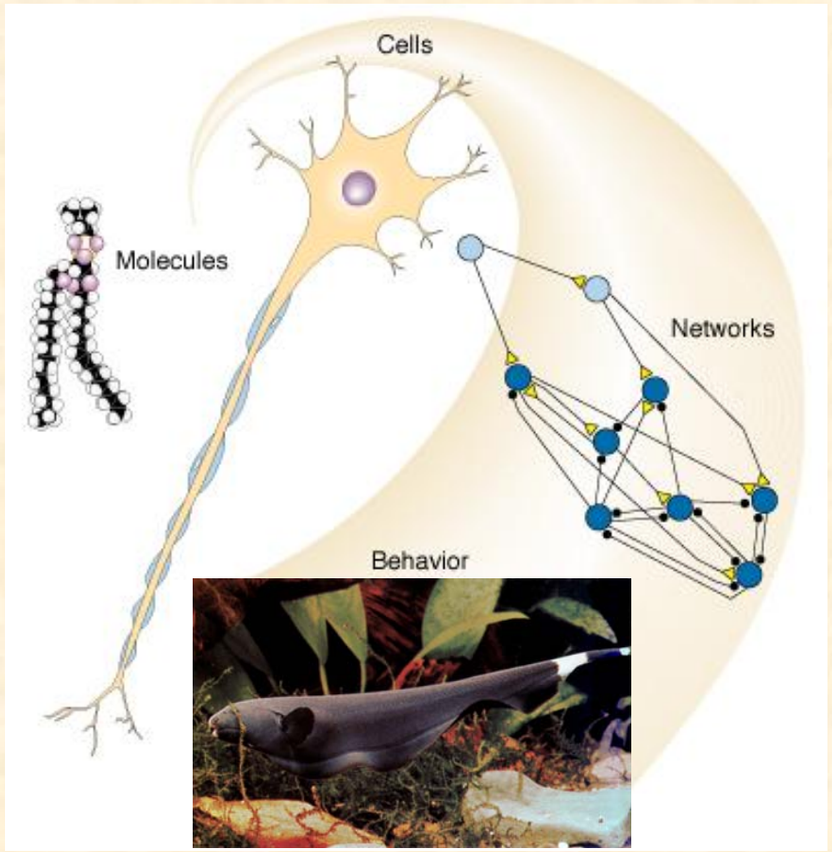
180,000 km nerve fiber

10^{15} synapses



10^{18} synaptic proteins

Multiscale Organization of the Nervous System



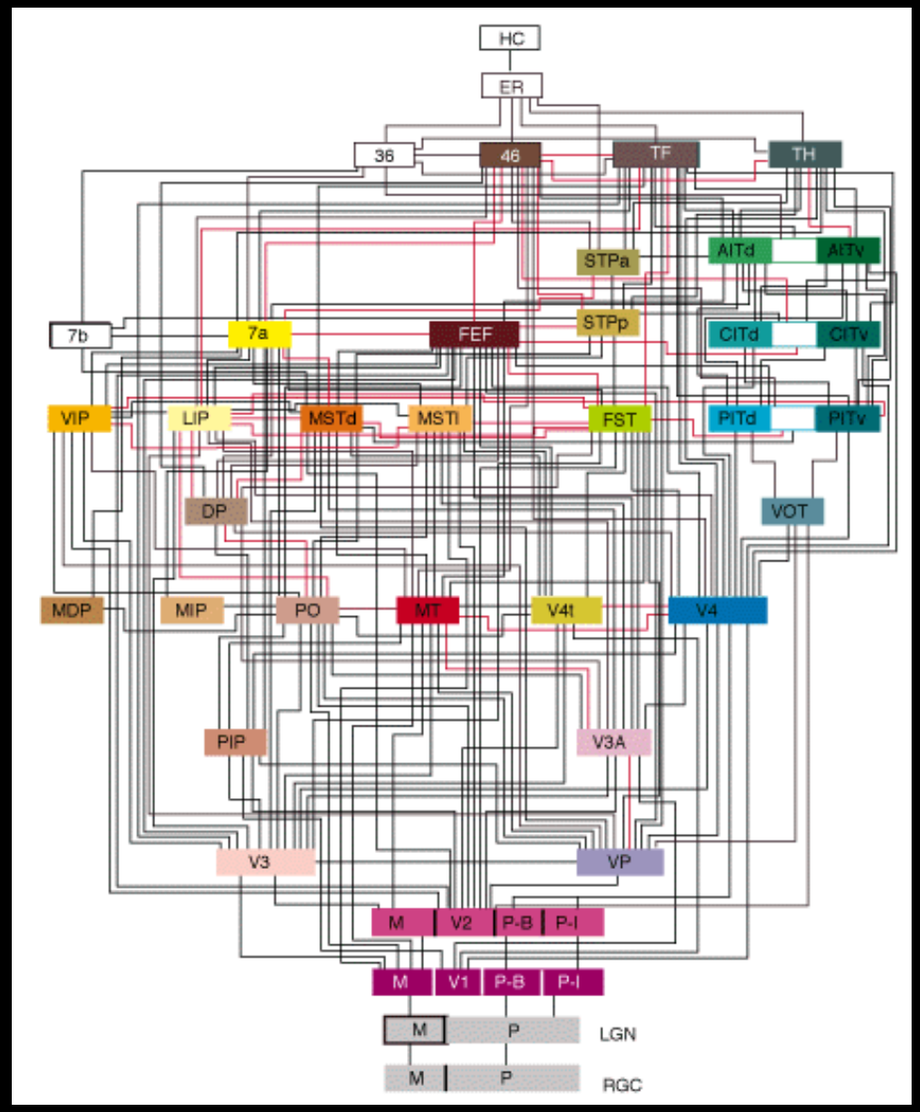
Delcomyn 1998

Organism	1 m
System	10 cm
Map	1 cm
Column	1 mm
Neuron	10 μm
Synapse	1 μm
Molecule	10 Å

Multiple Temporal Scale

- Action potential (spike): 1 msec
- Membrane integration time: 10 msec
- Synaptic integration time: 1-100 msec
- Short term synaptic plasticity: 0.1-1 sec
- Long term synaptic plasticity: hours-days

Van Essen Wiring Diagram of Visual Processing



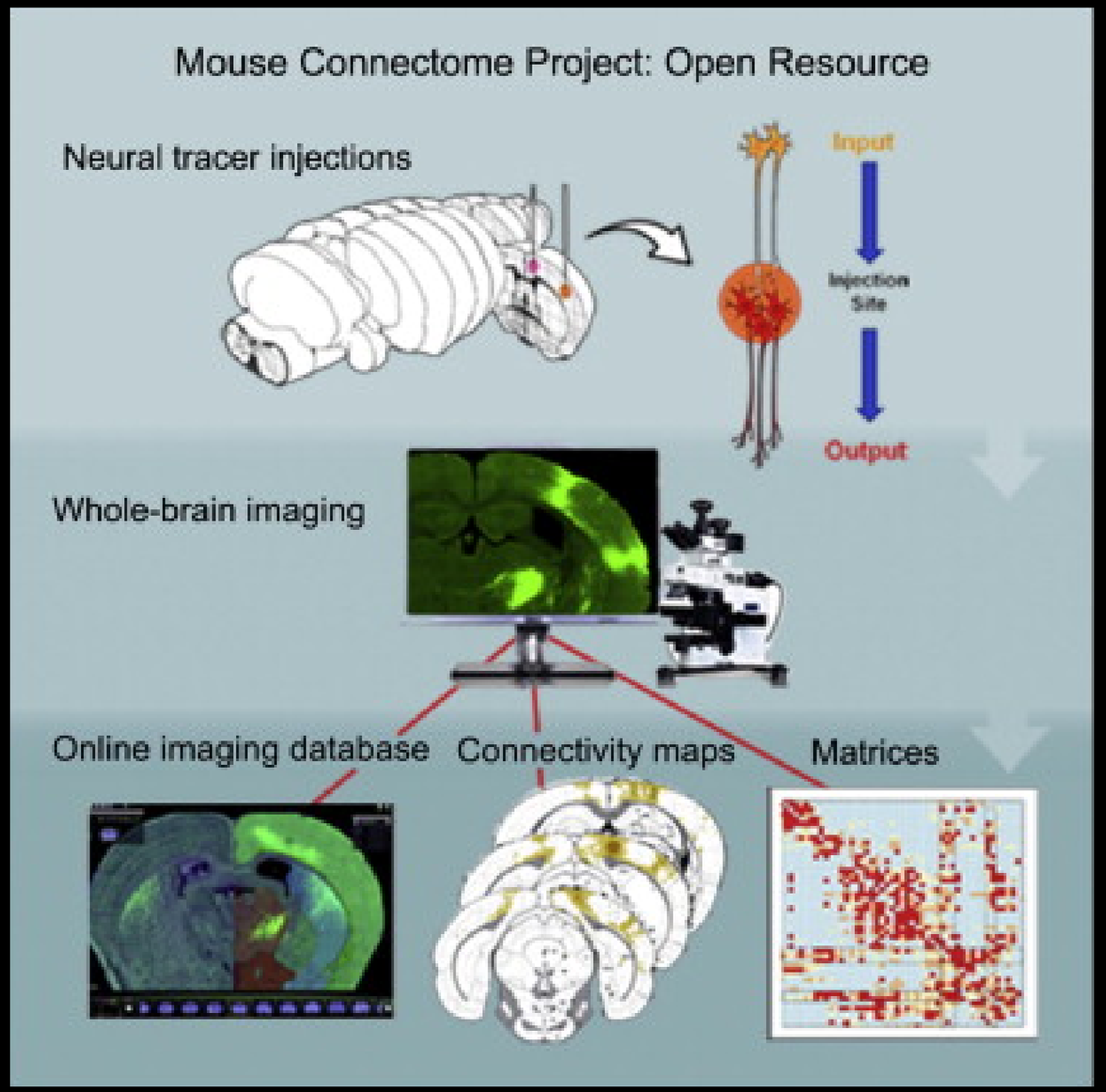
Algorithmic and Implementation levels cannot be easily decoupled!

Challenges

- Feedback connections
- Lateral connections
- Local recurrent connections
- Limited separation of scales
- Heterogeneity
- Distributed vs sparse neural code
- Fast vs slow processing
- ...

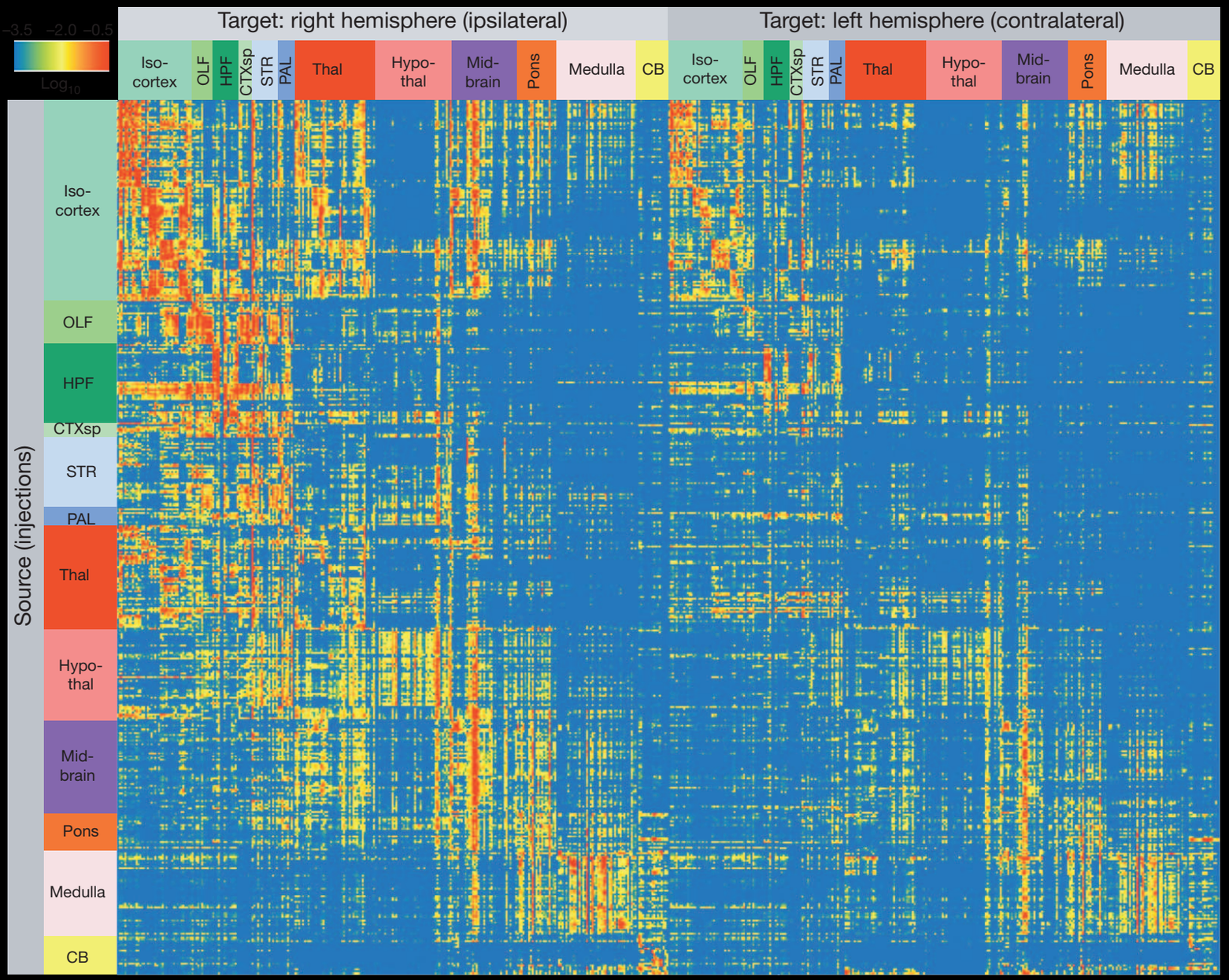
Reverse engineering the brain

Mapping the connectome (mesoscale)

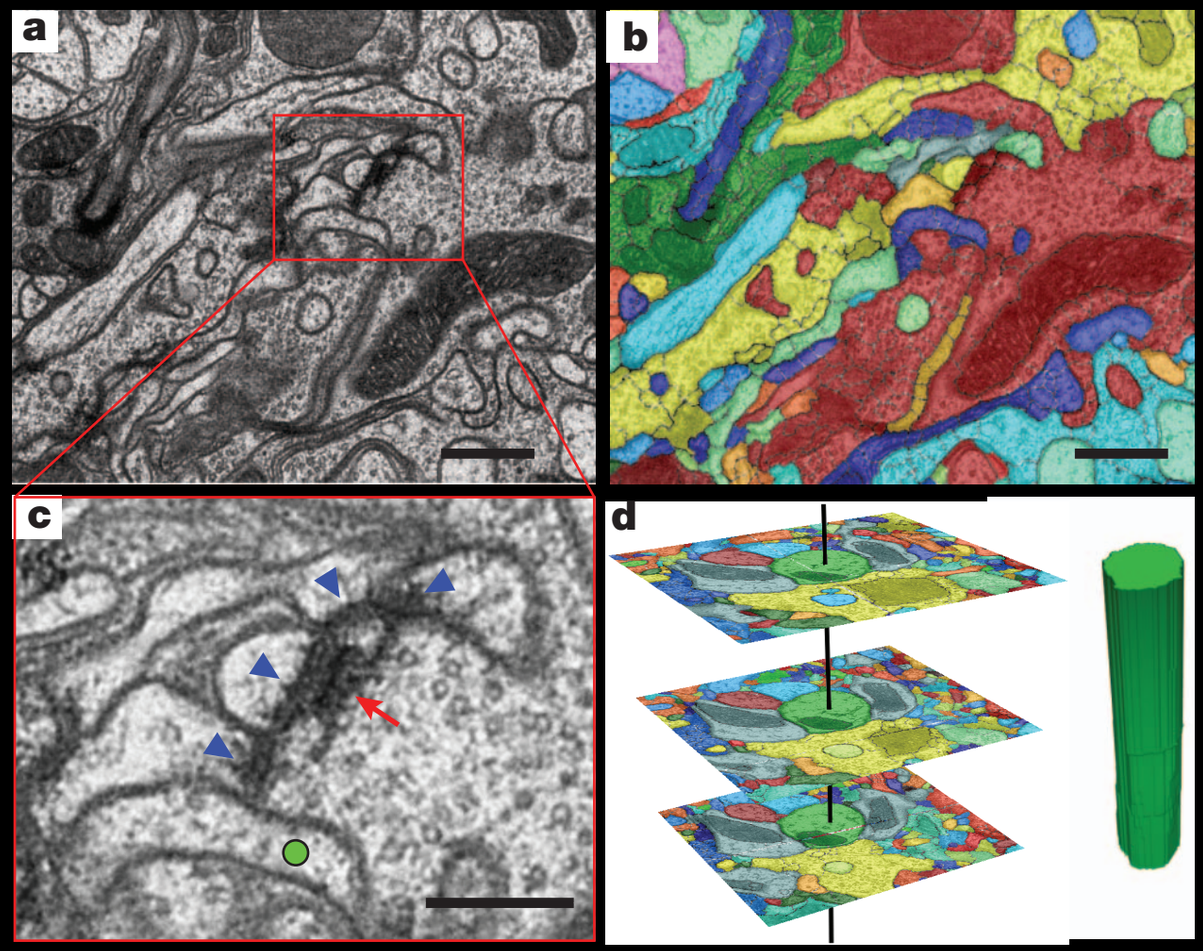


Zingg B, et.al, Cell (2015)

Mapping the connectome (mesoscale)

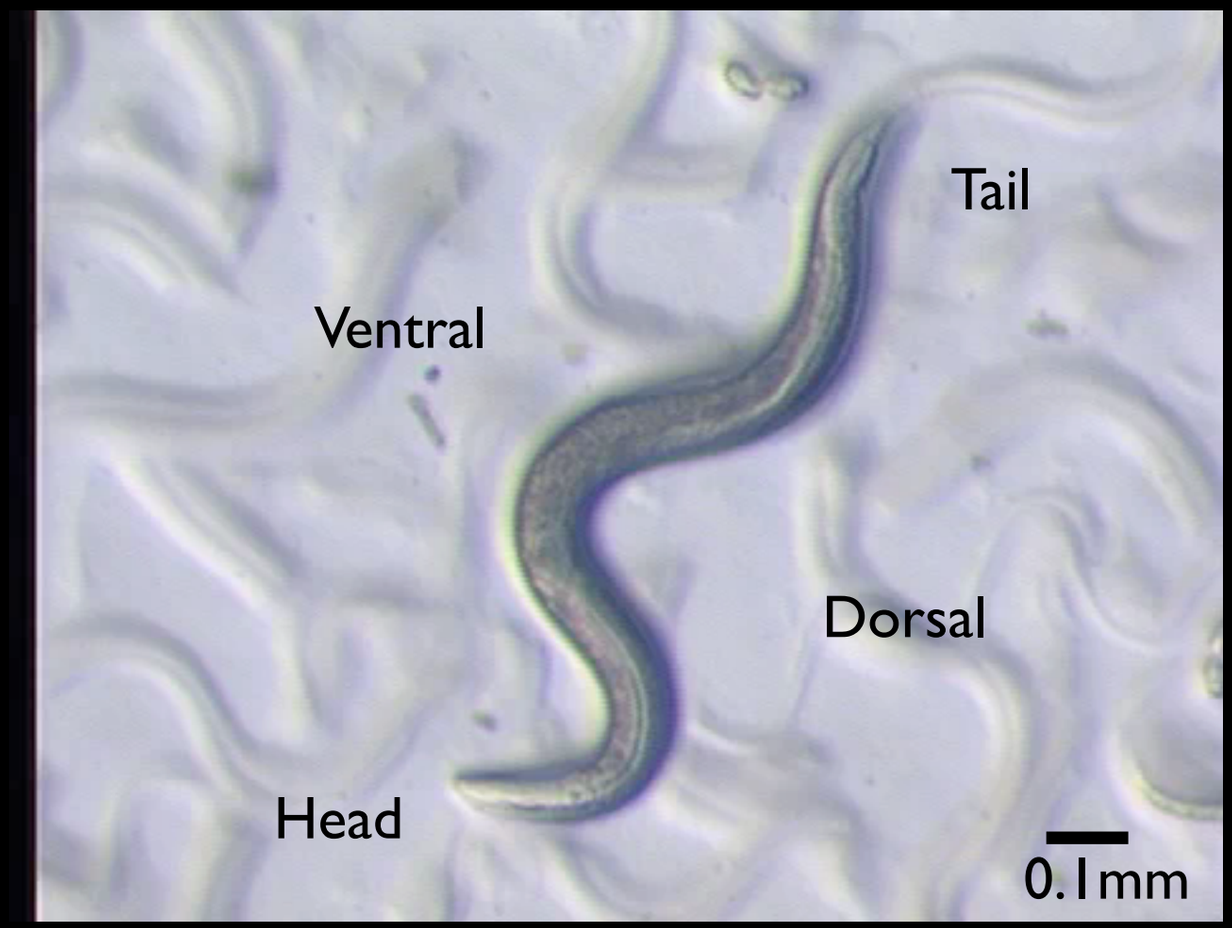


Mapping the connectome
(Electron Microscopy)

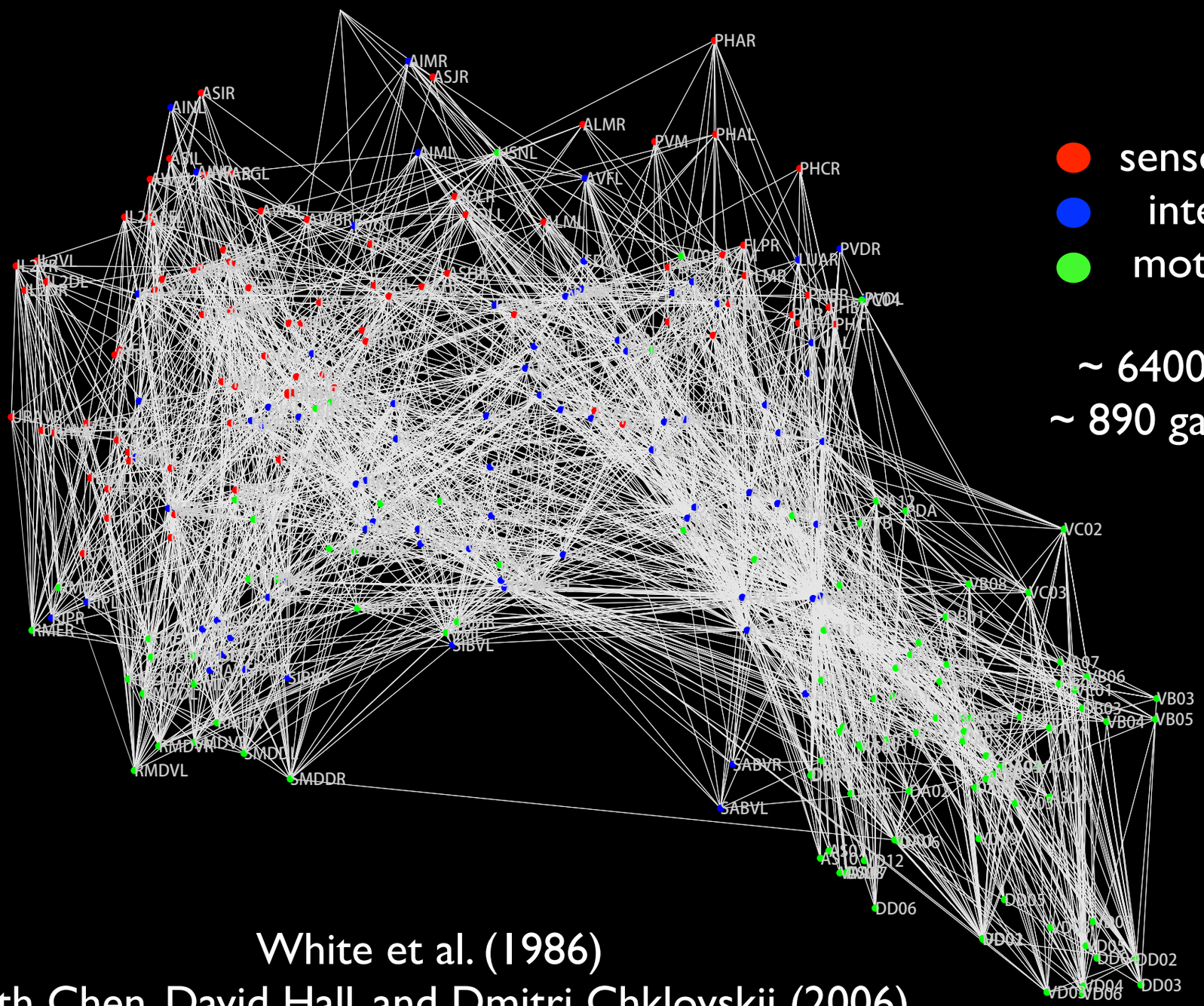


Takemura S, et. al, 2013 Nature

Caenorhabditis elegans



Worm Connectome

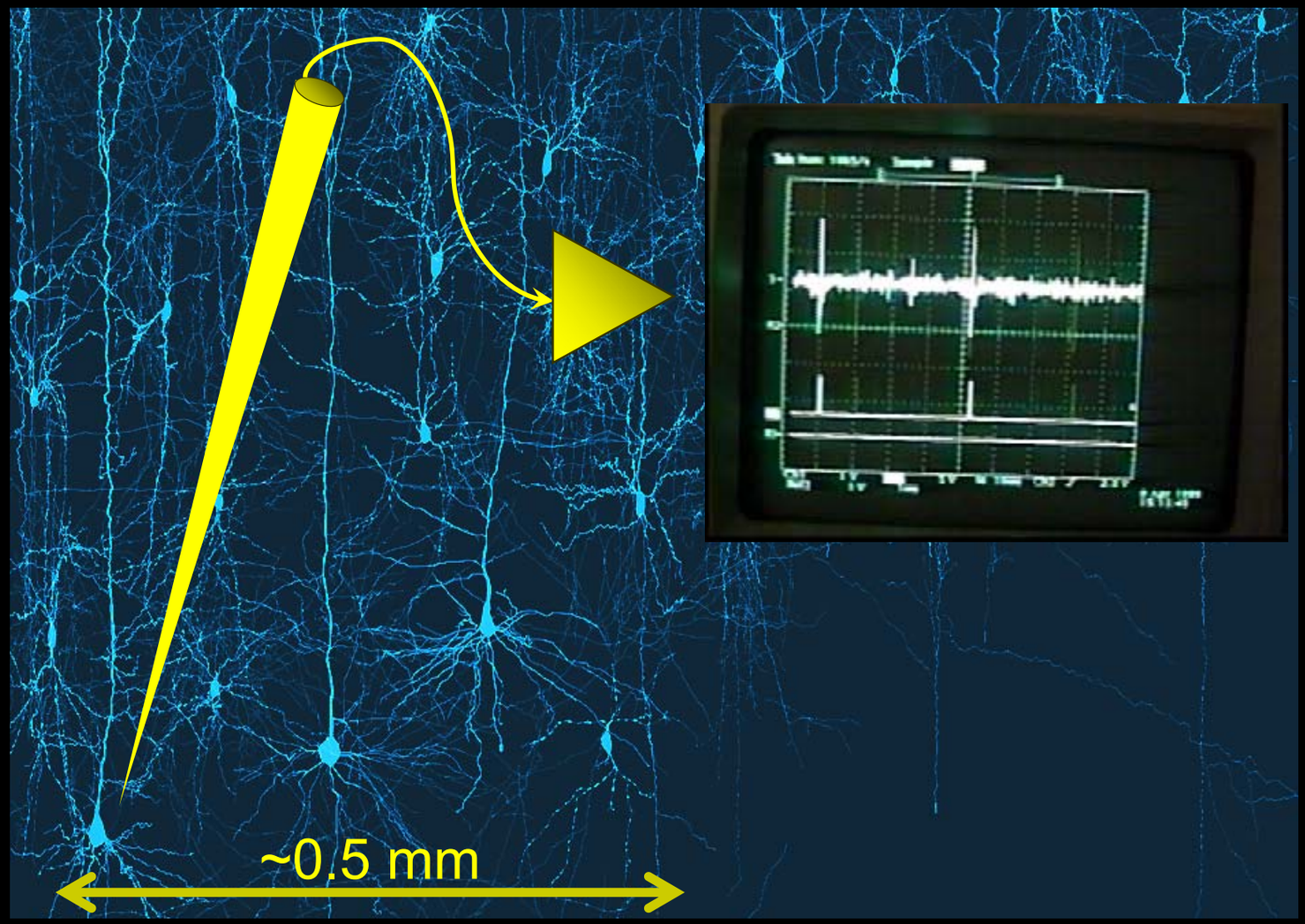


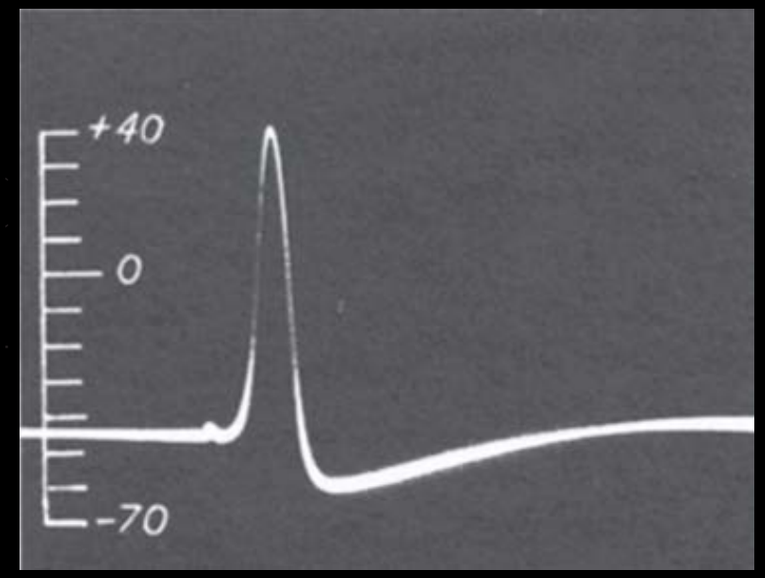
- sensory neuron
- inter neuron
- motor neuron

~ 6400 synapses
~ 890 gap junctions

White et al. (1986)
Beth Chen, David Hall, and Dmitri Chklovskii (2006)

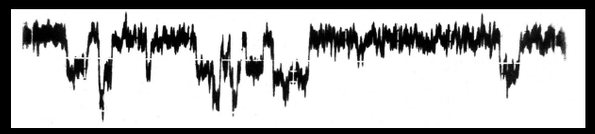
Electrophysiology

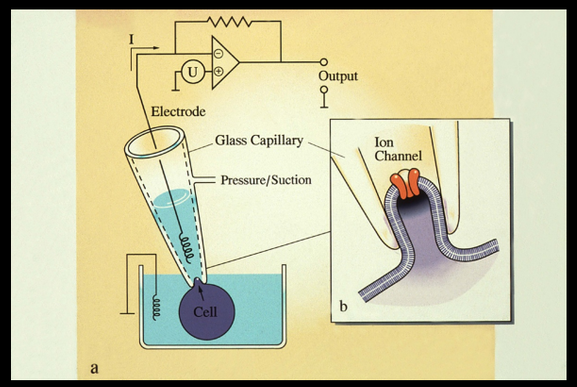


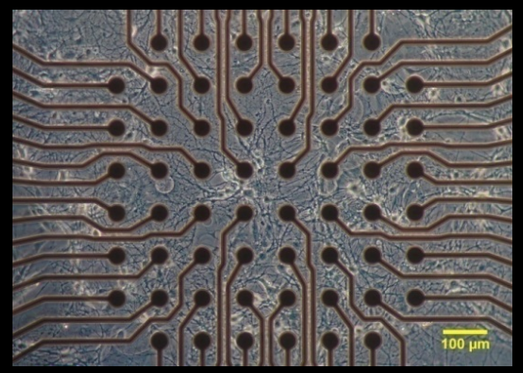


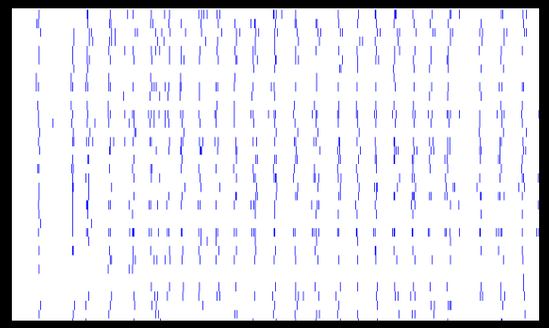
2 ms

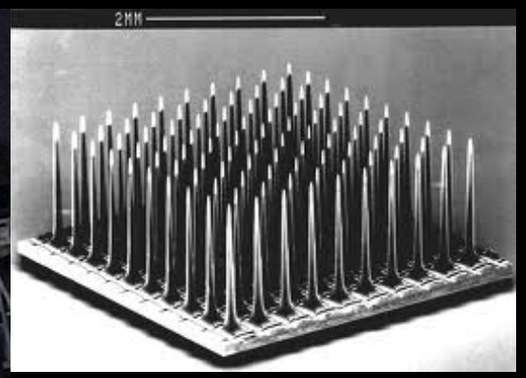
Electrophysiology







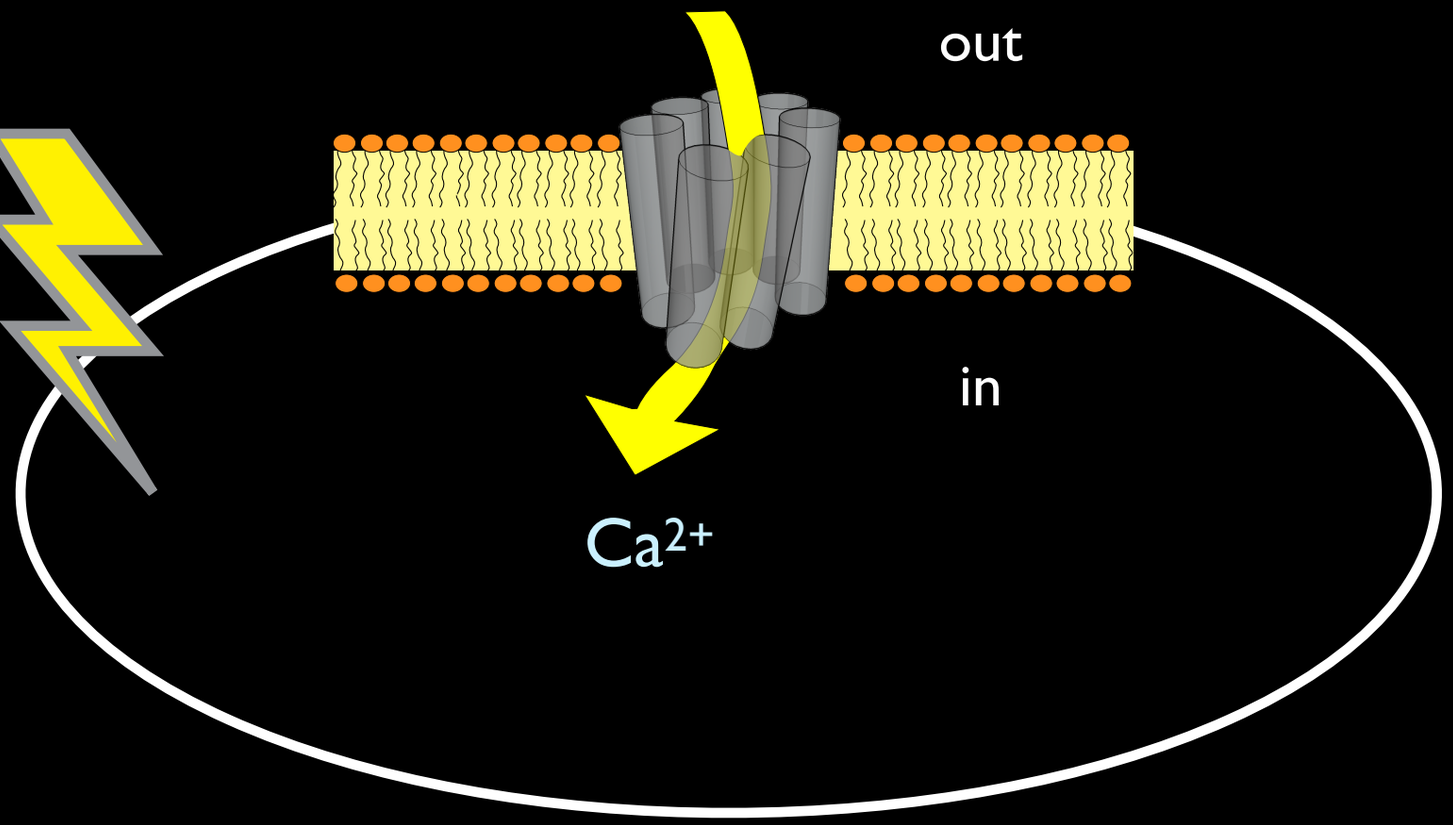




Optical Neurophysiology

using proteins to optically *monitor* neural activities

Infer neural activity from calcium activity



Optically recording neural activity using Cameleon

Cyan fluorescent protein (CFP)

CaM

M13

Yellow fluorescent protein (YFP)

Cyan fluorescent protein (CFP)

CaM

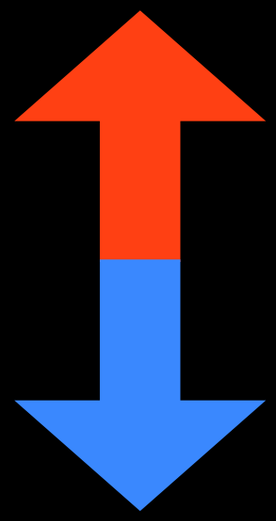
Ca^{2+} Ca^{2+}

M13

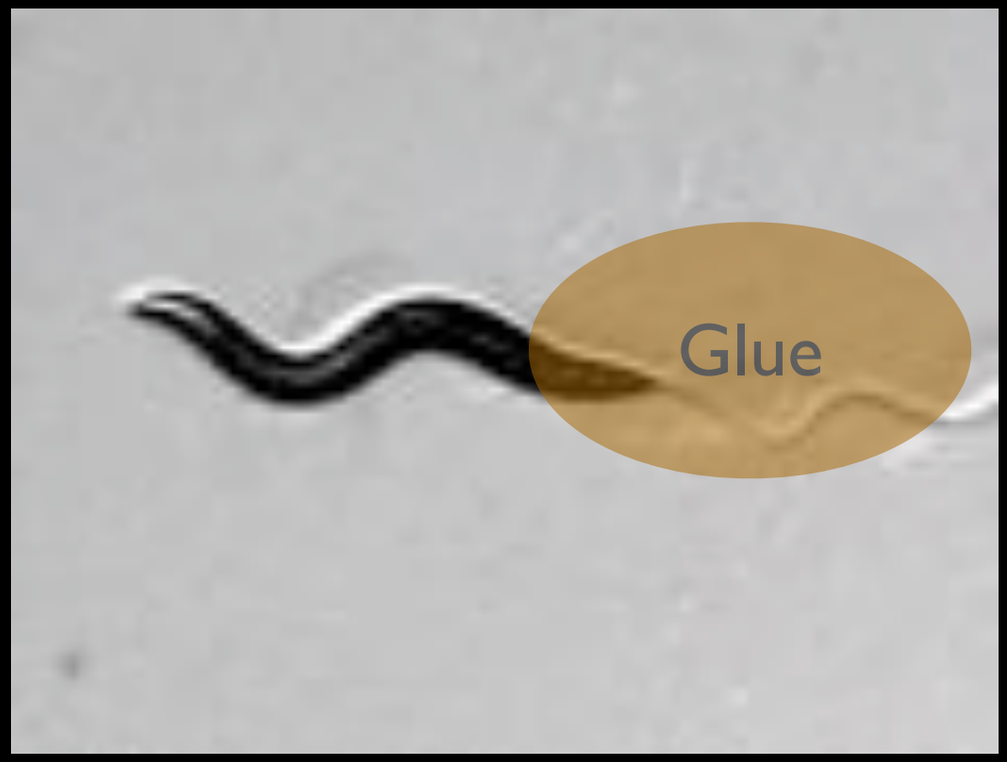
Yellow fluorescent protein (YFP)

Recording calcium activity in a thermosensory neuron AFD

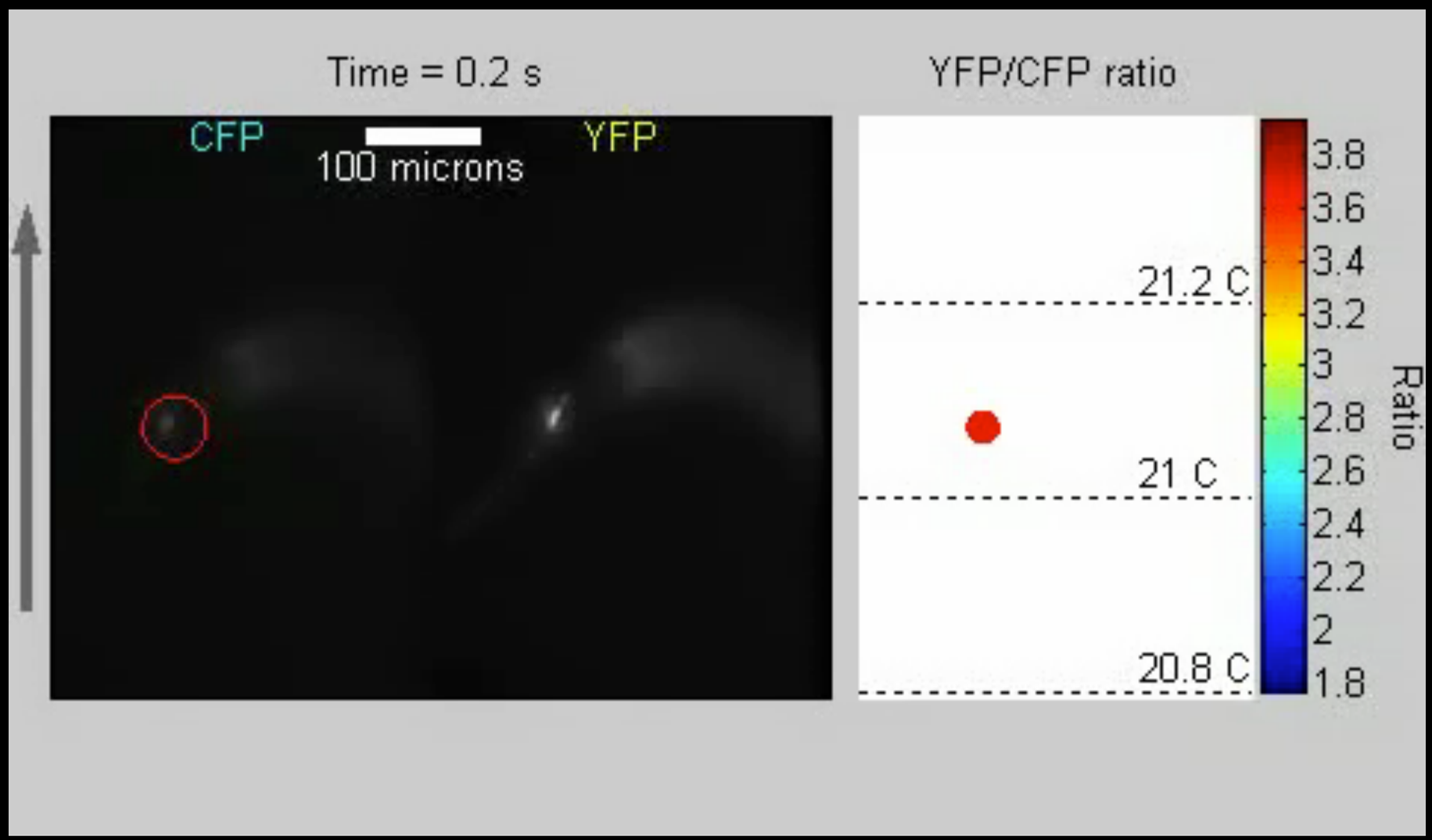
heat



cool



Recording calcium activity in a thermosensory neuron AFD



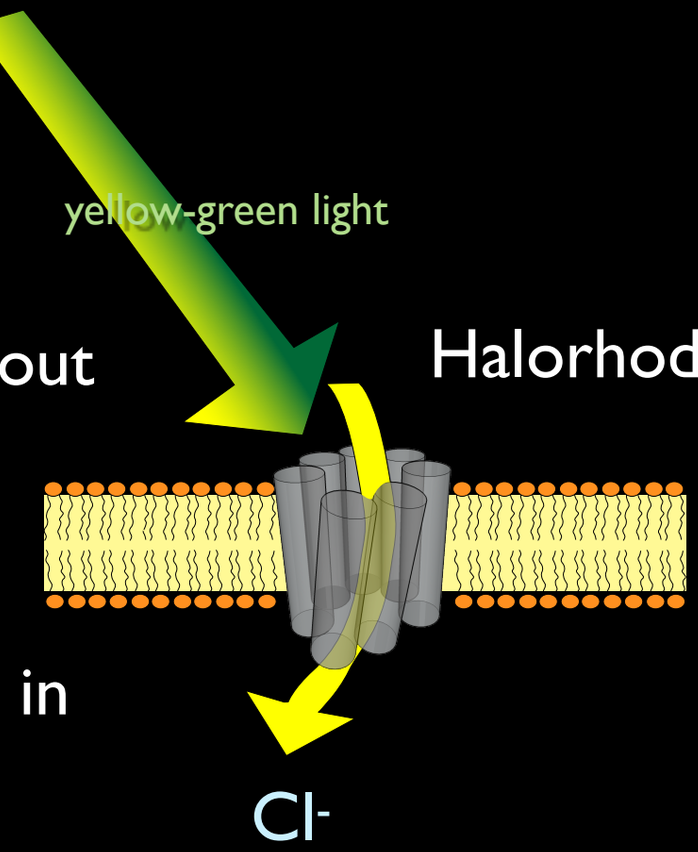
Optical Neurophysiology

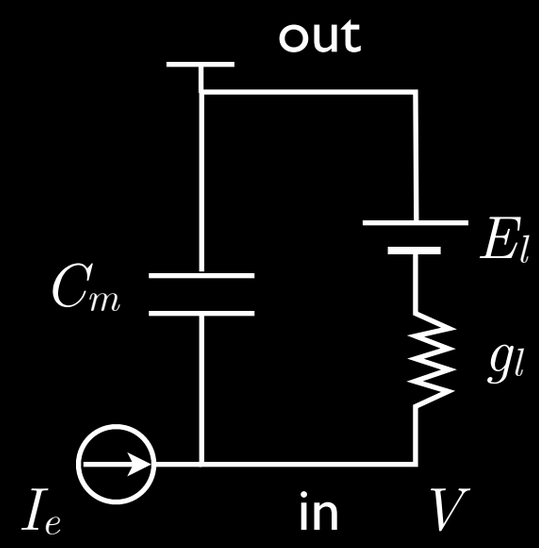
using proteins to optically *manipulate* neural activities

Optogenetics

dead sea

Optogenetics

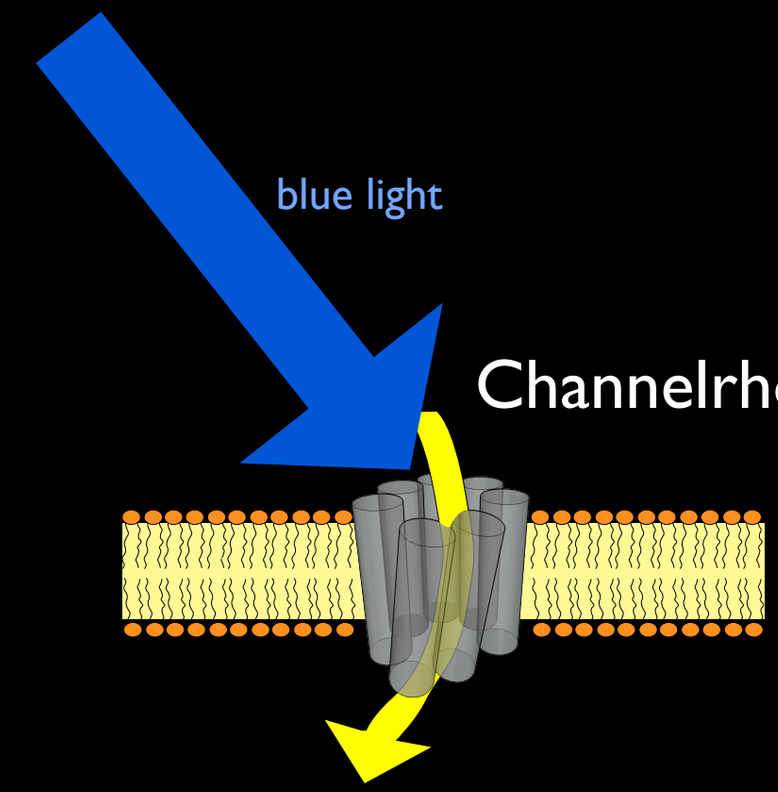




Inhibit cell activity

$$C_m dV/dt = -g_l(V-E_l)+I_e$$

Optogenetics



excite cell activity

Fiberoptic Control of Locomotion in ChR2 Mouse

History of Computational Neuroscience

First Breakthrough

Single neuron computation (1950-1960)

- Theory of action potential generation (Hodgkin and Huxley, 1962 Nobel Prize)
- Cable Theory for signal transduction in dendrites and axons (Wilfred Rall)
- Dendritic Integration (Christopher Koch et. al. 1980-1990)

Second Breakthrough
Coding and Memory (1970-2000)

- Receptive field in visual cortex (Hubel and Wiesel, Nobel Prize 1980)
- Hopfield Network for memory storage (JJ Hopfield 1982, Dirac Medal in theoretical physics)
- Information Theory in sensory coding (William Bialek, 1990)
- Sparse coding (Bruno Olshausen, 1990)

What will we learn in this semester?

Selected questions

- **Wiring**: how do neurons connect to one another to form functional circuits?
- **Coding and Processing**: how does a neural circuit represent and process information?
- **Learning**: how does a neural circuit reconfigure themselves in response to external inputs?
- **Motor**: how does a neural circuit generate complex yet flexible motor behaviors?
- **Emergence**: where do consciousness and free will come from?

课程规划

- The basic organization of the brain
- single neuron electronics
- synapses and neural plasticity
- neural network, short term and long term memory
- information theory and sensory processing
- unsupervised and supervised learning

Textbook

- Liqun Luo *Principles of Neurobiology*
- Peter Dayan & Larry Abbott *Theoretical Neuroscience: Computational and Mathematical modeling of the Neural Systems*