

SYDE 556/750

Simulating Neurobiological Systems

Lecture 1: Introduction

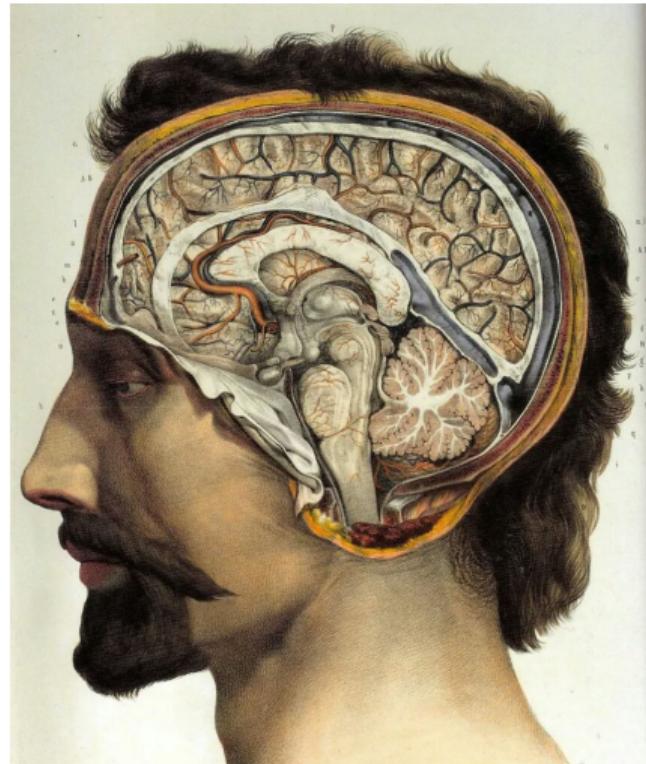
Chris Eliasmith

September 6, 2023

- ▶ Slide design: Andreas Stöckel
- ▶ Content: Terry Stewart, Andreas Stöckel, Chris Eliasmith



FACULTY OF
ENGINEERING



Goal of This Course

Image Sources. Left: "A chimpanzee brain at the Science Museum London", from Wikimedia. Centre: "Robot at a campus faire in São Paulo" from Wikimedia. Right: The Braindrop Neuromorphic hardware system, from "Braindrop: A Mixed-Signal Neuromorphic Architecture With a Dynamical Systems-Based Programming Model", Neckar et al., 2019.

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Building Large-Scale Brain Models

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Why?



Understand how Brains
Work

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Build Better AI Systems

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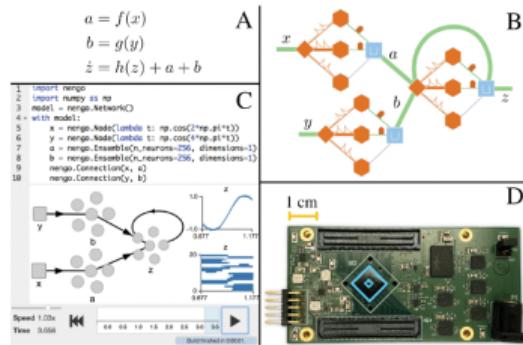
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Understand how Brains Work



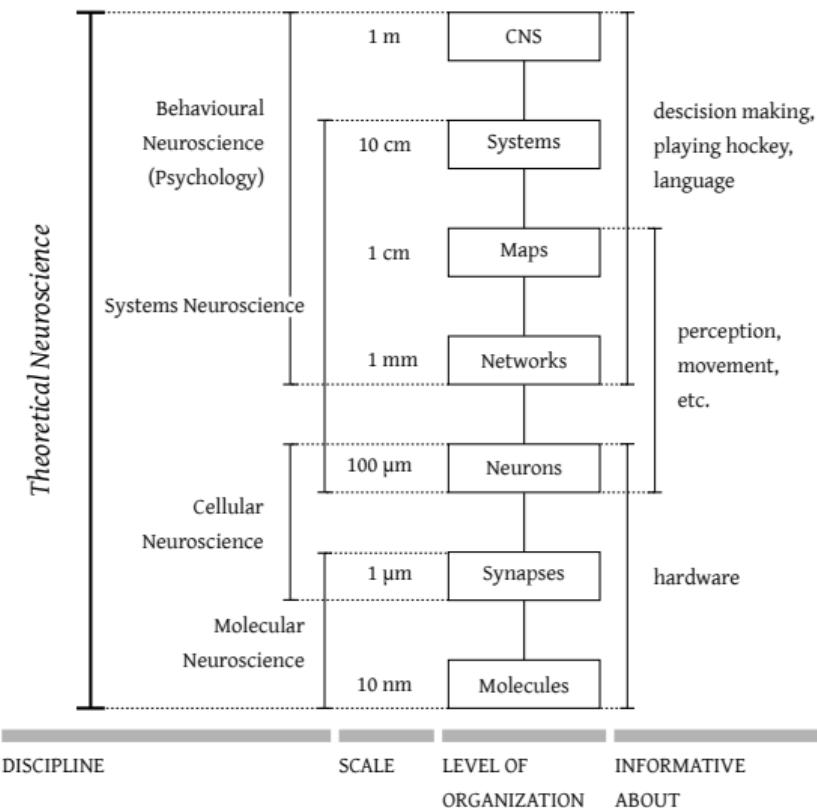
Build Better AI Systems



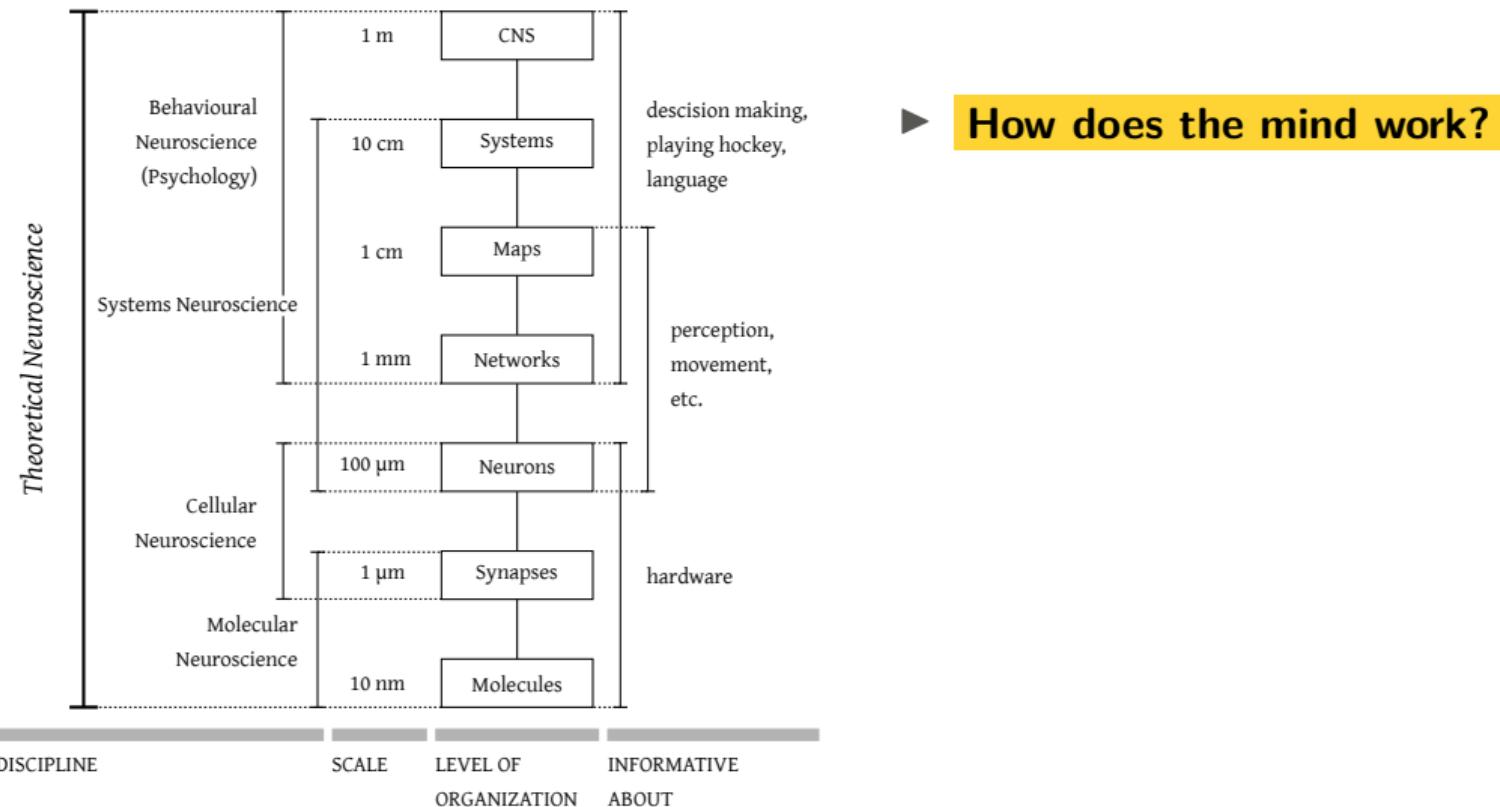
Program Neuromorphic Hardware

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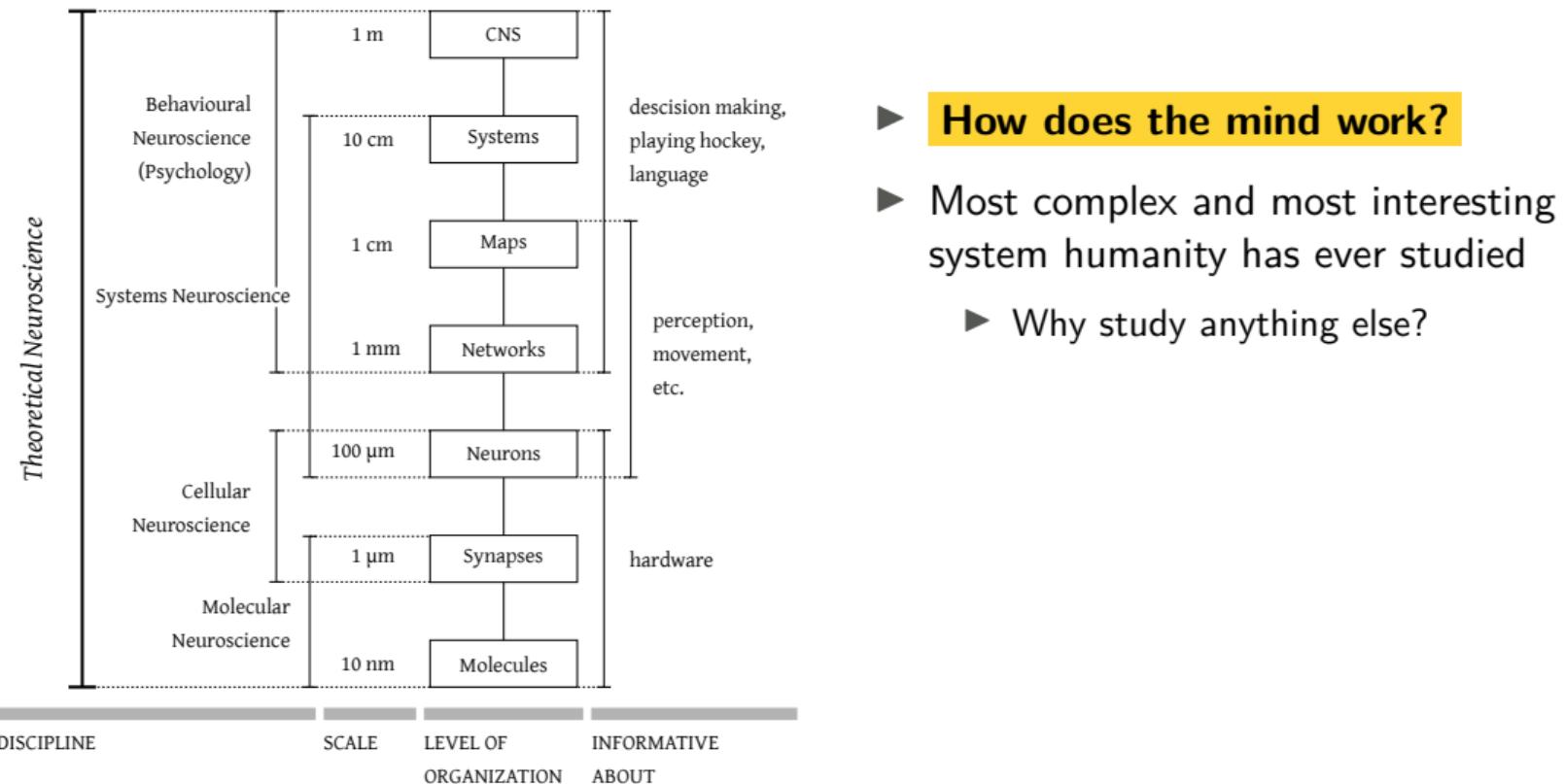
Our Focus: Theoretical Neuroscience



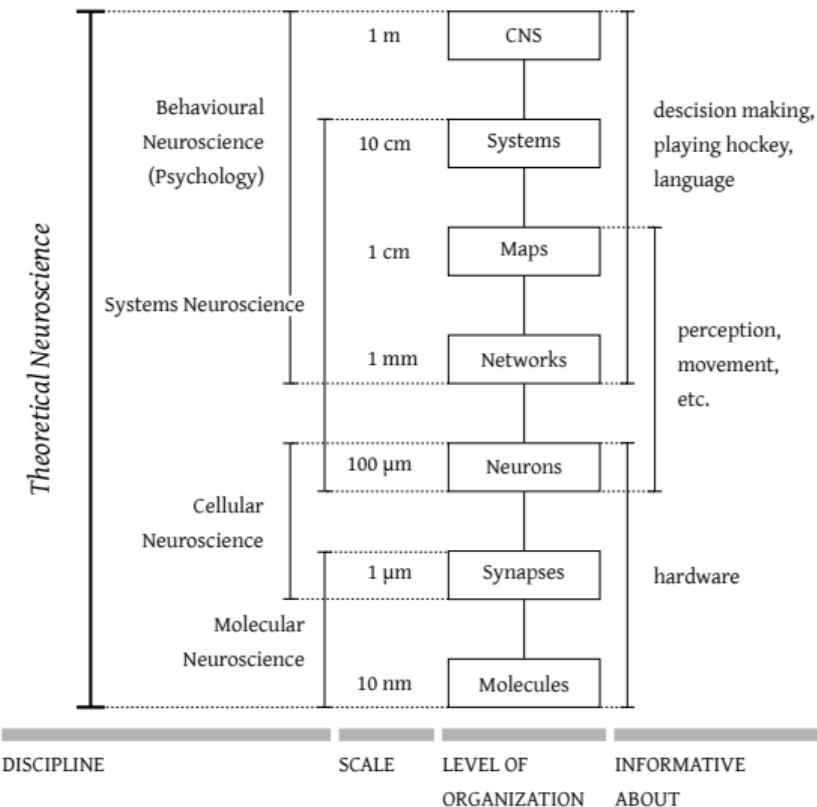
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Our Focus: Theoretical Neuroscience



- ▶ **How does the mind work?**
- ▶ Most complex and most interesting system humanity has ever studied
 - ▶ Why study anything else?
- ▶ How should we go about studying it?
 - ▶ What techniques/tools?
 - ▶ How do we know if we're making progress?
 - ▶ How do we deal with the complexity?

Theoretical Neuroscience vs. Theoretical Physics

	Theoretical physics	Theoretical neuroscience
Quantify phenomena	$F = ma$	$\hat{x} = Da$
Summarize lots of data	motion of objects	neural representation of information
Speculative (generate hypotheses)	true for all velocities	true for all stimuli

Theoretical Neuroscience vs. Theoretical Physics

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Similarities

- ▶ Methods are similar
- ▶ Goals are similar (quantification)

Theoretical Neuroscience vs. Theoretical Physics

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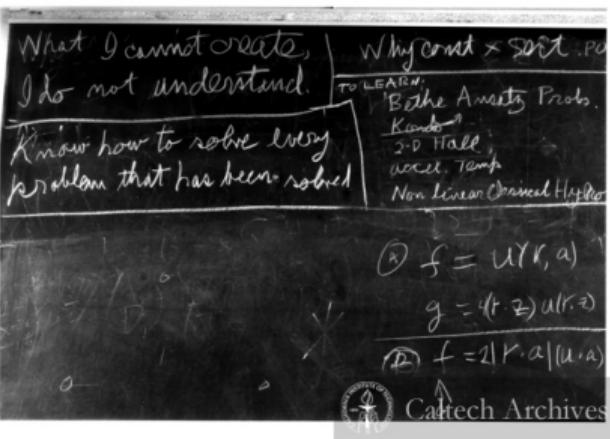
Similarities

- ▶ Methods are similar
- ▶ Goals are similar (quantification)

Differences

- ▶ “What exists?” vs. “Who are we?”
- ▶ Even more simulation in biology

Neural Modelling

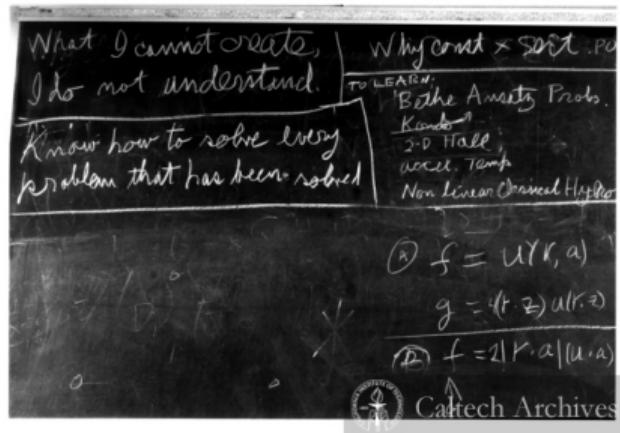


“What I cannot create, I do not
understand”
— Richard Feynman, 1988

Neural Modelling

► Let's build it

- Requires a mathematically detailed theory
- Often complex; need computer simulation

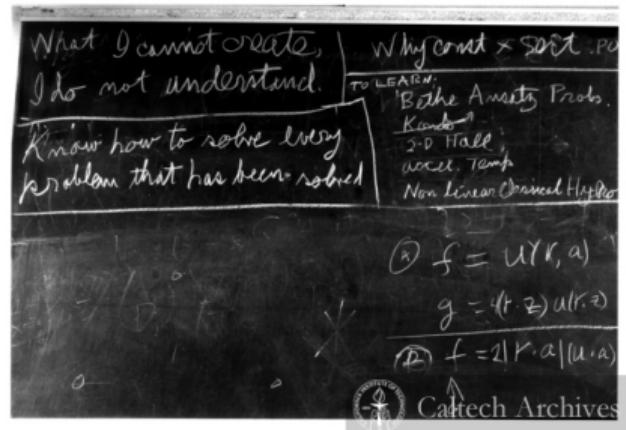


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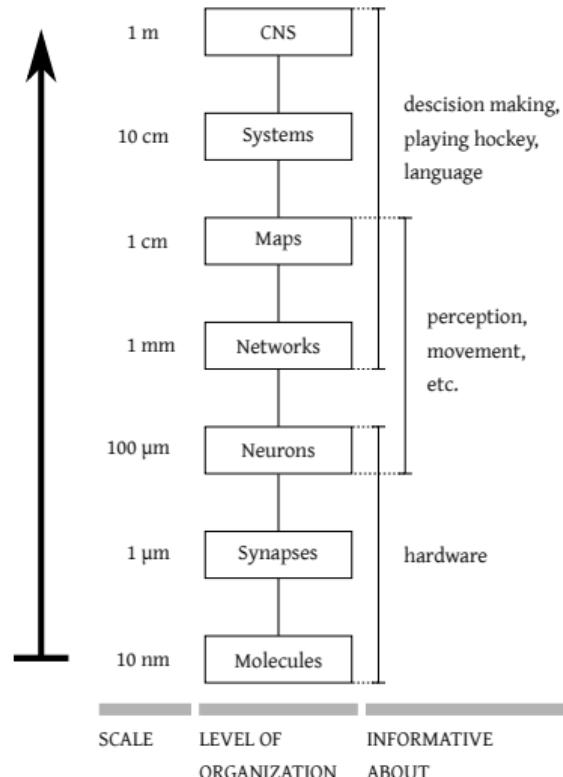
- Requires a mathematically detailed theory
- Often complex; need computer simulation
- Bring together levels and modelling methods
 - **Single neuron models**
Spikes, spatial structure, ion channels...
 - **Small network models**
Spiking neurons, rate neurons, mean fields...
 - **Large network/cognitive models**
Biophysics, pure computation, anatomy...



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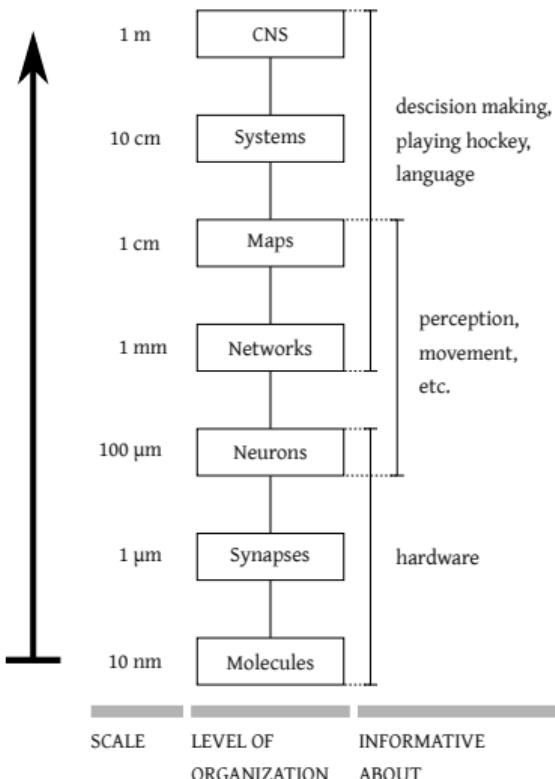
Problems With Current Approaches: Large-scale Neural Models

- **Bottom-up** approach



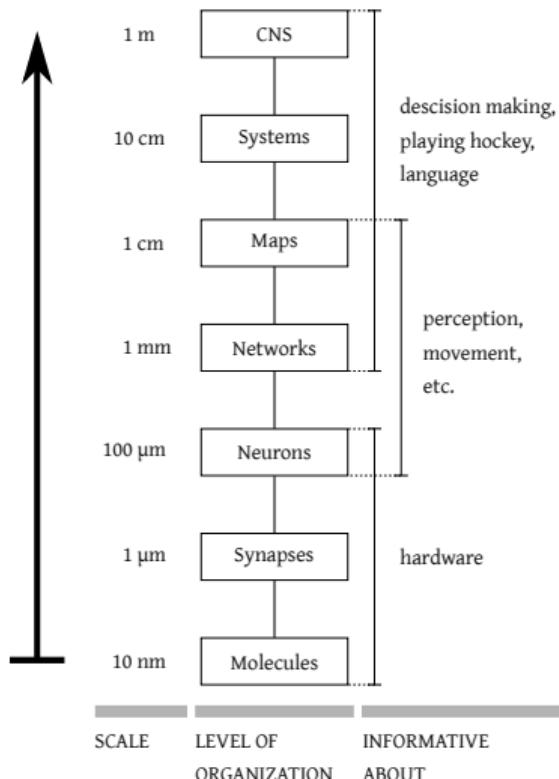
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- **Bottom-up** approach
 - 1. Gather low-level data



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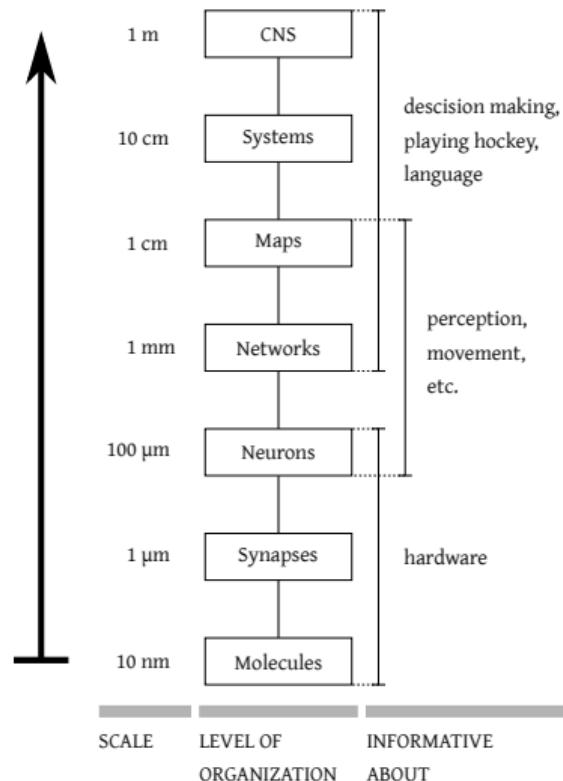
- **Bottom-up** approach
 - 1. Gather low-level data
 - 2. Build a detailed model



Problems With Current Approaches: Large-scale Neural Models

► **Bottom-up** approach

1. Gather low-level data
2. Build a detailed model
3. Simulate on special computers



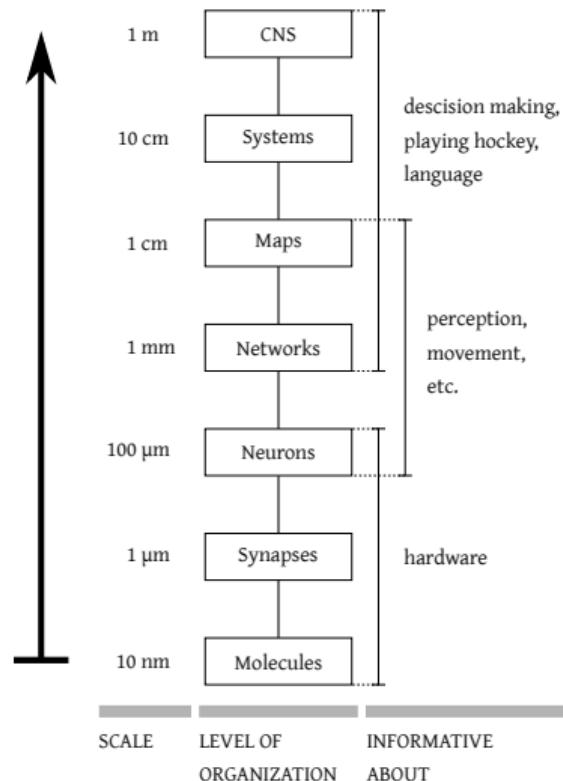
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- Examples

BlueBrain/Human Brain Project/SyNAPSE



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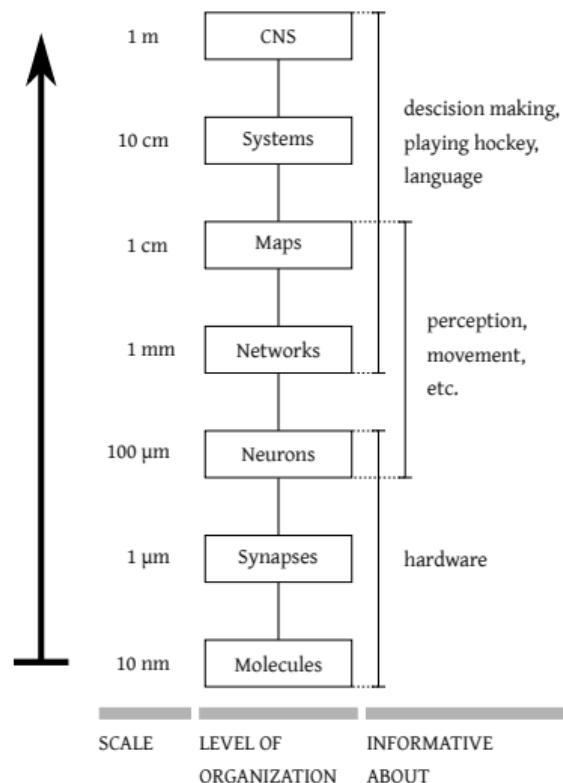
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- Shortcomings

- Lack of function \Rightarrow can't compare to Psychology
- Assumes canonical algorithm
- Expects intelligence to "emerge"



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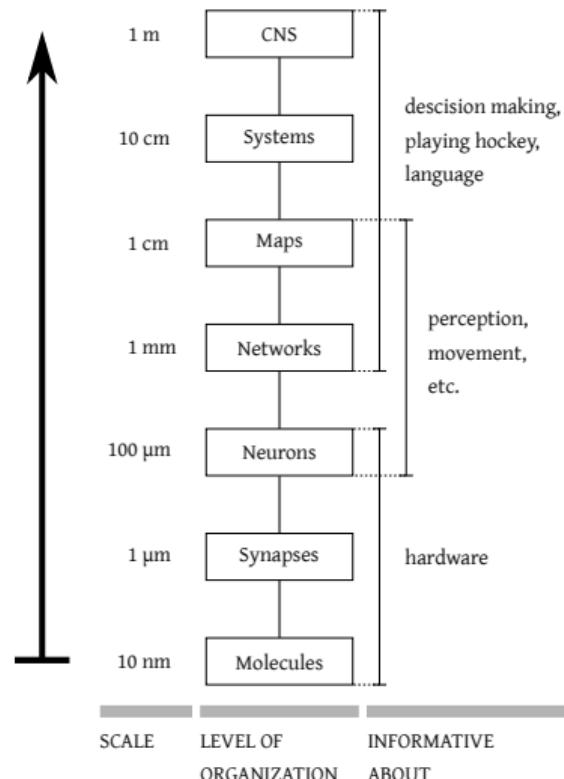
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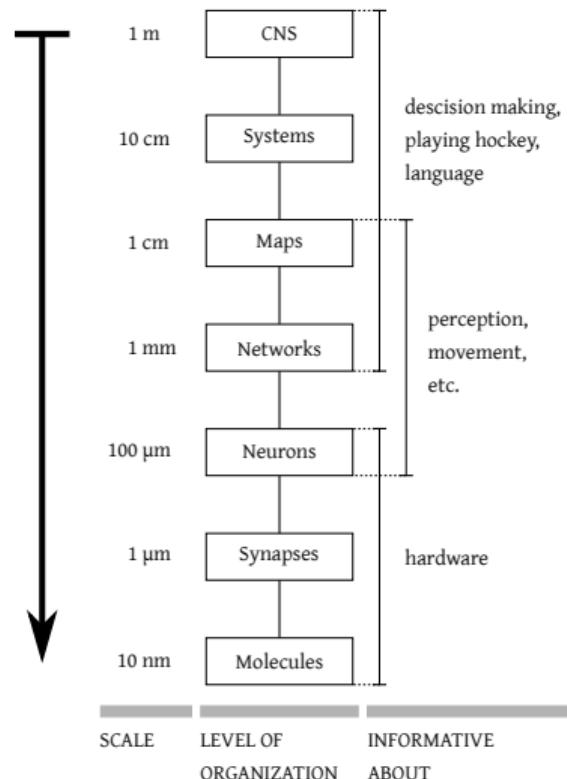
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⚠ This is still important research; these shortcomings are from the perspective of building a "functional" brain model.



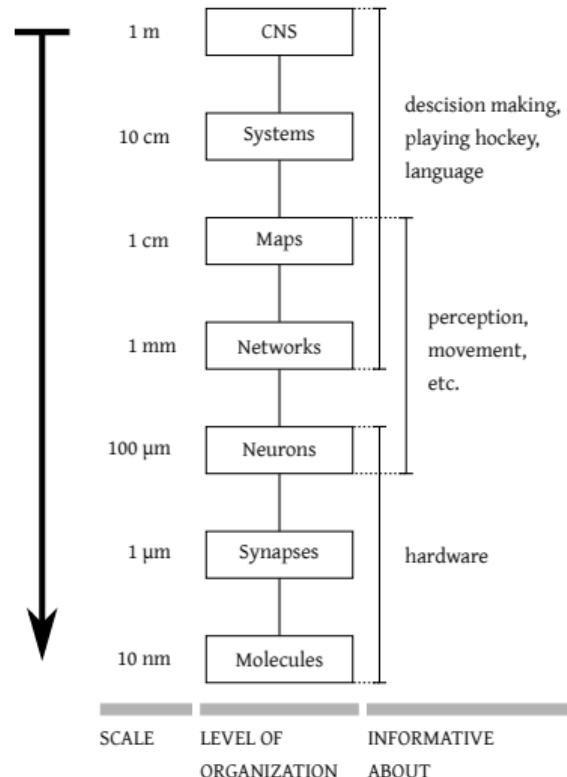
Problems With Current Approaches: Behavioural Models

- **Top-down** approach



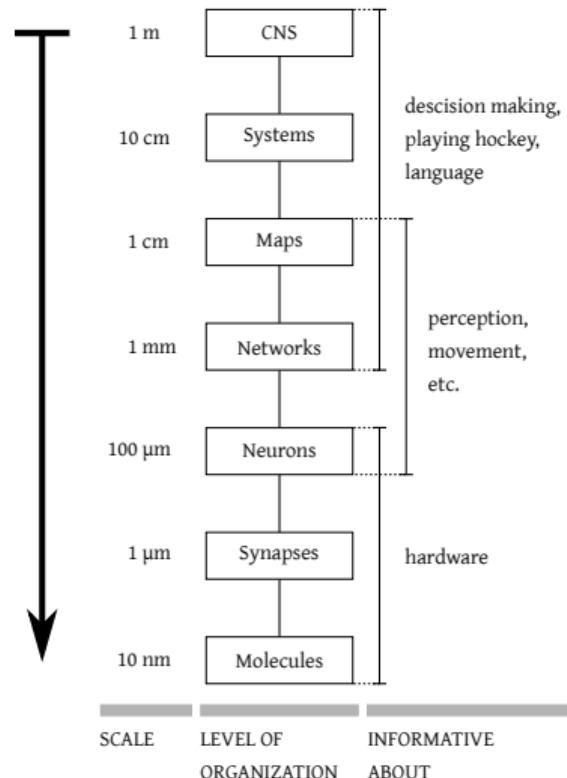
Problems With Current Approaches: Behavioural Models

- ▶ **Top-down** approach
- ▶ **Modeling Frameworks:** ACT-R, SOAR



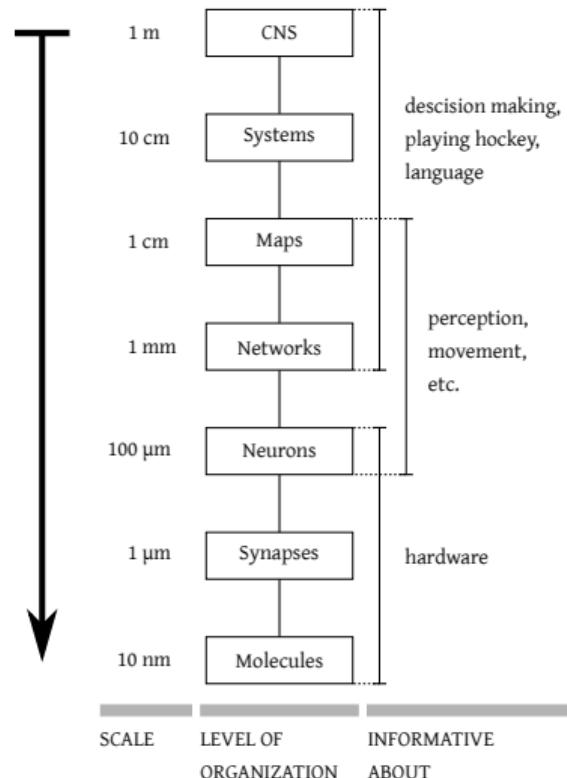
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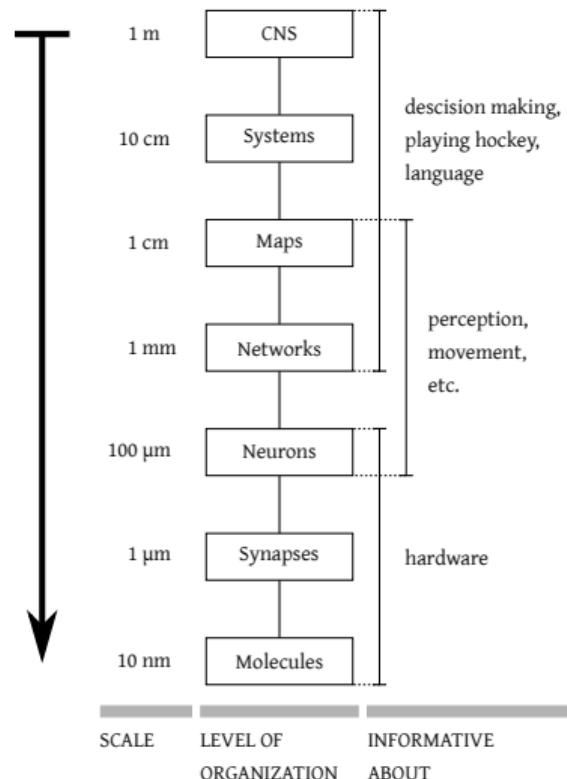
Problems With Current Approaches: Behavioural Models

- ▶ **Top-down** approach
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 - ▶ Can't compare to neural data



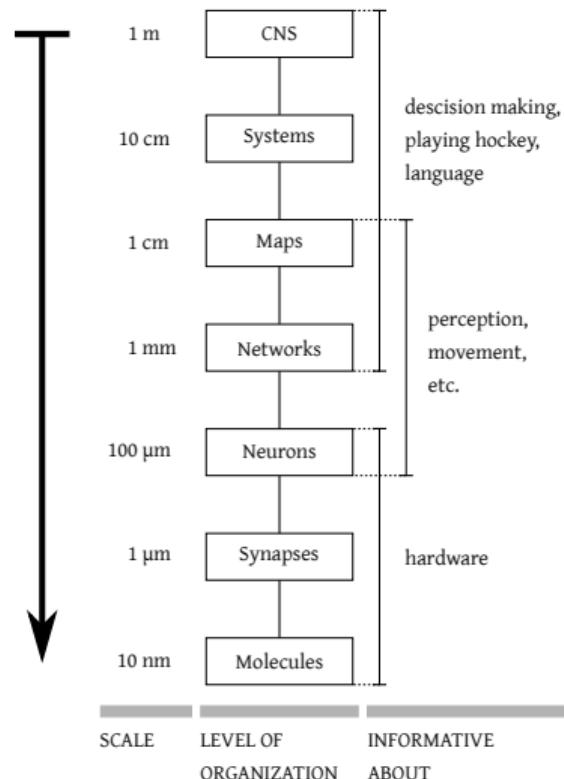
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 - ▶ No "bridging laws"



Problems With Current Approaches: Behavioural Models

- ▶ **Top-down** approach
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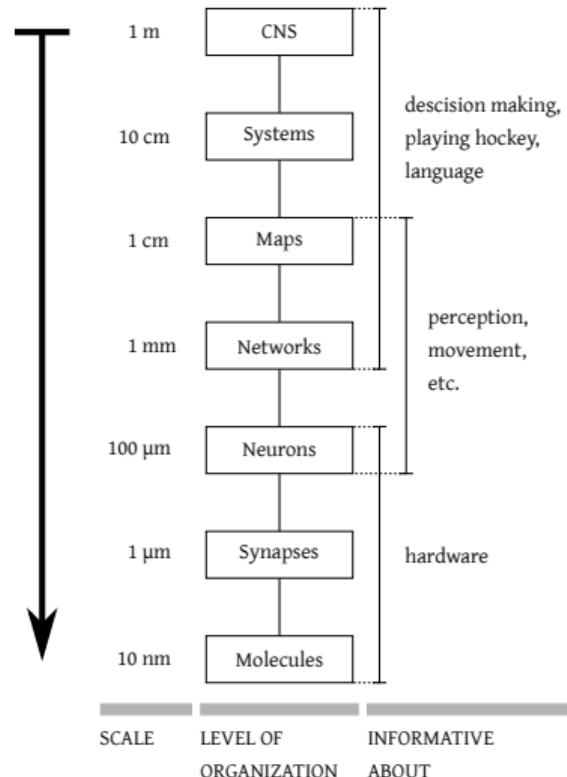
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⚠ **Maybe these shortcomings are okay.**

Do we understand the brain enough to derive
bridging laws and constrain theories?

When understanding a word processor, do we worry
about transistors?



The Brain

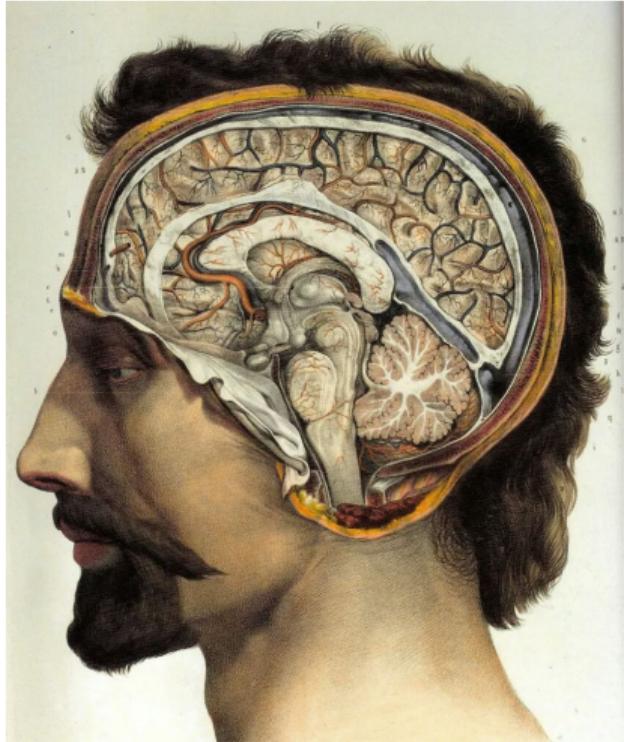
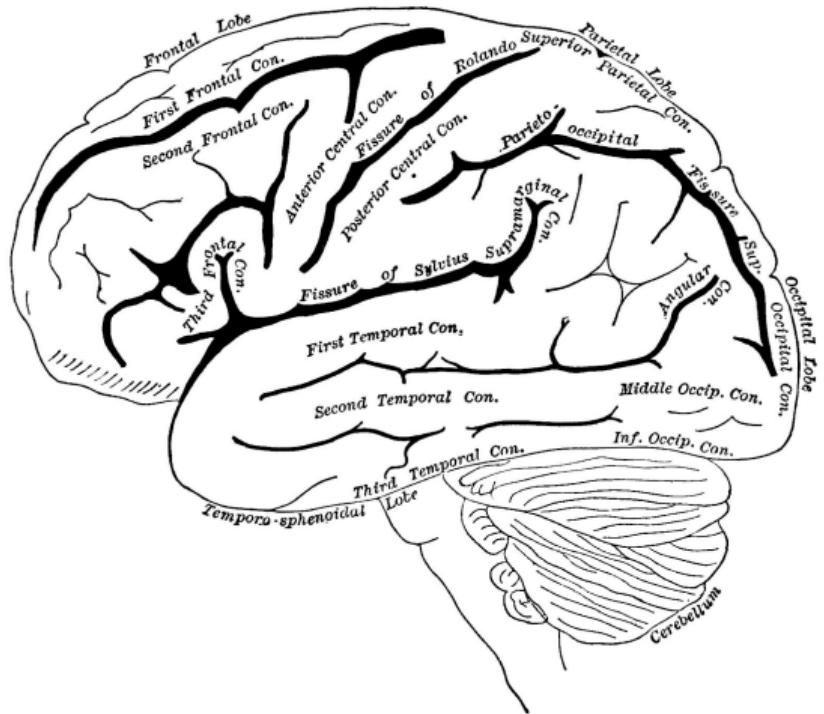


Image Sources. Left: "Labelled lateral view of the left hemisphere", from *Popular Science Monthly, Volume 35* (1889) via Wikimedia. Right: "Sagittal cross-section", illustration by Jean-Baptiste Marc Bourgery, *Traité complet de l'anatomie de l'homme* (1831 to 1854) via Wikimedia.

The Brain – Some Statistics

- ▶ **Weight:**
2 kg (2% of the body weight)
- ▶ **Power consumption:**
20 W (25% of the body's total power consumption)
- ▶ **Surface area:**
1500 cm² to 2000 cm² (roughly four A4/letter pages of paper)
- ▶ **Number of neurons:**
100 billion (10^{11} , 150 000 mm⁻²)
- ▶ **Number of synapses:**
100 trillion (10^{14} , about 1000 per neuron)

THE UNFIXED BRAIN

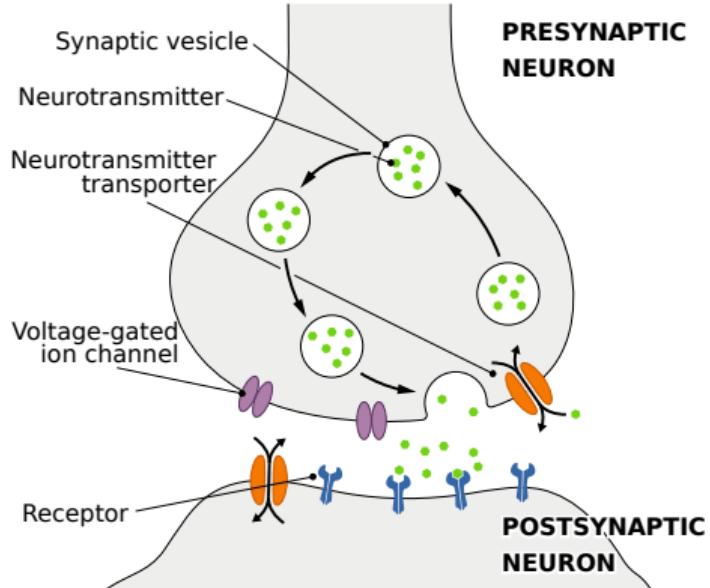
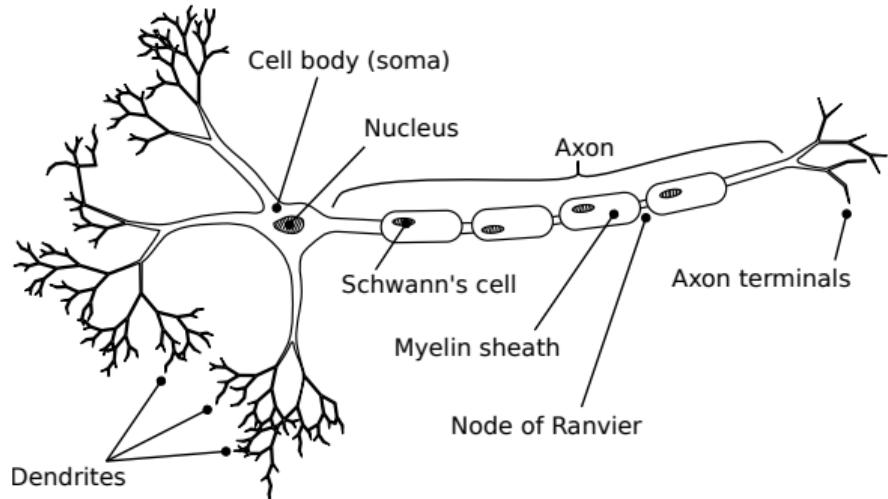


Suzanne Stensaas, PhD



Department of Neurobiology and Anatomy &
Spencer S. Eccles Health Sciences Library
University of Utah, Salt Lake City, Utah, USA

Neurons in the Brain



- ▶ 100's or 1000's of **distinct types**
(distinguished by anatomy/physiology)
- ▶ Axon length: from $100 \mu\text{m}$ to 5 m
- ▶ Vastly different input/output counts
(*convergence* and *divergence*)
- ▶ 100's of different neurotransmitters

What It Really Looks Like

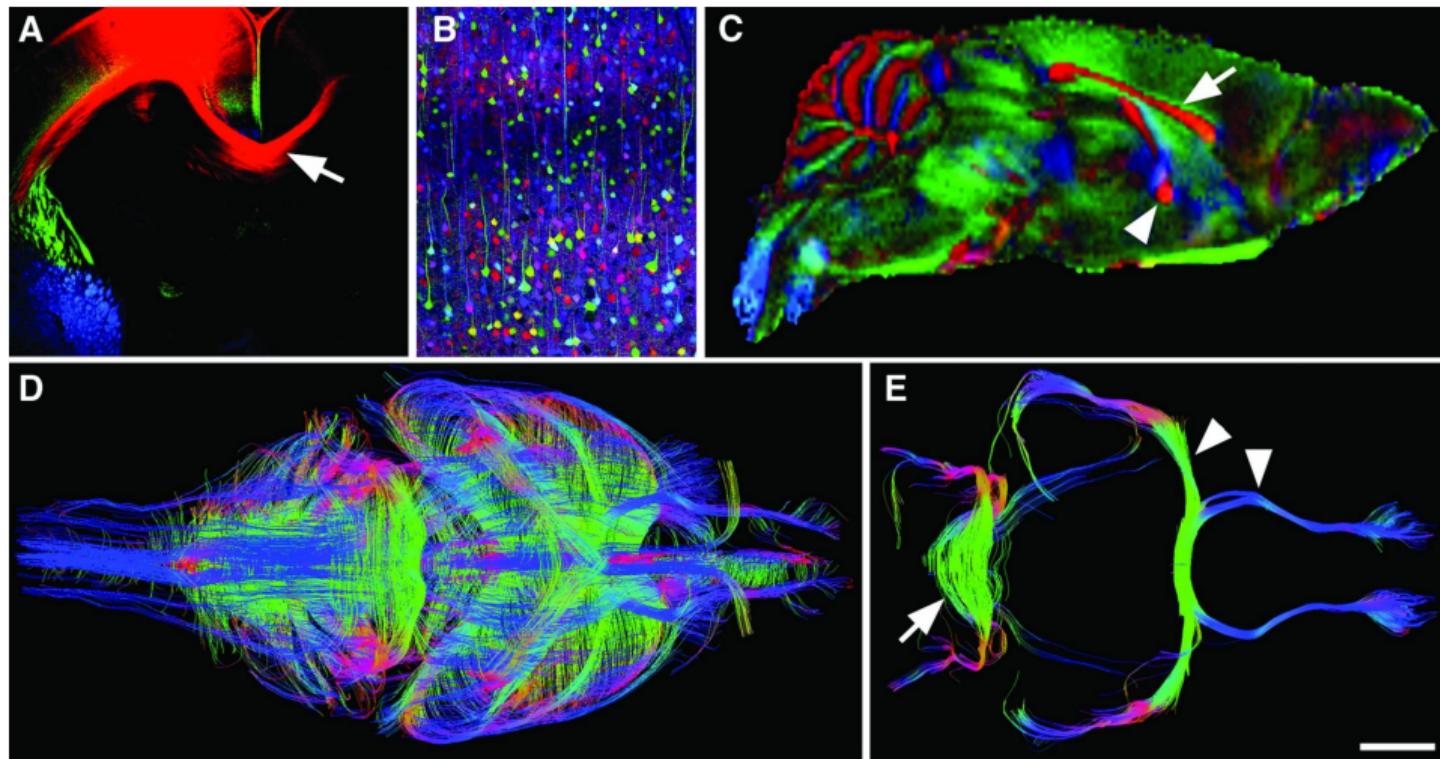
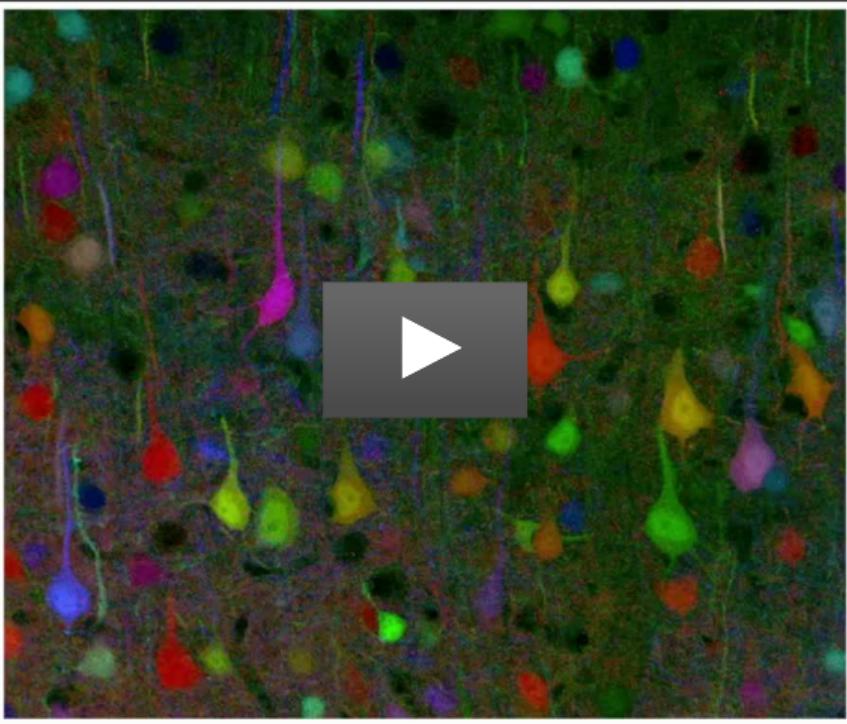


Image Sources. Alain Chédotal and Linda J Richards. *Wiring the Brain: The Biology of Neuronal Guidance*. Cold Spring Harbor perspectives in biology (2010)



R Draft & J Livet

x = independently organized TED event

TEDx Caltech

Kinds of Data From the Brain – Non-Invasive – fMRI

Functional Magnetic Resonance Tomography

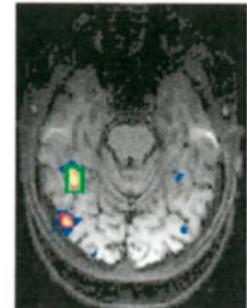
Measures *changes* in blood oxygenation (BOLD)

- + Whole-brain, 3D reconstruction
(individual activity voxels, volume elements)
- Yellow circle Medium spatial resolution (millimeters)
- Low temporal resolution (seconds)
- Signal is hard to interpret
(differences, indirect, i.e. not spiking activity)
- Has to be averaged over multiple trials

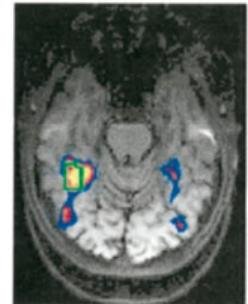
A catalogue of fMRI can be found at

[https://neurosynth.org/.](https://neurosynth.org/)

3a. Faces > Objects



3b. Intact Faces > Scrambled Faces



Kinds of Data From the Brain – Non-Invasive – EEG

Electroencephalography

Electric activity on top of the scalp

- ⊕ High time resolution
- ⊕ Relatively cheap
- ⊖ Artefacts
(eye movement, swallowing)
- ⊖ Low spatial resolution



Image Sources. Left: Electroencephalogram (image from Wikimedia). Right: EEG cap (image from Wikimedia).

Kinds of Data From the Brain – Invasive – Lesion Studies

What are the effects of **damaging parts** of the brain?

- ▶ **Occipital cortex** ↪ vision
 - ▶ **Inferior frontal gyrus** ↪ producing speech (Broca's area),
 - ▶ **Posterior superior temporal gyrus** ↪ understanding speech (Wernicke's area),
 - ▶ **Fusiform gyrus** ↪ recognition of faces/visually complex objects,
 - ▶ **Medial prefrontal cortex** ↪ moral judgment (controversial; see: Phineas Gage).
- ⊕ Informative about the functional relevance of an area
- ⊖ Often permanently damaging

Kinds of Data From the Brain – Invasive – Single Cell Recording

Place **electrode near or in single cell**

e.g., record the neural activity given some stimulus

- + High temporal resolution (microseconds)
- + High specificity (single or few neurons)
- Limited to a few cells
- Damaging over time

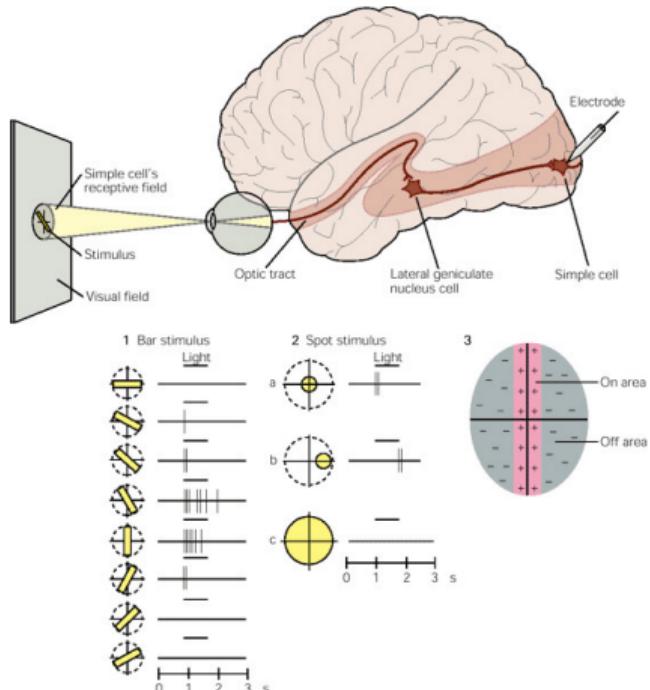


Image Sources. "Depiction of Hubel and Wiesels experiment." Kandel et al., 2012, Principles of Neural Science, 5th ed., Figure 27-11.

Visual Cortex



Mapping receptive fields

Kinds of Data From the Brain – Invasive – Multi-electrode recordings

Insert **tetrode** or a **Microelectrode Array** (MEA; “Utah Array”) into the brain

- + High temporal resolution
(microseconds)
- Up to ≈ 100 cells with one array
- Requires post-processing
(e.g., extraction of individual neurons
from local field potentials, LFPs)

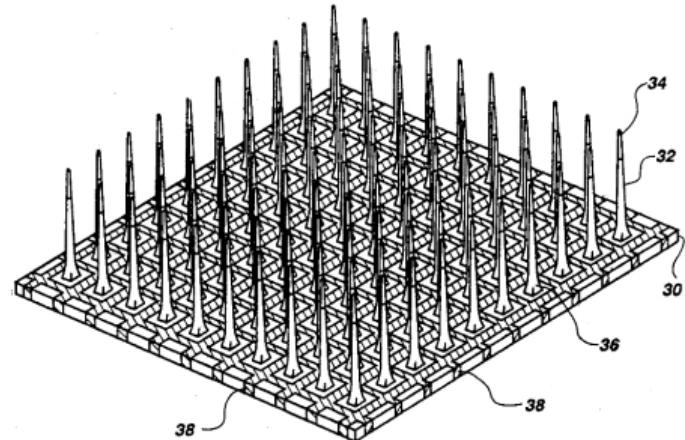
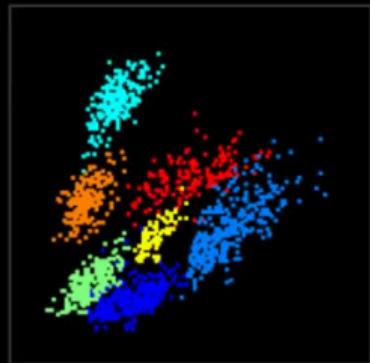


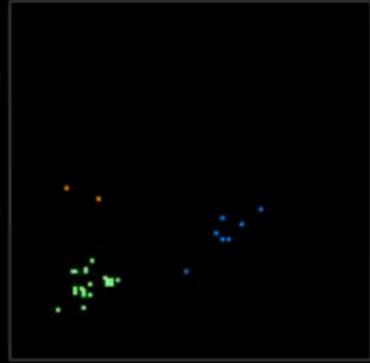
Image Sources. “Depiction of a Utah Array”. From: US Patent #5,215,088

cell activity

overall



ongoing



behavior



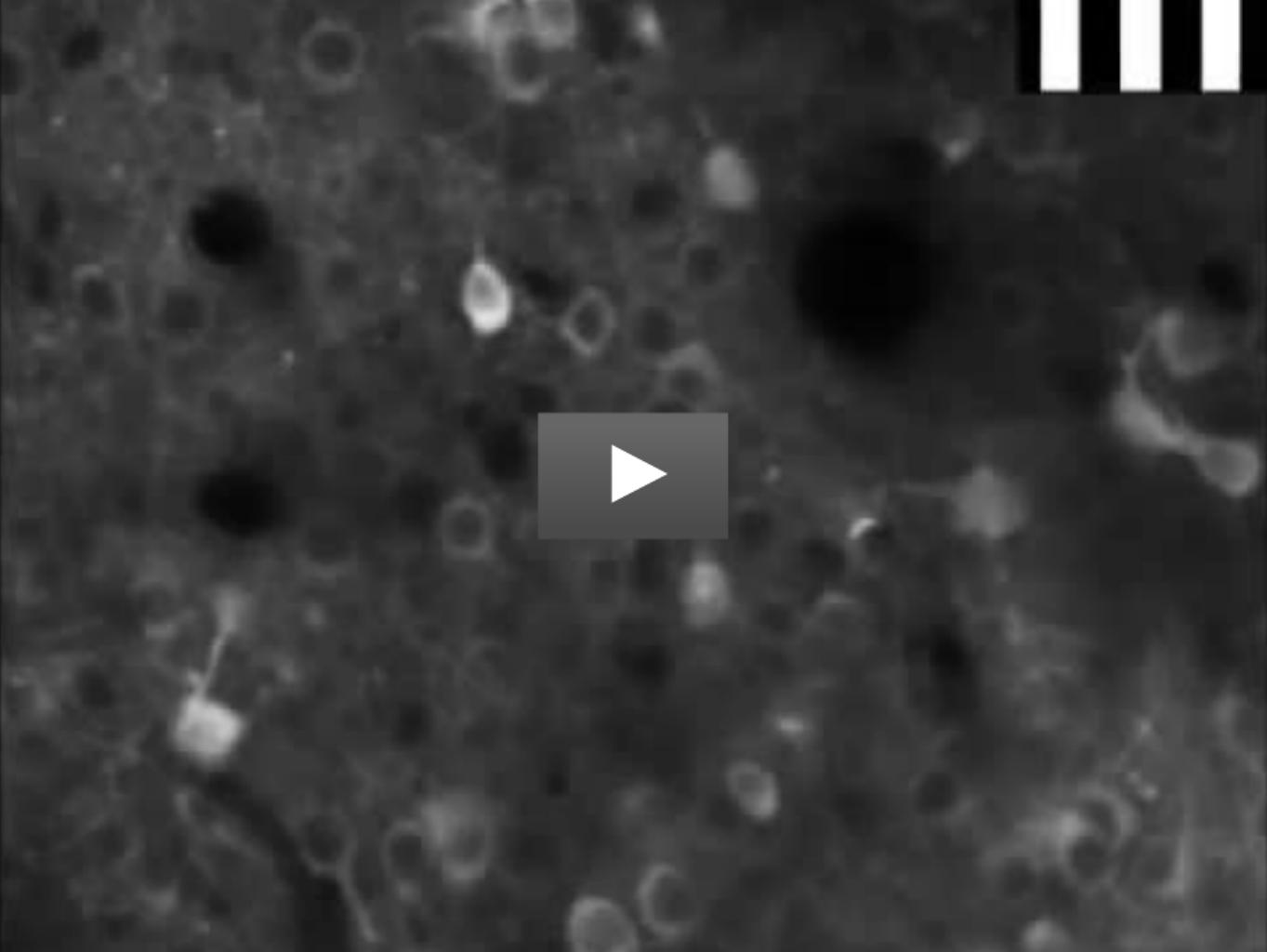
Kinds of Data From the Brain – Invasive – Calcium Imaging

Use **fluorescent calcium indicator** to indicate the presence of Ca^{2+} ions.

Indicator can be chemical or produced by genetic modification.

- + High temporal resolution
- + High spatial resolution

- Local
- Invasive



Kinds of Data From the Brain – Invasive – Optogenetics

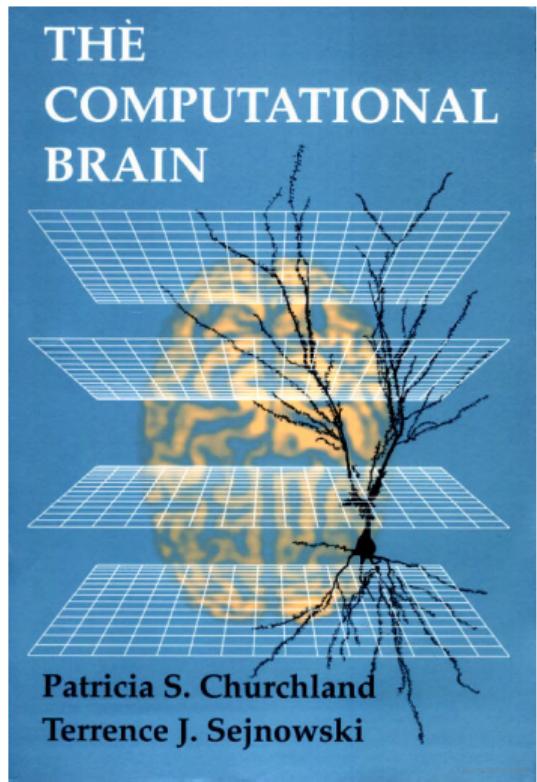
Make certain neuron types **sensitive to light** by genetic modification

Can either **excite** or **inhibit** neurons via light

- + High temporal resolution
- + Targets individual cell types
- + Can examine function of brain circuits
- Invasive

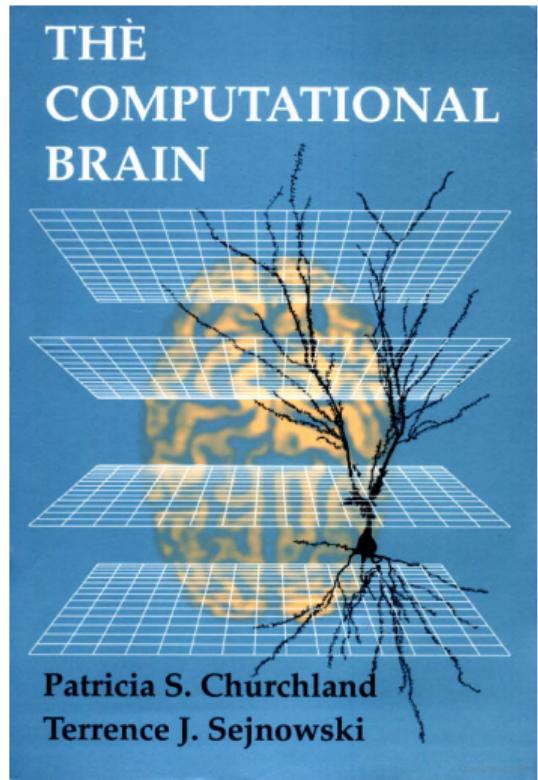


What do we know so far?



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- ▶ Lots of details

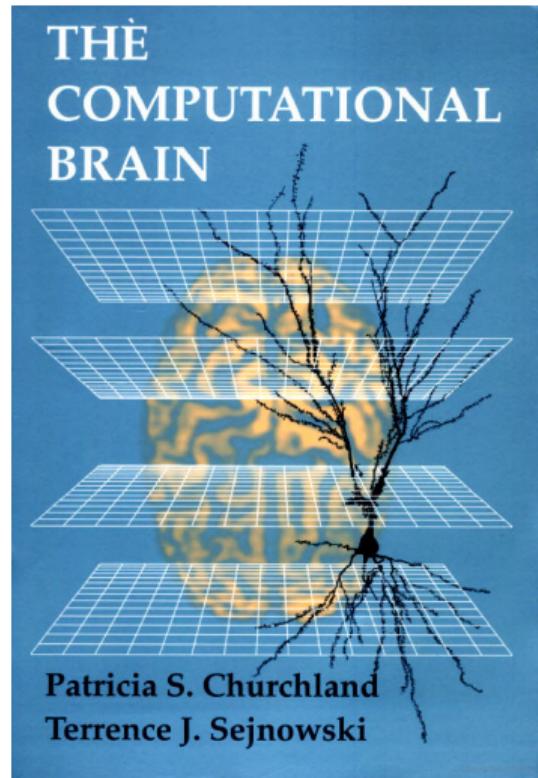


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“The proportion of type *A* neurons in area *X* is *Y*.”



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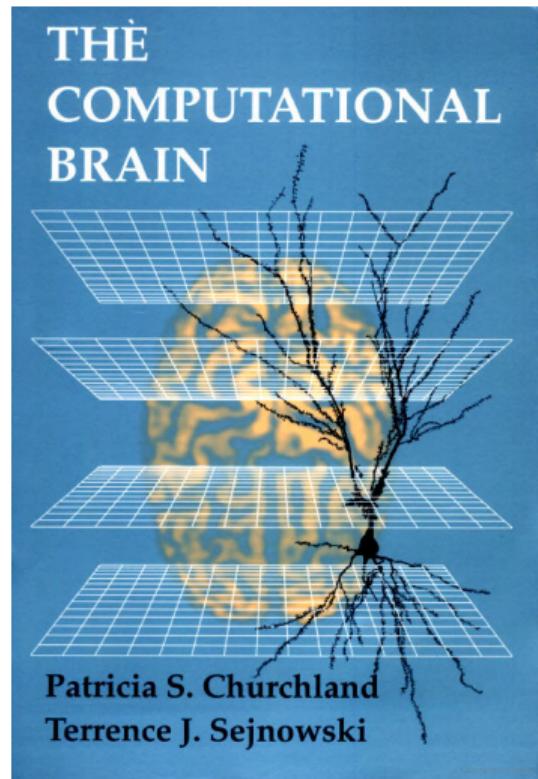
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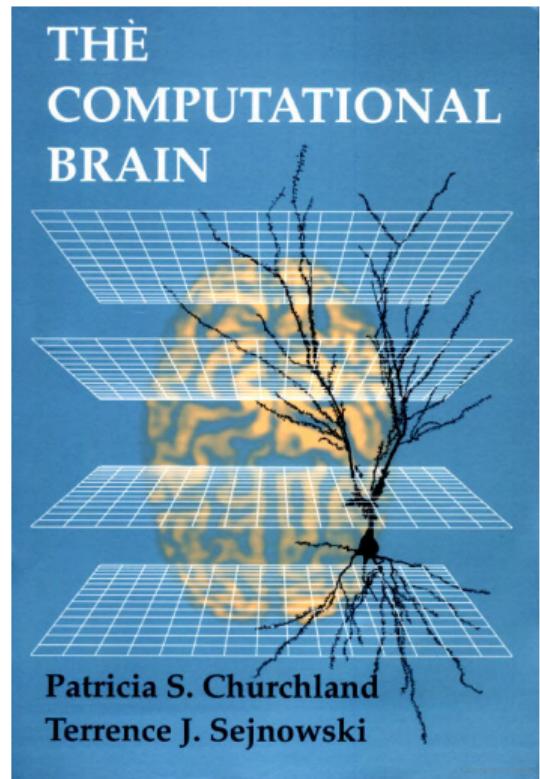
- ▶ **Conclusion:**

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 - ▶ **Conclusion:**
“The proportion of type *A* neurons in area *X* is *Y*.”
- ▶ Hard to get a big picture
 - ▶ No good methods for generalizing from data



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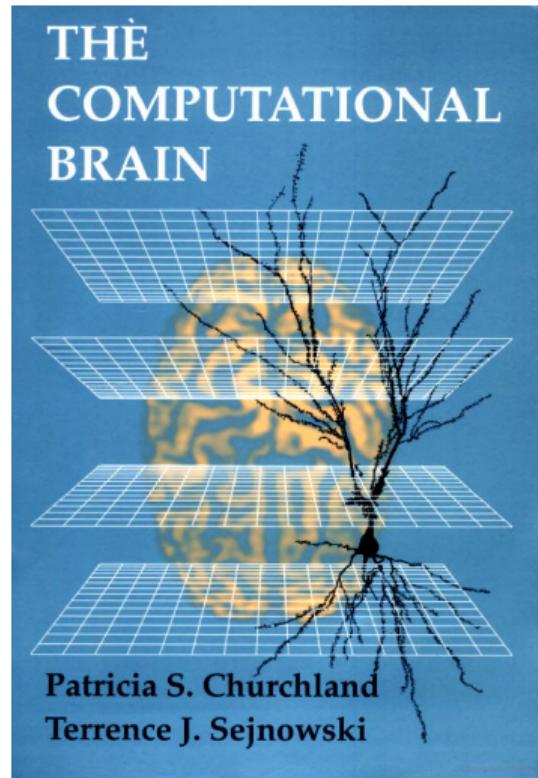
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- ▶ No good methods for generalizing from data

- ▶ Need some way to connect these details



What do we know so far?

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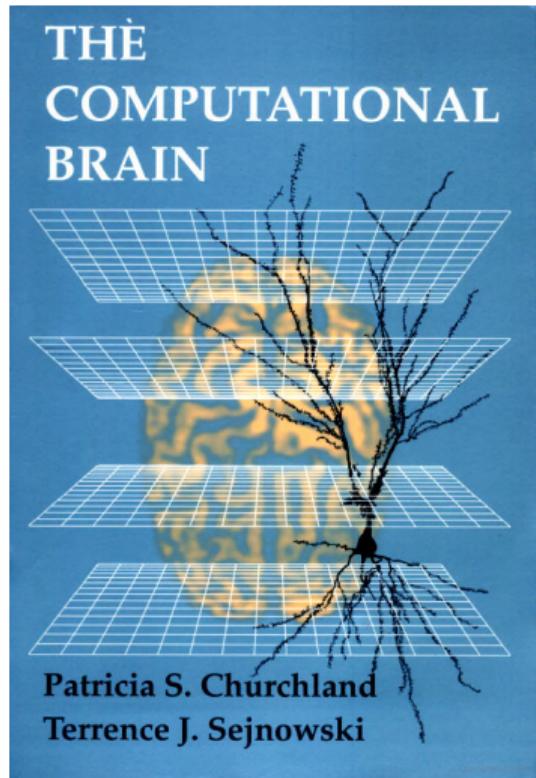
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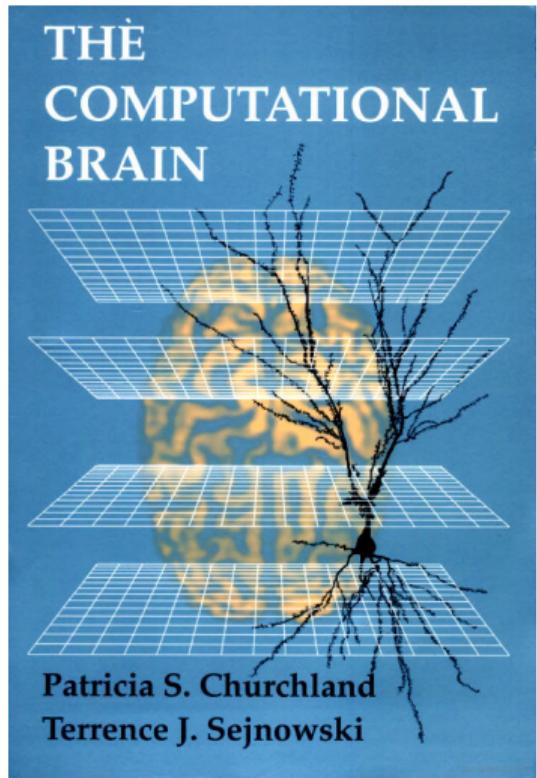
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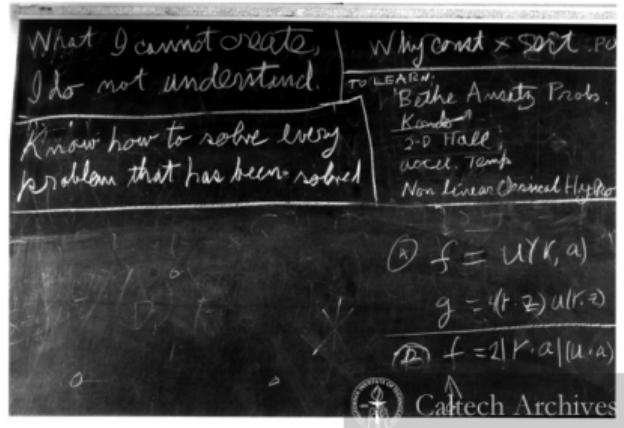
“Neuroscience is data-rich and theory poor”
— Churchland & Sejnowski, 1994



Recall: Neural Modelling

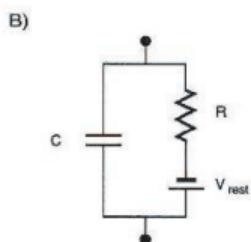
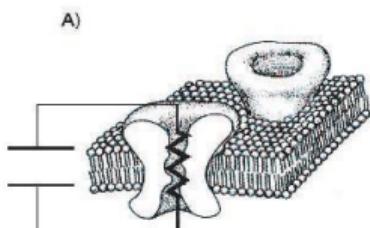
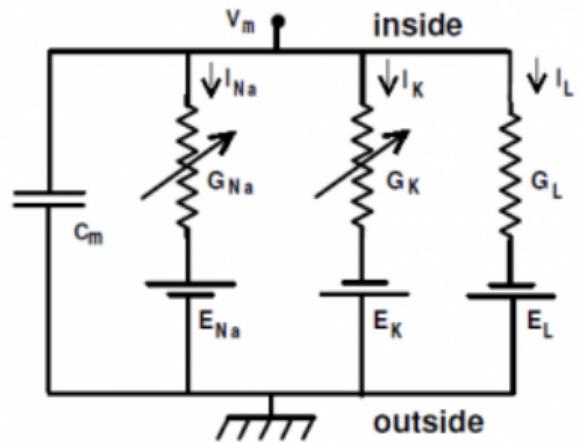
► Let's build it

- Requires a mathematically detailed theory
- Let's try to do to neuroscience what Newton did to Physics
- Not analytically tractable, requires computer simulation
- Can we use this to connect levels?

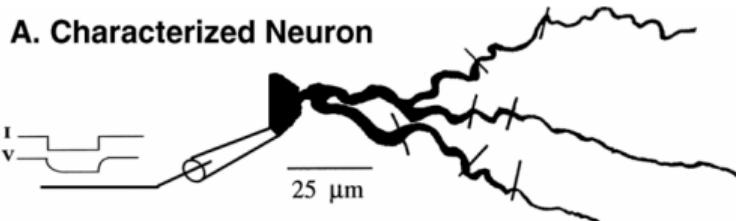


“What I cannot create, I do not understand”
— Richard Feynman, 1988

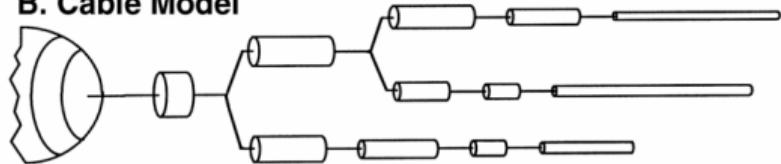
Single neuron simulation



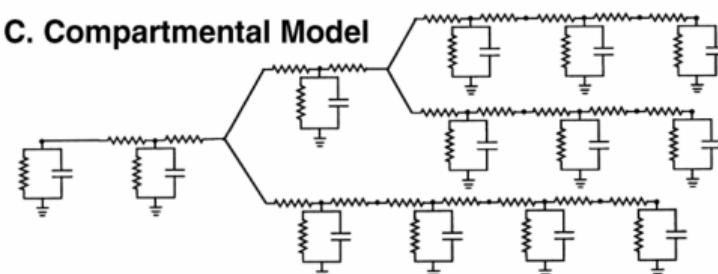
A. Characterized Neuron



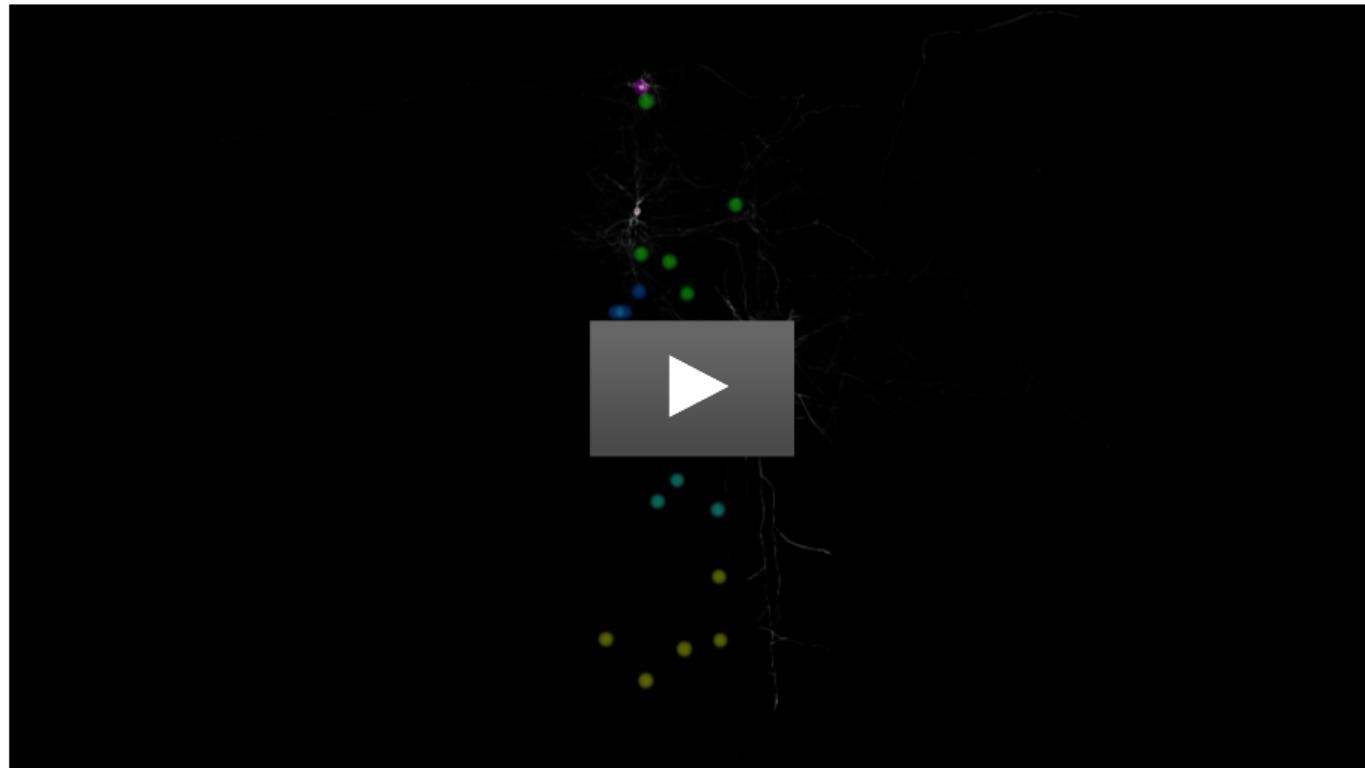
B. Cable Model



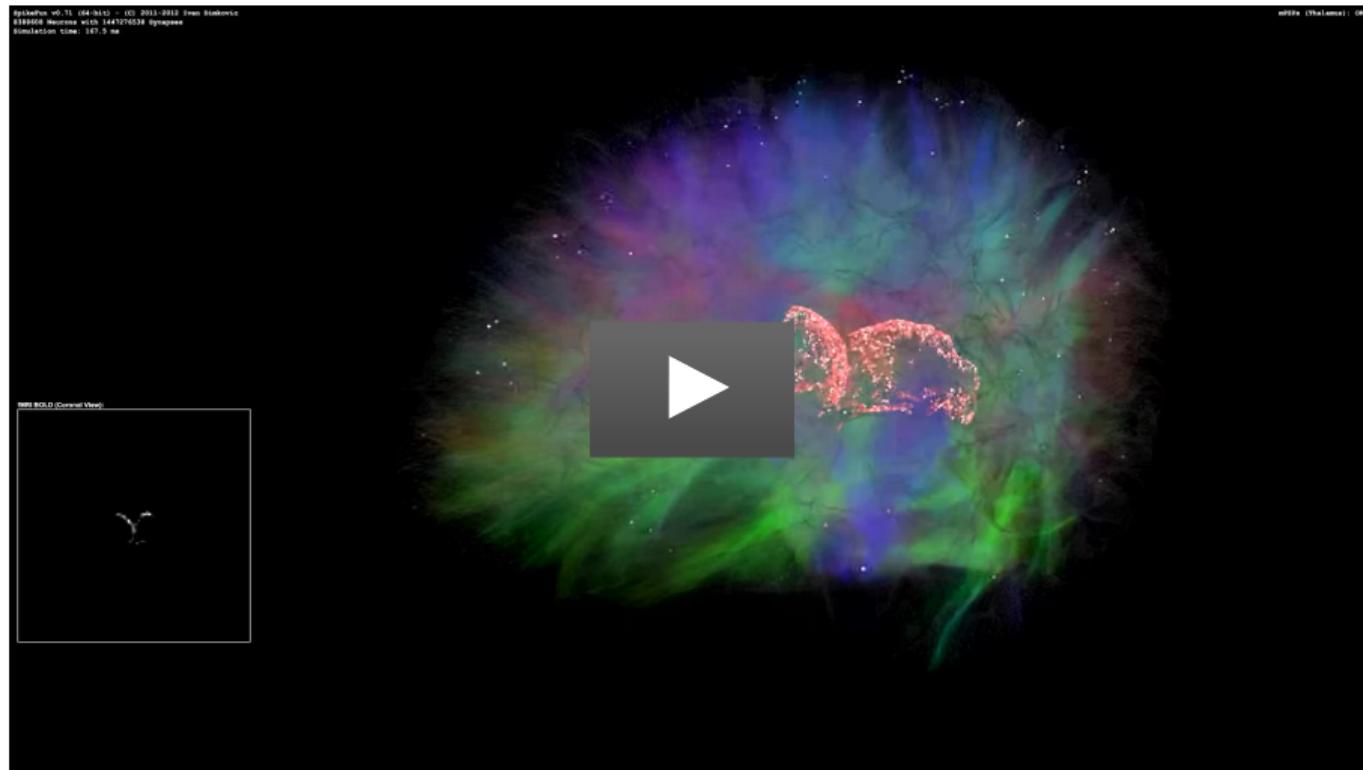
C. Compartmental Model



Simulating millions of neurons...



Simulating billions of neurons...



The Controversy

- **What level of detail** for the neurons?

How should they be connected?

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 - ▶ Billions of neurons, very simple models
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Dear Bernie,

You told me you would **string this guy up by the toes** the last time Mohda made his stupid statement about simulating the mouse's brain. [...]

1. These are **point neurons** (missing 99.999% of the brain; no branches; no detailed ion channels; the simplest possible equation you can imagine to simulate a neuron, totally trivial synapses; and using the STDP learning rule I discovered in this way is also a joke). [...]

Source: IEEE Spectrum, "Cat Fight Brews Over Cat Brain" (2009)

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What actually matters...

Connecting brain models to **behaviour**

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How can we build models that actually do something?

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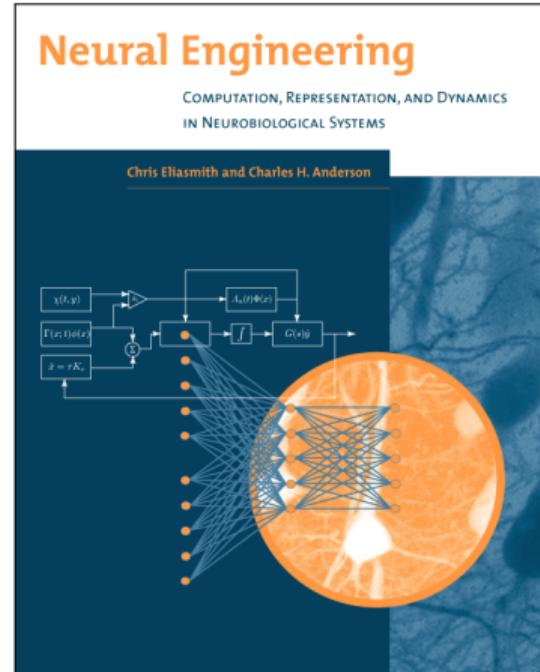
Connecting brain models to **behaviour**

How can we build models that actually do something?

How should we connect “realistic” neurons so they work together?

The Neural Engineering Framework

- ▶ Our attempt
 - ▶ Probably wrong, but got to start somewhere
- ▶ **Three principles**
 - ▶ Representation
 - ▶ Transformation
 - ▶ Dynamics
- ▶ Building **behaviour** out of **detailed low-level components**



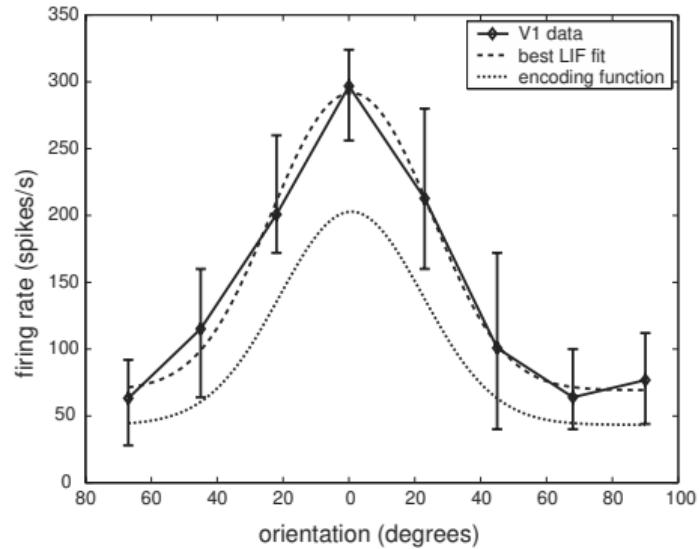
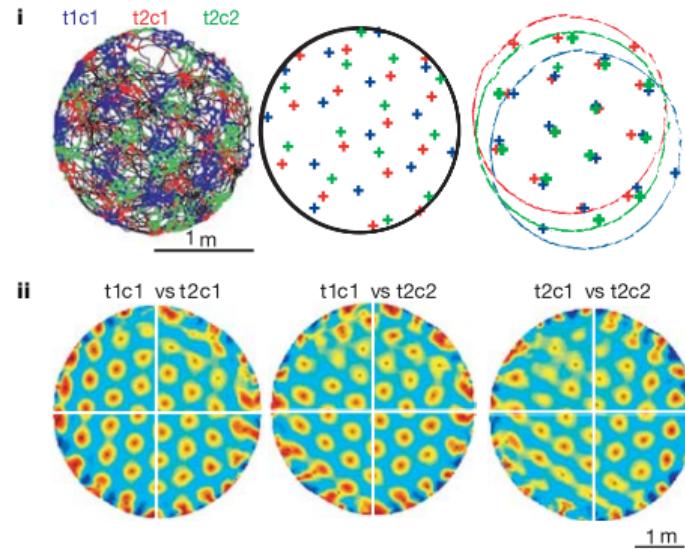
Representation

- ▶ How do neurons represent information? (What is the neural code?)

Image Sources. Left: Grid cells, from Hafting et al., *Microstructure of a Spatial Map in the Entorhinal Cortex* Nature (2005), fig. 3. Right: Example of visual orientation tuning in primary visual cortex, from "Neural Engineering", fig. 3.1.

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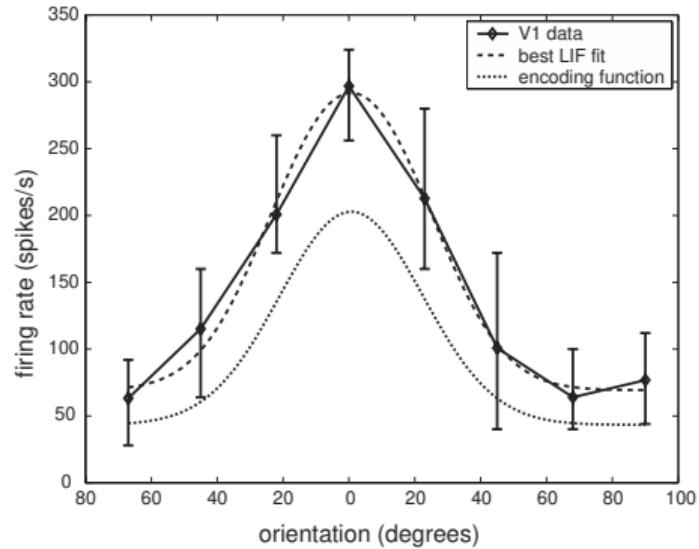
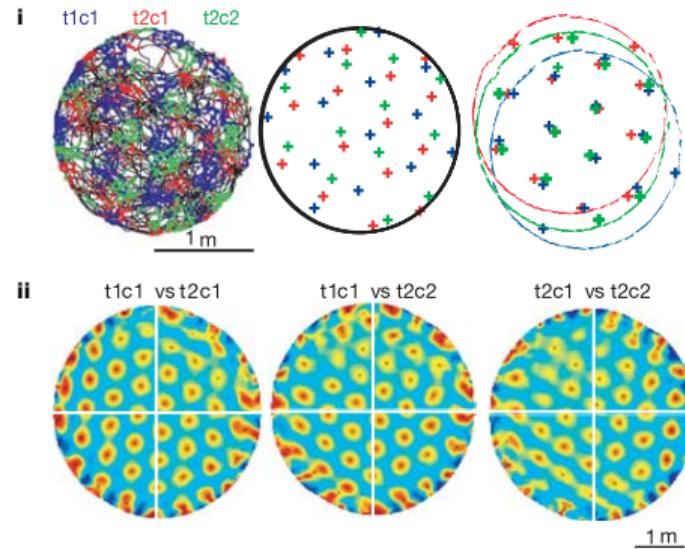


- ▶ What is the mapping between a value and the activity of a group of neurons?

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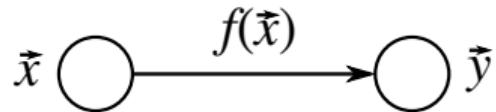
- ▶ How do neurons represent information? (What is the neural code?)



- ▶ What is the mapping between a value and the activity of a group of neurons?
- ▶ Every group of neurons can be thought of as **representing a vector**

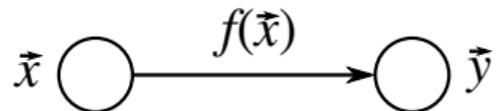
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Transformation



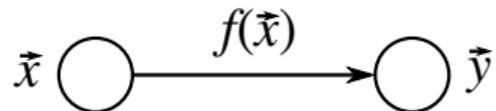
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Transformation



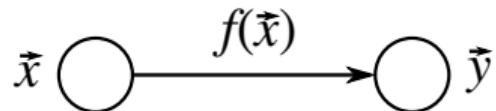
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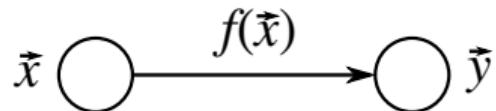
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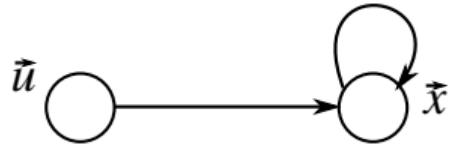
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- ▶ Can analyse which f can be computed

Dynamics

$$\frac{d\vec{x}}{dt} = f(\vec{u}, \vec{x})$$

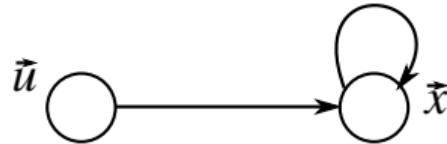


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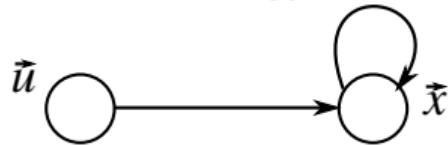
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- ▶ Great for implementing control theoretical concepts
- ▶ Memory as an integrator

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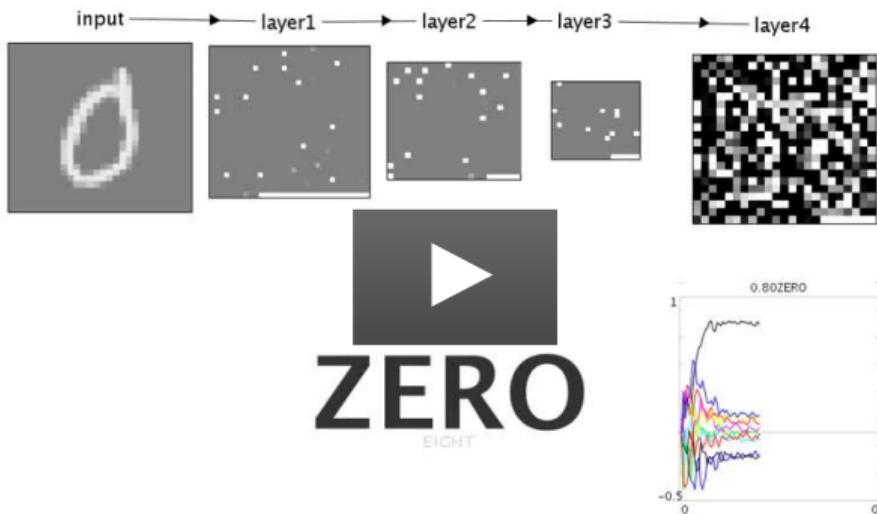
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- ▶ Framework for high-level cognition: **Semantic Pointer Architecture (SPA)**
- ▶ World's largest functional brain model: **SPAUN**

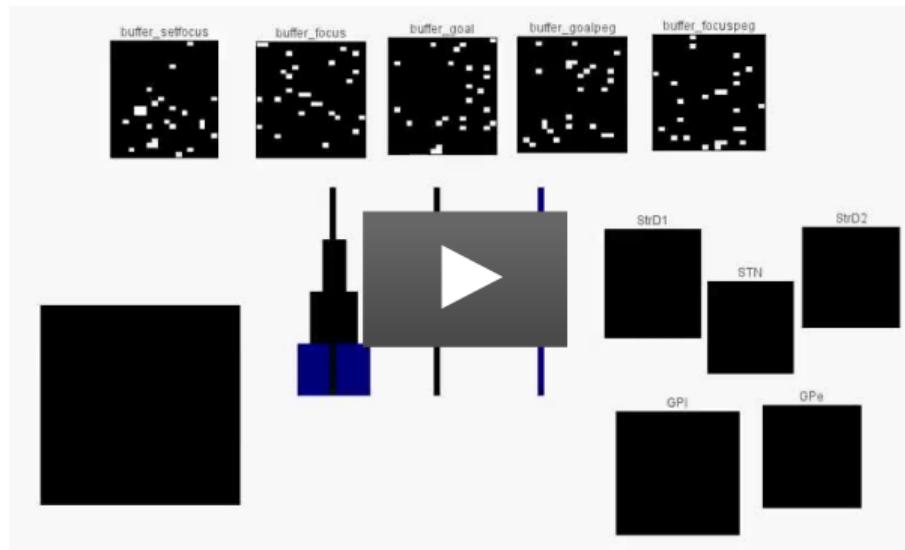
Examples: Recognizing Handwritten Digits



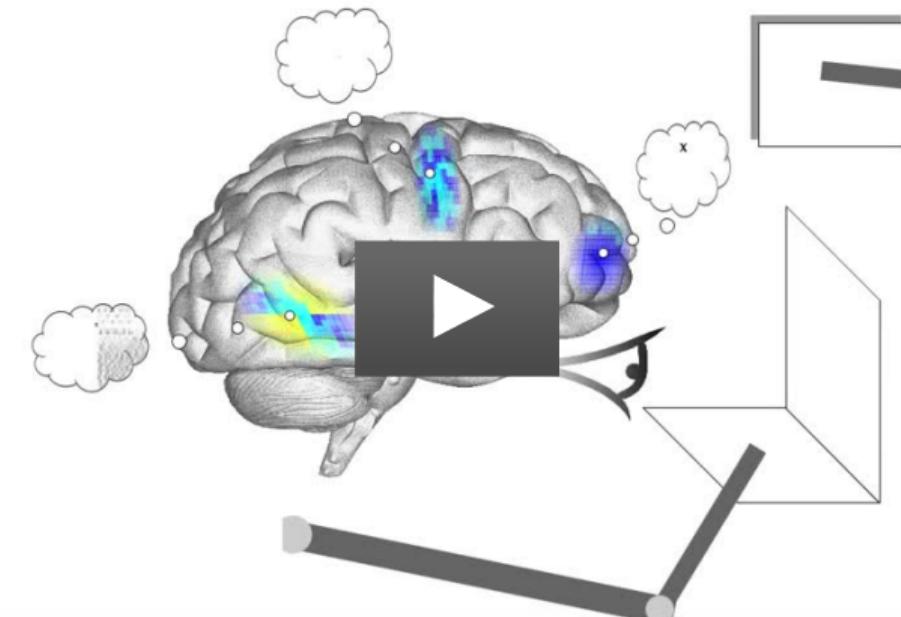
Examples: Recognizing Natural Images



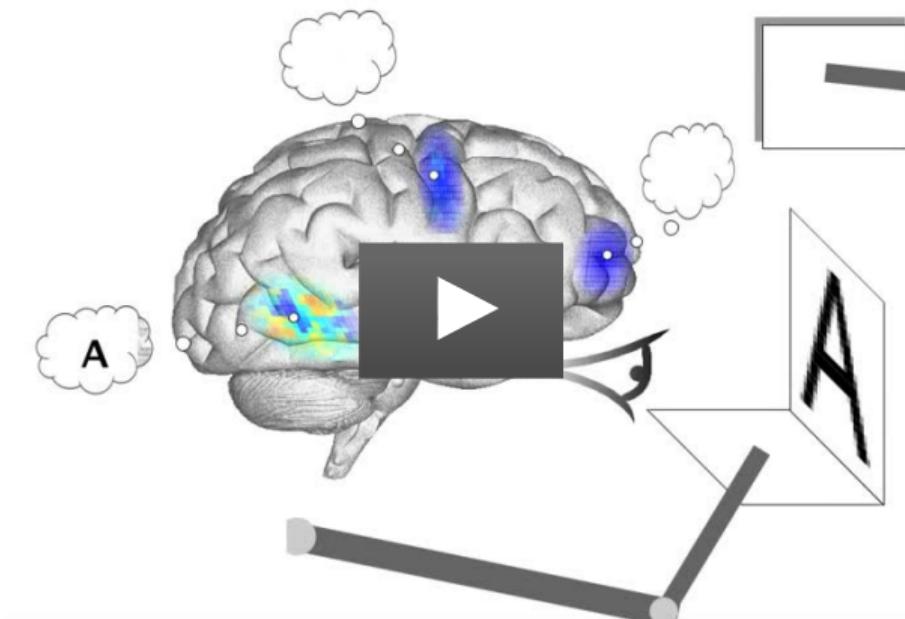
Examples: Playing Towers of Hanoi



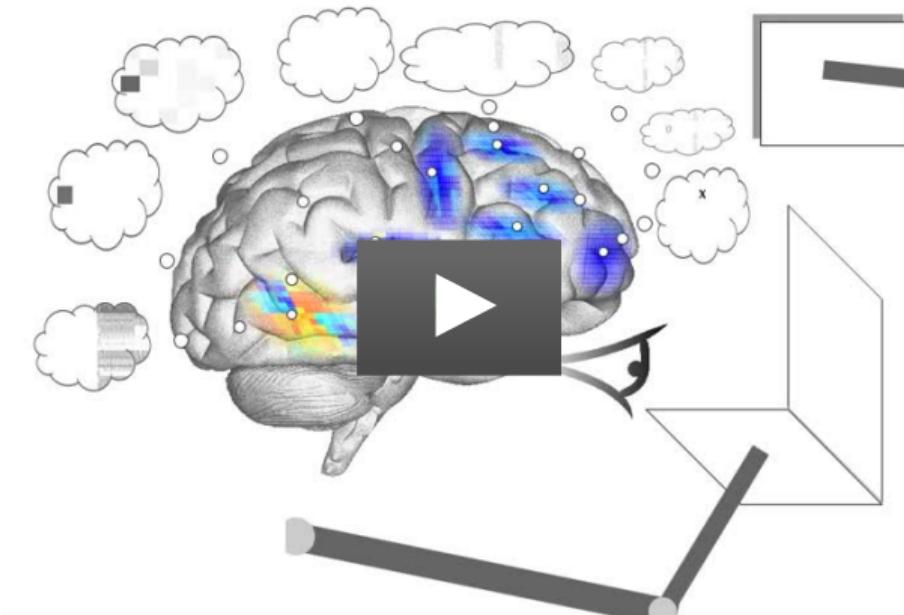
Examples: SPAUN Copy Drawing



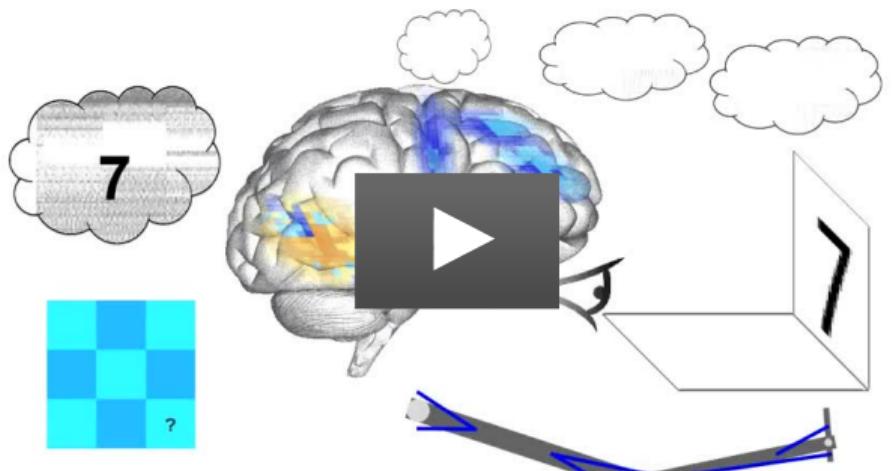
Examples: SPAUN Recognizing Digits



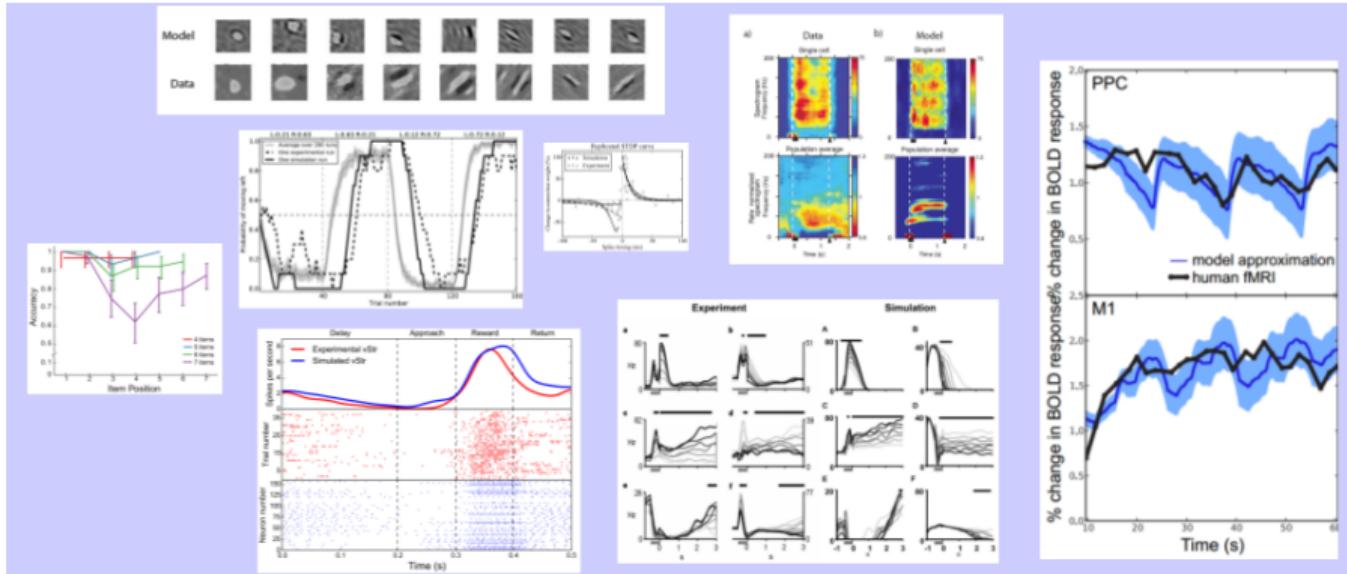
Examples: SPAUN Silent Addition



Examples: SPAUN Pattern Completion



Benefits



- ▶ No one else can do this
- ▶ New ways to test theories
- ▶ Suggests different types of algorithms

- ▶ Potential medical applications
- ▶ New ways of understanding the mind and who we are

Homework

- ▶ Get the **textbook**, read the first chapter
("Neural Engineering", Chris Eliasmith and Charles Anderson, 2003)
- ▶ Be able to run **jupyter lab** or (**jupyter notebook**) with **Python 3**
Install numpy, scipy, and matplotlib. You may want to use Anaconda, which ships with these packets preinstalled.