

**SYDE 556/750**

**Simulating Neurobiological Systems**  
**Lecture 1: Introduction**

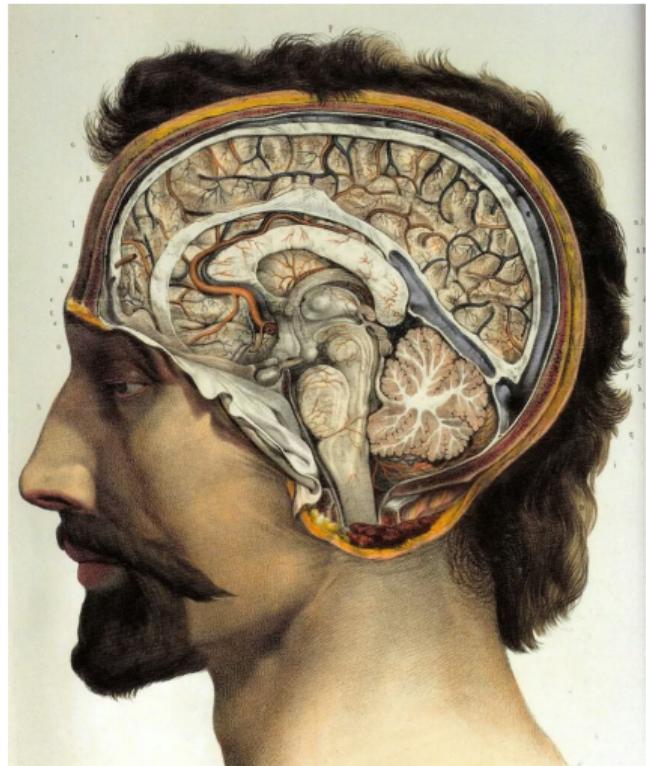
Andreas Stöckel

January 7, 2020



UNIVERSITY OF  
**WATERLOO**

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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## Building Large-Scale Brain Models

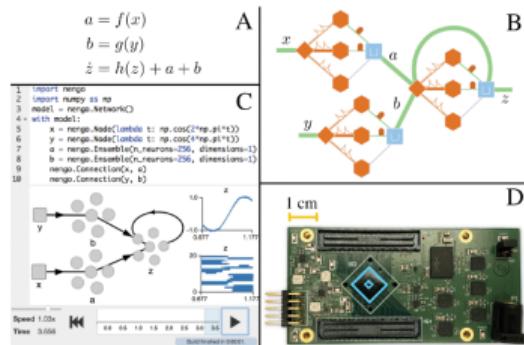
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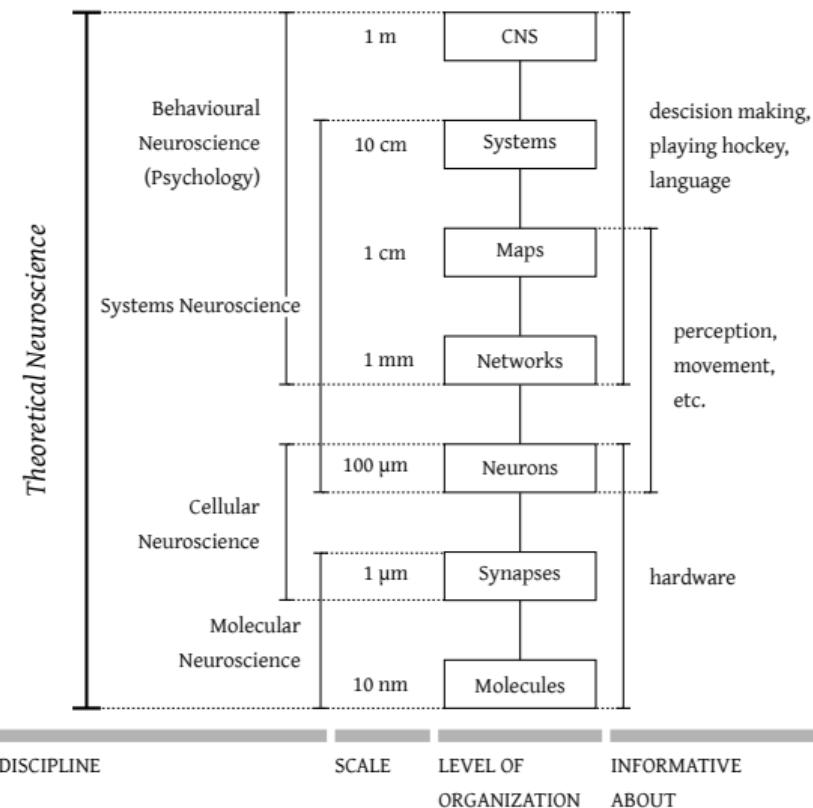
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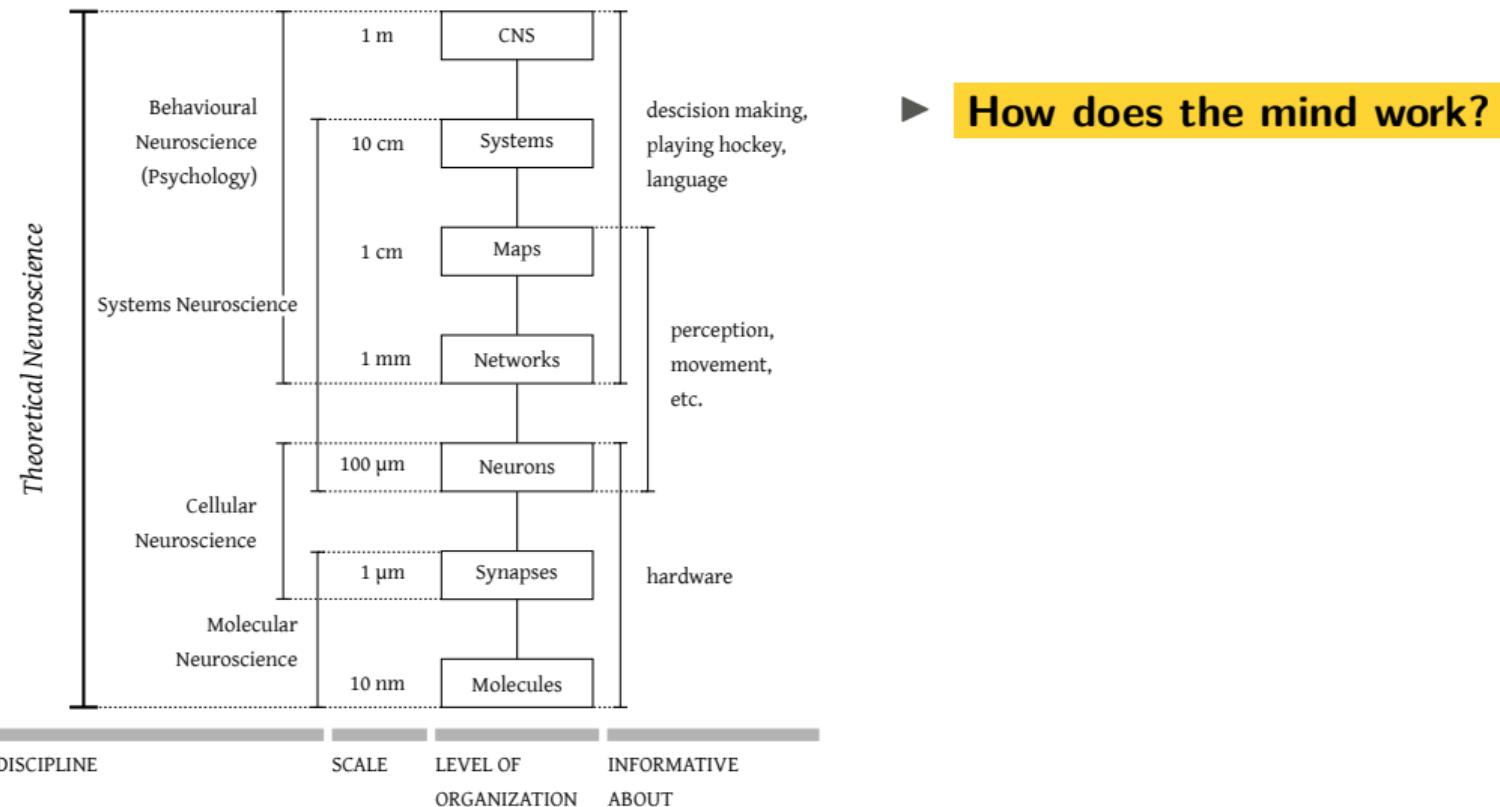
Program Neuromorphic  
Hardware

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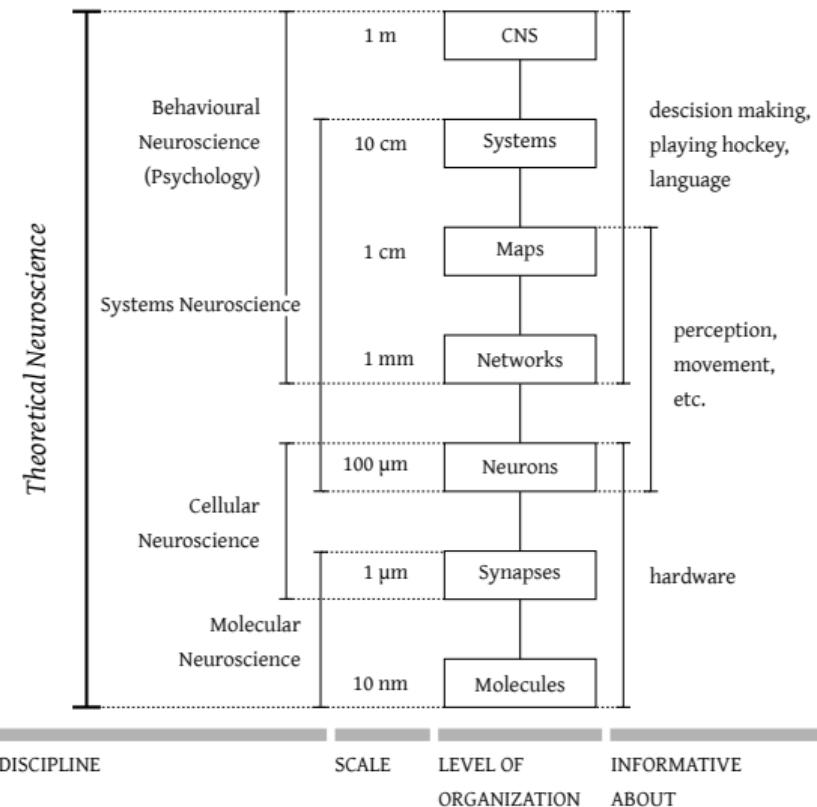
# Our Focus: Theoretical Neuroscience



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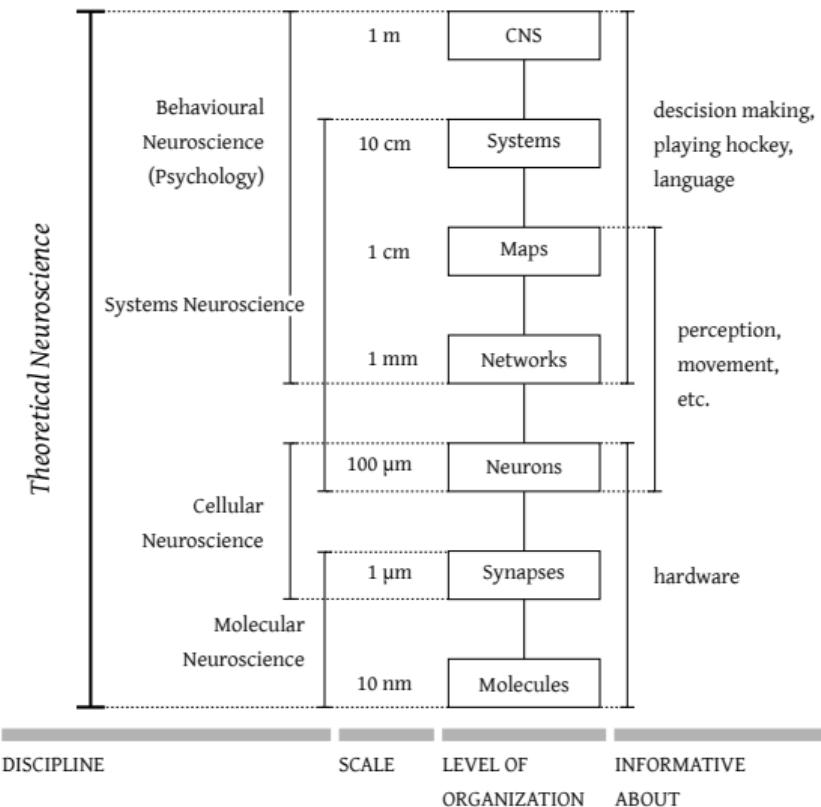


# Our Focus: Theoretical Neuroscience



- ▶ **How does the mind work?**
- ▶ Most complex and most interesting system humanity has ever studied
- ▶ Why study anything else?

# 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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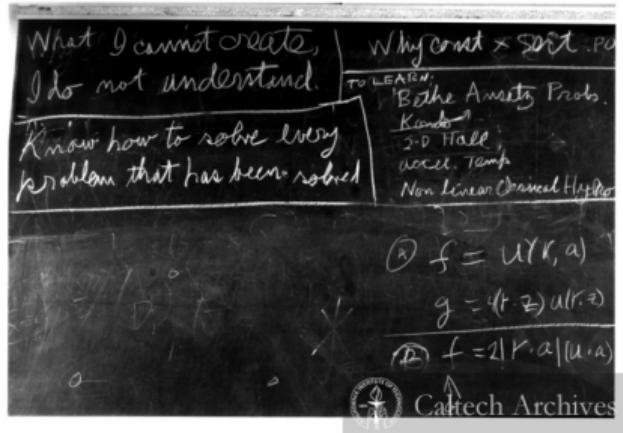
## Similarities

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

## Differences

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

# Neural Modelling



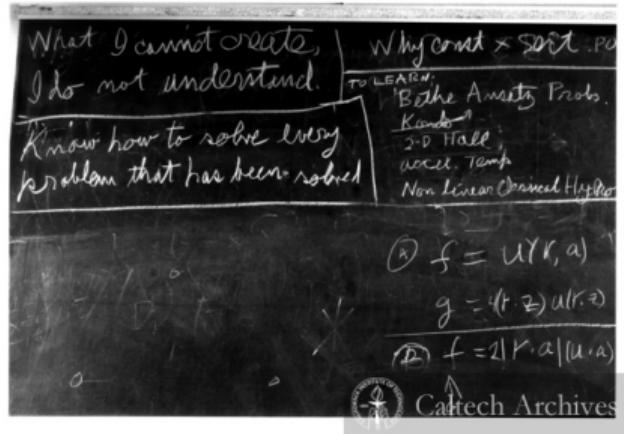
“What I cannot create, I do not understand”  
— Richard Feynman, 1988

Image Sources. “Richard Feynman’s blackboard at time of his death” (1988), from Caltech Archives.

# Neural Modelling

## ► Let's build it

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

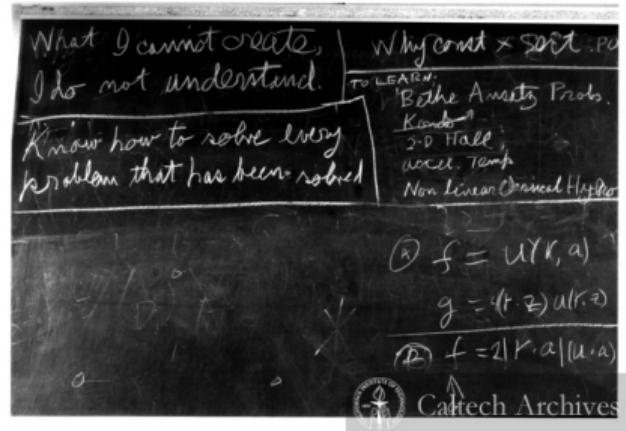


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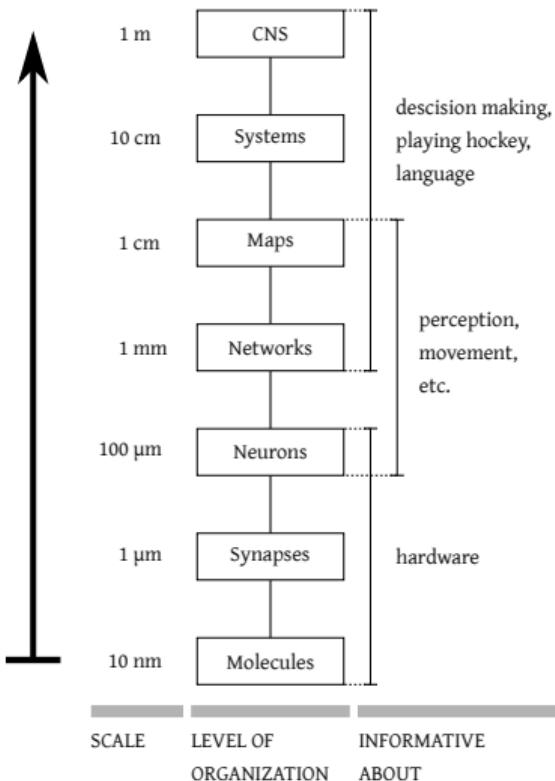
- Requires a mathematically detailed theory
- Often complex; need computer simulation
- Bring together levels and modelling methods
  - **Single neuron models**  
Spikes, spatial structure, ion channels...
  - **Small network models**  
Spiking neurons, rate neurons, mean fields...
  - **Large network/cognitive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



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# Problems With Current Approaches: Large-scale Neural Models

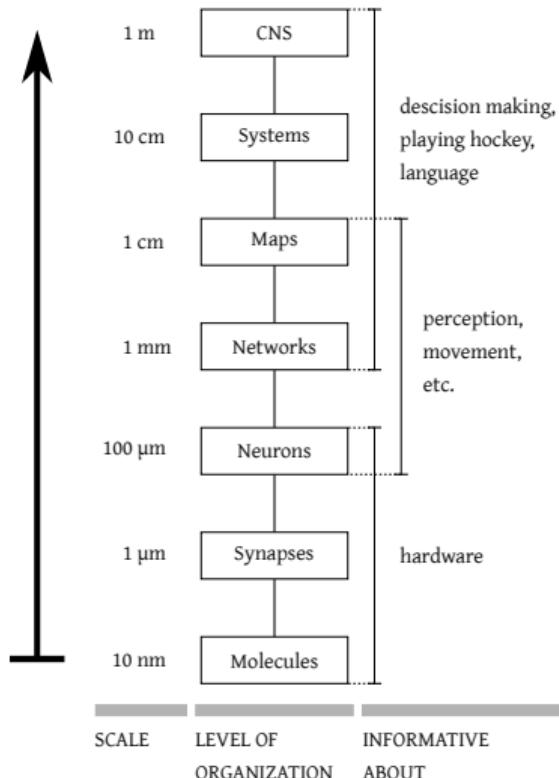
- **Bottom-up** approach



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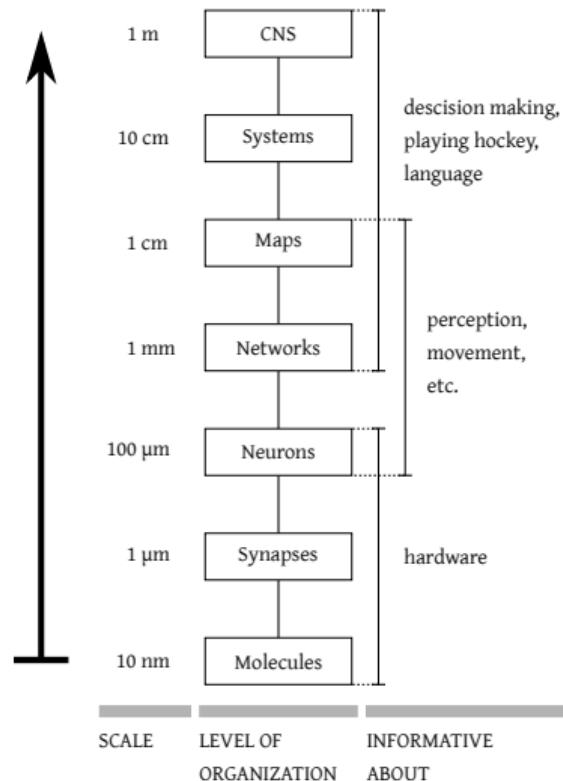
## ► **Bottom-up** approach

1. Gather low-level data



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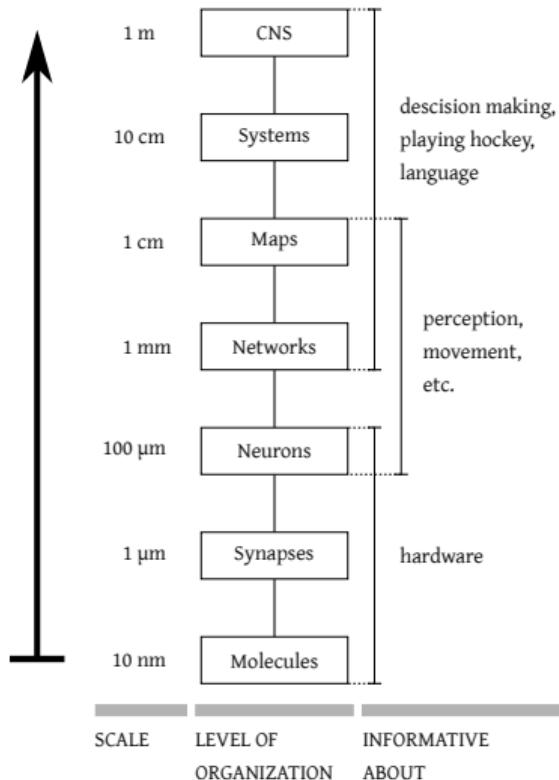
- **Bottom-up** approach
  - 1. Gather low-level data
  - 2. Build a detailed model



# 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



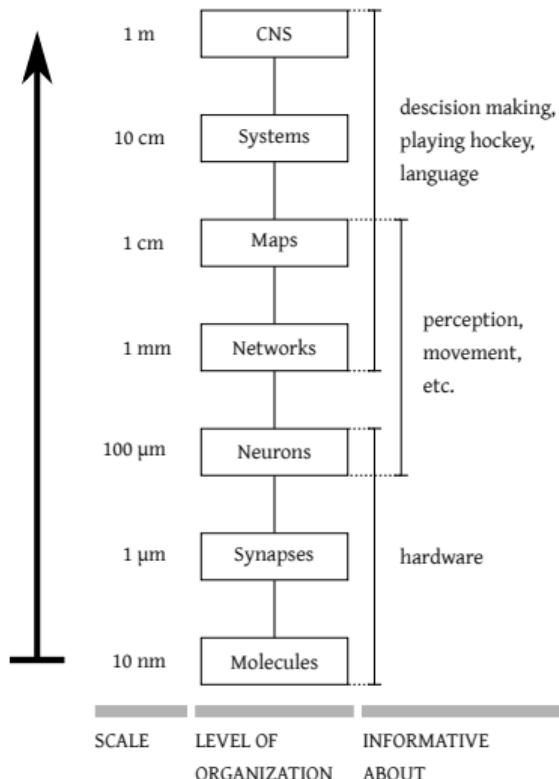
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## ► Examples

BlueBrain/Human Brain Project/SyNAPSE



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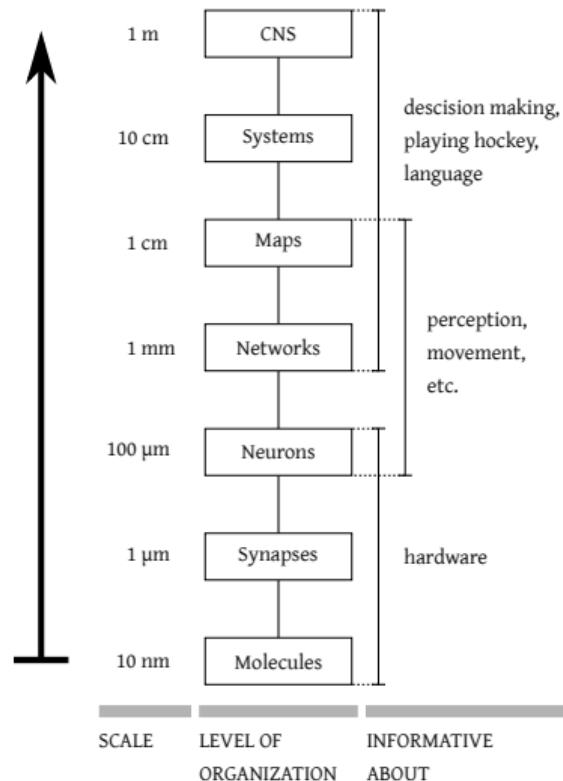
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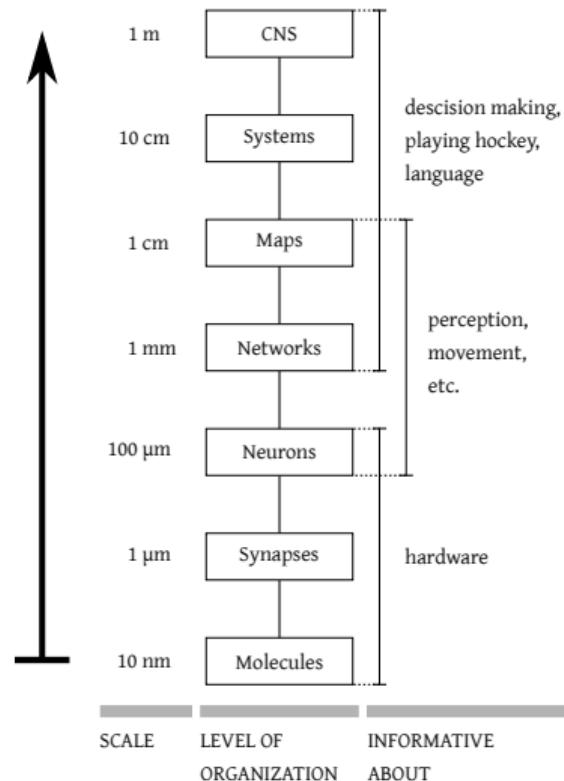
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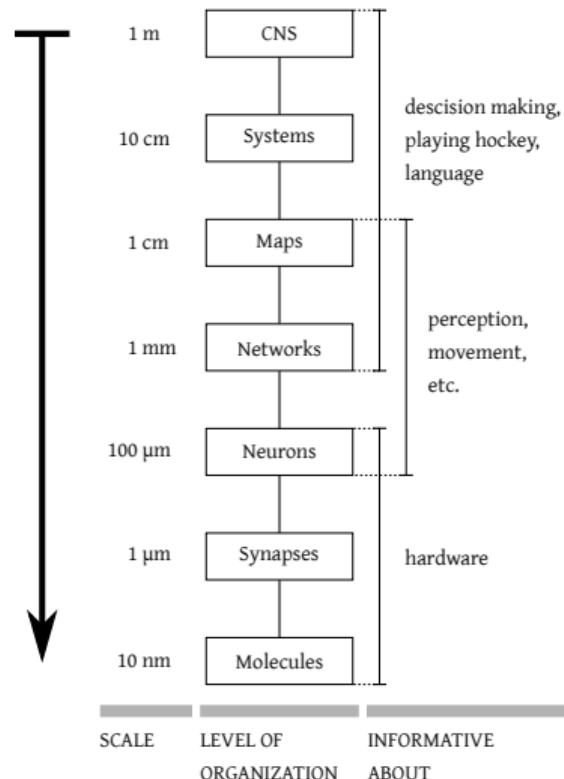
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**⚠ This is still important research; these shortcomings are from the perspective of building a “functional” brain model.**



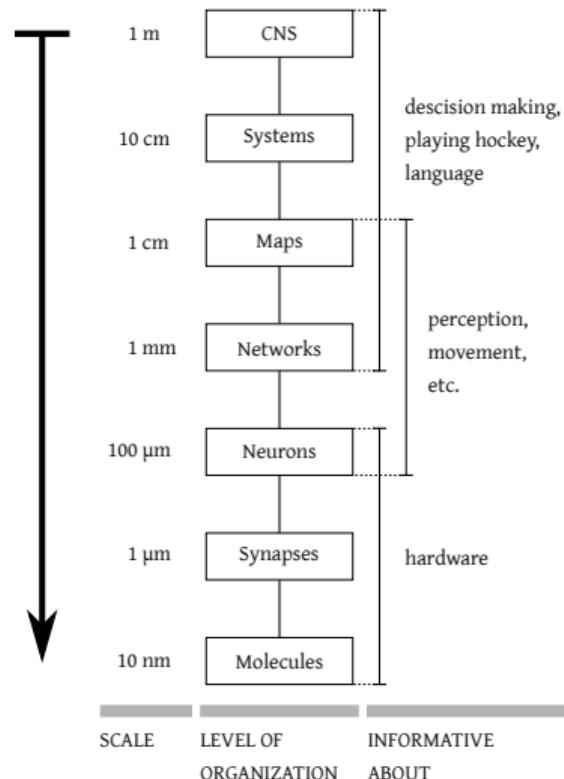
# Problems With Current Approaches: Behavioural Models

- **Top-down** approach



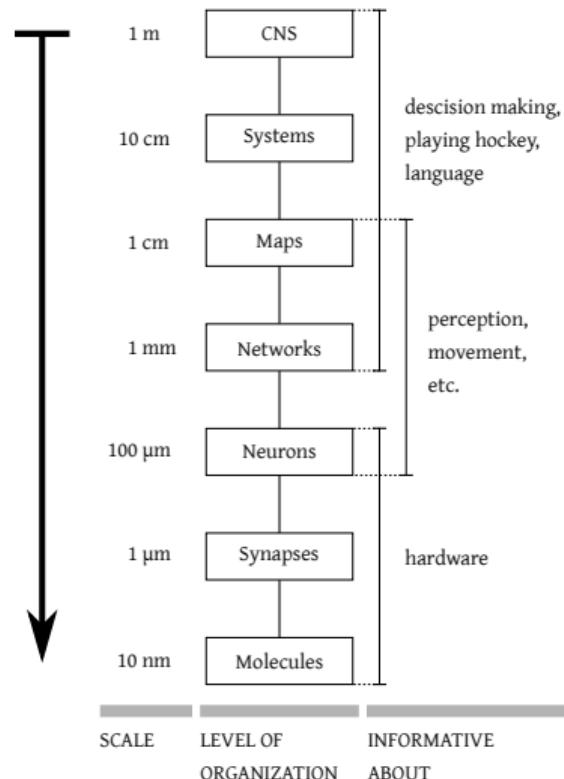
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- ▶ **Top-down** approach
- ▶ **Modeling Frameworks:** ACT-R, SOAR



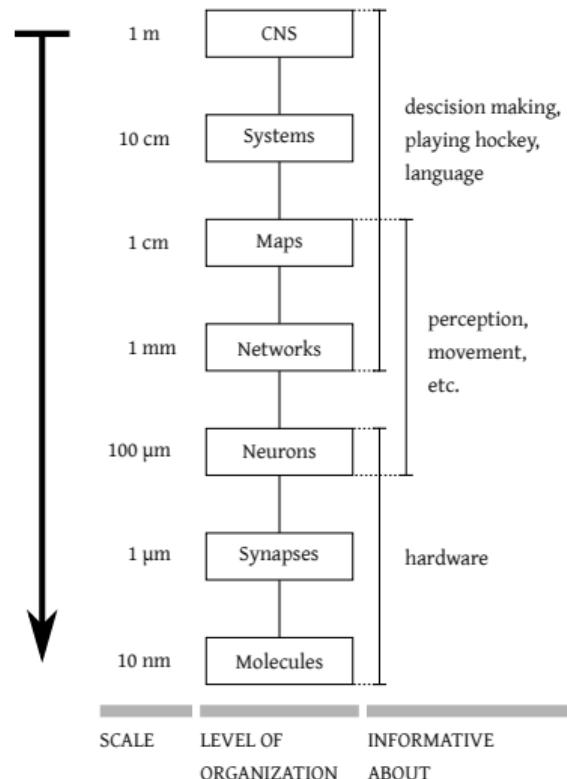
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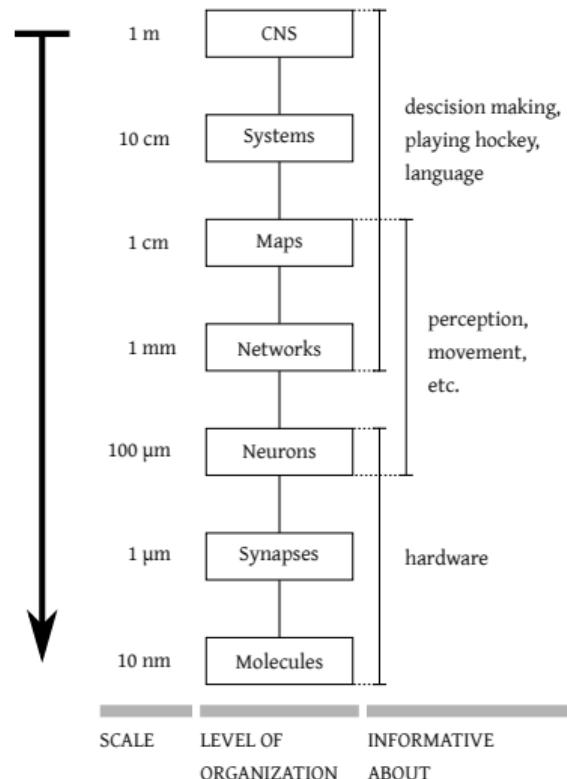
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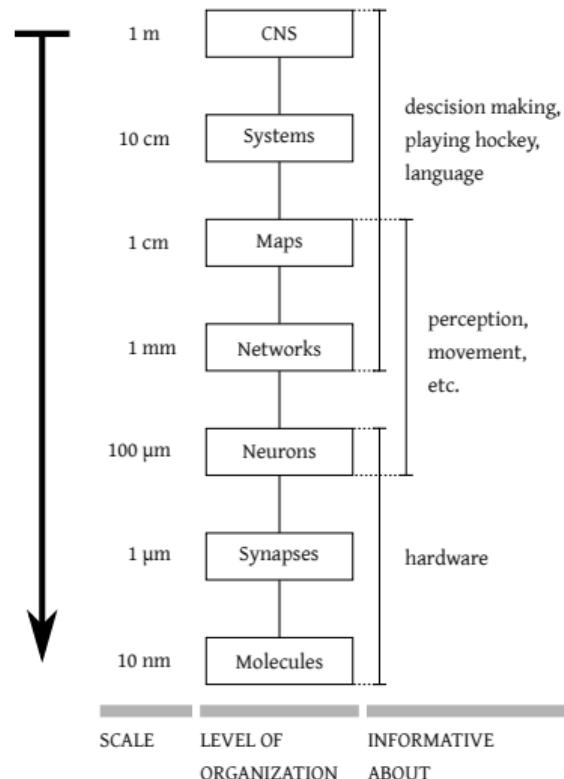
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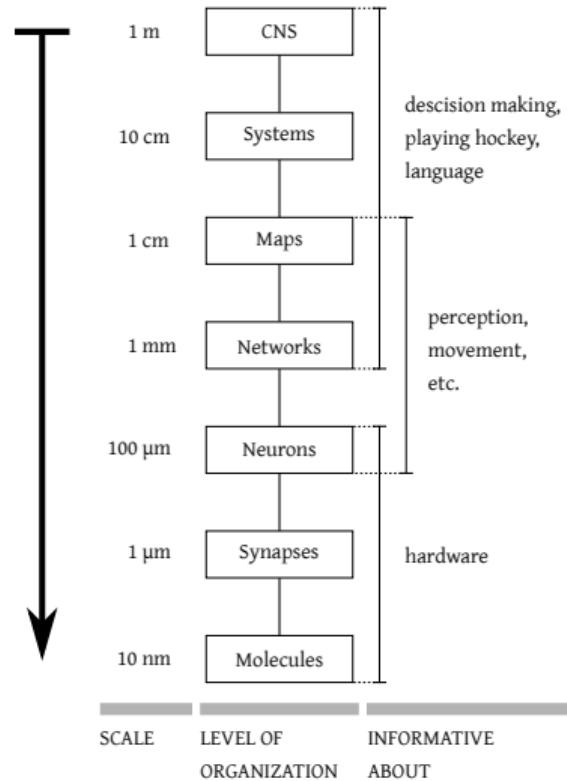
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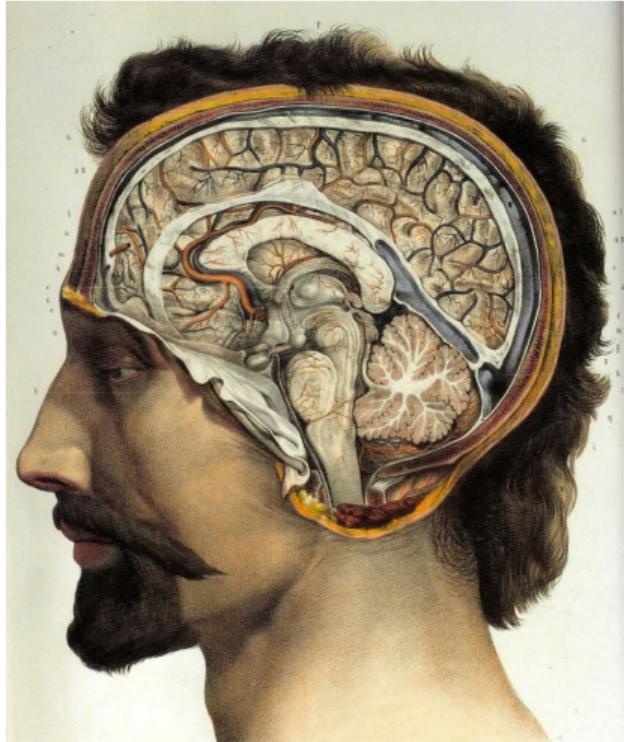
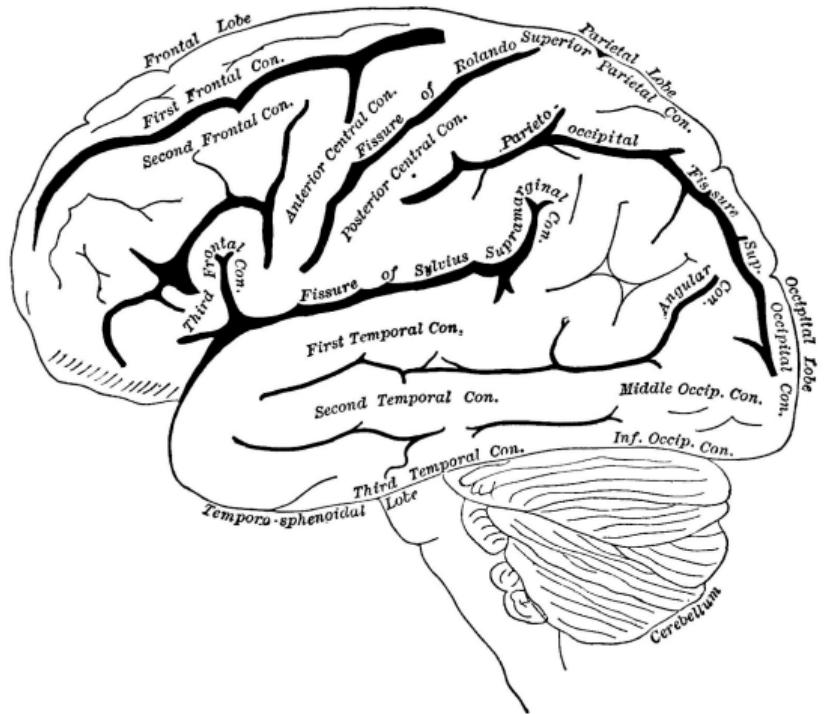
⚠ **Maybe these shortcomings are okay.**

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 cm<sup>2</sup> to 2000 cm<sup>2</sup> (roughly four A4/letter pages of paper)
- ▶ **Number of neurons:**  
100 billion ( $10^{11}$ , 150 000 mm<sup>-2</sup>)
- ▶ **Number of synapses:**  
100 trillion ( $10^{14}$ , about 1000 per neuron)

# THE UNFIXED BRAIN

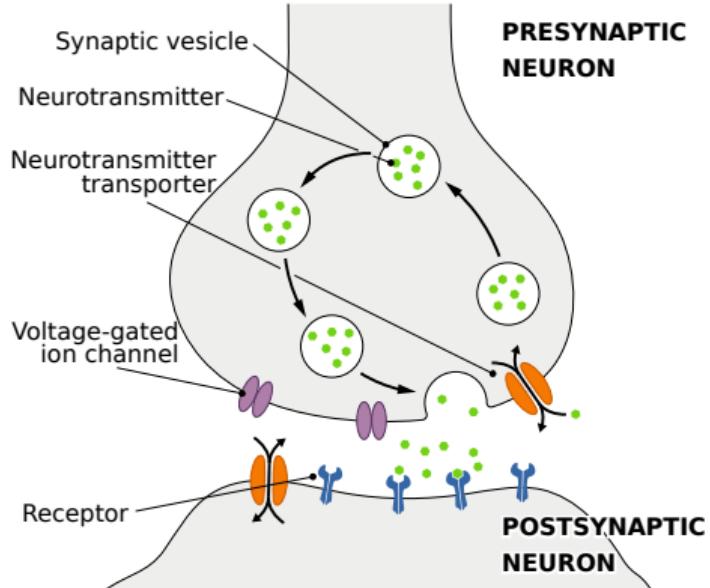
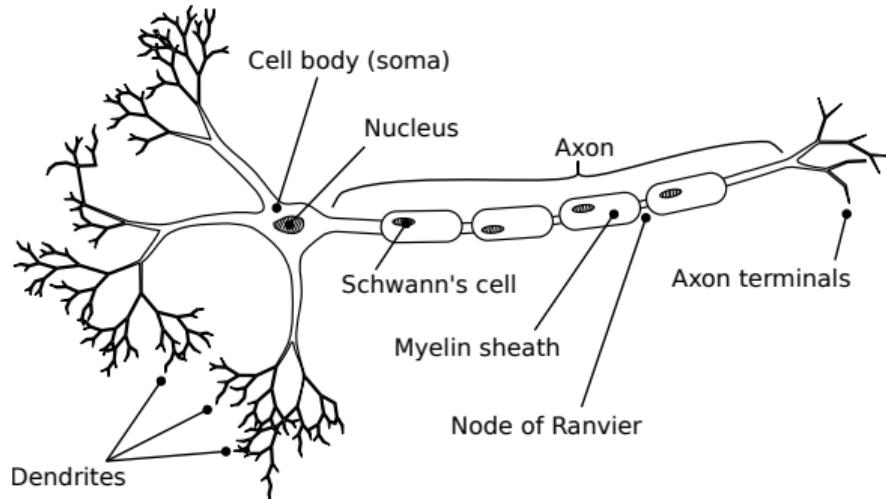


**Suzanne Stensaas, PhD**



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  $100\text{ }\mu\text{m}$  to  $5\text{ m}$
- ▶ Vastly different input/output counts (*convergence* and *divergence*)
- ▶ 100's of different neurotransmitters

# What It Really Looks Like

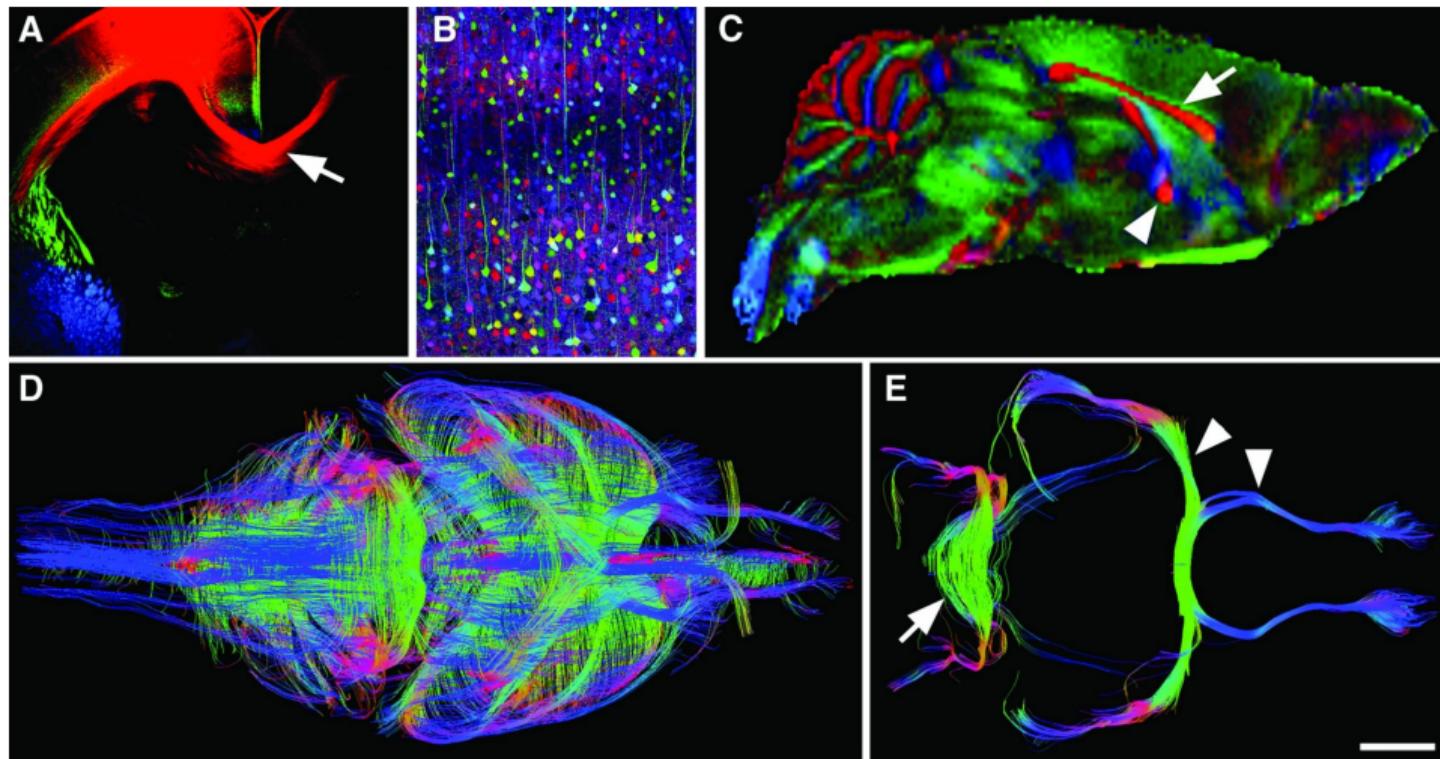
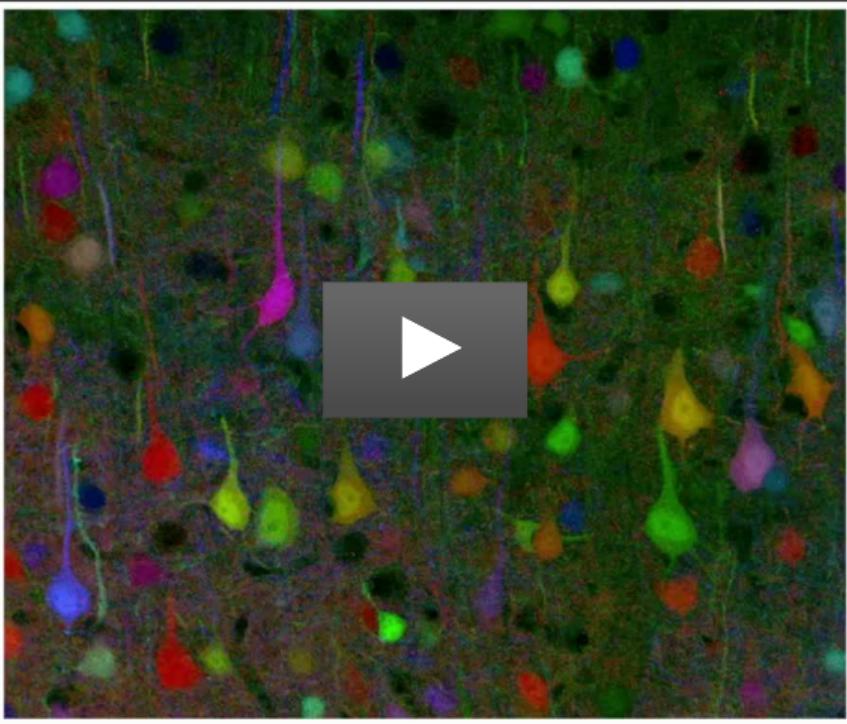


Image Sources. Alain Chédotal and Linda J Richards. *Wiring the Brain: The Biology of Neuronal Guidance*. Cold Spring Harbor perspectives in biology (2010)



R Draft & J Livet

x = independently organized TED event

**TEDx** Caltech

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

## Functional Magnetic Resonance Tomography

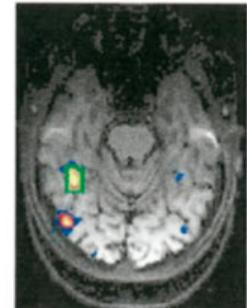
Measures *changes* in blood oxygenation (BOLD)

- + 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

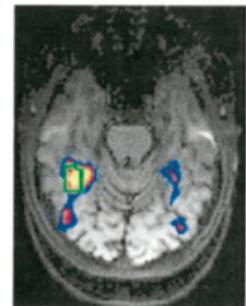
A catalogue of fMRI can be found at

[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

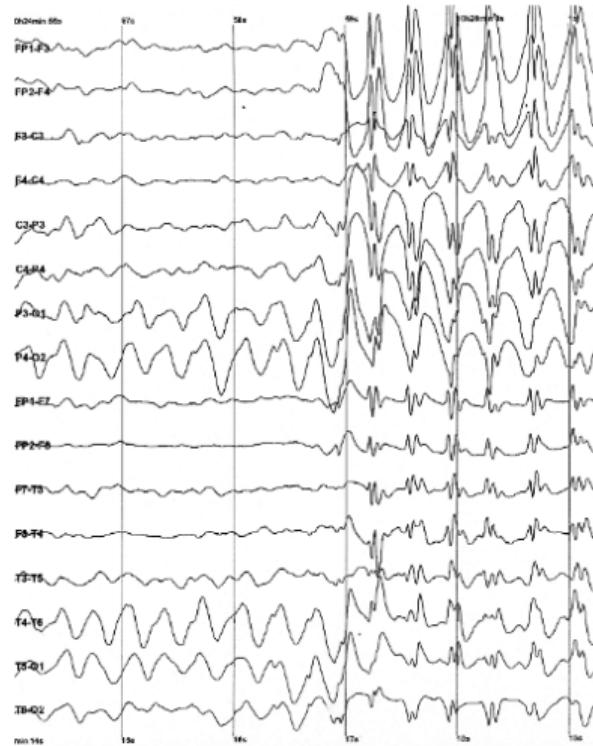


Image Sources. Left: Electroencephalogram (image from Wikimedia). Right: EEG cap (image from Wikimedia).

## Kinds of Data From the Brain – Invasive – Lesion Studies

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

- ▶ **Occipital cortex leads** ↪ 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

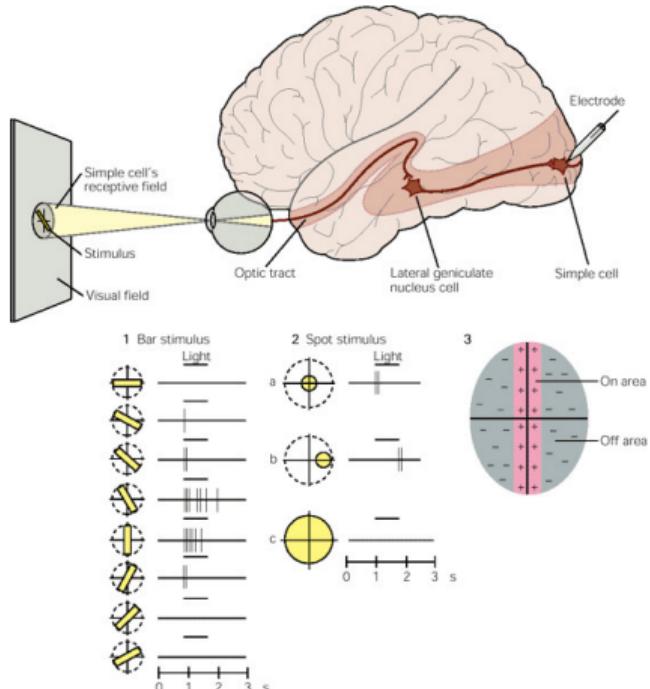


Image Sources. "Depiction of Hubel and Wiesels experiment." Kandel et al., 2012, Principles of Neural Science, 5th ed., Figure 27-11.

# 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  $\approx 100$  cells with one array
- Requires post-processing  
(e.g., extraction of individual neurons  
from local field potentials, LFPs)

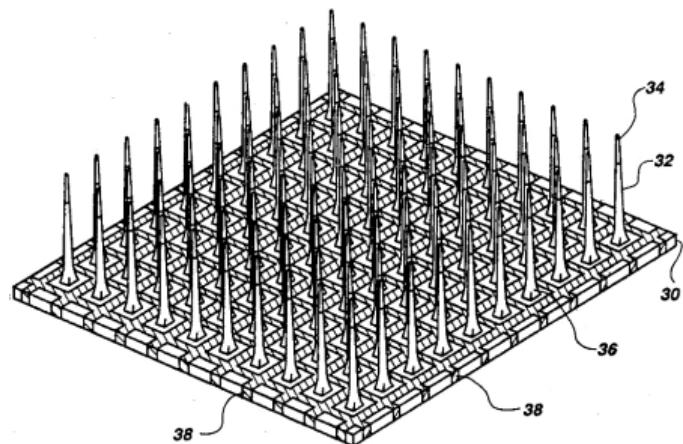
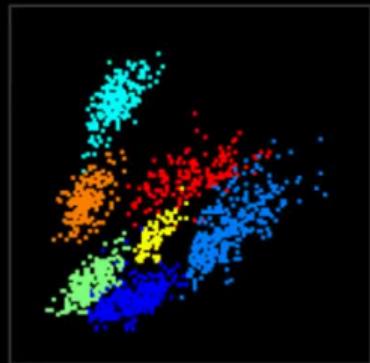


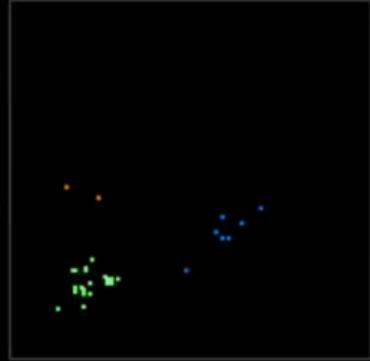
Image Sources. “Depiction of a Utah Array”. From: US Patent #5,215,088

cell activity

overall



ongoing



behavior



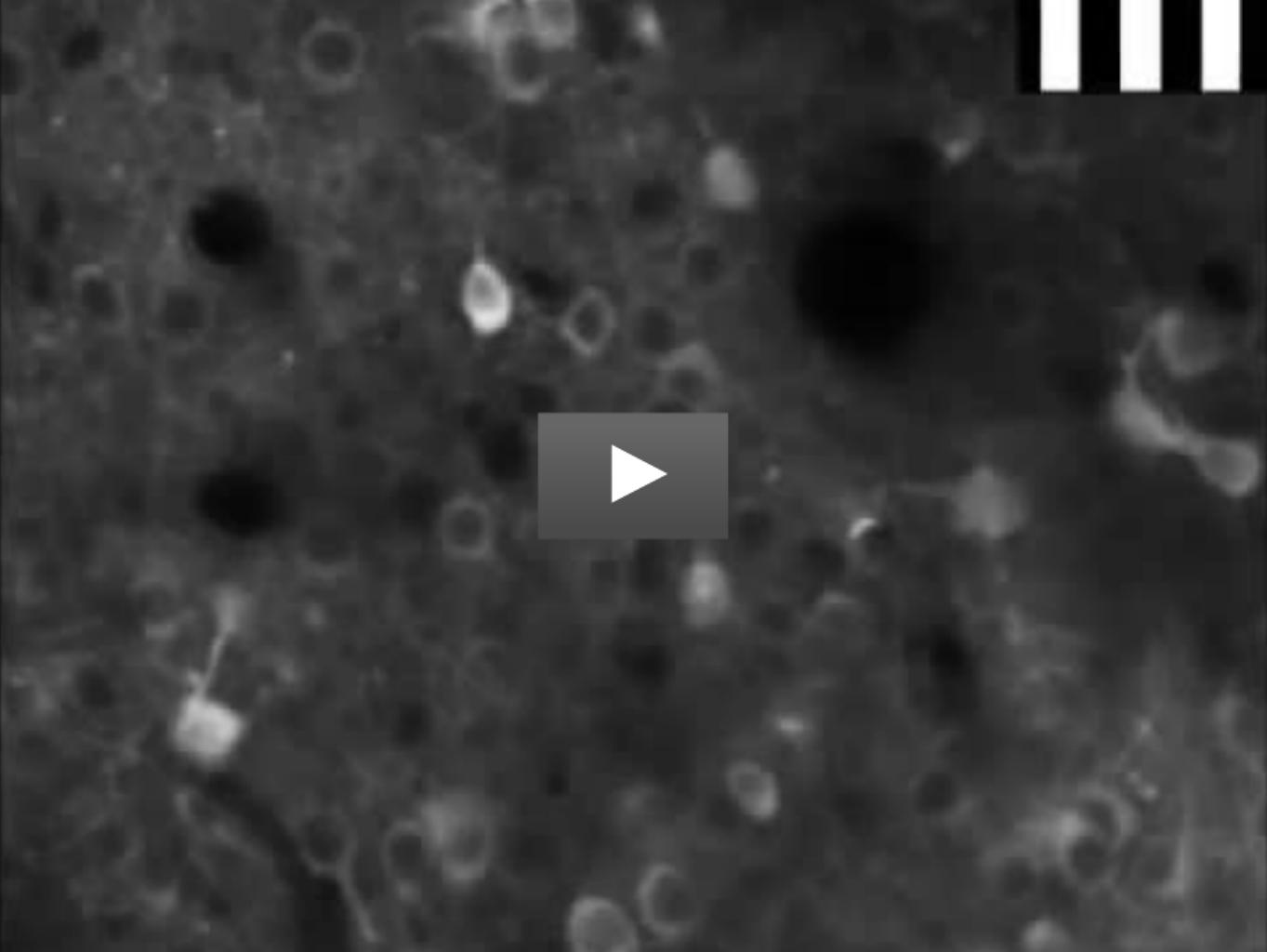
## Kinds of Data From the Brain – Invasive – Calcium Imaging

Use **fluorescent calcium indicator** to indicate the presence of  $\text{Ca}^{2+}$  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

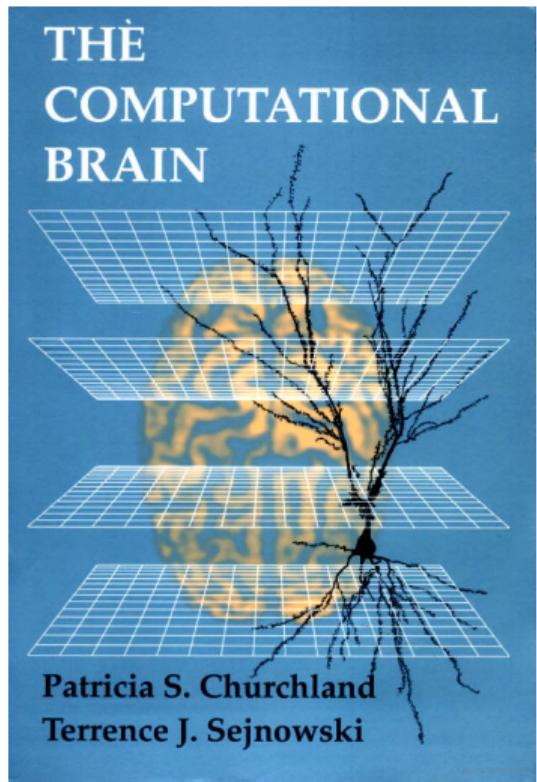
Make certain neuron types **sensitive to light** by genetic modification

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

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

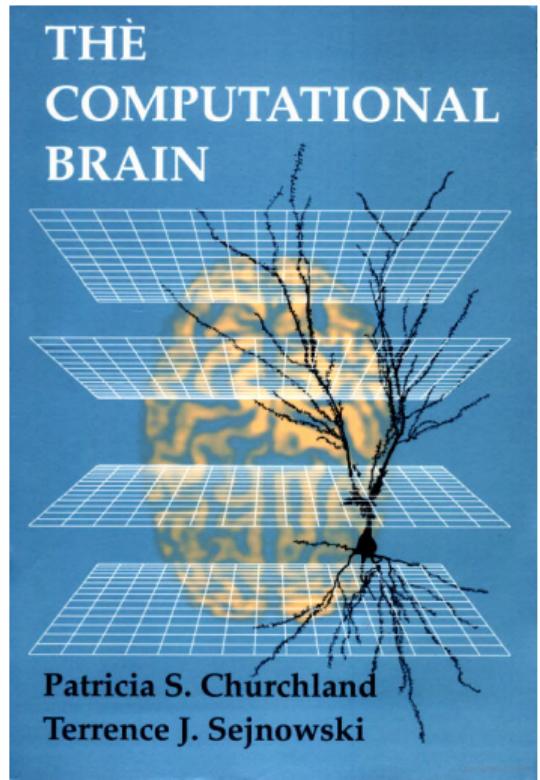


What do we know so far?



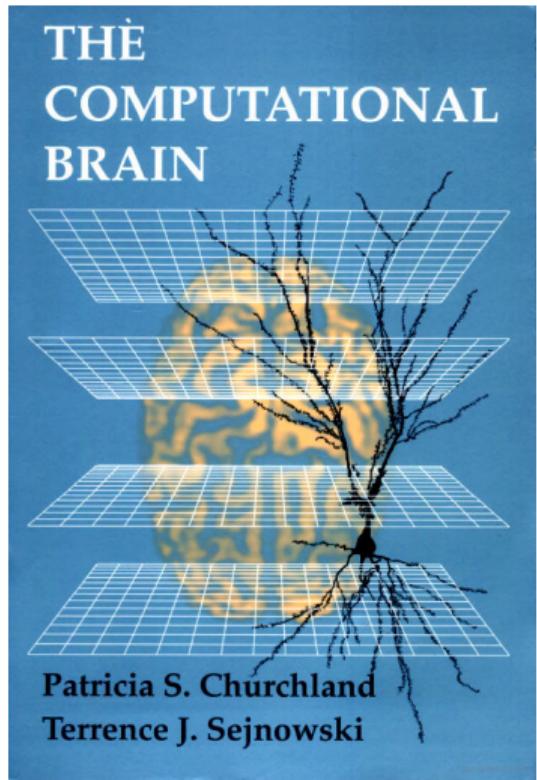
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- ▶ **Data:**  
“The proportion of type *A* neurons in area *X* is *Y*.”



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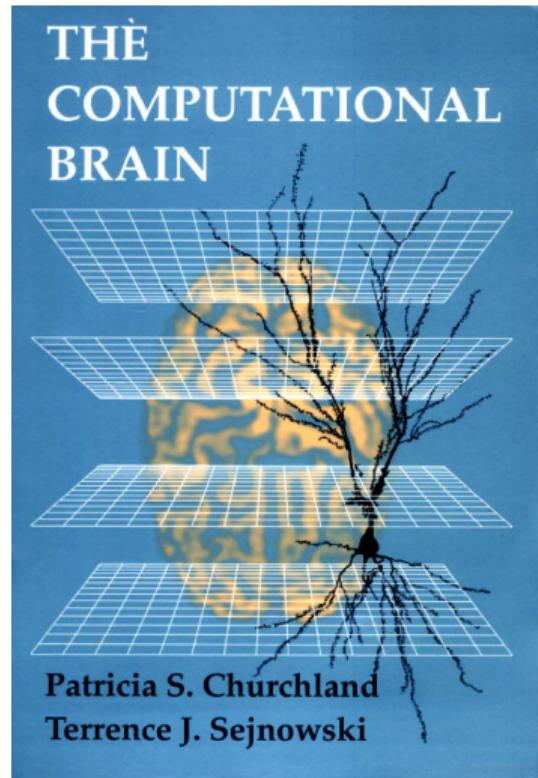
- ▶ **Lots of details**

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- ▶ **Conclusion:**

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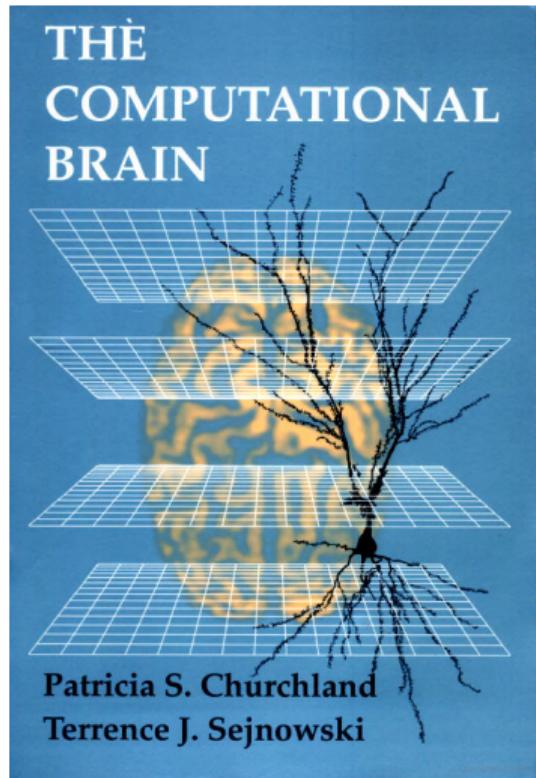
- "The proportion of type *A* neurons in area *X* is *Y*."

- ▶ **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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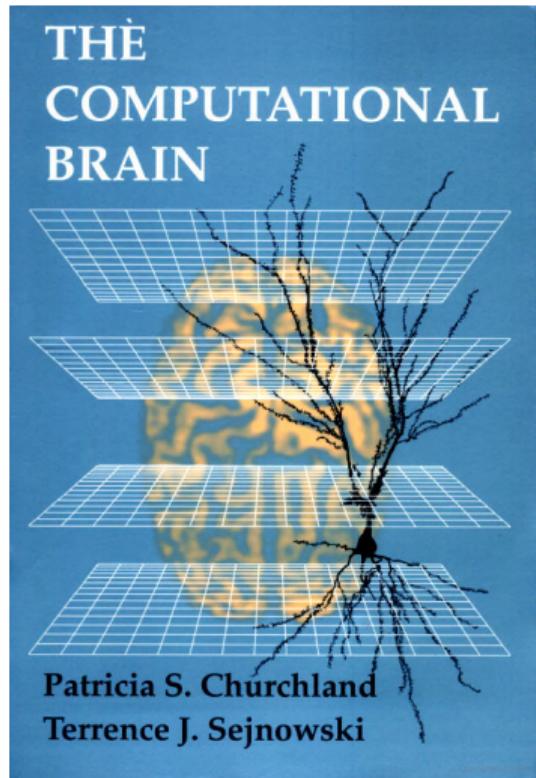
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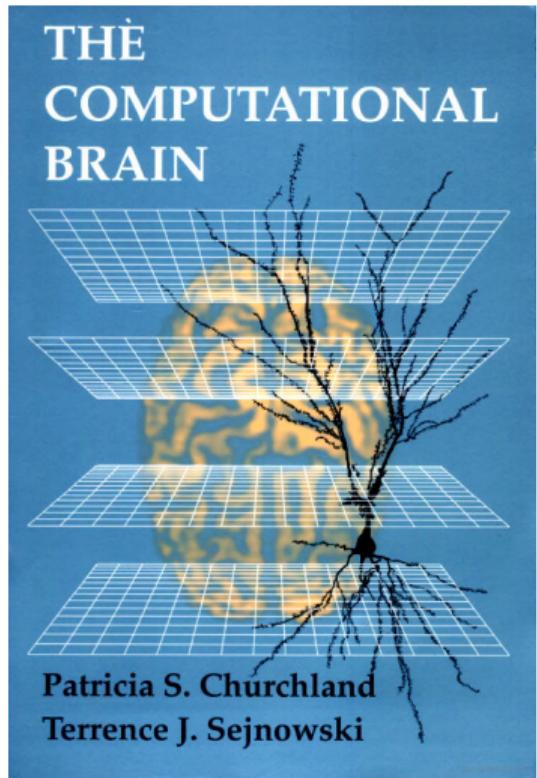
- ▶ No good methods for generalizing from data

- ▶ Need some way to connect these details



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- ▶ Need some way to connect these details
- ⇒ Need unifying theory

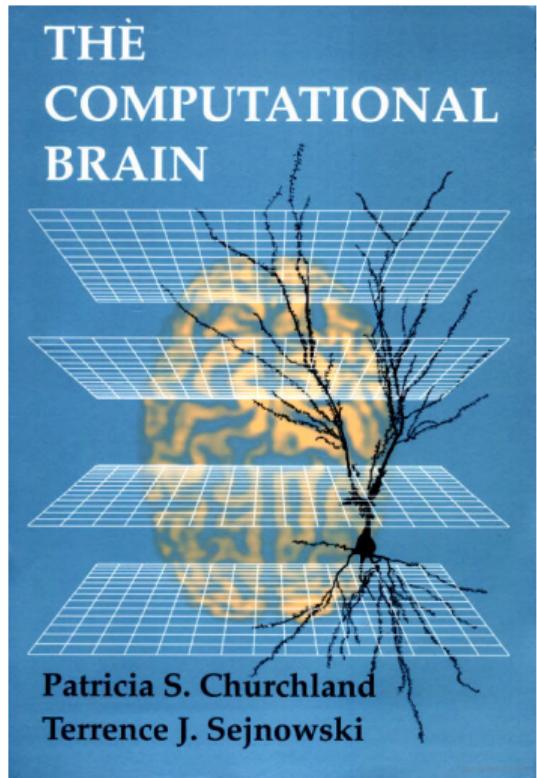


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  - ▶ Need some way to connect these details
- ⇒ Need unifying theory

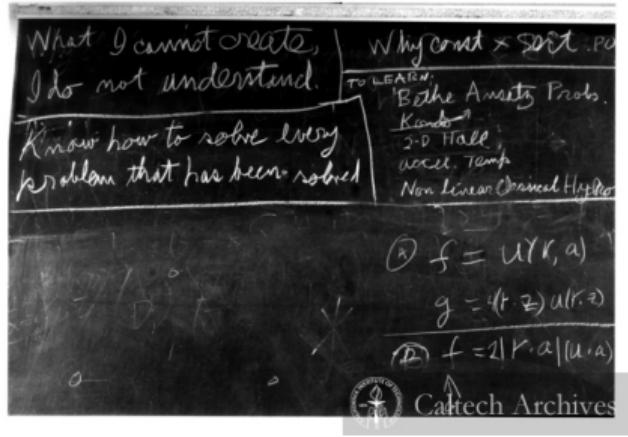
“Neuroscience is data-rich and theory poor”  
— Churchland & Sejnowski, 1994



# Recall: Neural Modelling

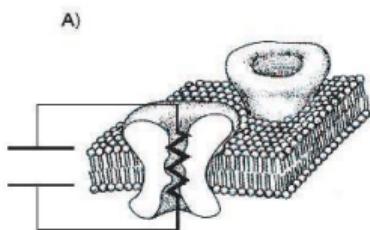
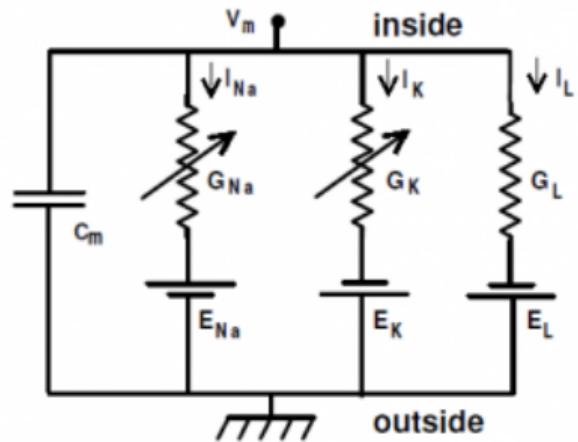
## ► Let's build it

- 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?

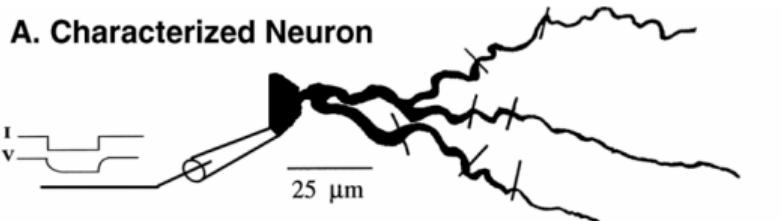


“What I cannot create, I do not understand”  
— Richard Feynman, 1988

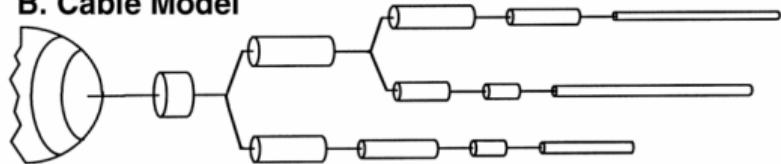
# Single neuron simulation



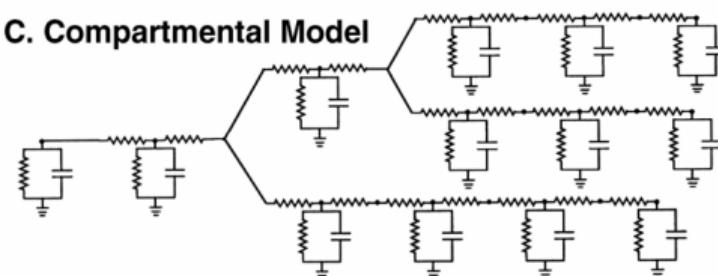
**A. Characterized Neuron**



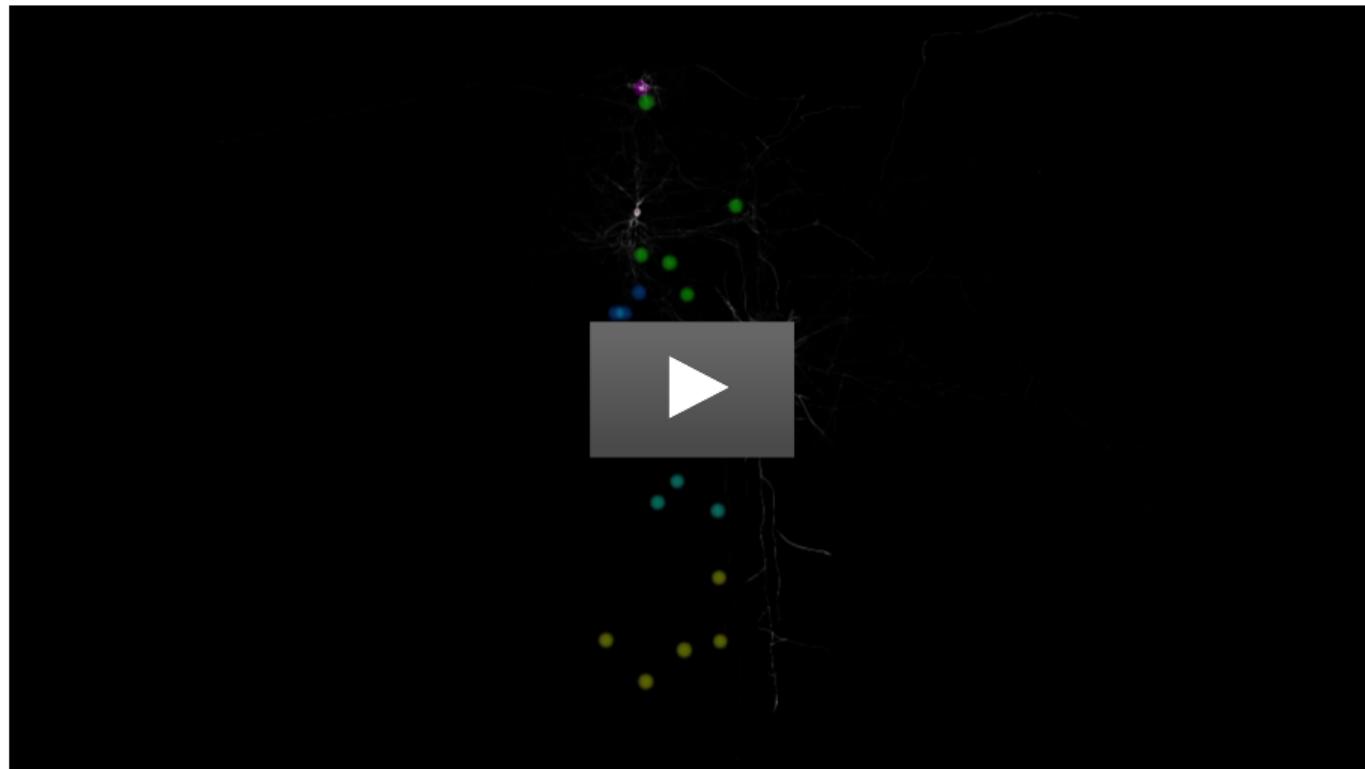
**B. Cable Model**



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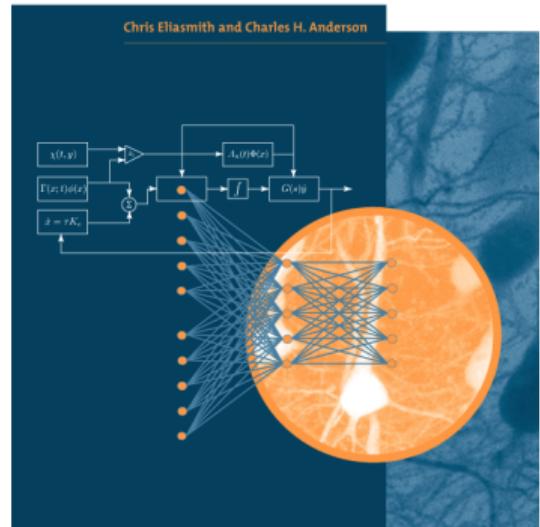
How should we connect “realistic” neurons so they work together?

# 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**

## Neural Engineering

COMPUTATION, REPRESENTATION, AND DYNAMICS  
IN NEUROBIOLOGICAL SYSTEMS

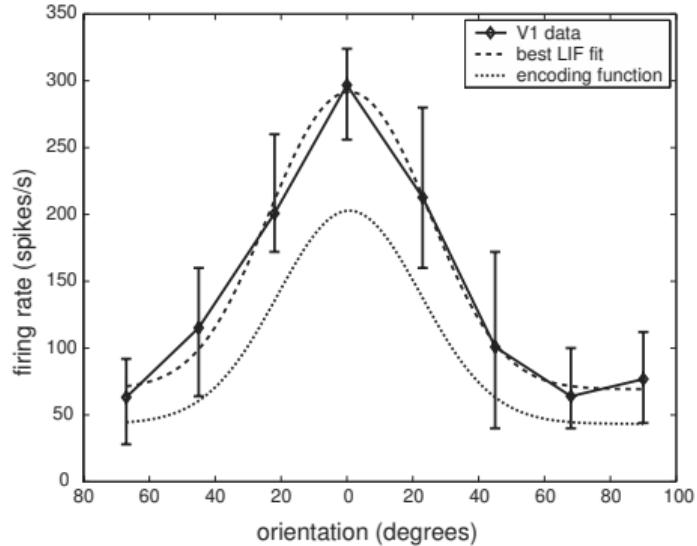
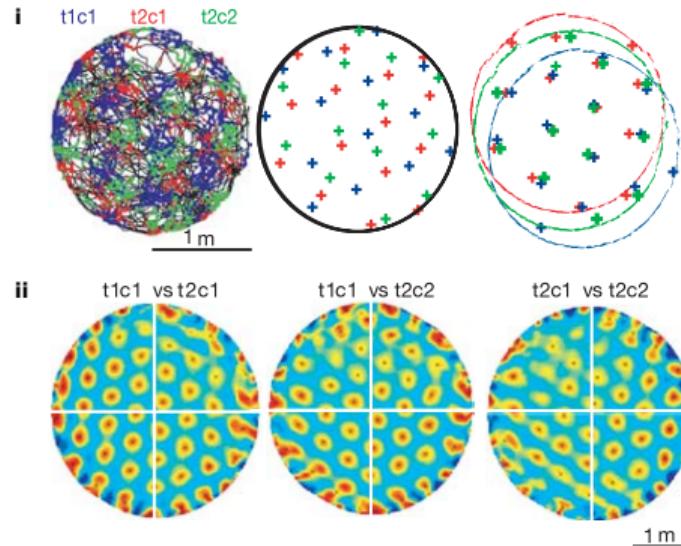


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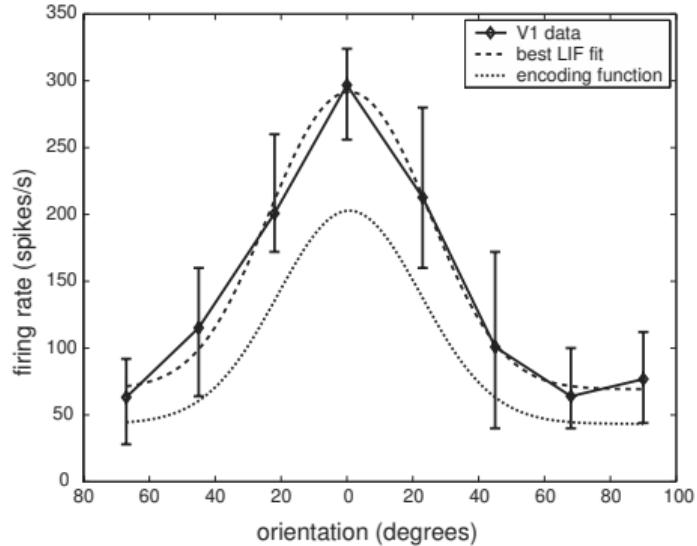
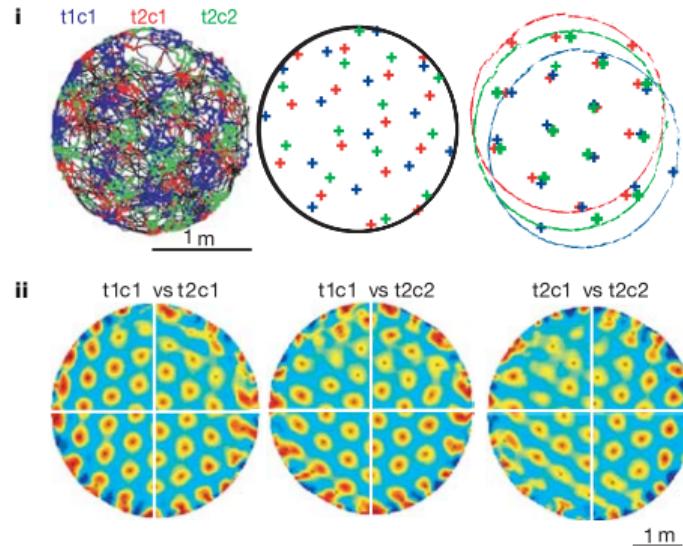


- ▶ What is the mapping between a value and the activity of a group of neurons?

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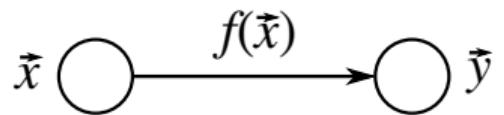
- ▶ How do neurons represent information? (What is the neural code?)



- ▶ 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**

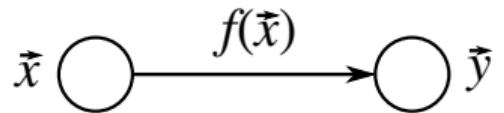
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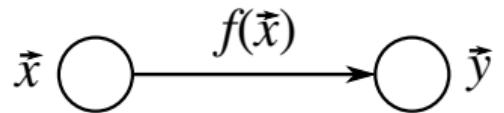
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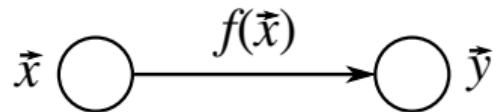
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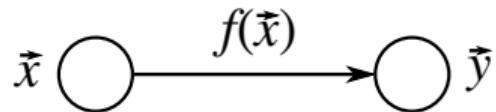
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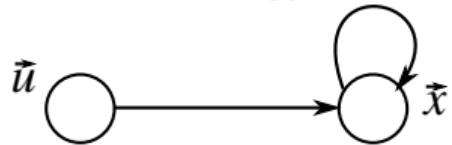
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# Dynamics

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

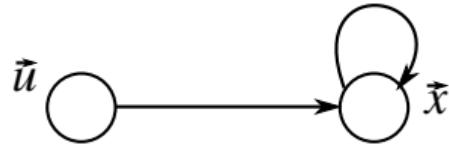


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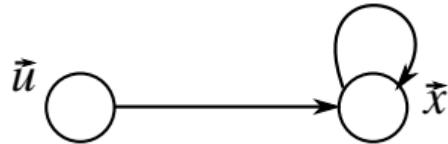
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- ▶ Memory as an integrator

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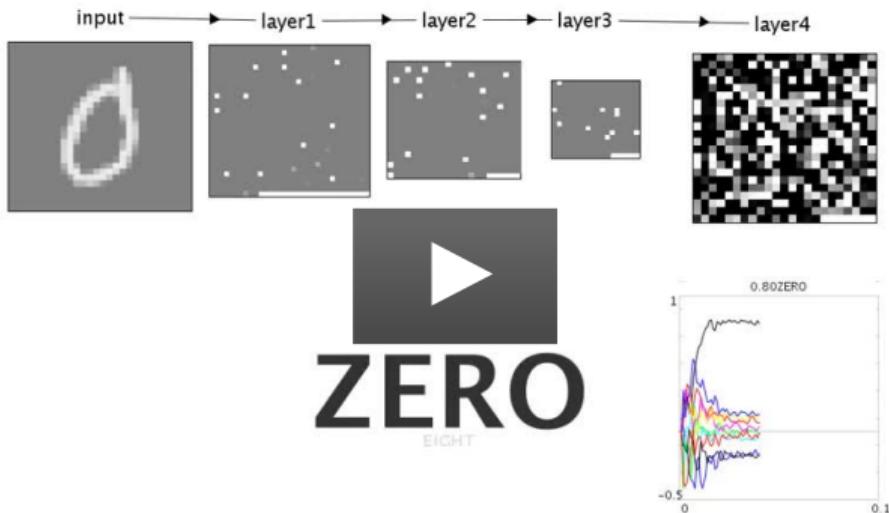
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- ▶ Framework for high-level cognition: **Semantic Pointer Architecture (SPA)**
- ▶ World's largest functional brain model: **SPAUN**

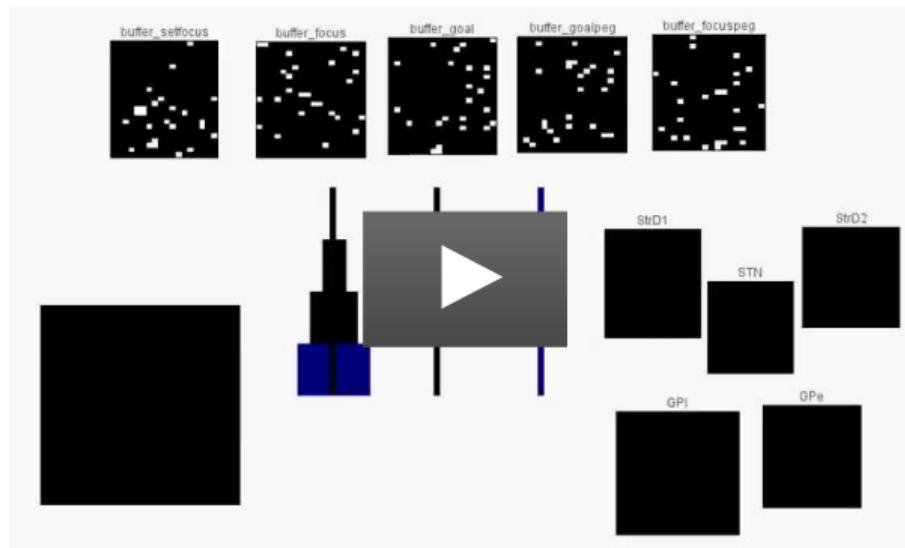
## Examples: Recognizing Handwritten Digits



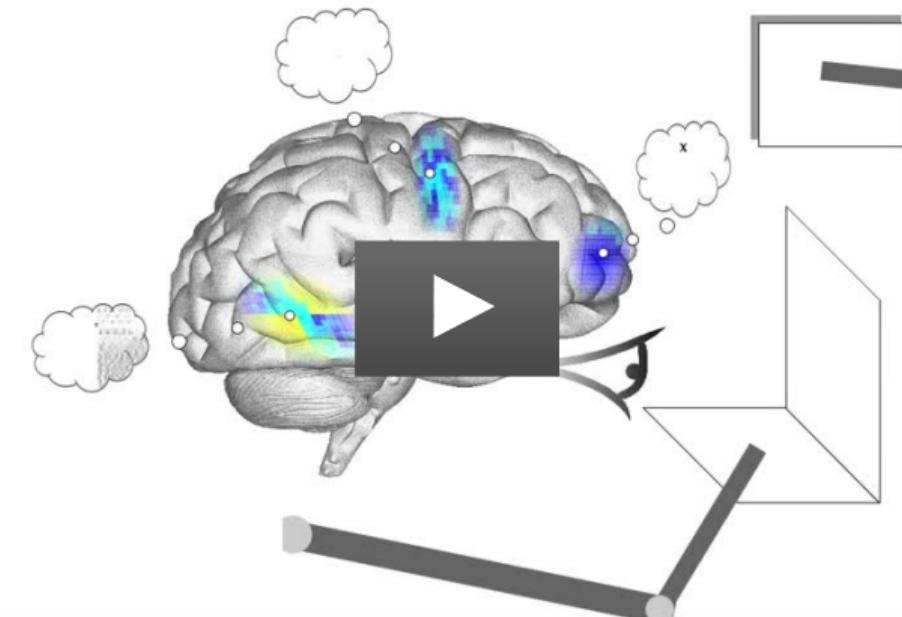
# Examples: Recognizing Natural Images



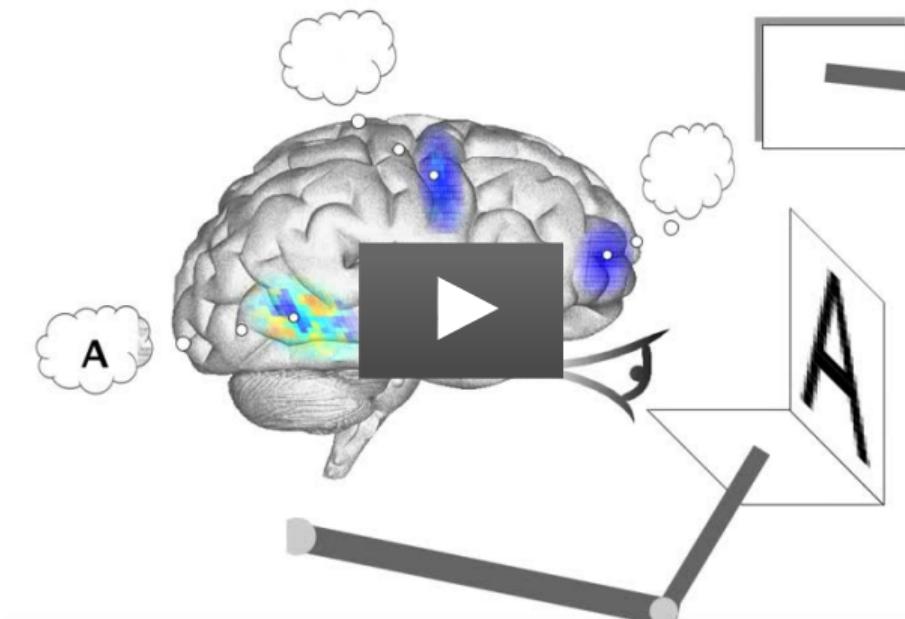
# Examples: Playing Towers of Hanoi



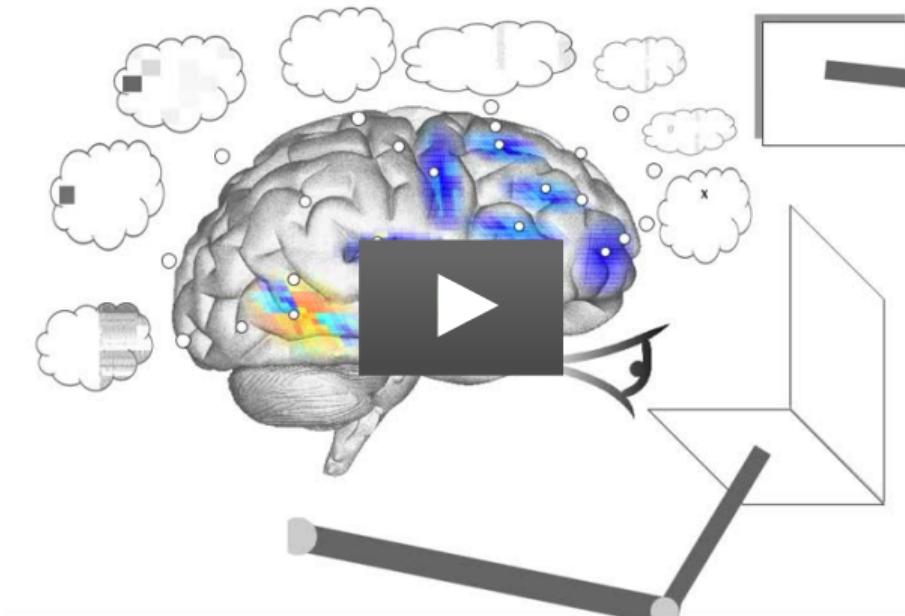
## Examples: SPAUN Copy Drawing



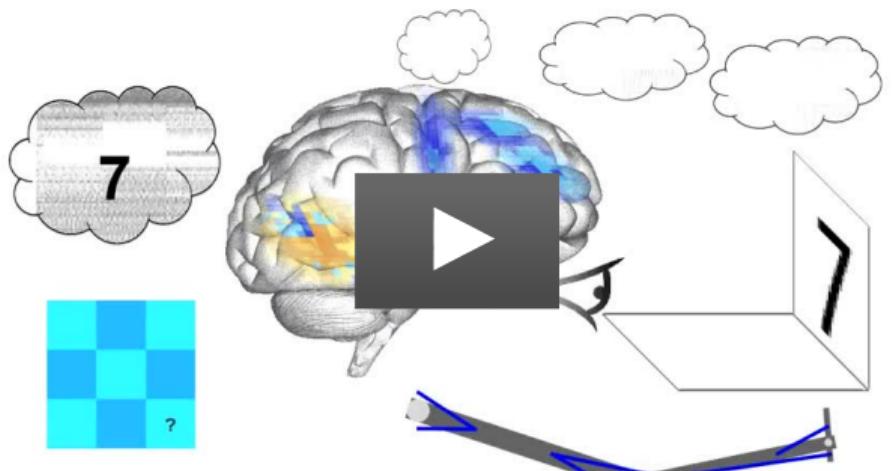
## Examples: SPAUN Recognizing Digits



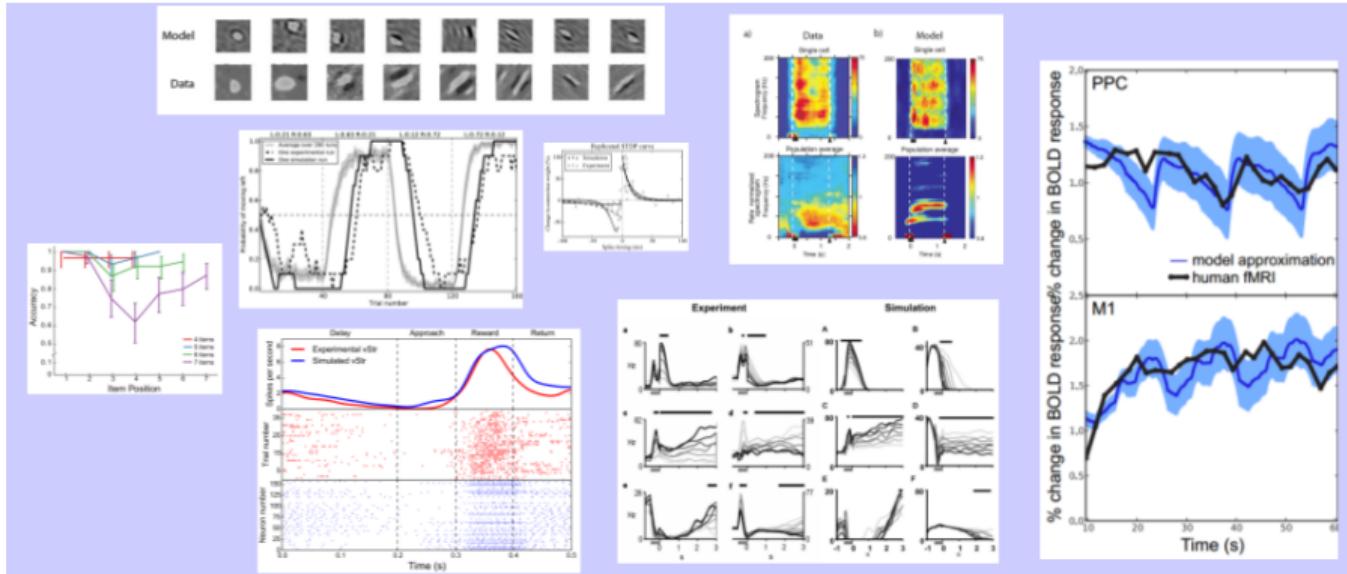
## Examples: SPAUN Silent Addition



## 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