

**SYDE 556/750**

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

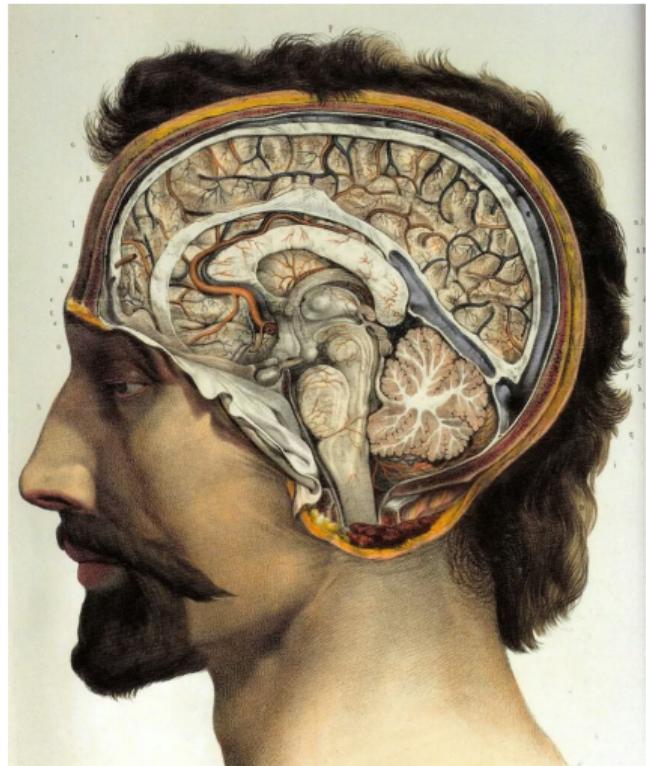
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January 7, 2020



UNIVERSITY OF  
**WATERLOO**

FACULTY OF  
ENGINEERING



# Goal of This Course

## Building Large-Scale Brain Models

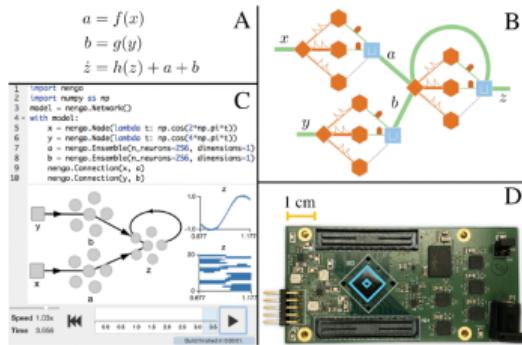
Why?



Understand how Brains Work



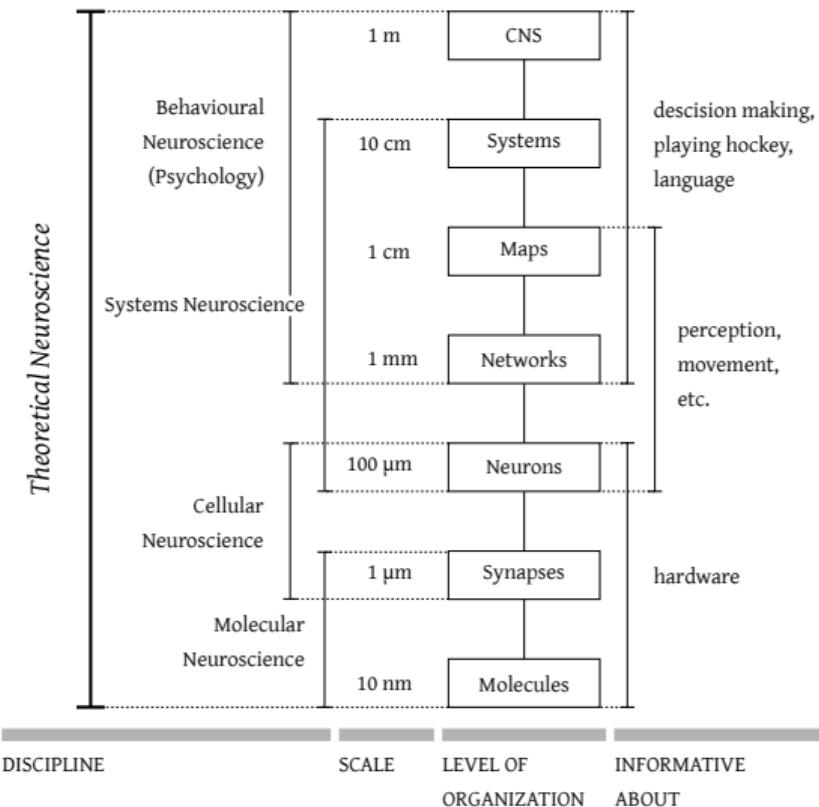
Build Better AI Systems



Program Neuromorphic Hardware

**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.

# 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

## Similarities

- Methods are similar
- Goals are similar (quantification)

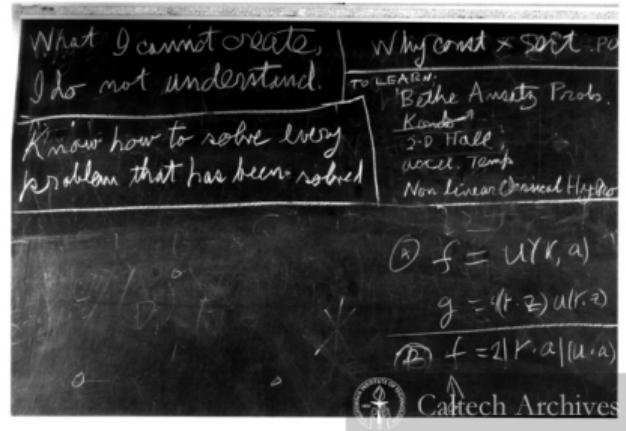
## Differences

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

# Neural Modelling

## ► Let's build it

- 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...



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

# 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

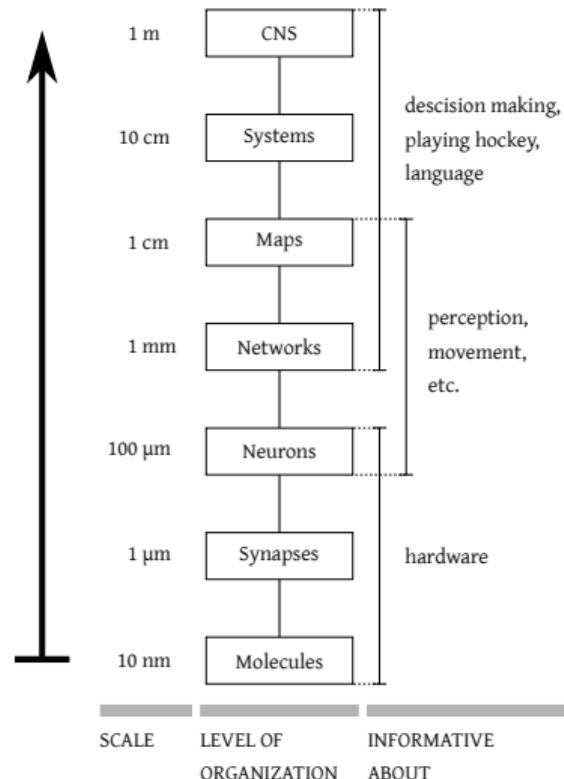
## ► Examples

BlueBrain/Human Brain Project/SyNAPSE

## ► Shortcomings

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

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



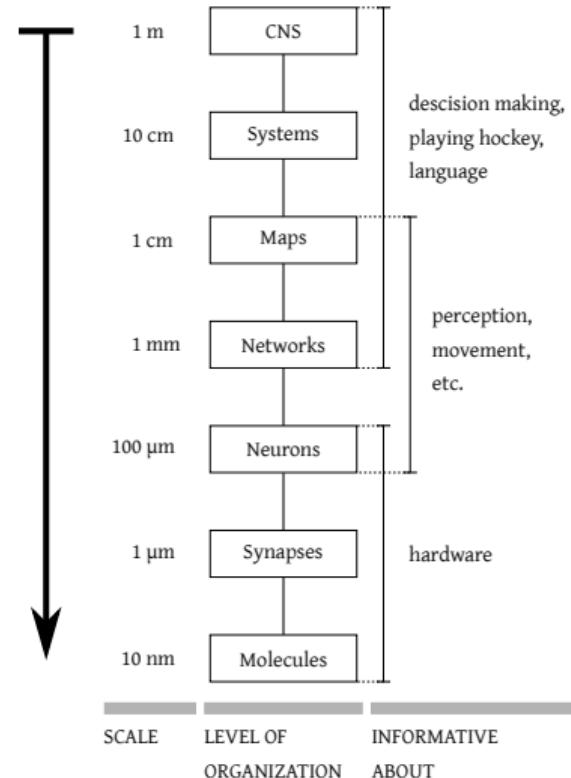
# Problems With Current Approaches: Behavioural Models

- ▶ **Top-down** approach
- ▶ **Modeling Frameworks:** ACT-R, SOAR
- ▶ **Shortcomings**
  - ▶ Can't compare to neural data
  - ▶ No "bridging laws"
  - ▶ No constraints on the equations

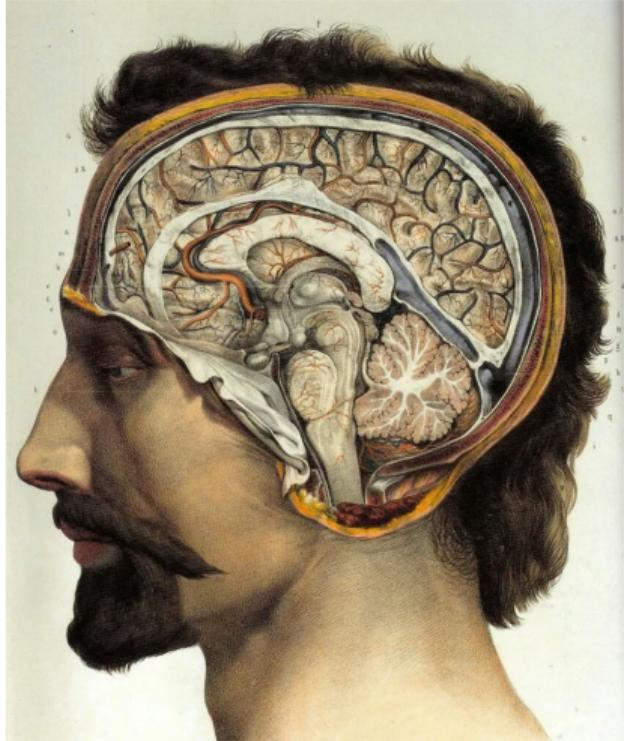
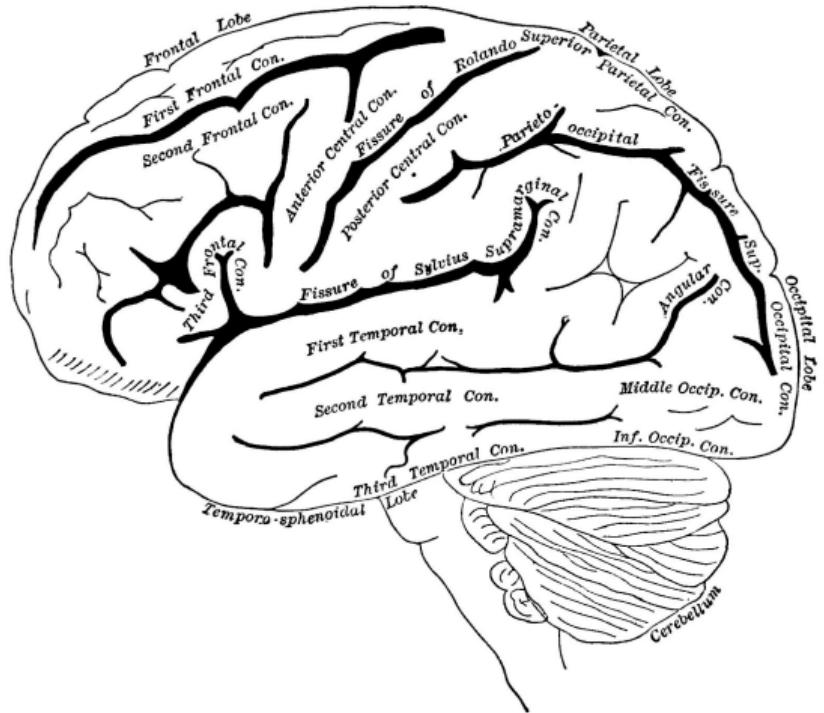
⚠ **Maybe these shortcomings are okay.**

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

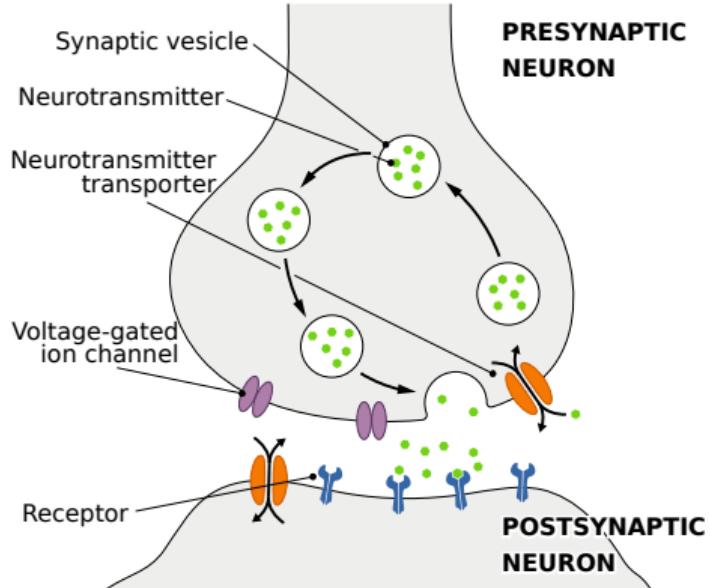
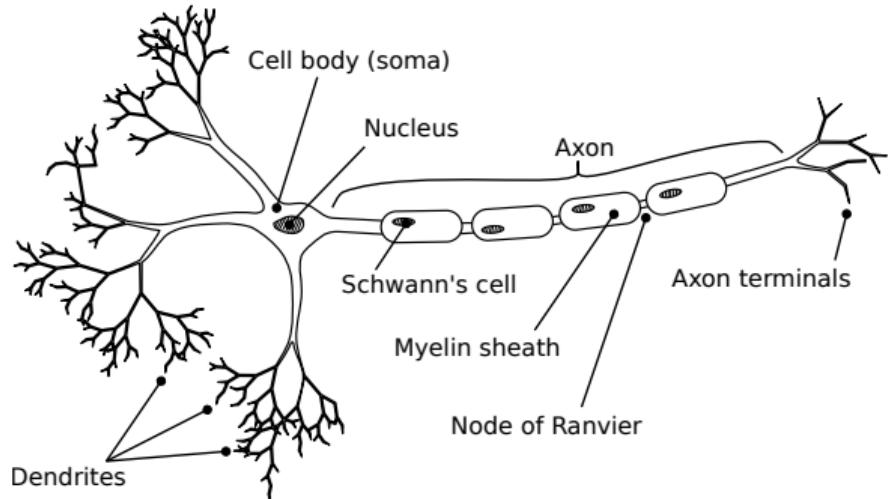


**Suzanne Stensaas, PhD**



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

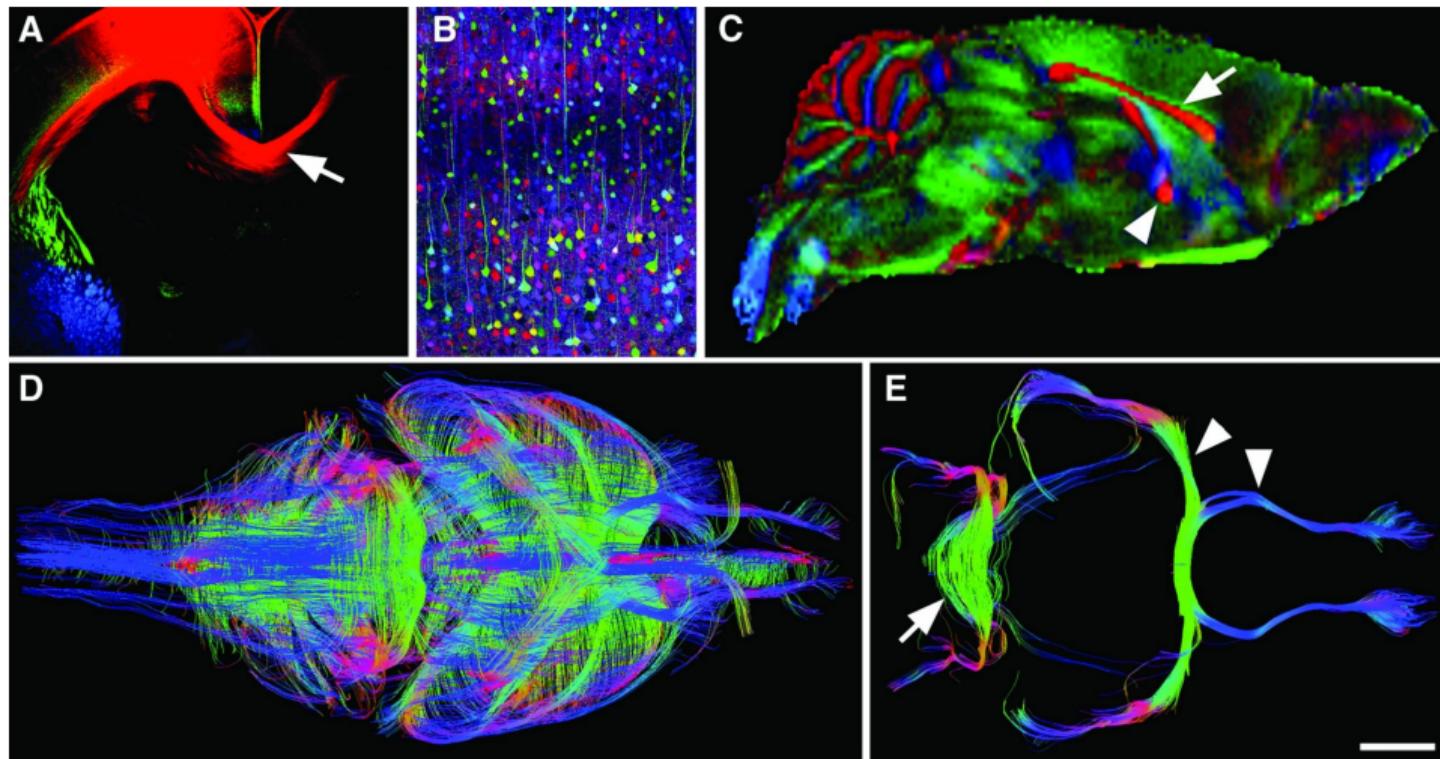
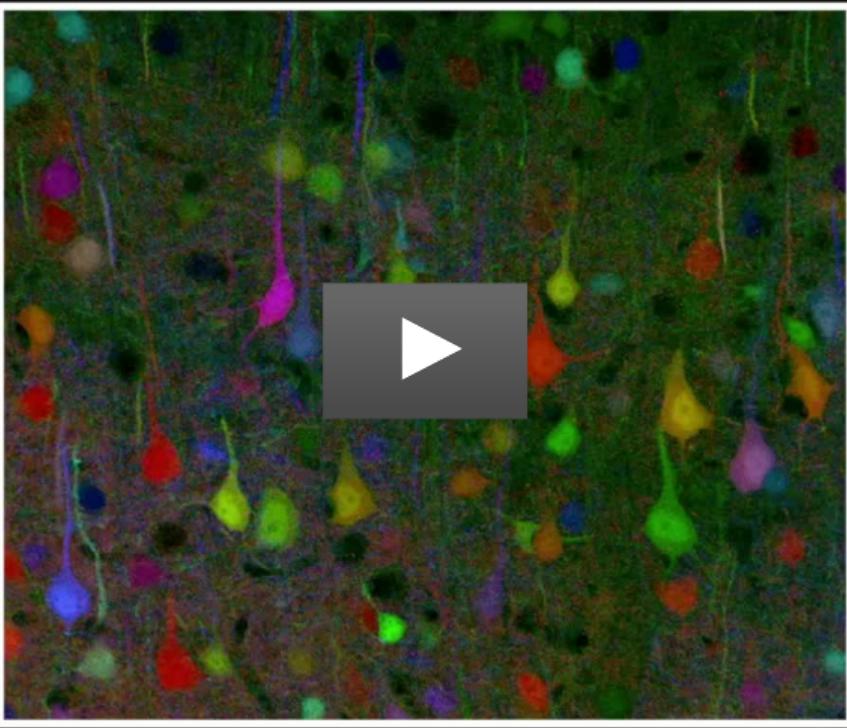


Image Sources. Alain Chédotal and Linda J Richards. *Wiring the Brain: The Biology of Neuronal Guidance*. Cold Spring Harbor perspectives in biology (2010)



R Draft & J Livet

x = independently organized TED event

**TEDx** Caltech

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

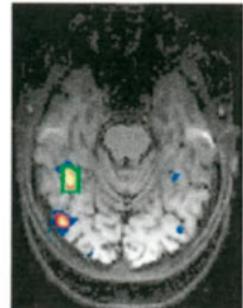
## Functional Magnetic Resonance Tomography

Measures *changes* in blood oxygenation (BOLD)

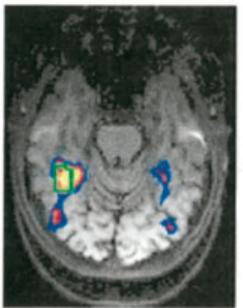
- + Whole-brain, 3D reconstruction  
(individual activity voxels, volume elements)
- Yellow circle Medium spatial resolution (millimeters)
- Low temporal resolution (seconds)
- Signal is hard to interpret  
(differences, indirect, i.e. not spiking activity)
- Has to be averaged over multiple trials

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

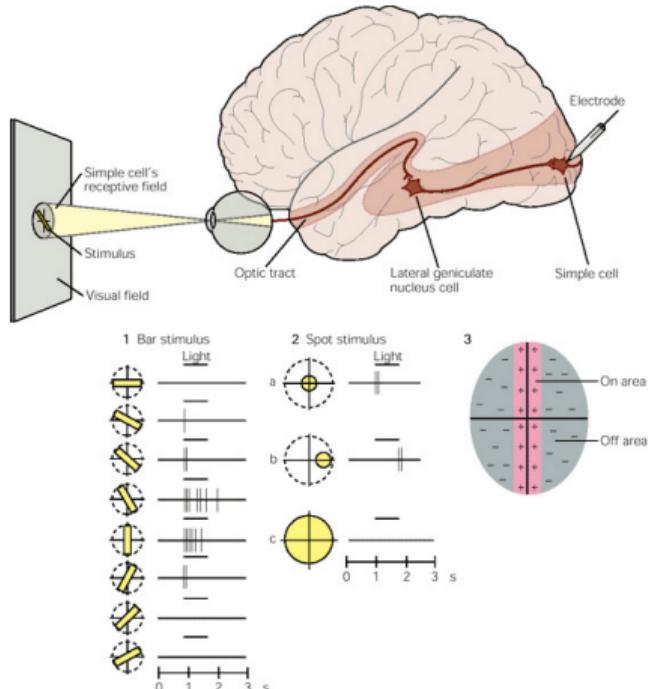


Image Sources. "Depiction of Hubel and Wiesels experiment." Kandel et al., 2012, Principles of Neural Science, 5th ed., Figure 27-11.

# 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)

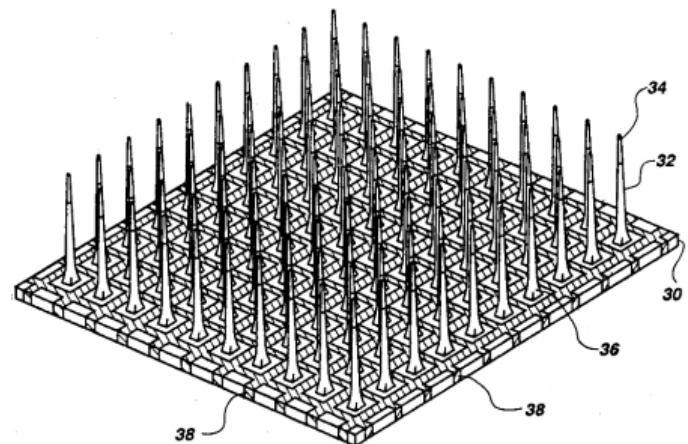
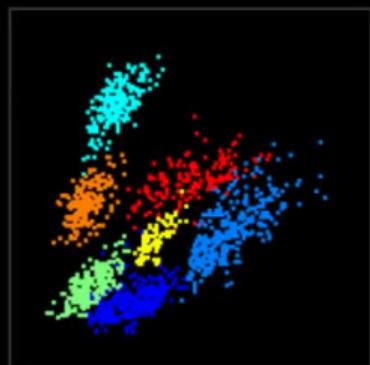


Image Sources. “Depiction of a Utah Array”. From: US Patent #5,215,088

cell activity

overall



ongoing



behavior



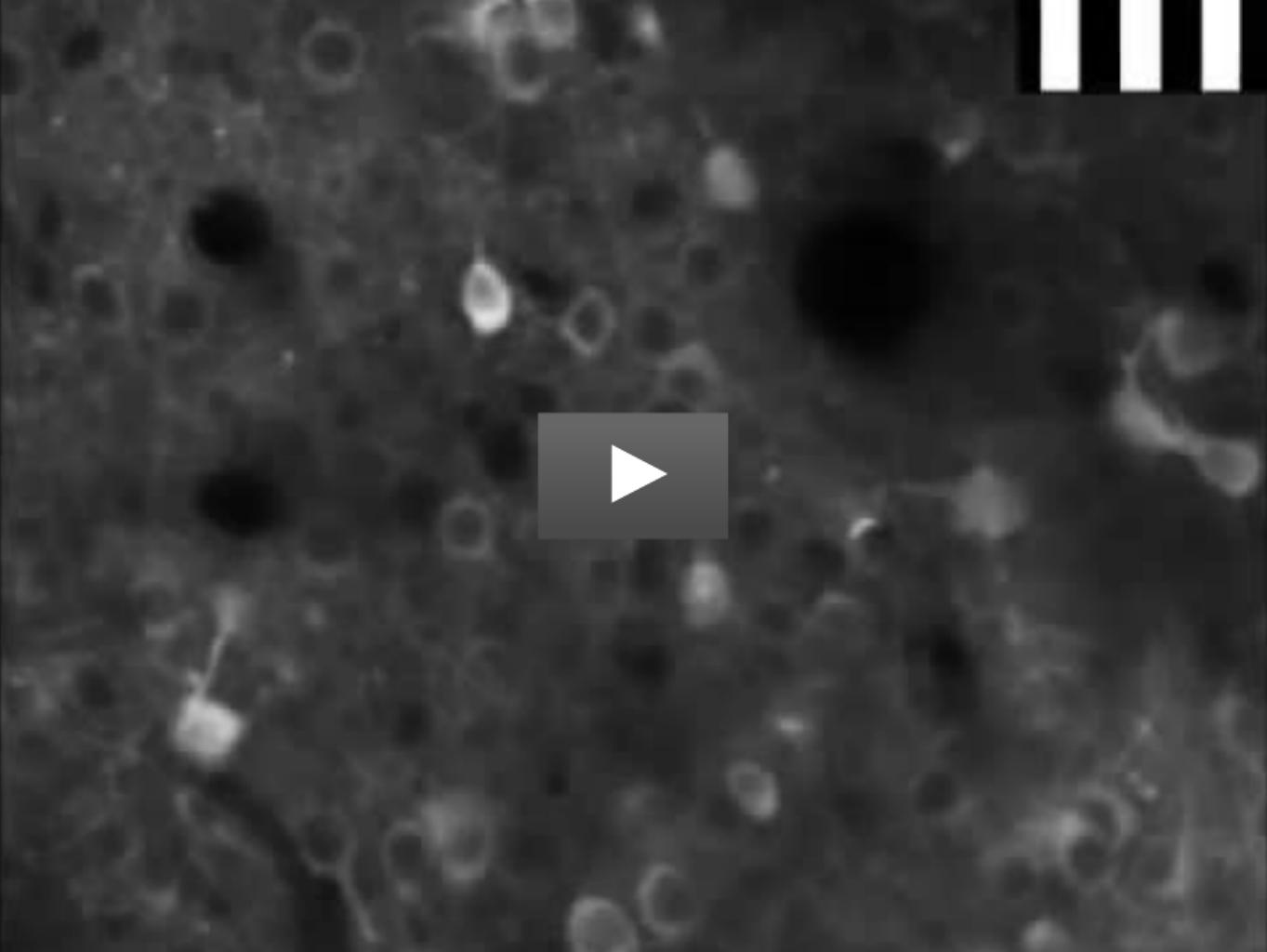
## Kinds of Data From the Brain – Invasive – Calcium Imaging

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?

- ▶ **Lots of details**

- ▶ **Data:**

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

- ▶ **Conclusion:**

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

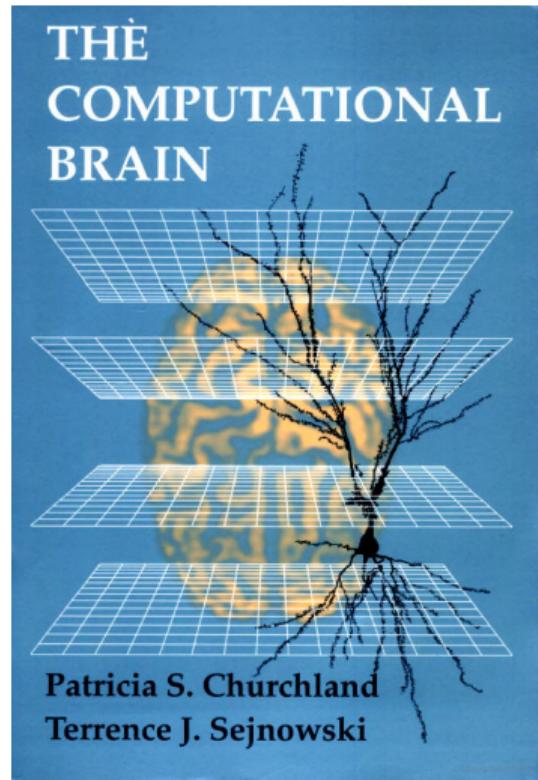
- ▶ Hard to get a big picture

- ▶ No good methods for generalizing from data

- ▶ Need some way to connect these details

- ⇒ Need unifying theory

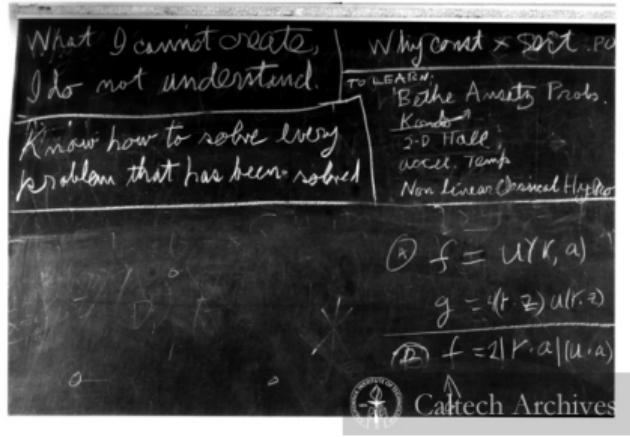
“Neuroscience is data-rich and theory poor”  
— Churchland & Sejnowski, 1994



# Recall: Neural Modelling

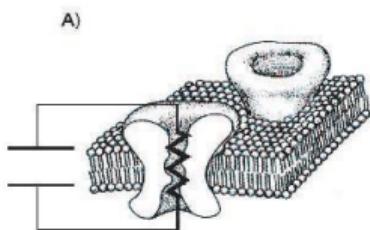
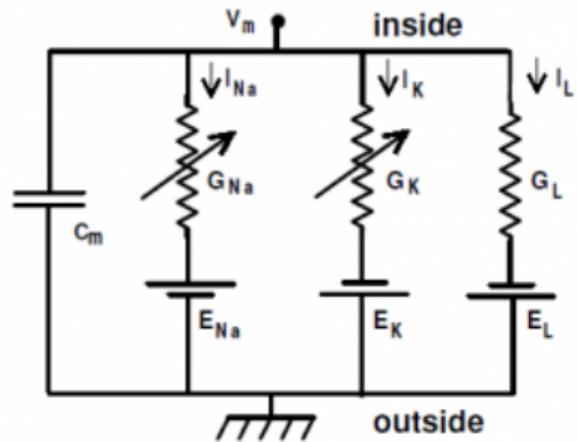
## ► Let's build it

- 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?

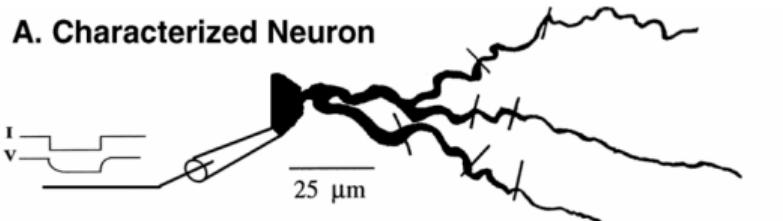


“What I cannot create, I do not understand”  
— Richard Feynman, 1988

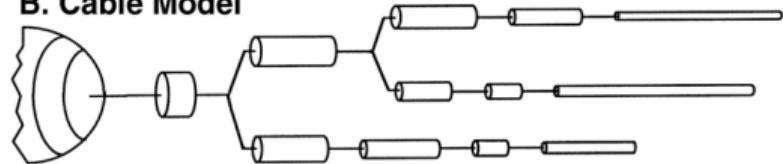
# Single neuron simulation



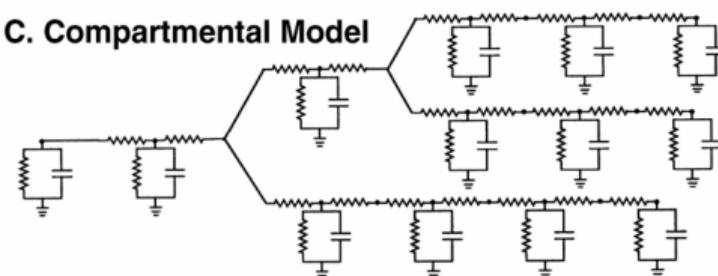
**A. Characterized Neuron**



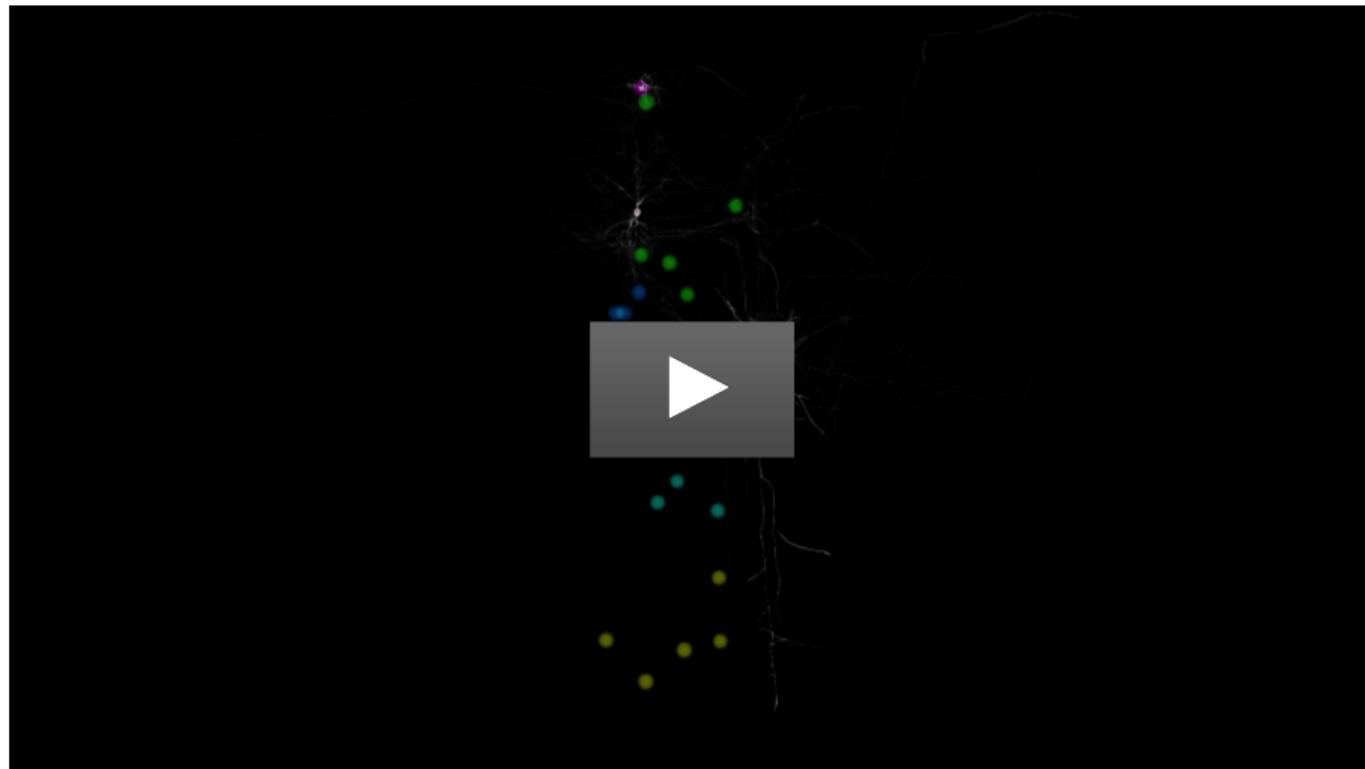
**B. Cable Model**



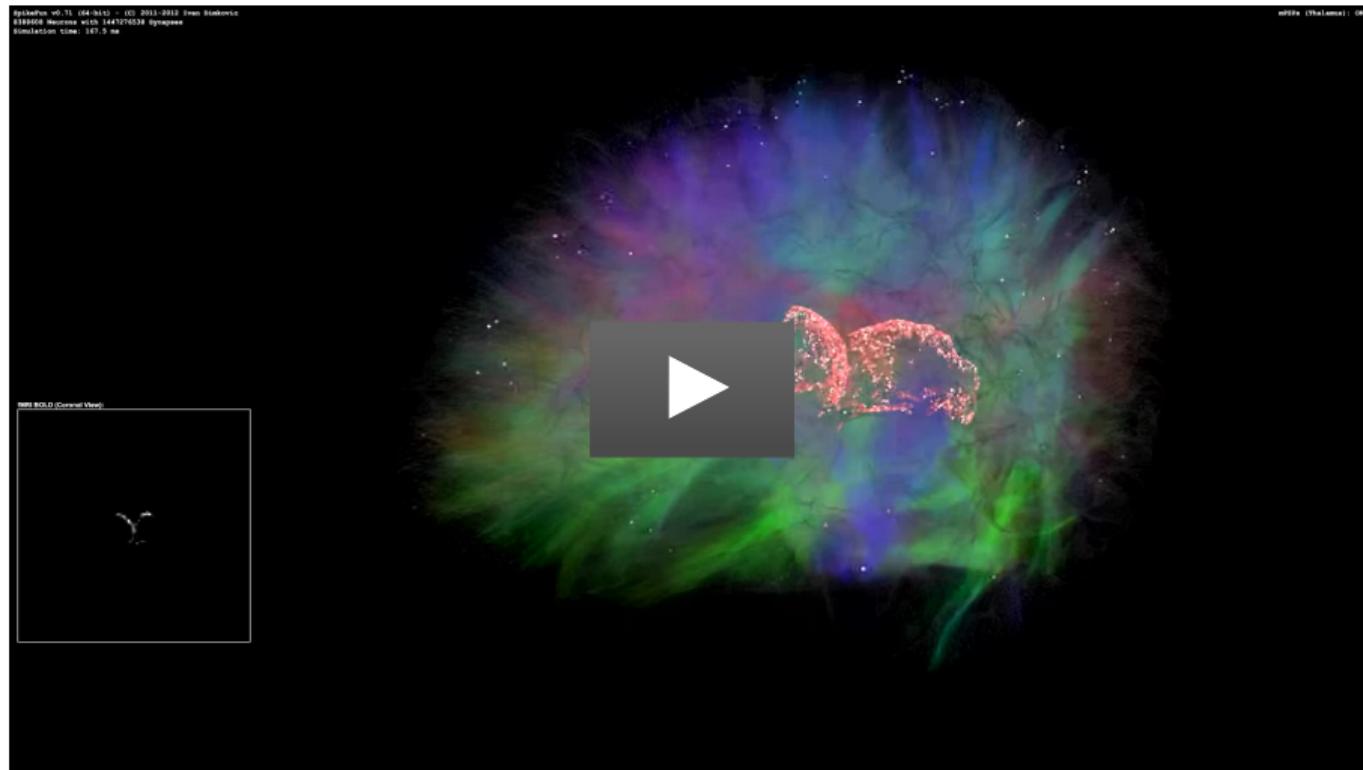
**C. Compartmental Model**



Simulating millions of neurons...



# Simulating billions of neurons...



# The Controversy

- ▶ **What level of detail** for the neurons?  
How should they be connected?
- ▶ IBM SyNAPSE project (Modha)
  - ▶ Billions of neurons, very simple models
  - ▶ Randomly connected
  - ▶ 2009: "Cat"-scale brain
  - ▶ 2012: "Human"-scale brain
- ▶ Blue Brain/HBP (Markram)
  - ▶ Much more detailed neuron models
  - ▶ Statistically connected
- ▶ How much detail is enough?
- ▶ How could we know?

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" (2019)

# What actually matters...

Connecting brain models to **behaviour**

How can we build models that actually do something?

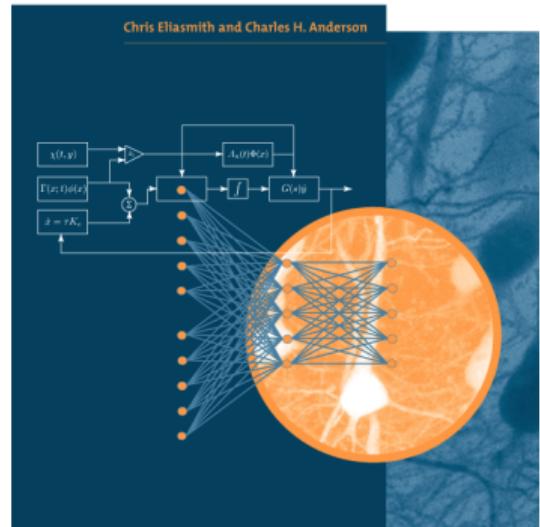
How should we connect “realistic” neurons so they work together?

# 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**

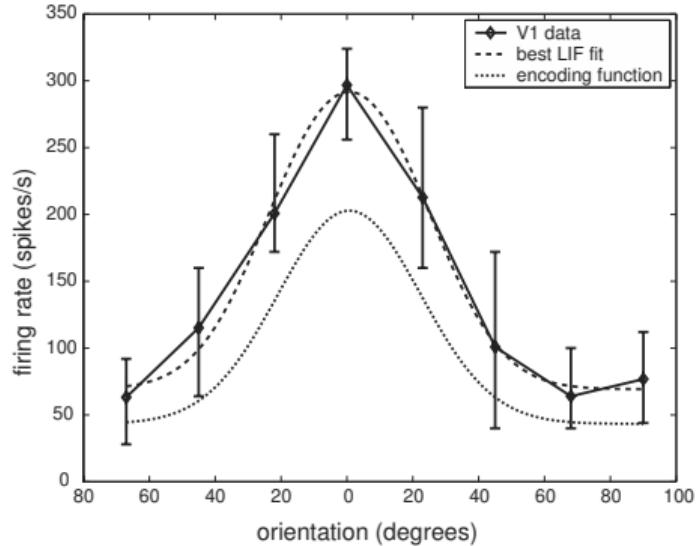
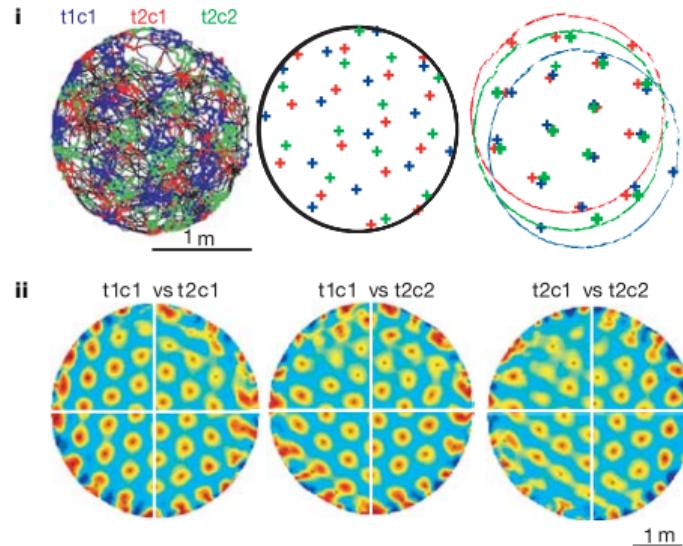
## Neural Engineering

COMPUTATION, REPRESENTATION, AND DYNAMICS  
IN NEUROBIOLOGICAL SYSTEMS



# Representation

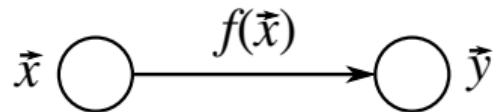
- ▶ How do neurons represent information? (What is the neural code?)



- ▶ 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**

**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.

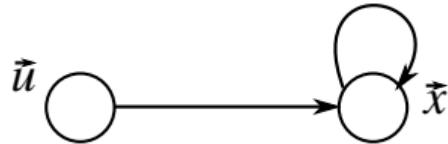
# Transformation



- ▶ **Connections compute functions** on those vectors
- ▶ One group of neurons may represent  $\mathbf{x} \in \mathbb{R}^m$ , another group a vector  $\mathbf{y} \in \mathbb{R}^n$
- ▶ Connection determines  $f : \mathbb{R}^m \rightarrow \mathbb{R}^n$  with  $f(\mathbf{x}) = \mathbf{y}$
- ▶ We can systematically find connection weights  $\mathbf{W}$  that approximate a certain  $f$
- ▶ Can analyse which  $f$  can be computed

# Dynamics

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



- ▶ Recurrent connections (feedback) implement **dynamical systems**

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

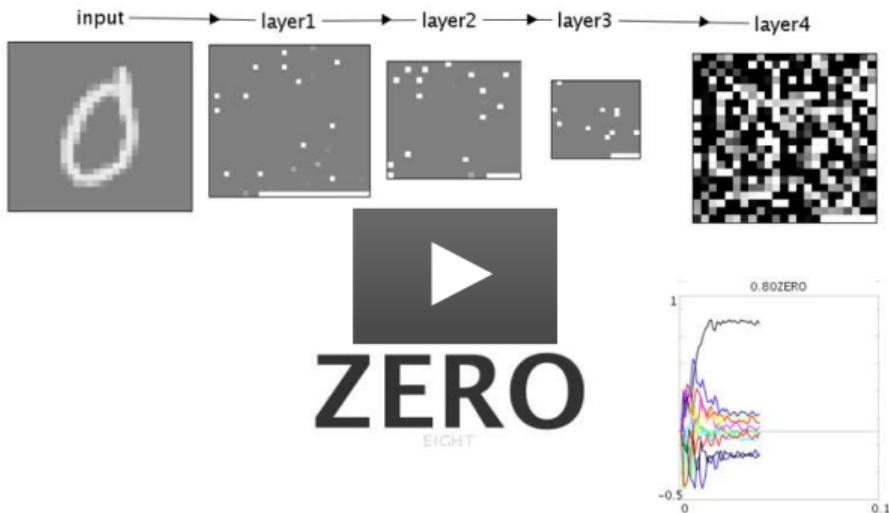
- ▶ Great for implementing control theoretical concepts
- ▶ Memory as an integrator

$$\frac{d}{dt}\mathbf{x}(t) = \mathbf{u}(t)$$

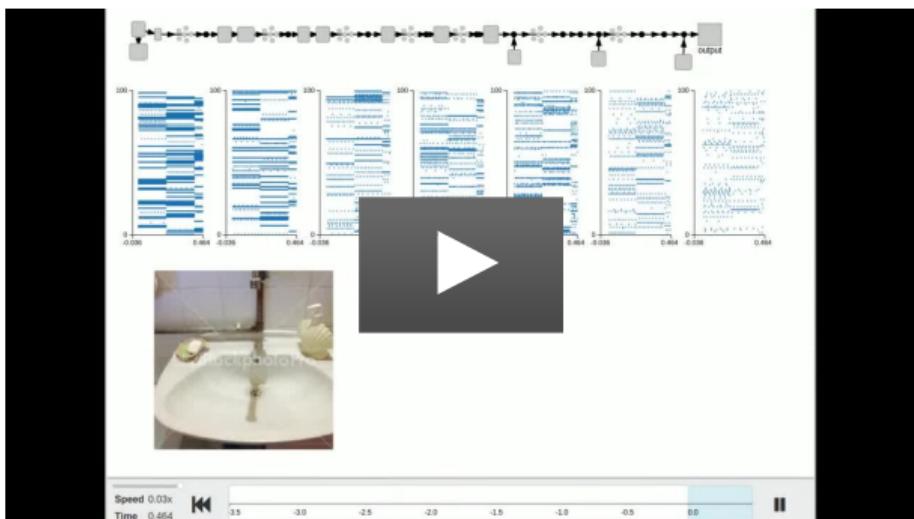
## Examples

- ▶ This approach gives us a **neural compiler**
- ▶ Solve for the connections weights that approximate a **behaviour**
- ▶ Works for a wide variety of **neuron models**
- ▶ Number of neurons affects **accuracy**
- ▶ Neuron properties influence **timing** and computation
- ▶ Framework for high-level cognition: **Semantic Pointer Architecture (SPA)**
- ▶ World's largest functional brain model: **SPAUN**

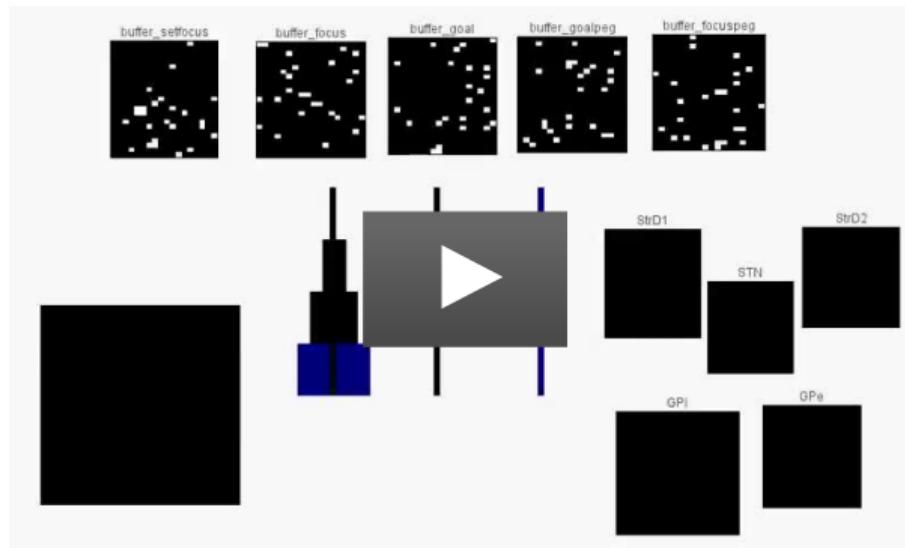
## Examples: Recognizing Handwritten Digits



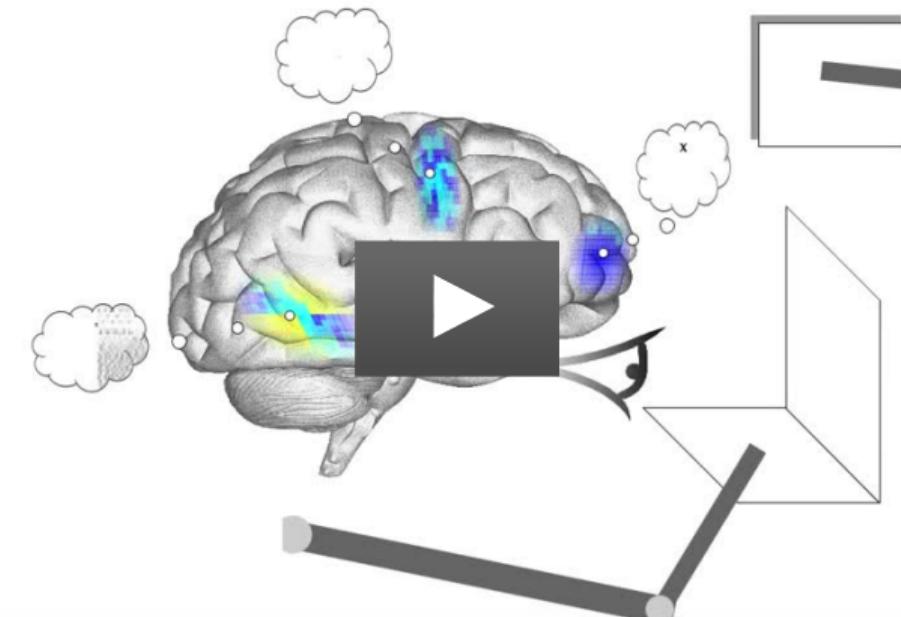
# Examples: Recognizing Natural Images



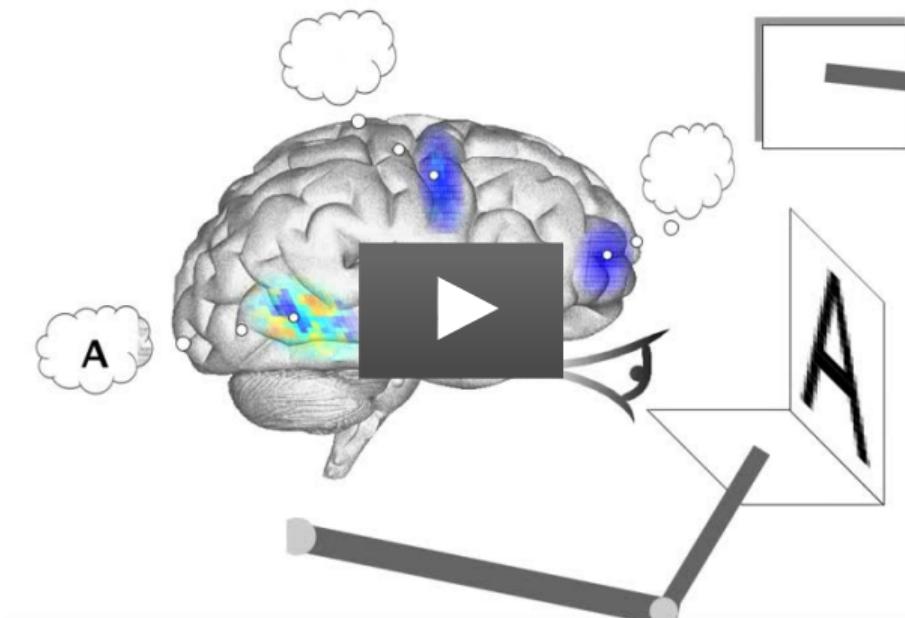
## Examples: Playing Towers of Hanoi



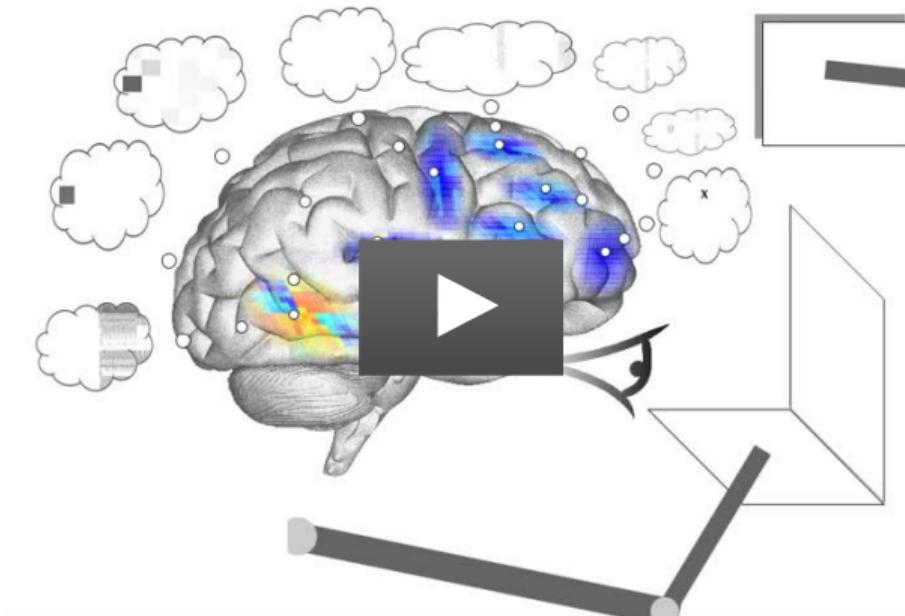
## Examples: SPAUN Copy Drawing



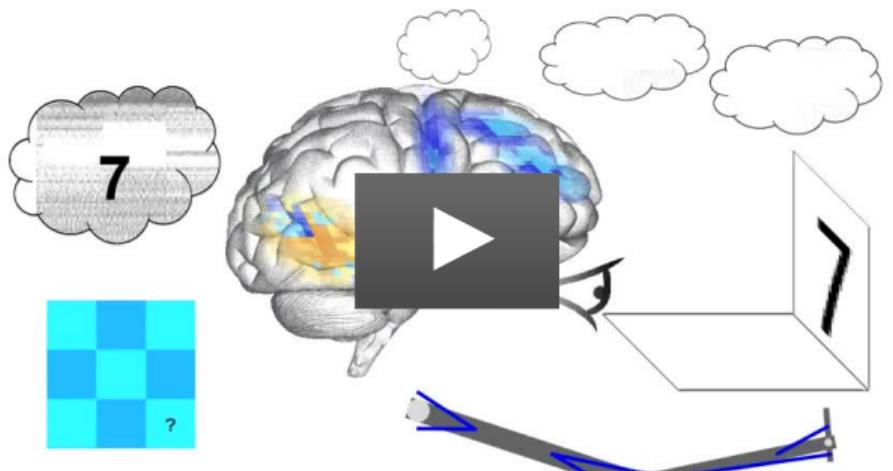
## Examples: SPAUN Recognizing Digits



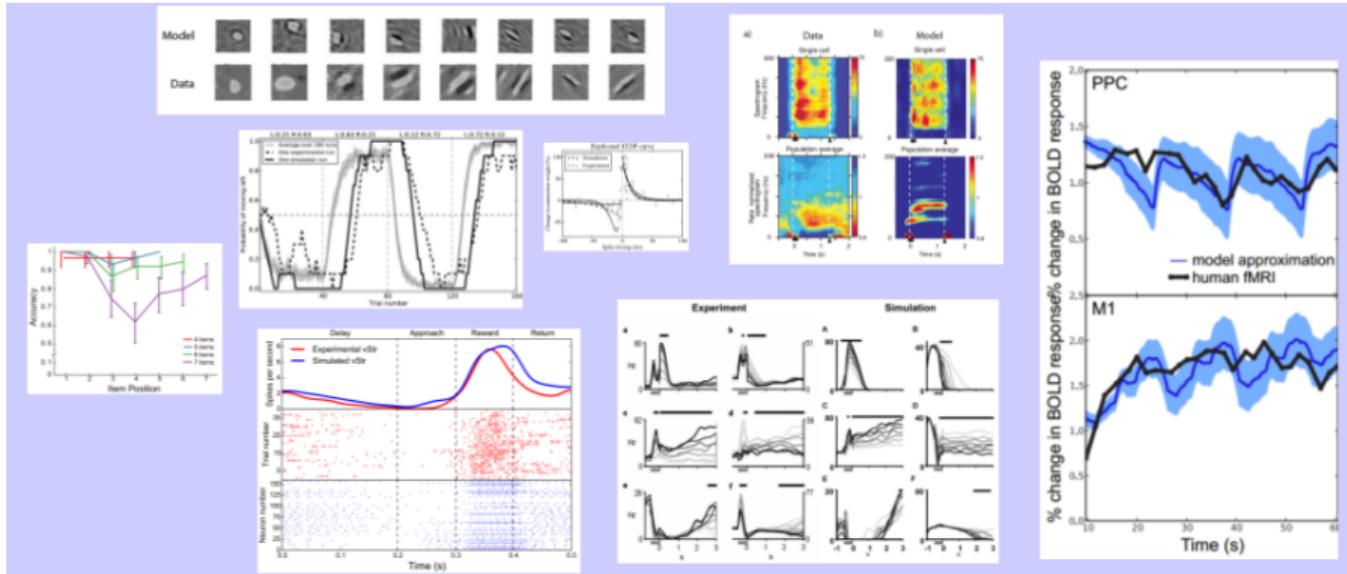
## Examples: SPAUN Silent Addition



## 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