

**SYDE 556/750**

## **Simulating Neurobiological Systems**

### **Lecture 1: Introduction**

Chris Eliasmith

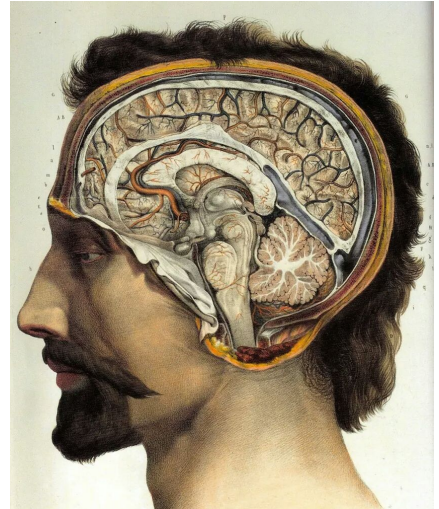
September 4, 2024

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



**UNIVERSITY OF  
WATERLOO**

**FACULTY OF  
ENGINEERING**



# Goal of This Course

## Building Large-Scale Brain Models

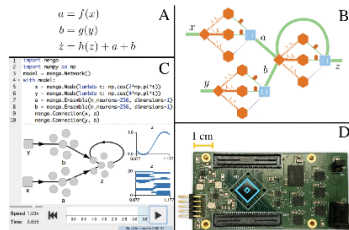
Why?



Understand how Brains  
Work



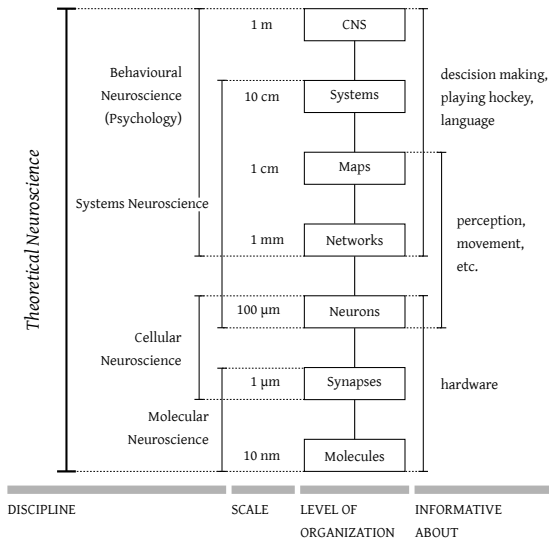
Build Better AI Systems



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

	<b>Theoretical physics</b>	<b>Theoretical neuroscience</b>
<i>Quantify</i> phenomena	$\mathbf{F} = m\mathbf{a}$	$\hat{\mathbf{x}} = \mathbf{D}\mathbf{a}$
<i>Summarize</i> lots of data	motion of objects	neural representation of information
Speculative (generate hypotheses)	true for all velocities	true for all stimuli

## Similarities

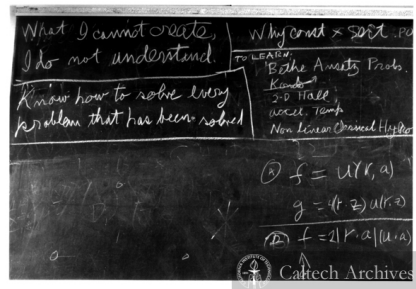
- ▶ Methods are similar
- ▶ Goals are similar (quantification)

## 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”

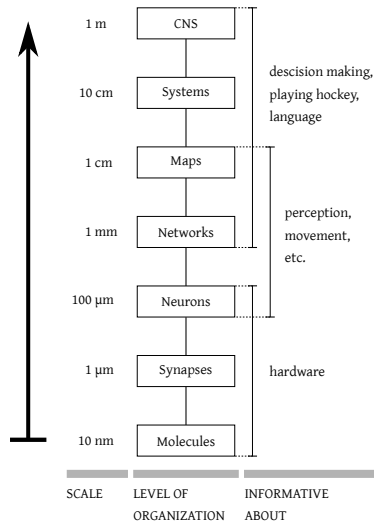
— Richard Feynman, 1988

# 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.



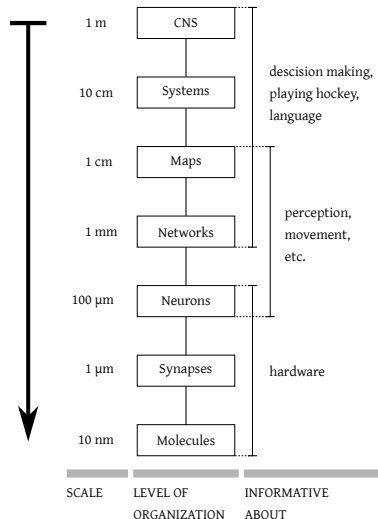
# Problems With Current Approaches: Behavioural Models

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

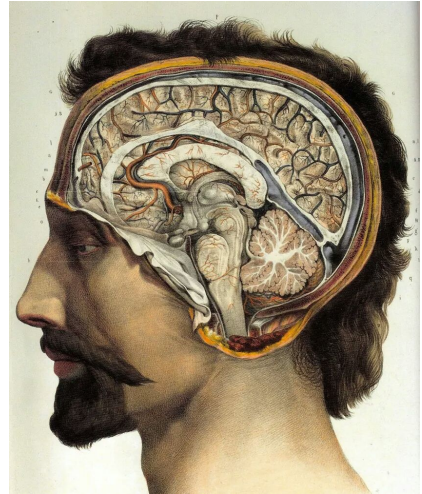
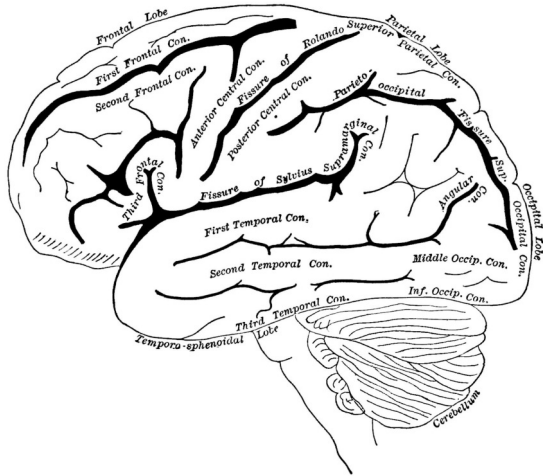
⚠ **Maybe these shortcomings are okay.**

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 Bourger, *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

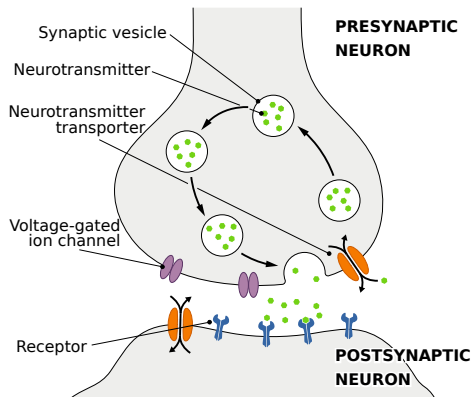
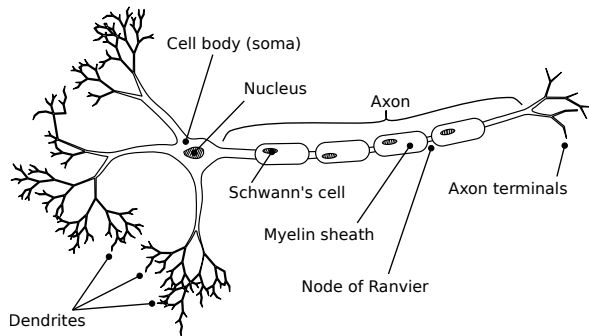


**Suzanne Stensaas, PhD**



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  $\mu\text{m}$  to 5 m

- ▶ Vastly different input/output counts (*convergence* and *divergence*)
- ▶ 100's of different neurotransmitters

# What It Really Looks Like

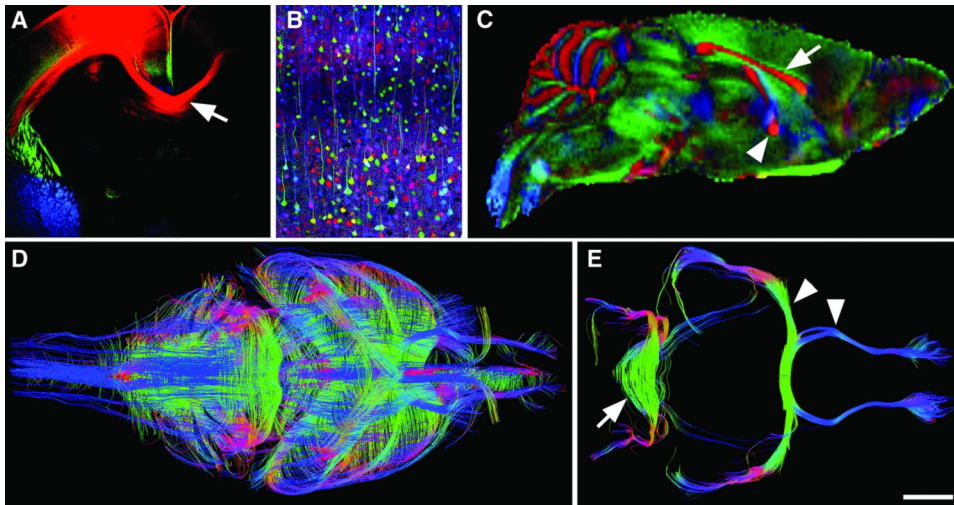


Image Sources. Alain Chédotal and Linda J Richards. *Wiring the Brain: The Biology of Neuronal Guidance*. Cold Spring Harbor perspectives in biology (2010)

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

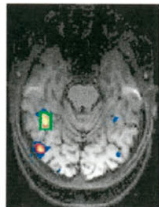
## Functional Magnetic Resonance Tomography

Measures *changes* in blood oxygenation (BOLD)

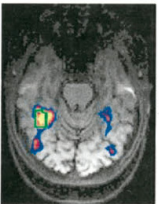
- + Whole-brain, 3D reconstruction  
(individual activity voxels, volume elements)
- Medium spatial resolution (millimeters)
- Low temporal resolution (seconds)
- Signal is hard to interpret  
(differences, indirect, i.e. not spiking activity)
- Has to be averaged over multiple trials

A catalogue of fMRI can be found at  
<https://neurosynth.org/>.

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



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

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

- ▶ **Occipital cortex**  $\rightsquigarrow$  vision
- ▶ **Inferior frontal gyrus**  $\rightsquigarrow$  producing speech (Broca's area),
- ▶ **Posterior superior temporal gyrus**  $\rightsquigarrow$  understanding speech (Wernicke's area),
- ▶ **Fusiform gyrus**  $\rightsquigarrow$  recognition of faces/visually complex objects,
- ▶ **Medial prefrontal cortex**  $\rightsquigarrow$  moral judgment (controversial; see: Phineas Gage).

⊕ Informative about the functional relevance of an area

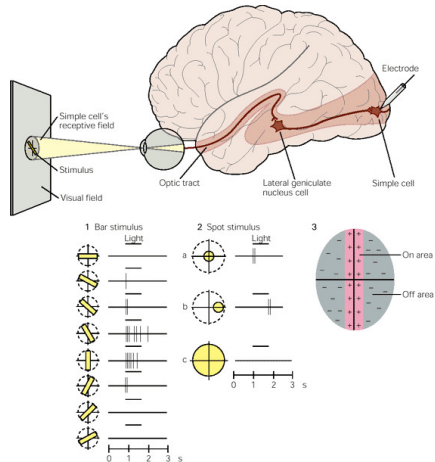
⊖ Often permanently damaging

# 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





# Visual Cortex



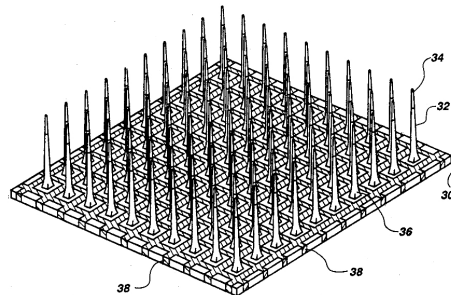
## Mapping receptive fields

# 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)

– Damaging over time



cell activity

behavior

overall



ongoing



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

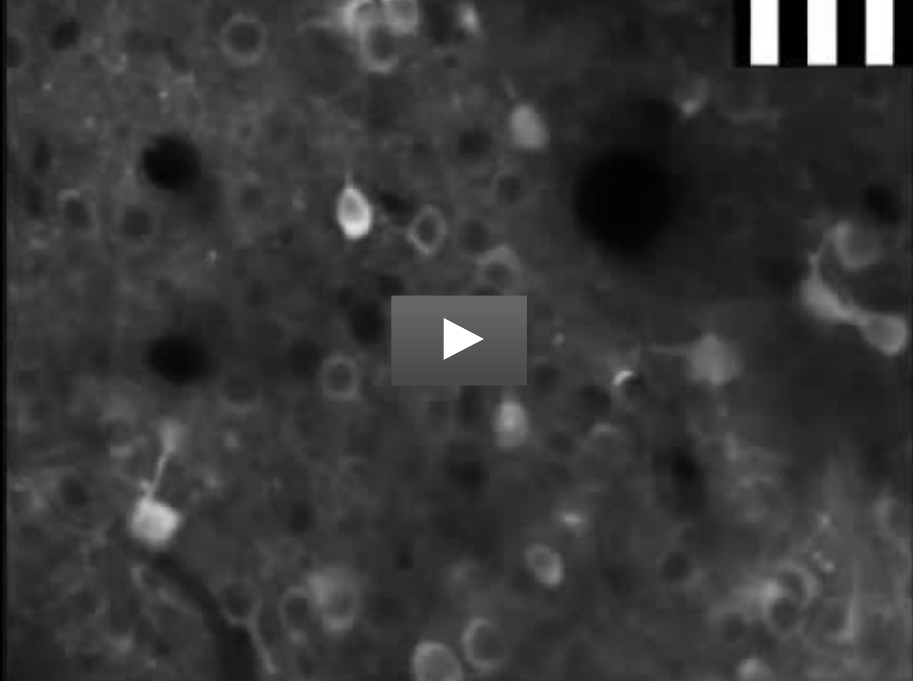
Use **fluorescent calcium indicator** to indicate the presence of  $\text{Ca}^{2+}$  ions.  
Indicator can be chemical or produced by genetic modification.

⊕ High temporal resolution

⊖ Local

⊕ High spatial resolution

⊖ 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

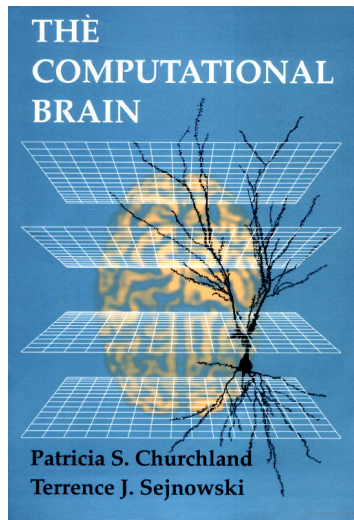
- ▶ No good methods for generalizing from data

- ▶ Need some way to connect these details

⇒ Need unifying theory

“Neuroscience is data-rich and theory poor”

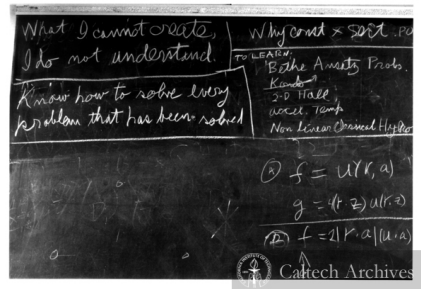
— Churchland & Sejnowski, 1994





# Recall: Neural Modelling

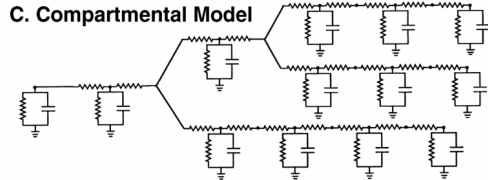
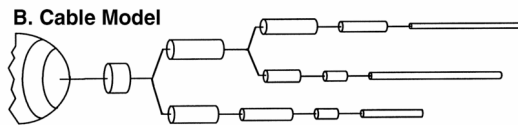
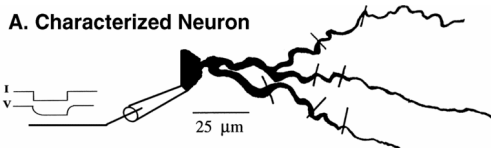
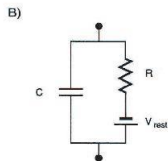
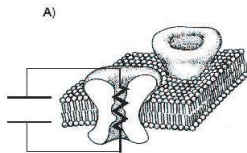
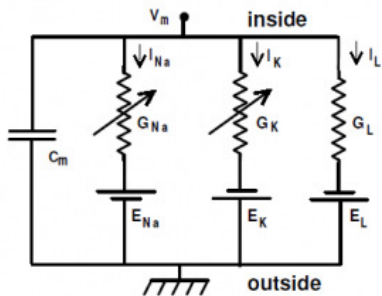
- ▶ **Let's build it**
  - ▶ Requires a mathematically detailed theory
  - ▶ Let's try to do to neuroscience what Newton did to Physics
  - ▶ Not analytically tractable, requires computer simulation
- ▶ Can we use this to connect levels?



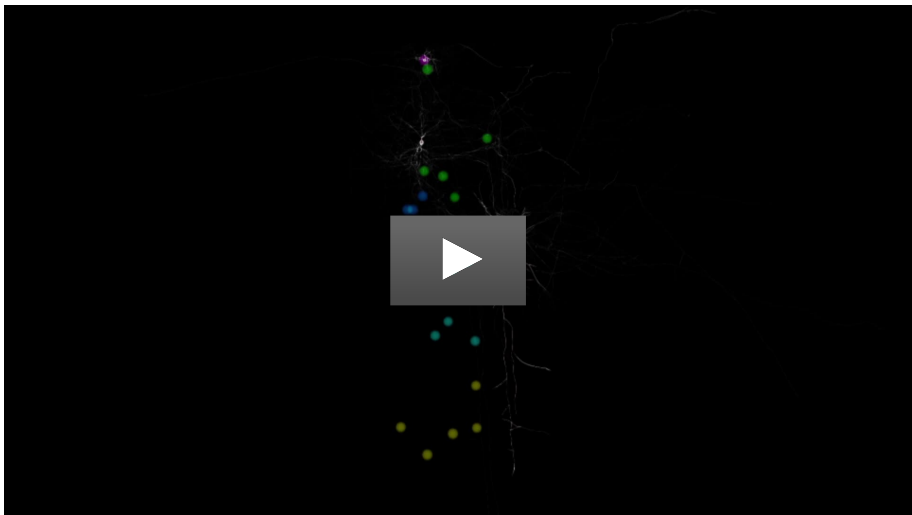
“What I cannot create, I do not understand”

— Richard Feynman, 1988

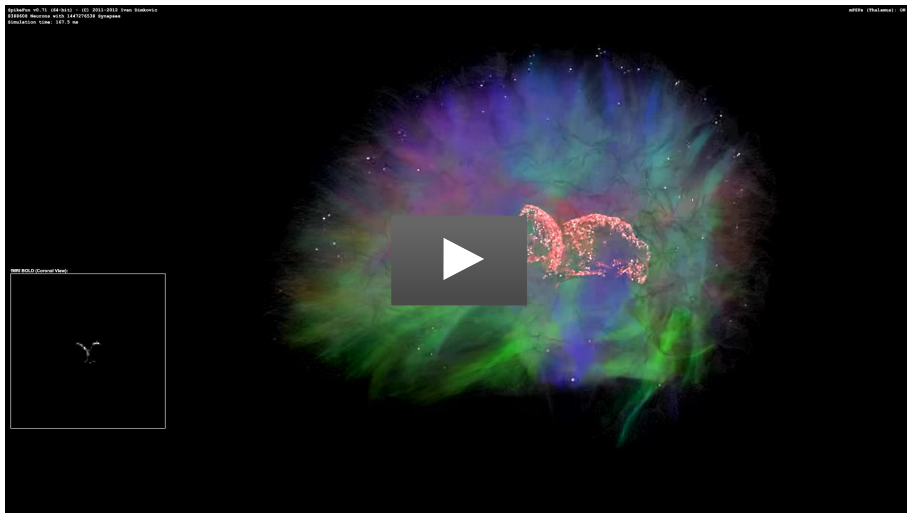
# Single neuron simulation



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 is a joke). [...]

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

# What actually matters. . .

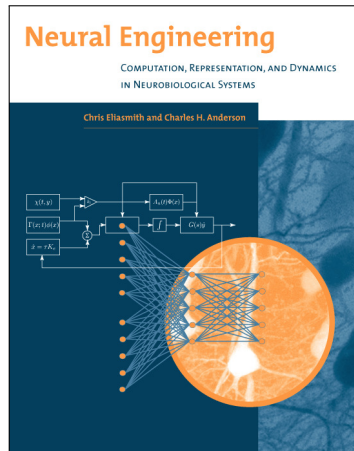
Connecting brain models to **behaviour**

How can we build models that actually do something?

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

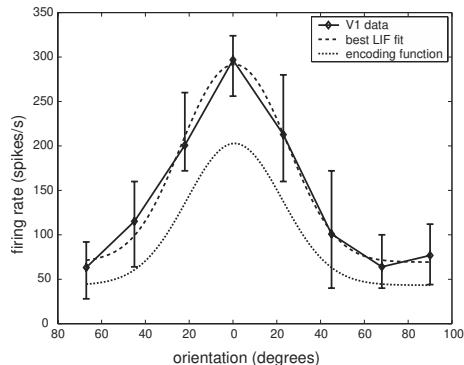
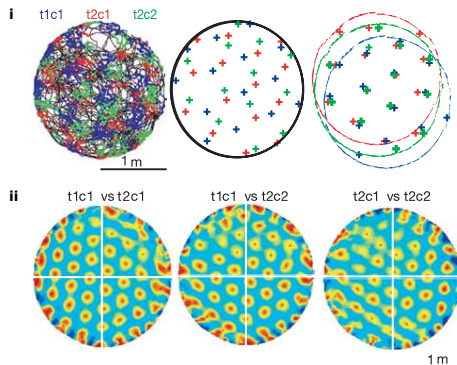
# The Neural Engineering Framework

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



# Representation

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

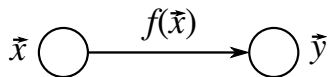


- What is the mapping between a value and the activity of a group of neurons?
- Every group of neurons can be thought of as **representing a vector**

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.

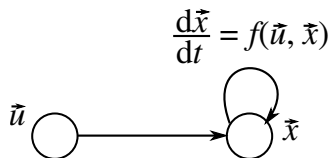


# Transformation



- ▶ **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



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

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

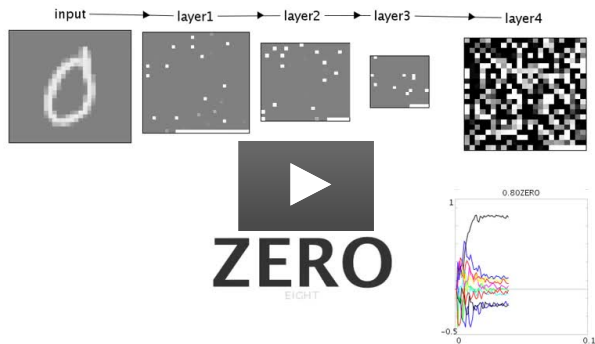
- Great for implementing control theoretical concepts
- Memory as an integrator

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

# 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**

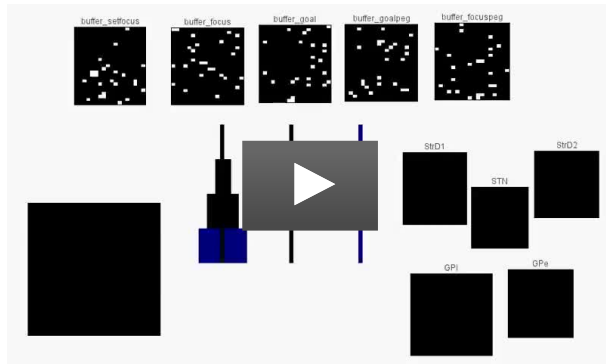
## Examples: Recognizing Handwritten Digits



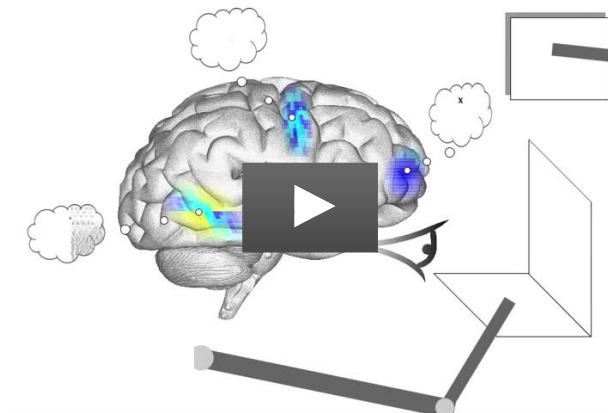
# Examples: Recognizing Natural Images



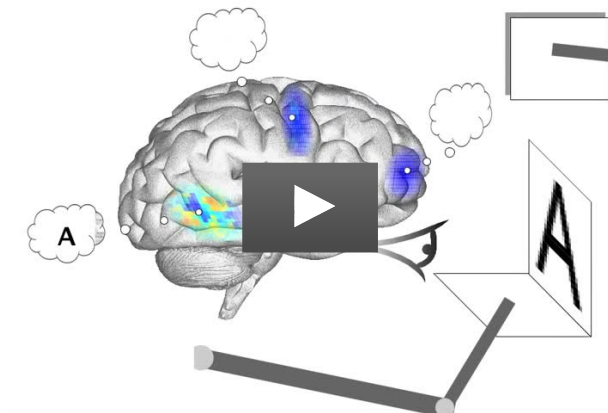
## Examples: Playing Towers of Hanoi



## Examples: SPAUN Copy Drawing

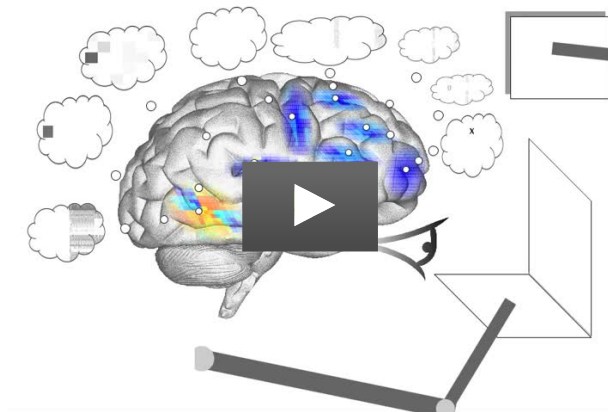


## Examples: SPAUN Recognizing Digits

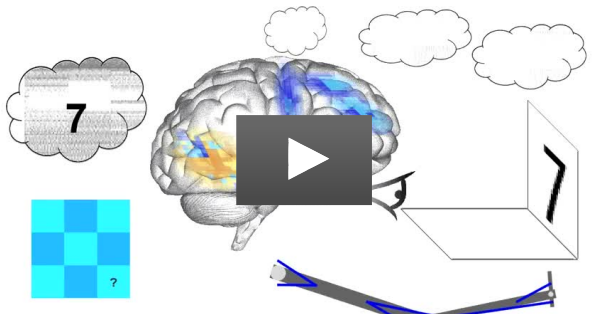




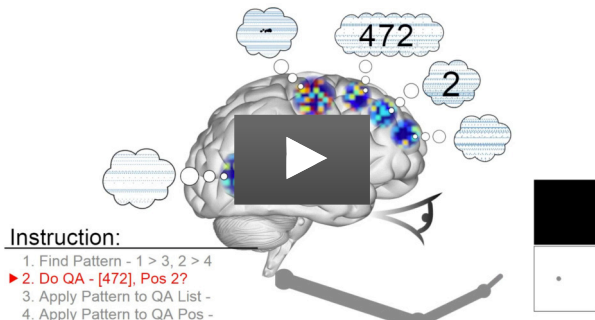
## Examples: SPAUN Silent Addition



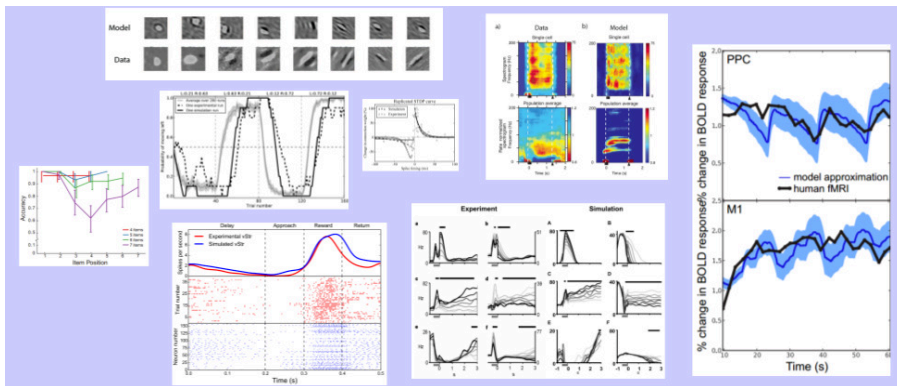
## Examples: SPAUN Pattern Completion



## Examples: SPAUN Instruction Following aka 'Mental Gymnastics'



# 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.