SYDE 556/750

Simulating Neurobiological Systems
Lecture 1: Introduction

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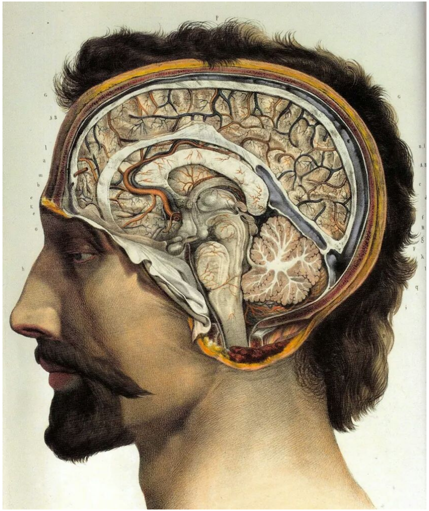
UNIVERSITY OF WATERLOO | FACULTY OF ENGINEERING

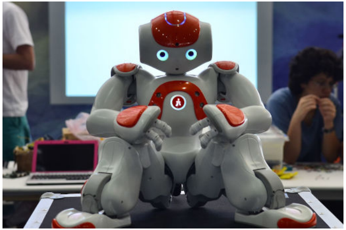


Goal of This Course

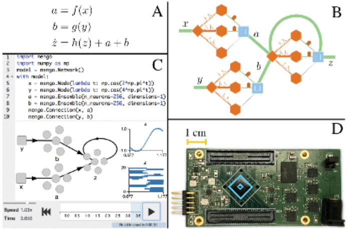
Building Large-Scale Brain Models

Why?

Understand how Brains Work



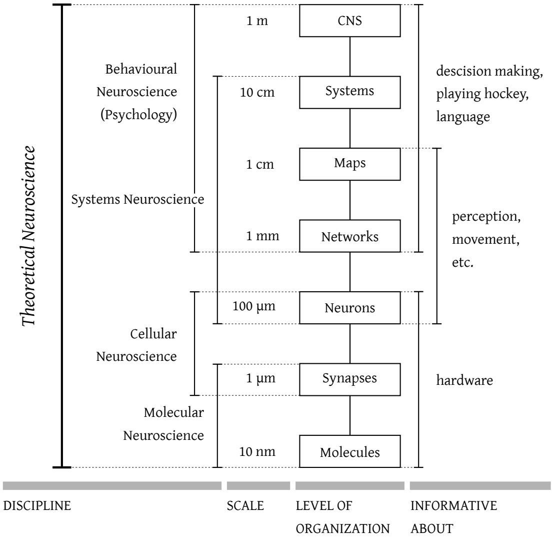
Build Better AI Systems



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	$\mathbf{F} = m\mathbf{a}$	$\hat{\mathbf{x}} = \mathbf{D}\mathbf{a}$
Summarize lots of data	motion of objects	neural representation of information
Speculative (generate hypotheses)	true for all velocities	true for all stimuli

Similarities

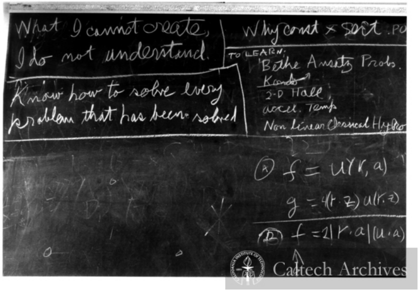
- Methods are similar
- Goals are similar (quantification)

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...

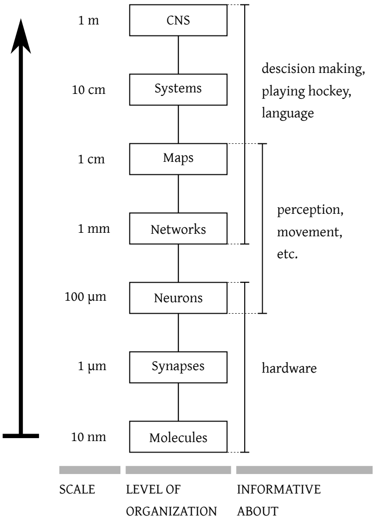


"What I cannot create, I do not understand"
— Richard Feynman, 1988

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 ⇒ can't compare to Psychology
  - Assumes canonical algorithm
  - Expects intelligence to "emerge"

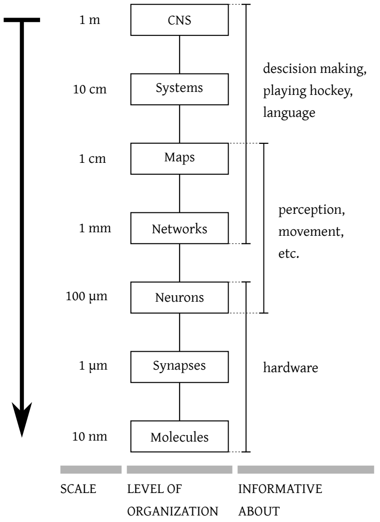
⚠ **This is still important research; these shortcomings are from the perspective of building a "functional" brain model.**



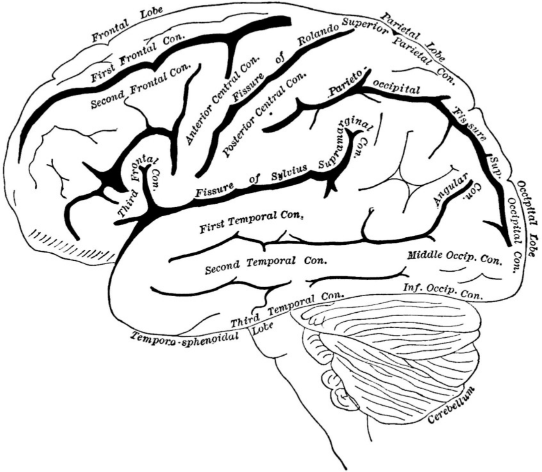
Problems With Current Approaches: Behavioural Models

- **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



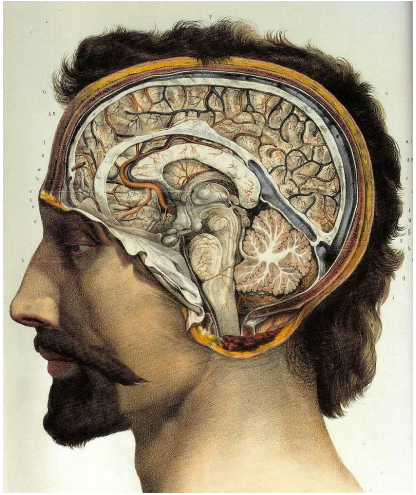


Image Sources. Left: "Labelled lateral view of the left hemisphere", from *Popular Science Monthly, Volume 35* (1889) via Wikimedia. Right: "Sagittal cross-section", illustration by Jean-Baptiste Marc Bourgery, *Traité complet de l'anatomie de l'homme* (1831 to 1854) via Wikimedia.

The Brain – Some Statistics

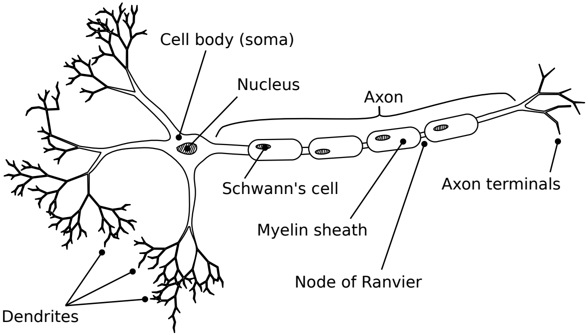
- **Weight:**
  $2\,\mathrm{kg}$ (2% of the body weight)
- **Power consumption:**
  $20\,\mathrm{W}$ (25% of the body's total power consumption)
- **Surface area:**
  $1500\,\mathrm{cm}^2$ to $2000\,\mathrm{cm}^2$ (roughly four A4/letter pages of paper)
- **Number of neurons:**
  100 billion $(10^{11},\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

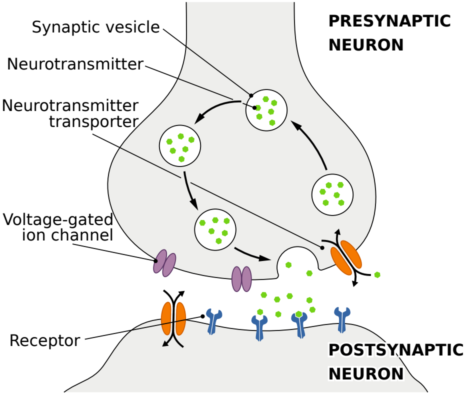
THE UNFIXED BRAIN

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

What It Really Looks Like

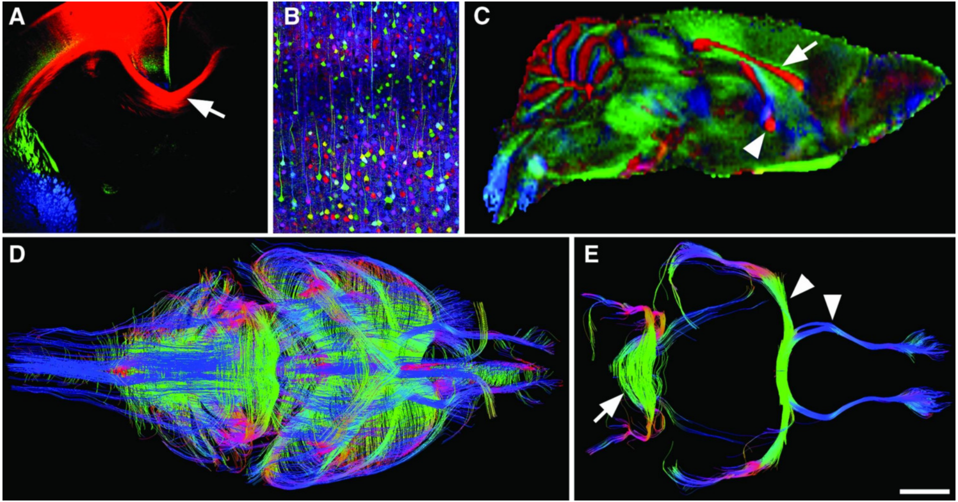


Image Sources. Alain Chédotal and Linda J Richards. *Wiring the Brain: The Biology of Neuronal Guidance.* Cold Spring Harbor perspectives in biology (2010)

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/`.

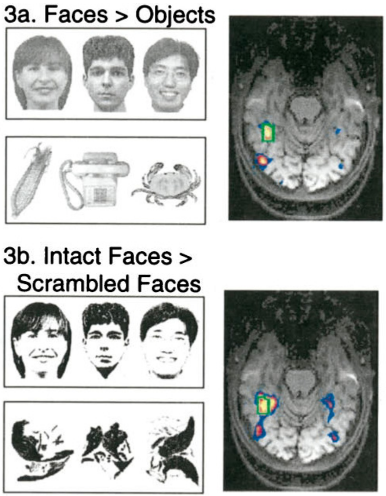


Image Sources. fMRI study of the "Fusiform Face Area" in the "Fusiform Gyrus", from: Nancy Kanwisher, Josh McDermott, and Marvin M. Chun, *The Fusiform Face Area: A Module in Human Extrastriate Cortex Specialized for Face Perception*, Journal of Neuroscience (1997)

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 prefontal 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

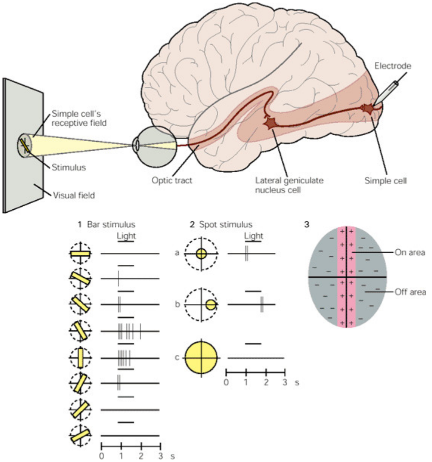


Image Sources. "Depiction of Hubel and Wiesels experiment." Kandel et al., 2012, Principles of Neural Science, 5th ed., Figure 27-11.

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)

- ⊖ Damaging over time

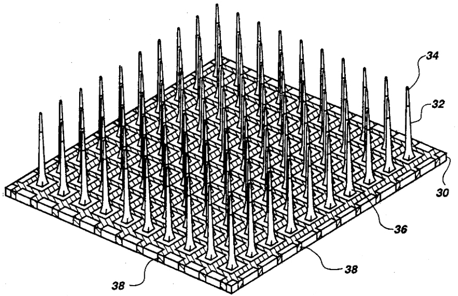


Image Sources. "Depiction of a Utah Array". From: US Patent #5,215,088


cell activity
behavior
overall
ongoing

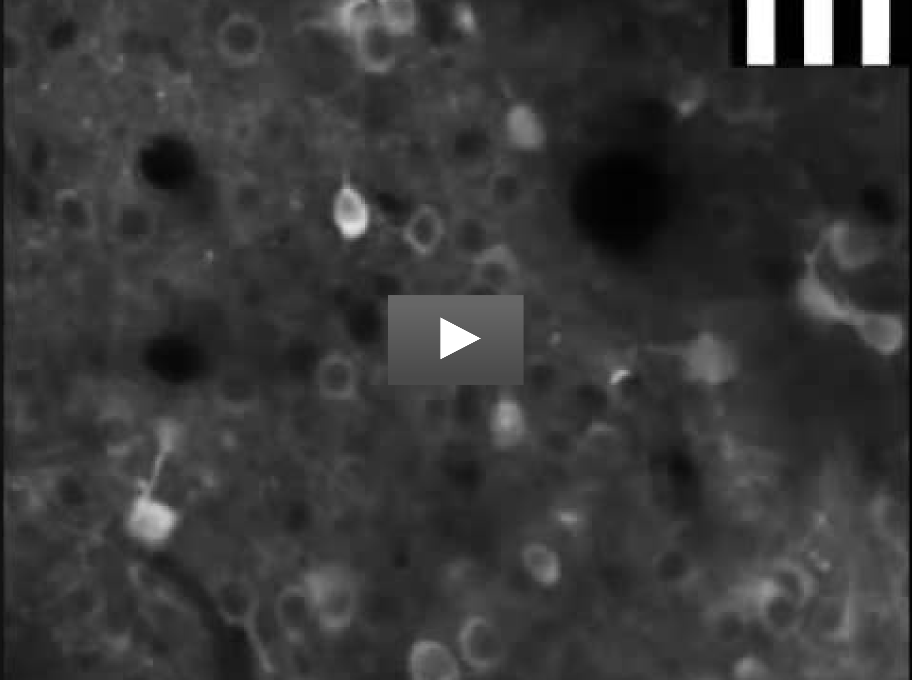
Kinds of Data From the Brain – Invasive – Calcium Imaging

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

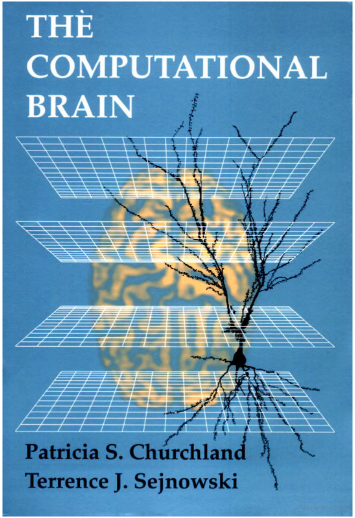
- ⊖ Invasive

What do we know so far?

- **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

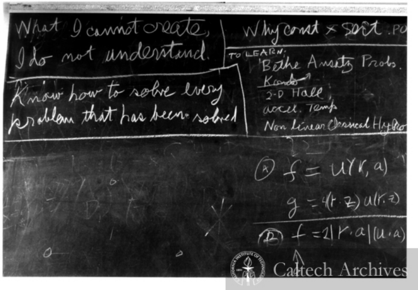
$\Rightarrow$ Need unifying theory

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



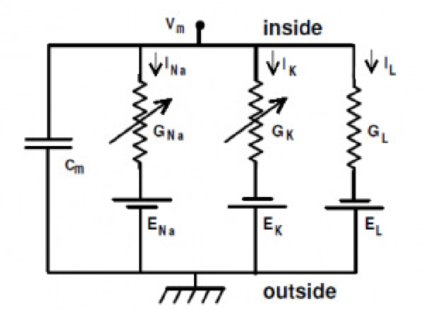
Recall: Neural Modelling

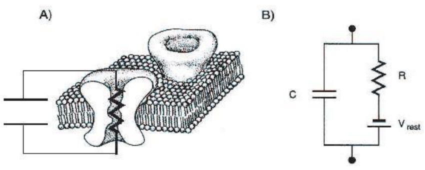
- **Let's build it**
  - Requires a mathematically detailed theory
  - Let's try to do to neuroscience what Newton did to Physics
  - Not analytically tractable, requires computer simulation
- Can we use this to connect levels?

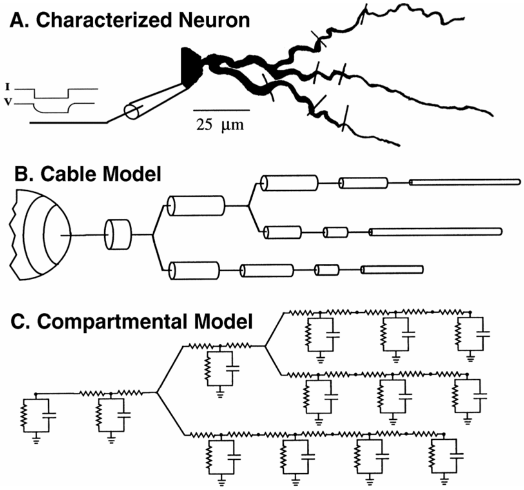


"What I cannot create, I do not understand"
— Richard Feynman, 1988

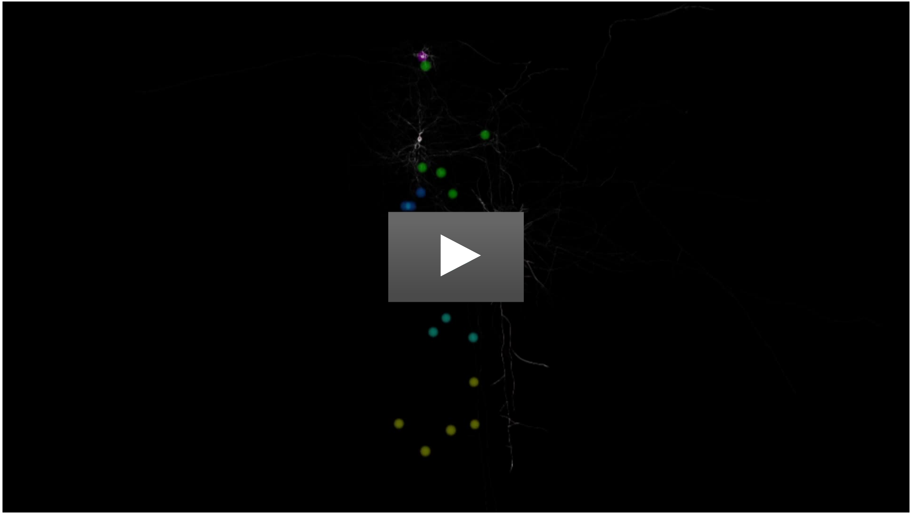
Single neuron simulation







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...

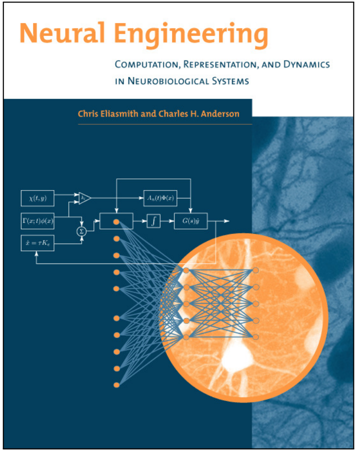
Connecting brain models to **behaviour**

How can we build models that actually do something?

How should we connect "realistic" neurons so they work together?

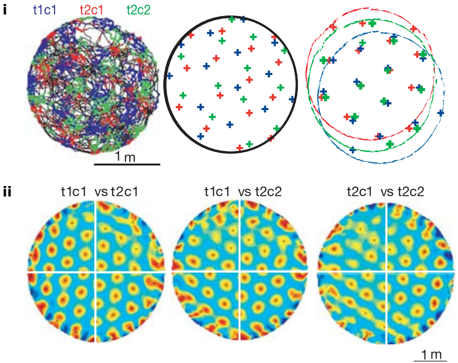
The Neural Engineering Framework

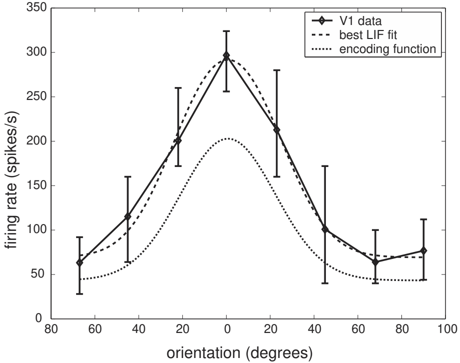
- Our attempt
  - Probably wrong, but got to start somewhere
- **Three principles**
  - Representation
  - Transformation
  - Dynamics
- Building **behaviour** out of **detailed low-level components**



Representation

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

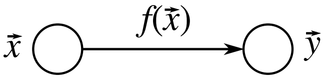




- What is the mapping between a value and the activity of a group of neurons?
- Every group of neurons can be thought of as **representing a vector**

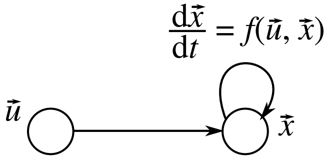
Image Sources. Left: Grid cells, from Hafting et al., *Microstructure of a Spatial Map in the Entorhinal Cortex* Nature (2005), fig. 3. Right: Example of visual orientation tuning in primary visual cortex, from "Neural Engineering", fig. 3.1.

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 $f : \mathbb{R}^m \to \mathbb{R}^n$ 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**

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

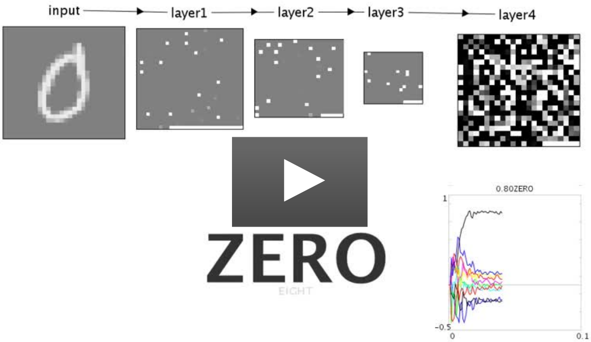
- Great for implementing control theoretical concepts
- Memory as an integrator

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

Examples

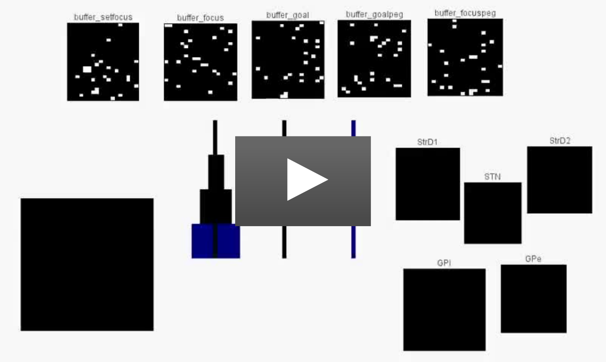
- This approach gives us a **neural compiler**
- Solve for the connections weights that approximate a **behaviour**
- Works for a wide variety of **neuron models**
- Number of neurons affects **accuracy**
- Neuron properties influence **timing** and computation
- Framework for high-level cognition: **Semantic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

Examples: Recognizing Handwritten Digits

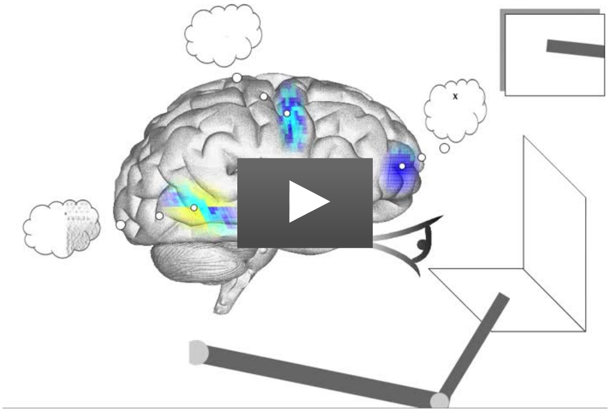


Examples: Recognizing Natural Images

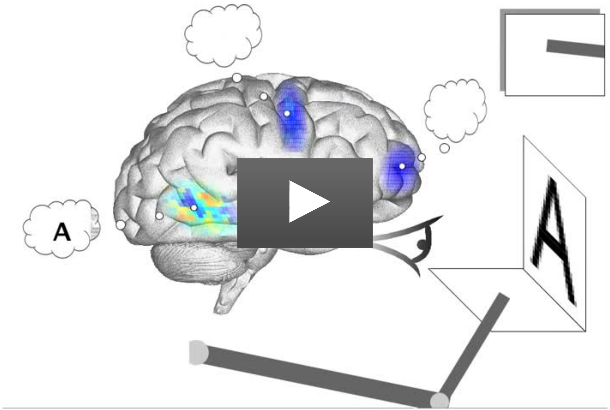
Examples: Playing Towers of Hanoi



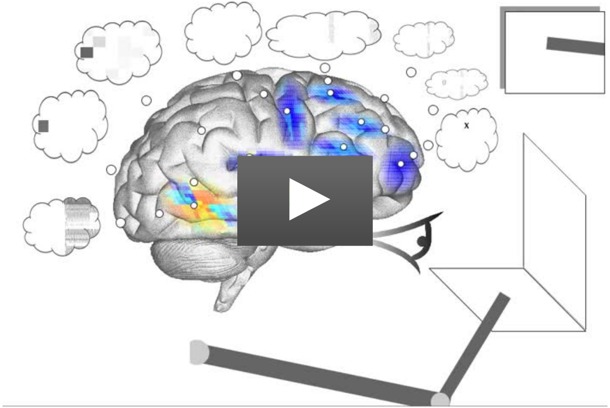
Examples: SPAUN Copy Drawing



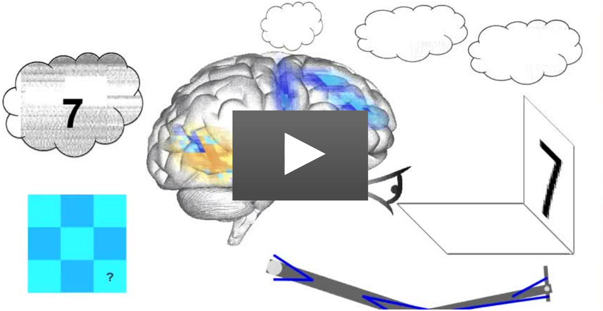
Examples: SPAUN Recognizing Digits



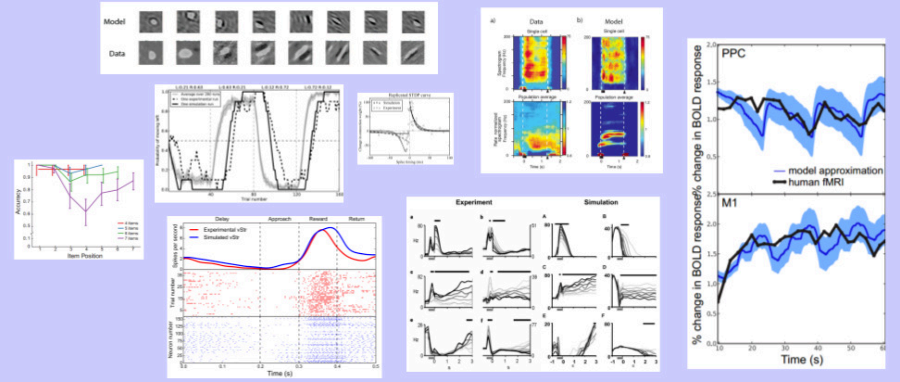
Examples: SPAUN Silent Addition



Examples: SPAUN Pattern Completion



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.