SYDE 556/750

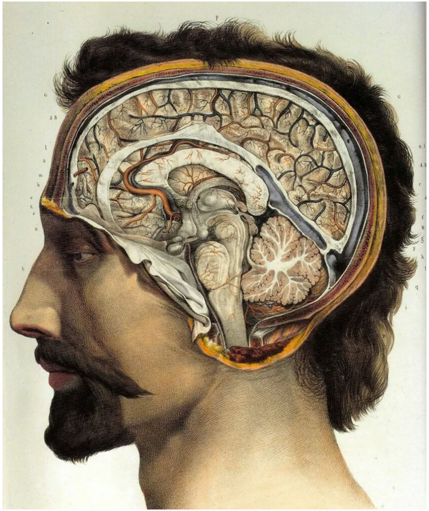
Simulating Neurobiological Systems
Lecture 1: Introduction

Terry Stewart

September 8, 2021

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

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.

Building Large-Scale Brain Models

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Building Large-Scale Brain Models

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Understand how Brains Work

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Building Large-Scale Brain Models

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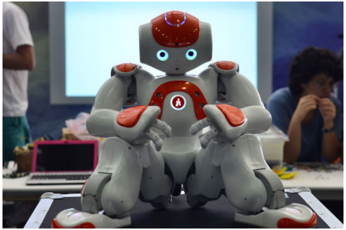

Build Better AI Systems

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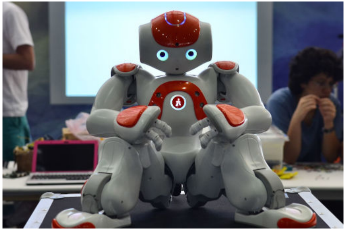
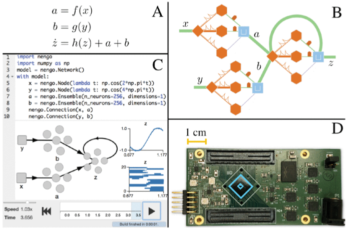


Build Better AI Systems



Program Neuromorphic Hardware

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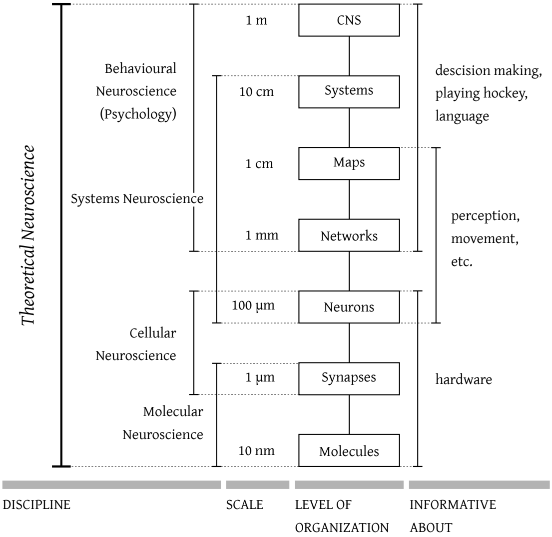
Our Focus: Theoretical Neuroscience



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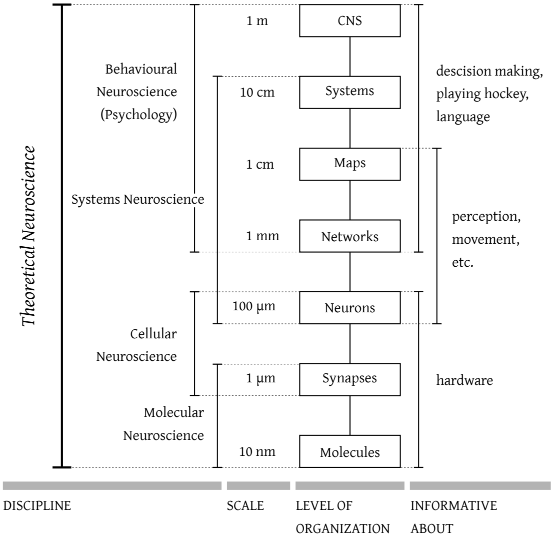
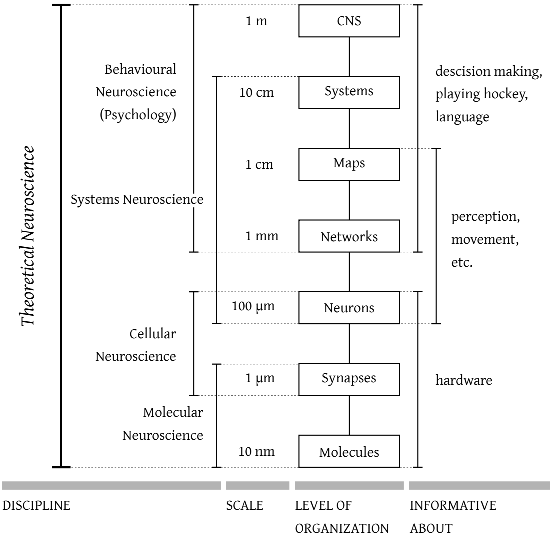


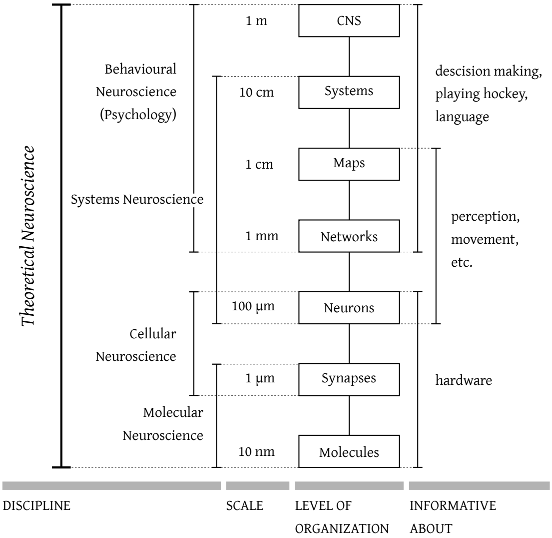
- **How does the mind work?**

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

Theoretical Neuroscience vs. Theoretical Physics

	Theoretical physics	**Theoretical neuroscience**
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Similarities

- Methods are similar
- Goals are similar (quantification)

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

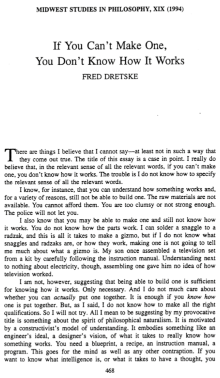
Similarities

- Methods are similar
- Goals are similar (quantification)

Differences

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

Neural Modelling



MIDWEST STUDIES IN PHILOSOPHY, XIX (1994)

If You Can't Make One,
You Don't Know How It Works

FRED DRETSKE

There are things I believe that I cannot say—at least not in such a way that they come out true. The title of this essay is a case in point. I really do believe that, in the relevant sense of all the relevant words, if you can't make one, you don't know how it works. The trouble is I do not know how to specify the relevant sense of all the relevant words.

I know, for instance, that you can understand how something works and, for a variety of reasons, still not be able to build one. The raw materials are not available. You cannot afford them. You are too clumsy or not strong enough. The police will not let you.

I also know that you may be able to make one and still not know how it works. You do not know how the parts work. I can solder a snaggle to a radzak, and this is all it takes to make a gizmo, but if I do not know what snaggles and radzaks are, or how they work, making one is not going to tell me much about what a gizmo is. My son once assembled a television set from a kit by carefully following the instruction manual. Understanding next to nothing about electricity, though, assembling one gave him no idea of how television worked.

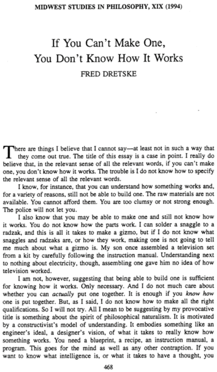
I am not, however, suggesting that being able to build one is sufficient for knowing how it works. Only necessary. And I do not much care about whether you can *actually* put one together. It is enough if you *know how* one is put together. But, as I said, I do not know how to make all the right qualifications. So I will not try. All I mean to be suggesting by my provocative title is something about the spirit of philosophical naturalism. It is motivated by a constructivist's model of understanding. It embodies something like an engineer's ideal, a designer's vision, of what it takes to really know how something works. You need a blueprint, a recipe, an instruction manual, a program. This goes for the mind as well as any other contraption. If you want to know what intelligence is, or what it takes to have a thought, you

468

"If you can't make one, you don't know how it works"
— Fred Dretske, 1994

Neural Modelling

- **Let's build it**
  - Requires a mathematically detailed theory
  - Often complex; need computer simulation



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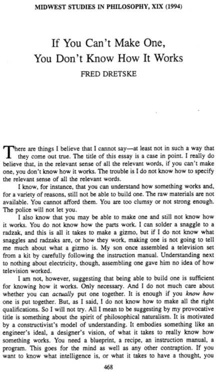
Neural Modelling

- **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...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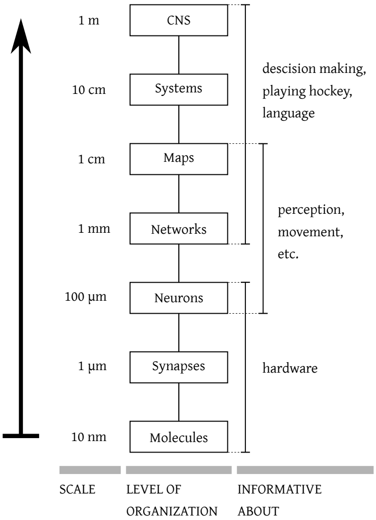
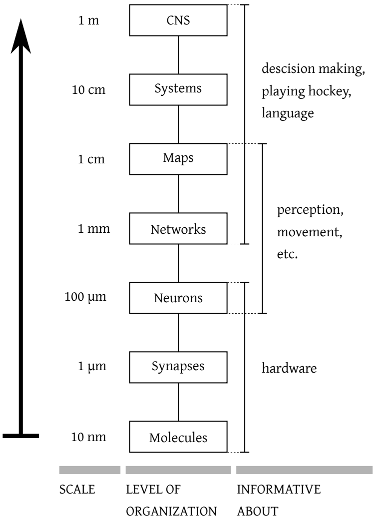
Problems With Current Approaches: Large-scale Neural Models

- **Bottom-up** approach



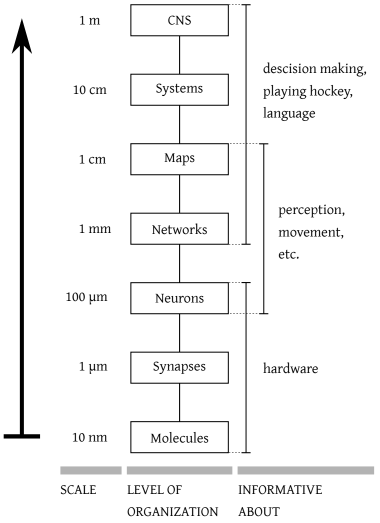
Problems With Current Approaches: Large-scale Neural Models

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



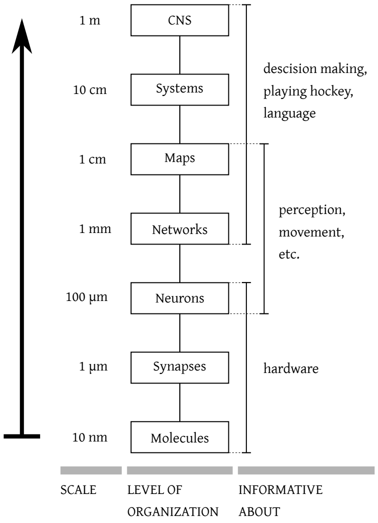
Problems With Current Approaches: Large-scale Neural Models

- **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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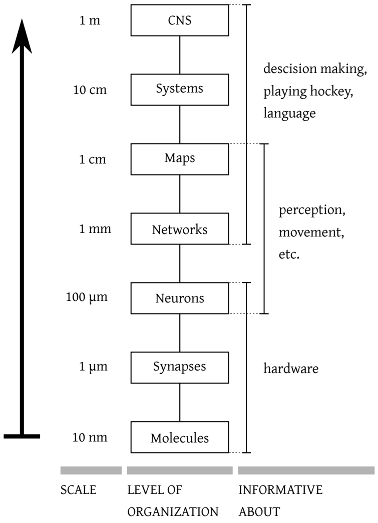
- **Examples**
  BlueBrain/Human Brain Project/SyNAPSE



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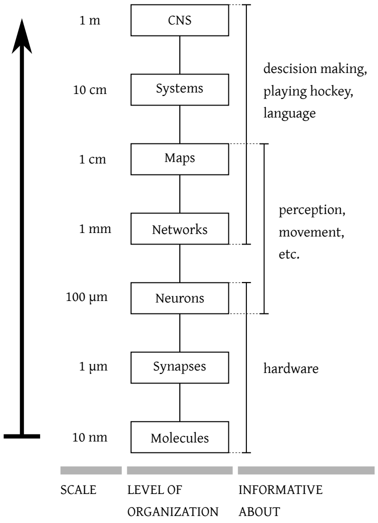
  - Lack of function $\Rightarrow$ can't compare to Psychology
  - Assumes canonical algorithm
  - Expects intelligence to "emerge"



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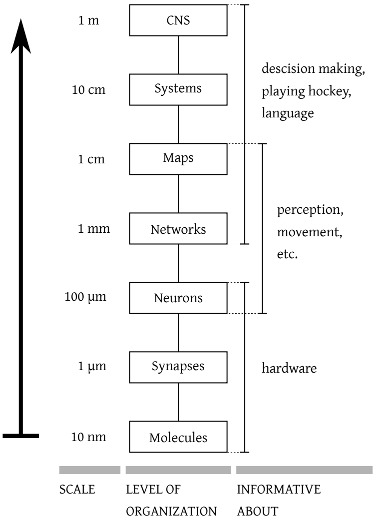
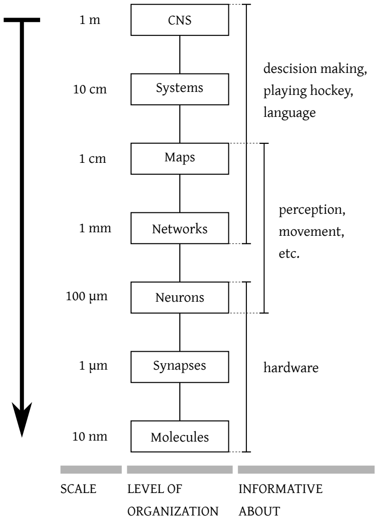
⚠ This is still important research; these shortcomings are from the perspective of building a "functional" brain model.



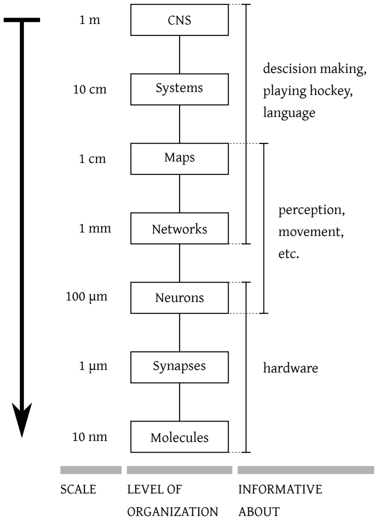
Problems With Current Approaches: Behavioural Models

- **Top-down** approach



Problems With Current Approaches: Behavioural Models

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



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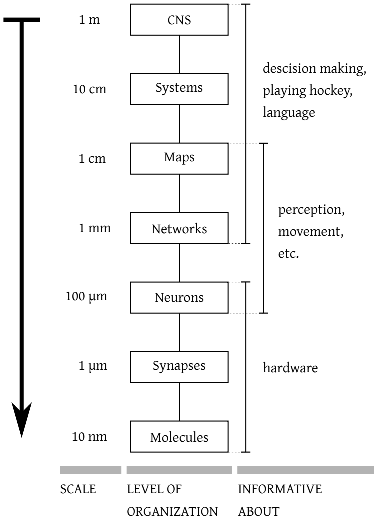

Problems With Current Approaches: Behavioural Models

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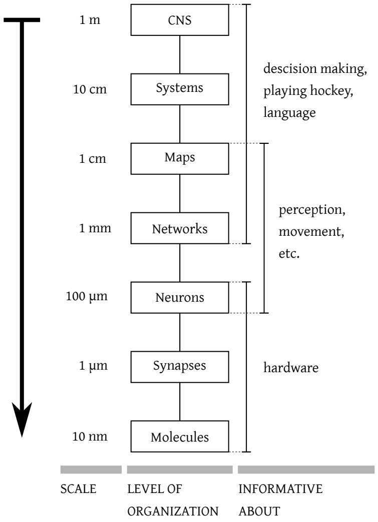
- **Shortcomings**
  - Can't compare to neural data



Problems With Current Approaches: Behavioural Models

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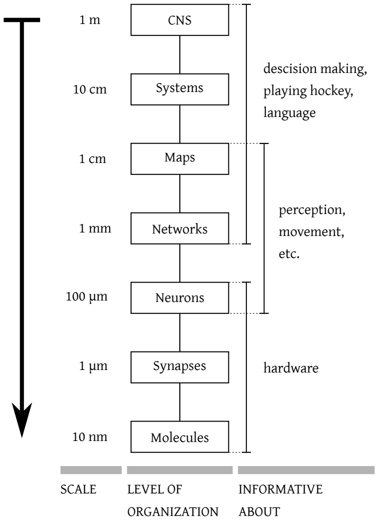
- **Shortcomings**
  - Can't compare to neural data
  - No "bridging laws"



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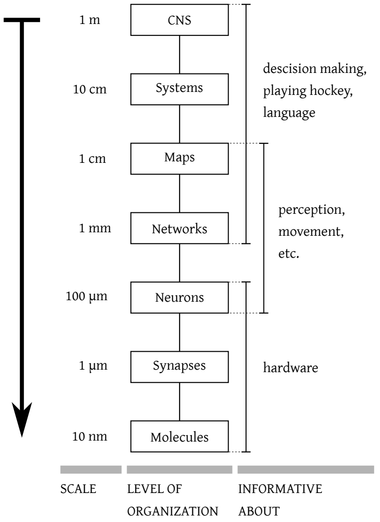

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- **Shortcomings**
  - Can't compare to neural data
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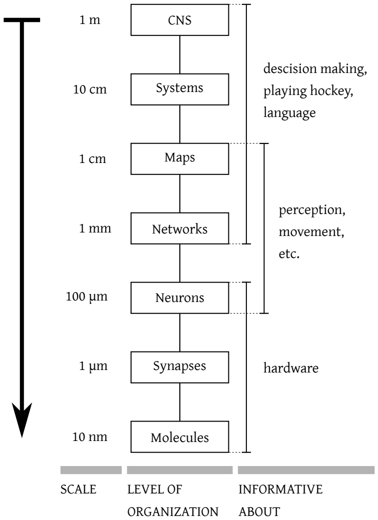
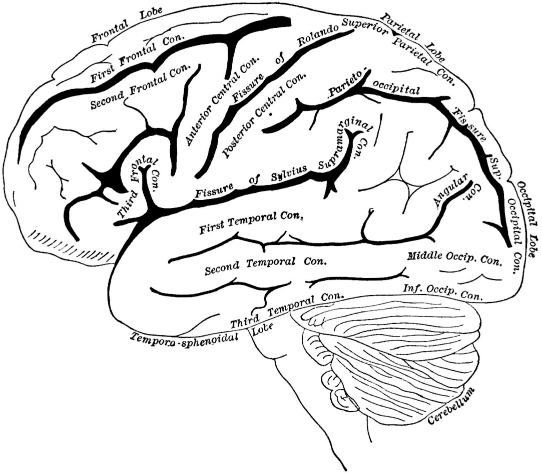
⚠ **Maybe these shortcomings are okay.**

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



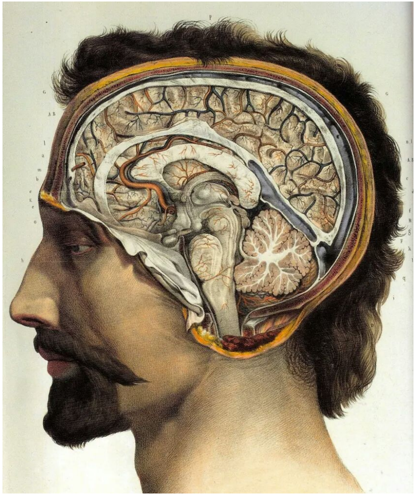


Image Sources. Left: "Labelled lateral view of the left hemisphere", from *Popular Science Monthly, Volume 35* (1889) via Wikimedia. Right: "Sagittal cross-section", illustration by Jean-Baptiste Marc Bourgery, *Traité complet de l'anatomie de l'homme* (1831 to 1854) via Wikimedia.

The Brain – Some Statistics

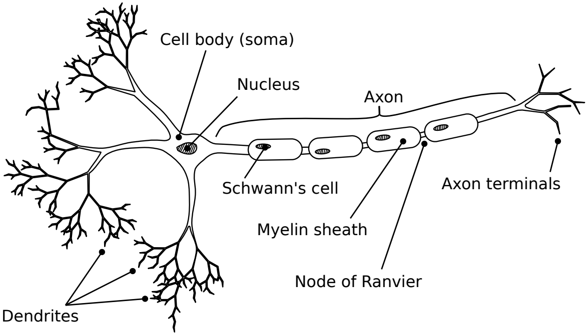
- **Weight:**
  2 kg (2% of the body weight)
- **Power consumption:**
  20 W (25% of the body's total power consumption)
- **Surface area:**
  1500 cm^2 to 2000 cm^2 (roughly four A4/letter pages of paper)
- **Number of neurons:**
  100 billion (10^{11}, 150 000 mm^{-2})
- **Number of synapses:**
  100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

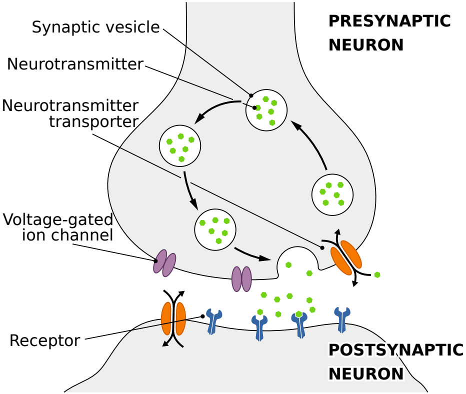
THE UNFIXED BRAIN

Suzanne Stensaas, PhD

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

Neurons in the Brain





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

What It Really Looks Like

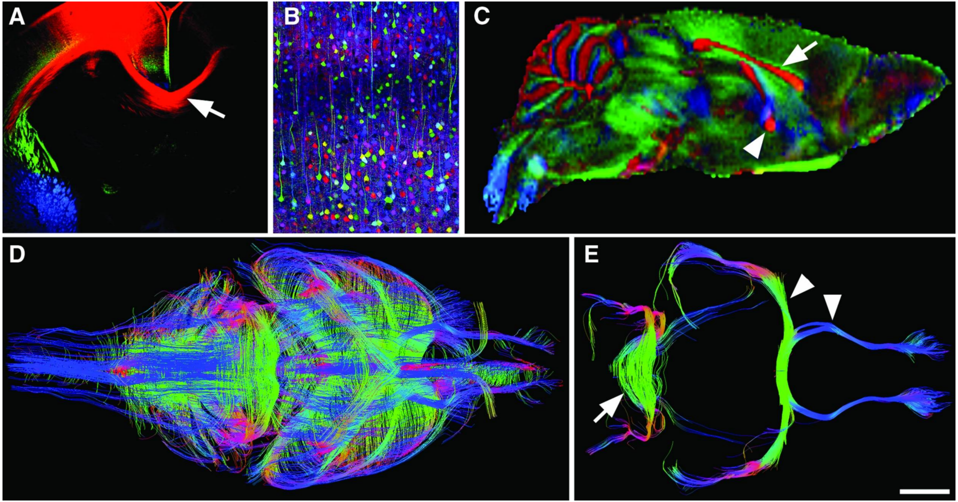
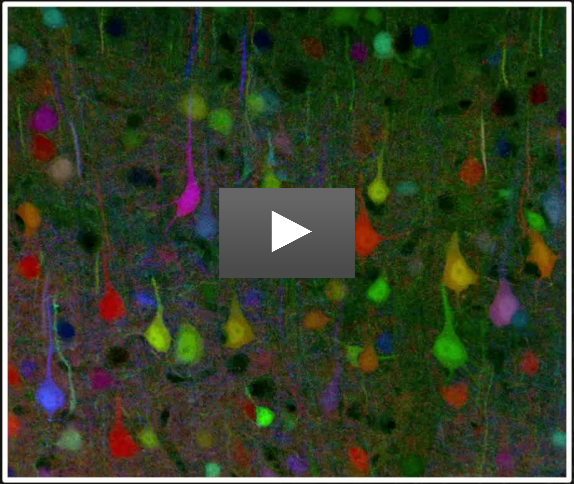


Image Sources. Alain Chédotal and Linda J Richards. *Wiring the Brain: The Biology of Neuronal Guidance*. Cold Spring Harbor perspectives in biology (2010)



R Draft & J Livet

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/`.

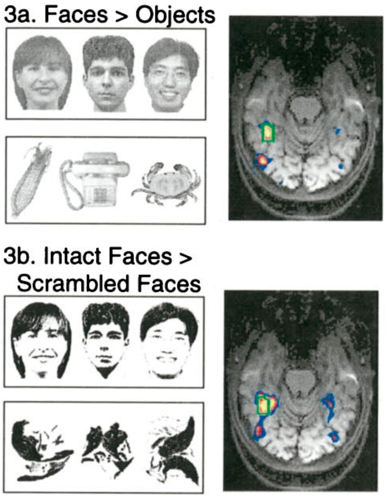


Image Sources. fMRI study of the "Fusiform Face Area" in the "Fusiform Gyrus", from: Nancy Kanwisher, Josh McDermott, and Marvin M. Chun, *The Fusiform Face Area: A Module in Human Extrastriate Cortex Specialized for Face Perception*, Journal of Neuroscience (1997)

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

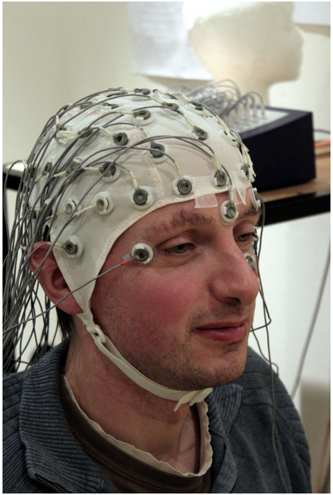


Image Sources. Left: Electroencephalogram (image from Wikimedia). Right: EEG cap (image from Wikimedia).

Kinds of Data From the Brain – Invasive – Lesion Studies

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

- **Occipital cortex leads** $\rightsquigarrow$ 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 prefontal 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

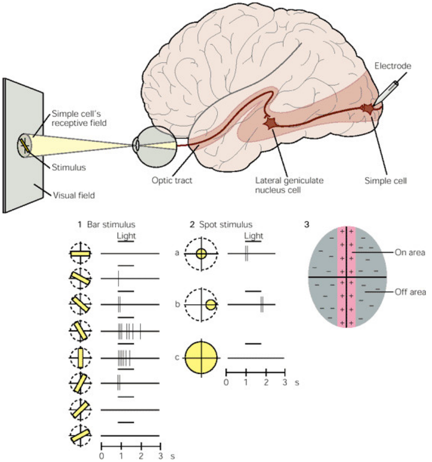


Image Sources. "Depiction of Hubel and Wiesels experiment." Kandel et al., 2012, Principles of Neural Science, 5th ed., Figure 27-11.

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

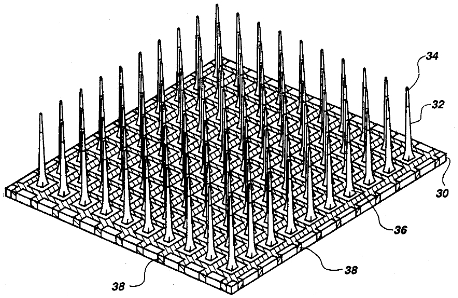


Image Sources. “Depiction of a Utah Array”. From: US Patent #5,215,088


cell activity
behavior
overall
ongoing

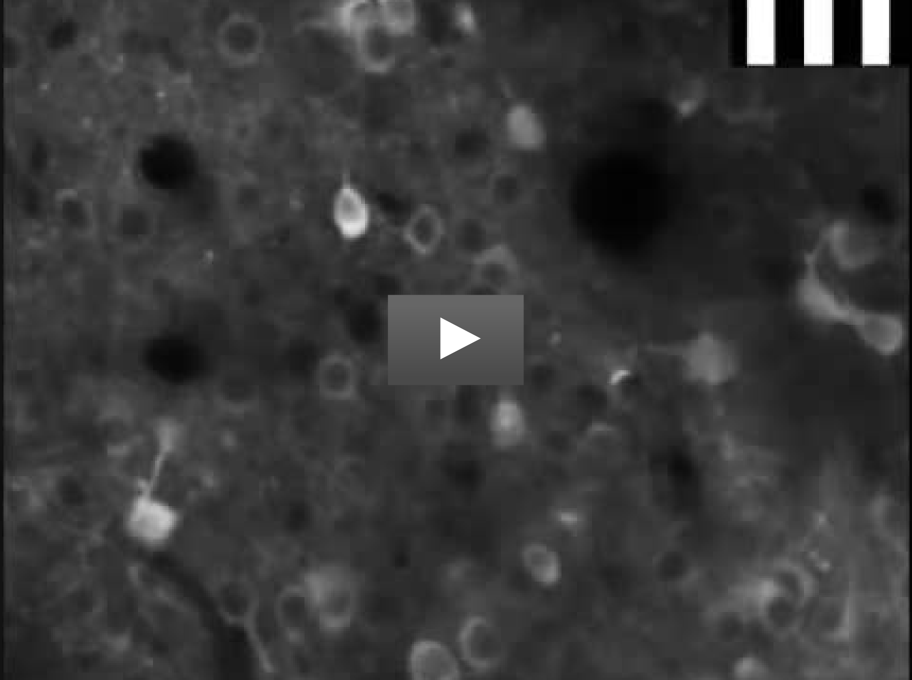
Kinds of Data From the Brain – Invasive – Calcium Imaging

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

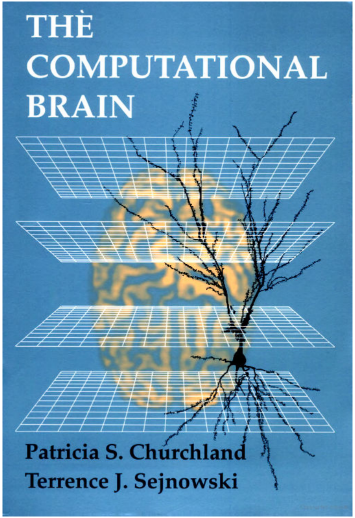
Make certain neuron types **sensitive to light** by genetic modification

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?



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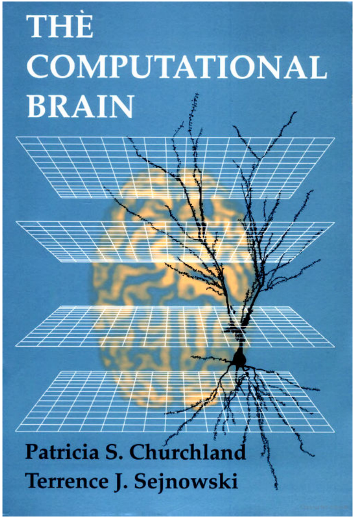

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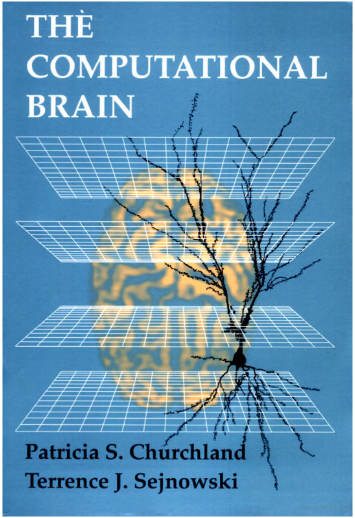
  - **Data:**
    "The proportion of type A neurons in area X is Y."



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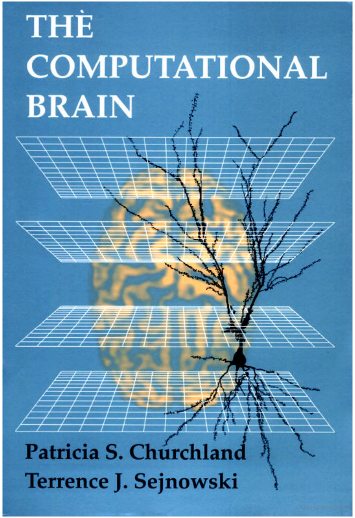

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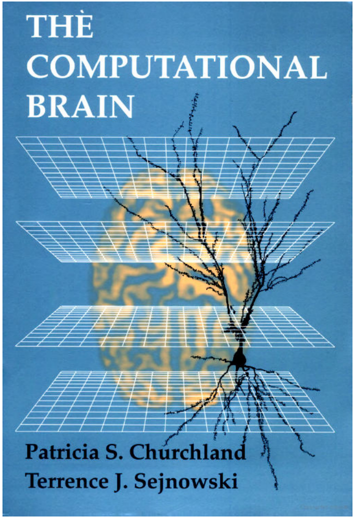

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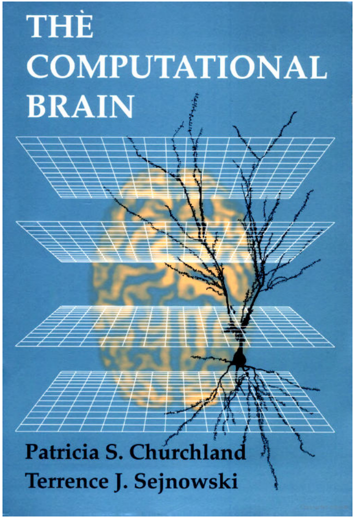

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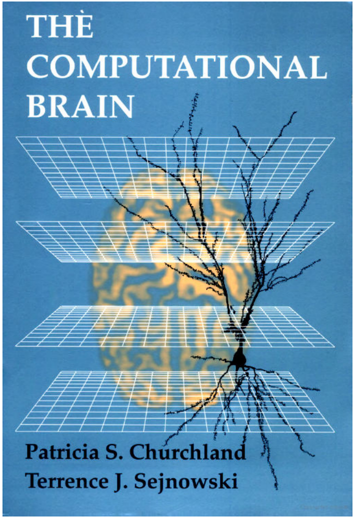
$\Rightarrow$ Need unifying theory



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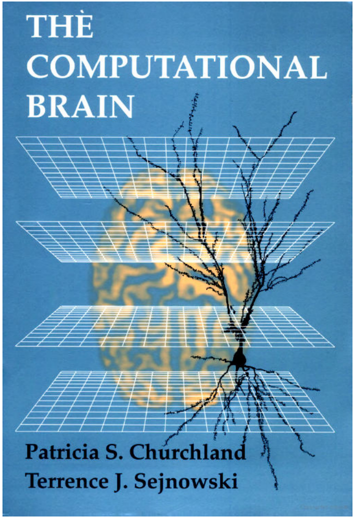
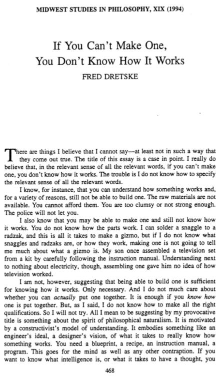
⇒ Need unifying theory

"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?



MIDWEST STUDIES IN PHILOSOPHY, XIX (1994)

If You Can't Make One, You Don't Know How It Works

FRED DRETSKE

There are things I believe that I cannot say—at least not in such a way that they come out true. The title of this essay is a case in point. I really do believe that, in the relevant sense of all the relevant words, if you can't make one, you don't know how it works. The trouble is I do not know how to specify the relevant sense of all the relevant words.

I know, for instance, that you can understand how something works and, for a variety of reasons, still not be able to build one. The raw materials are not available. You cannot afford them. You are too clumsy or not strong enough. The police will not let you.

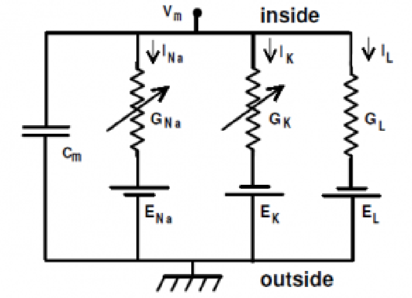
I also know that you may be able to make one and still not know how it works. You do not know how the parts work. I can solder a snaggle to a radzak, and this is all it takes to make a gizmo, but if I do not know what snaggles and radzaks are, or how they work, making one is not going to tell me much about what a gizmo is. My son once assembled a television set from a kit by carefully following the instruction manual. Understanding next to nothing about electricity, though, assembling one gave him no idea of how television worked.

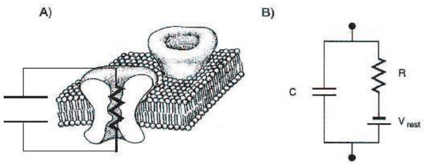
I am not, however, suggesting that being able to build one is sufficient for knowing how it works. Only necessary. And I do not much care about whether you can *actually* put one together. It is enough if you *know how* one is put together. But, as I said, I do not know how to make all the right qualifications. So I will not try. All I mean to be suggesting by my provocative title is something about the spirit of philosophical naturalism. It is motivated by a constructivist's model of understanding. It embodies something like an engineer's ideal, a designer's vision, of what it takes to really know how something works. You need a blueprint, a recipe, an instruction manual, a program. This goes for the mind as well as any other contraption. If you want to know what intelligence is, or what it takes to have a thought, you

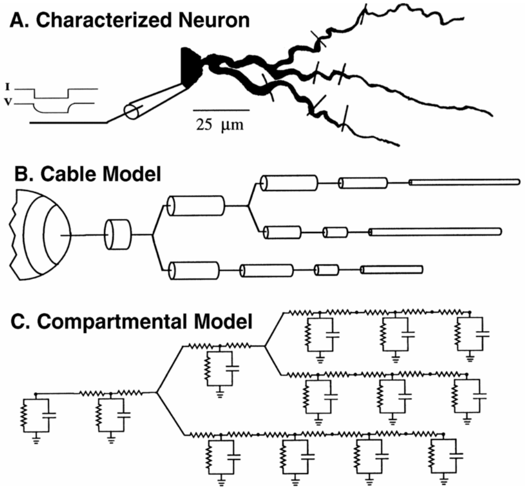
468

"If you can't make one, you don't know how it works"
— Fred Dretske, 1994

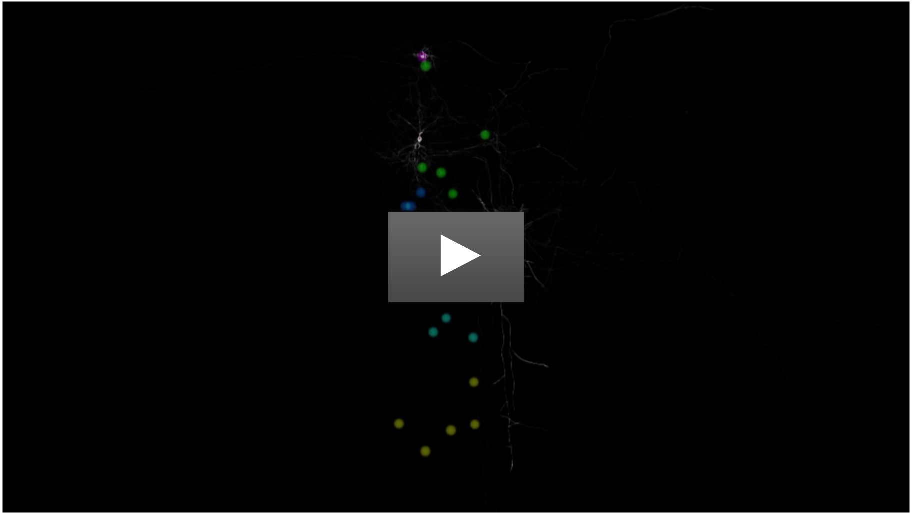
Single neuron simulation







Simulating millions of neurons. . .



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

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What actually matters...

Connecting brain models to **behaviour**

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How can we build models that actually do something?

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?)

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

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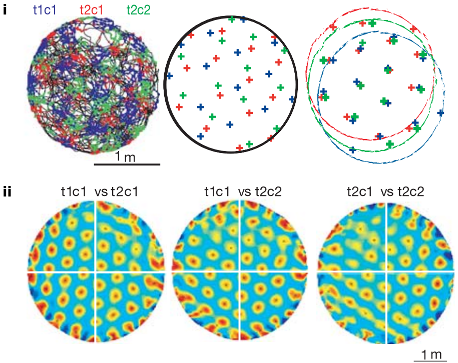

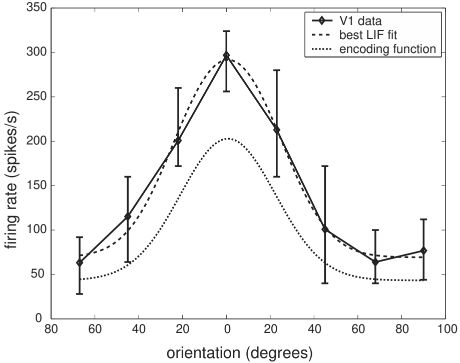

- What is the mapping between a value and the activity of a group of neurons?

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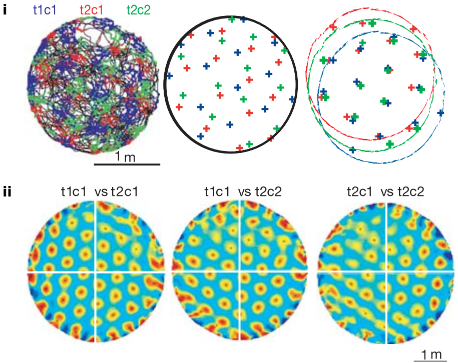

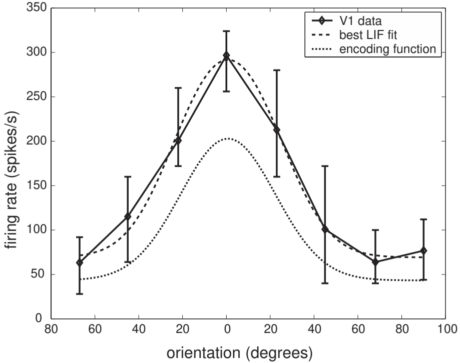

- What is the mapping between a value and the activity of a group of neurons?
- Every group of neurons can be thought of as **representing a vector**

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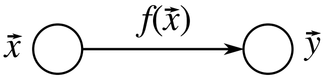
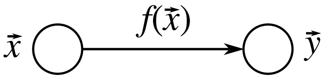
Transformation



- **Connections compute functions** on those vectors

Transformation



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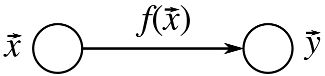

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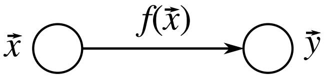

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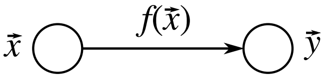

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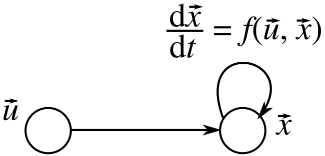
- Can analyse which f can be computed

Dynamics



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

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

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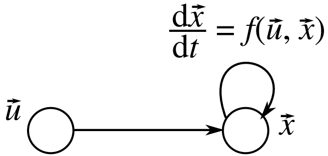

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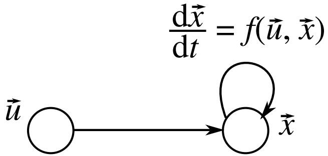

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- Great for implementing control theoretical concepts
- Memory as an integrator

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

Examples

- This approach gives us a **neural compiler**

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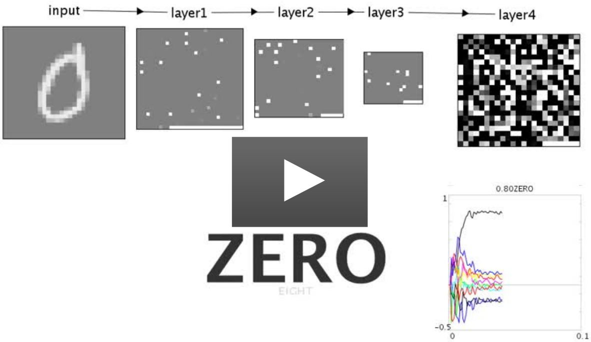
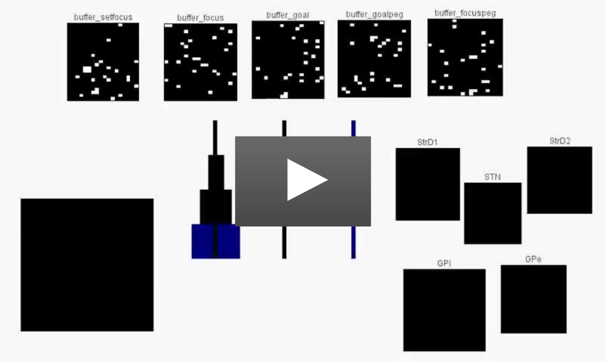
- Framework for high-level cognition: **Semantic Pointer Architecture (SPA)**
- World's largest functional brain model: **SPAUN**

Examples: Recognizing Handwritten Digits

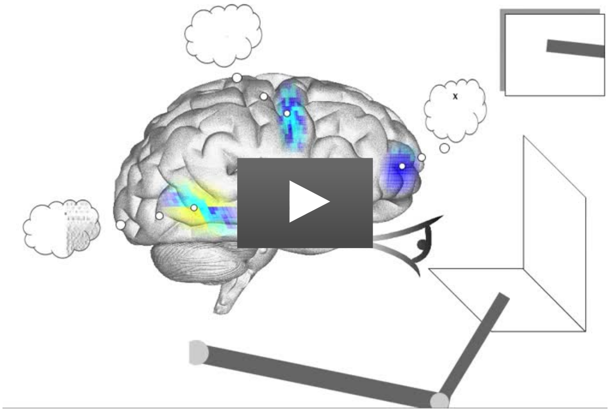


Examples: Recognizing Natural Images

Examples: Playing Towers of Hanoi



Examples: SPAUN Copy Drawing



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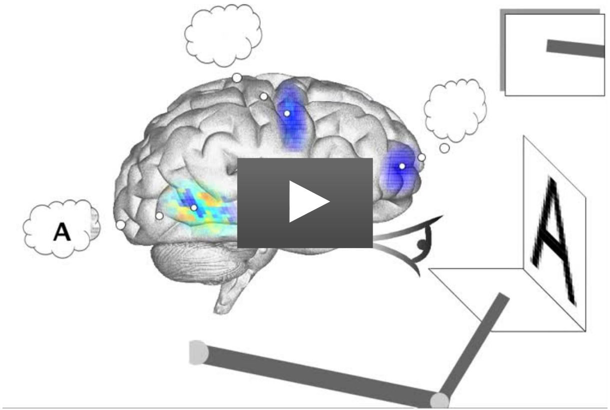
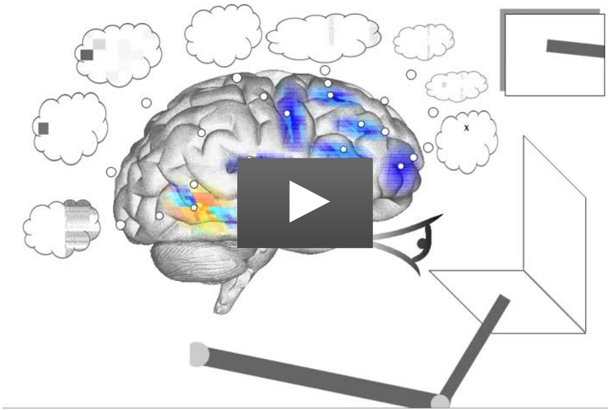
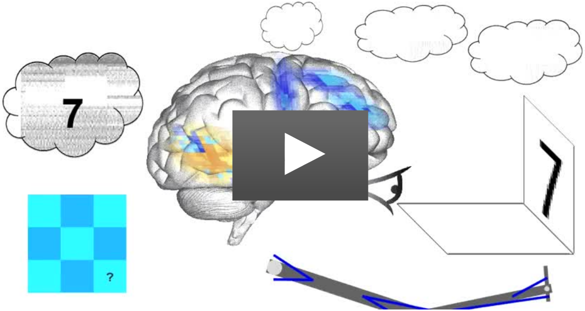


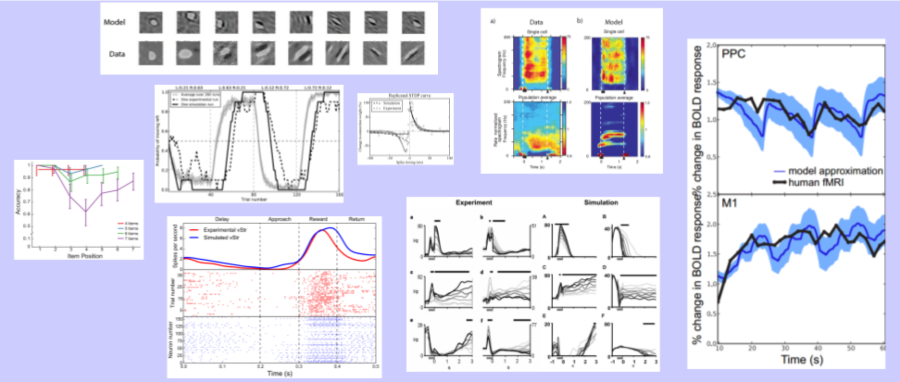
Examples: SPAUN Silent Addition



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.