Introduction to Modeling and Computational Neuroscience using Python

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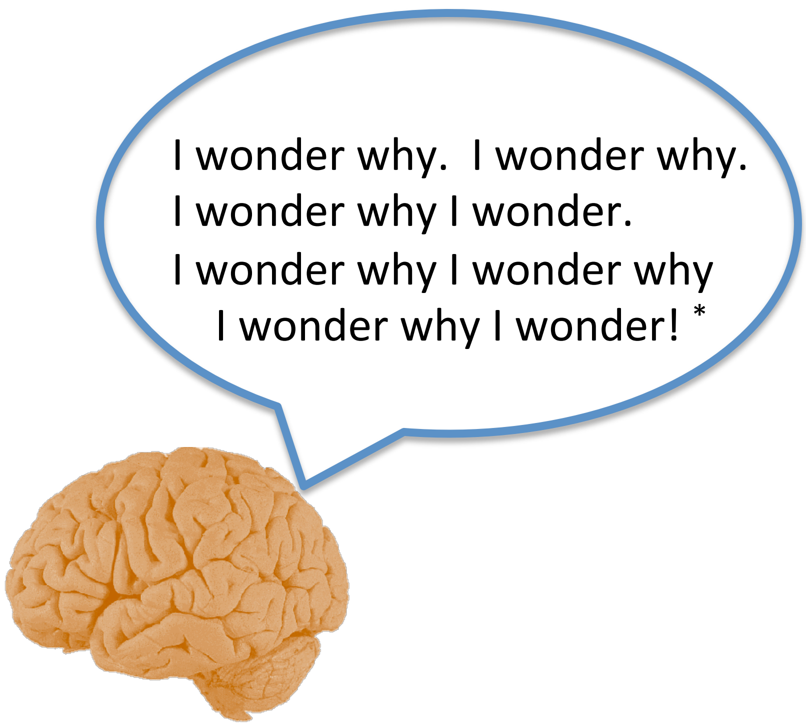


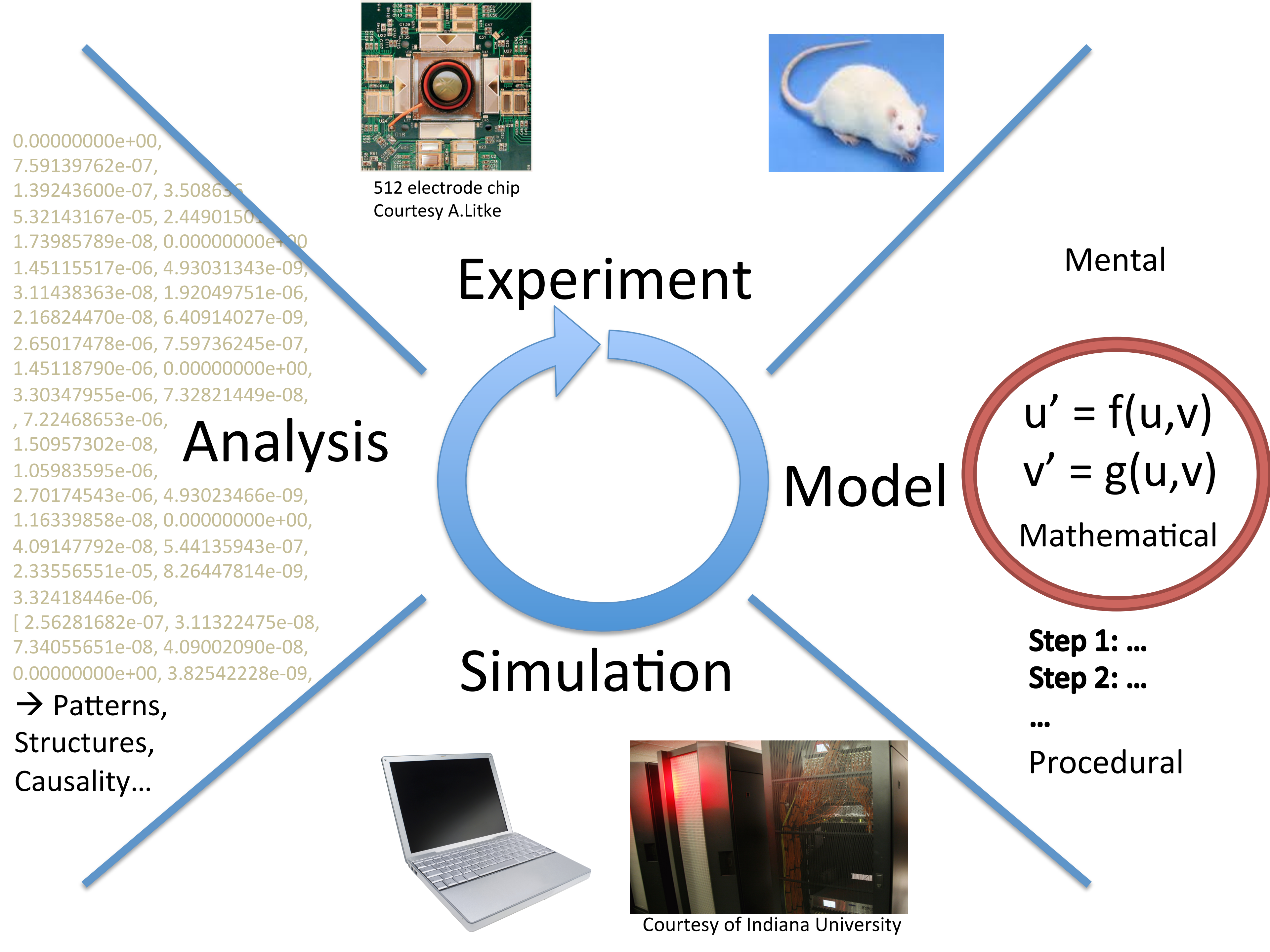
Society for Mathematical Biology Annual Meeting and Conference, July 25-28, 2012

* **Surely You're Joking, Mr. Feynman! (Adventures of a Curious Character),** Richard Feynman.

Overview

- Computational Science:

  Experiments, Models, Simulations, Analyses
- Modeling
- Neuroscience
- Python programming
- Questions? (+ short survey)



512 electrode chip
Courtesy A.Litke
Experiment
Mental
0.00000000e+00,
7.59139762e-07,
1.39243600e-07, 3.50863
5.32143167e-05, 2.4490150
1.73985789e-08, 0.00000000e+00
1.45115517e-06, 4.93031343e-09,
3.11438363e-08, 1.92049751e-06,
2.16824470e-08, 6.40914027e-09,
2.65017478e-06, 7.59736245e-07,
1.45118790e-06, 0.00000000e+00,
3.30347955e-06, 7.32821449e-08,
, 7.22468653e-06,
1.50957302e-08,
1.05983595e-06,
2.70174543e-06, 4.93023466e-09,
1.16339858e-08, 0.00000000e+00,
4.09147792e-08, 5.44135943e-07,
2.33556551e-05, 8.26447814e-09,
3.32418446e-06,
[2.56281682e-07, 3.11322475e-08,
7.34055651e-08, 4.09002090e-08,
0.00000000e+00, 3.82542228e-09,
→ Patterns,
Structures,
Causality…
Analysis
Model
u' = f(u,v)
v' = g(u,v)
Mathematical
Step 1: …
Step 2: …
…
Procedural
Simulation
Courtesy of Indiana University

Modeling

- Using math to approximate some process (or data)
  (physical, biological, chemical, social, …)

- Typically ignore some parameters for a more "reasonable" model (e.g., for your *F=ma* lab, you ignored friction)

- " all models are wrong, but some are useful"
  – Prof. Emer. George E. P. Box, Statistics, UW-Madison

Simulation

- Execution of a model in a computer program
- Several computer languages: C/C++, Java, etc.
- Higher level languages: MATLAB, Python, etc.
- Solving some models may require the use of parallel computing.

Python language

```
>>> (52*55)/3.0
953.3333333333334
>>> from math import *
>>> cos(pi)
-1.0
```

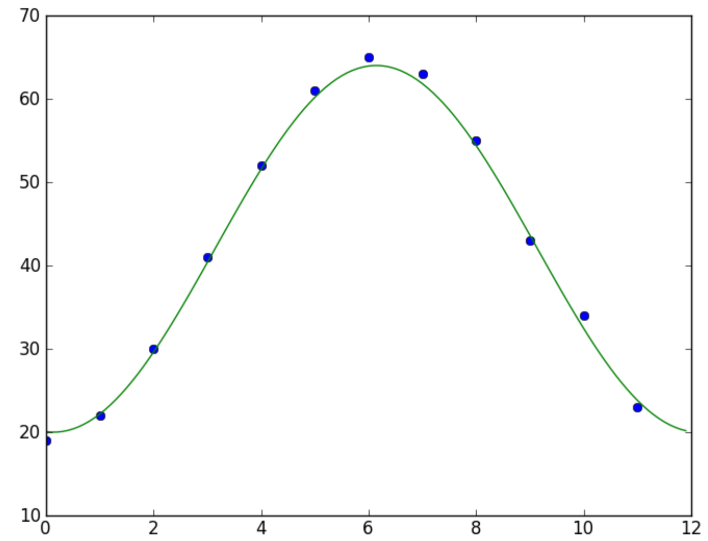
- Easy to use
- Interpreted
- Powerful
- Free (“open source”); runs on all computers
- Used in many computational science tools

Simple model in Python

Average monthly temperature
in Indiana (from weather.com)

→ A function as a model

```
lowTemp=[19,22,30,41,52,61,65,63,55,43,34,23]
plot(lowTemp,'o')      #  'o' → circular points
time = arange(0, 12, 0.1)
F = 22*sin(pi/6 * (time-pi)) + 42
plot(time,F)
```



(Note that Python is "0-based indexing")

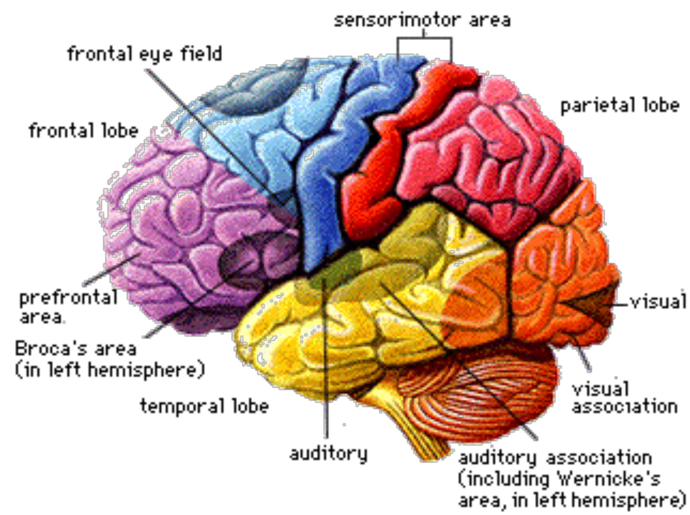
Neuroscience

- Goal: understand relationship between neural structures and functions

Why?

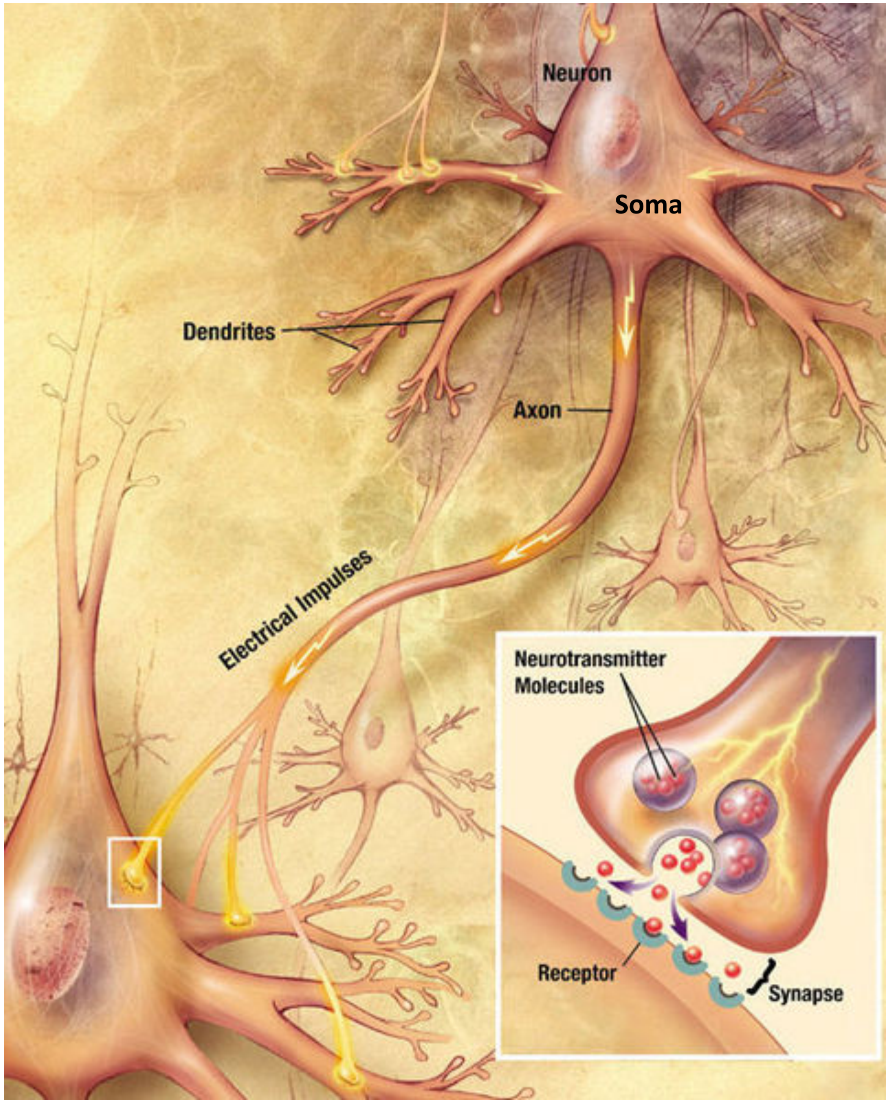
- Help solve important problems
  - Vision
  - Memory
  - Auditory

  …



- Ponder/explain interesting topics
  - Consciousness; self-awareness
  - Altruism

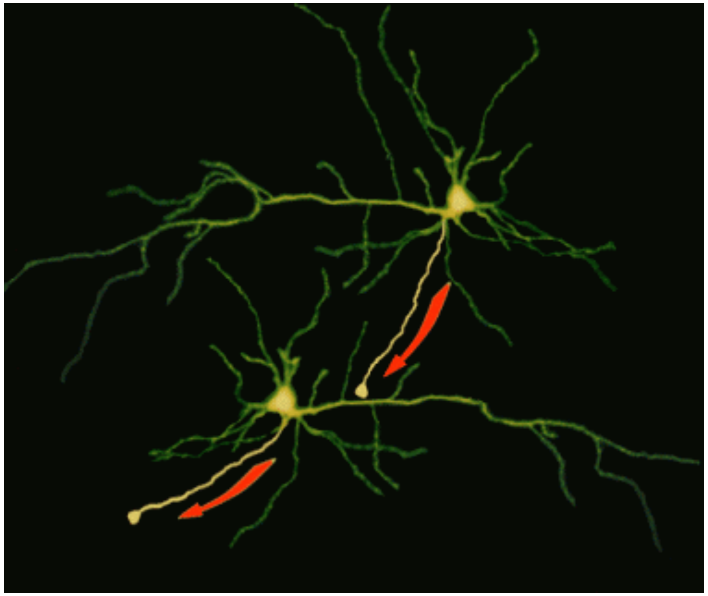
Concepts & Terminology



Illustrative image

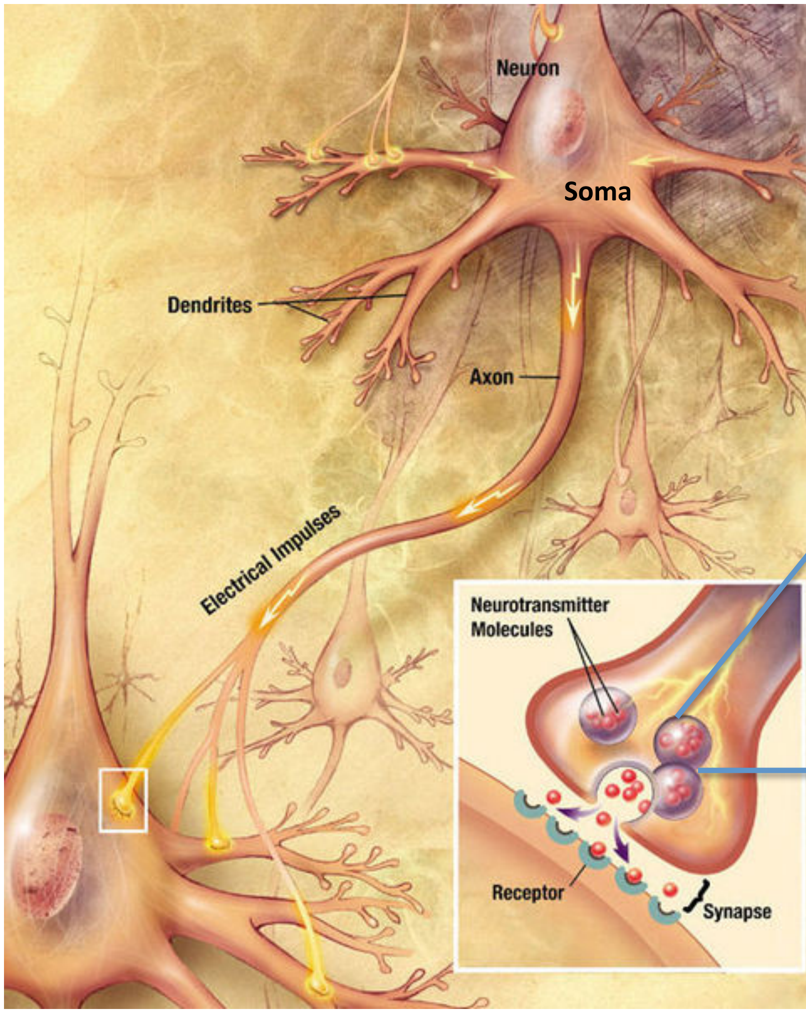
A neuron is a nerve cell.
It contains a soma, dendrites, and axon.

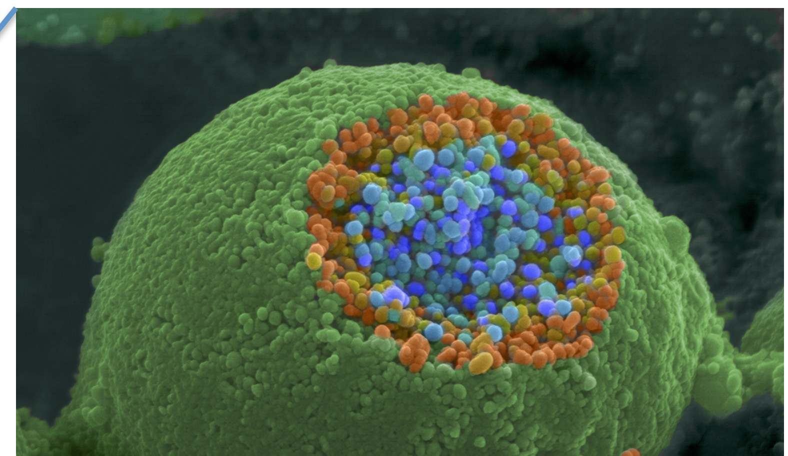
(Combination of biology, chemistry, and physics)



Microscopic image

Yes, it's quite complex



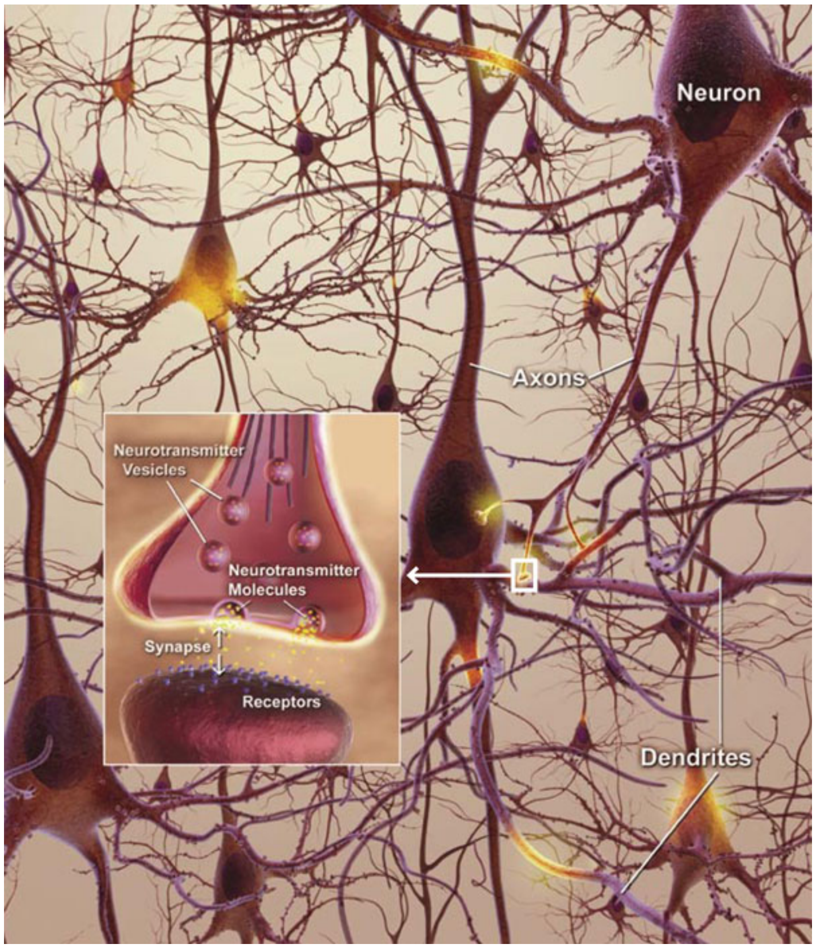


SEM image: cutaway of (mouse) nerve ending and its synaptic vesicles
(cellimagelibrary.org)

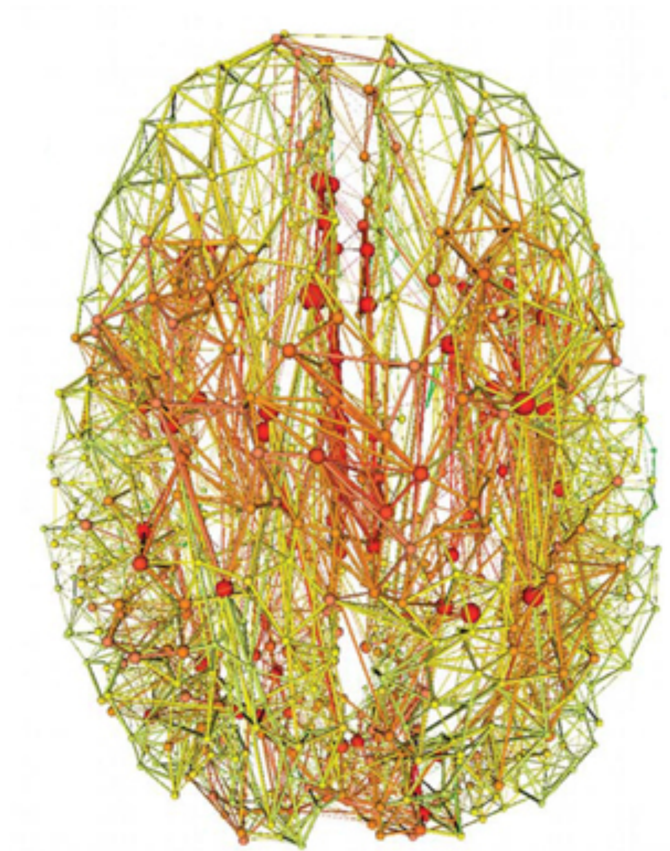
The scale of a model

- Models can be at different scales:
  molecular, cellular, multi-cellular, tissue, organ, organism, …
- A single neuron model is on a different space and time (“spatiotemporal”) scale than a brain region or whole brain model.

Larger number of neurons → complex signaling and networks



100 billion neurons in human brain

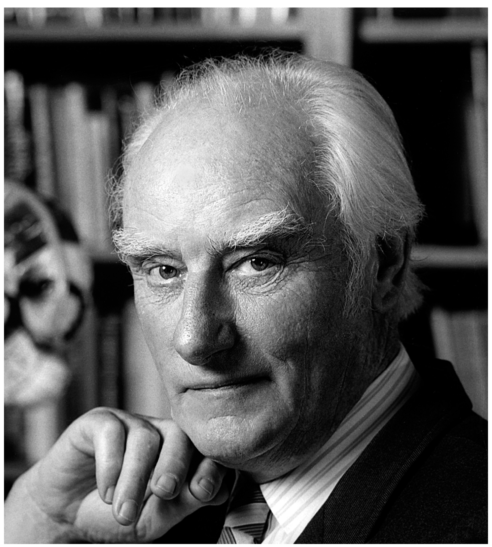


Rich-Club Organization of the Human Connectome.
M.P. van den Heuvel and O. Sporns. J. Neuroscience,
2 Nov 2011.

(Thanks to Journal of Neuroscience and authors for permission to use this image)

- “… it is intolerable that we do not have this information [connectional map] for the human brain. Without it there is little hope of understanding how our brains work…”

(Crick 1993)



Francis Crick, 1916-2004

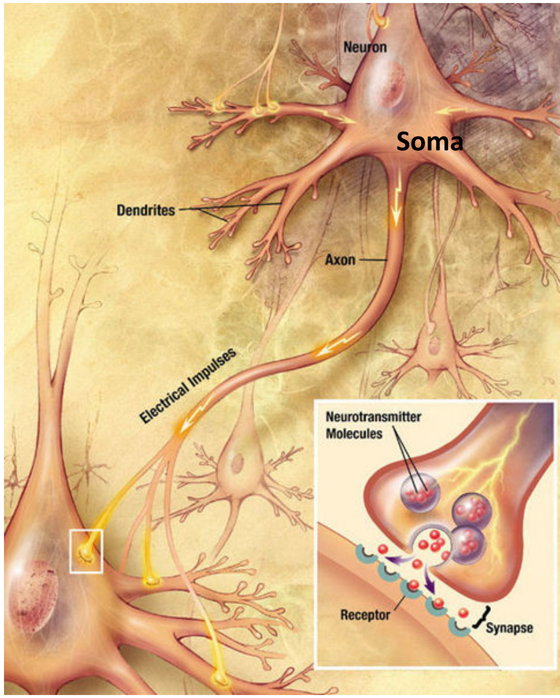
Q: who knows who Francis Crick was?
Hint: James Watson, Maurice Wilkins, Rosalind Franklin

Vision: conversion of light to electrical signals

Memory

- One of the main hypotheses in neuroscience is that memories are encoded in the strengths of synapses between neurons

- <u>Plasticity</u> – the ability to change as a result of experience



Overwhelmed yet?

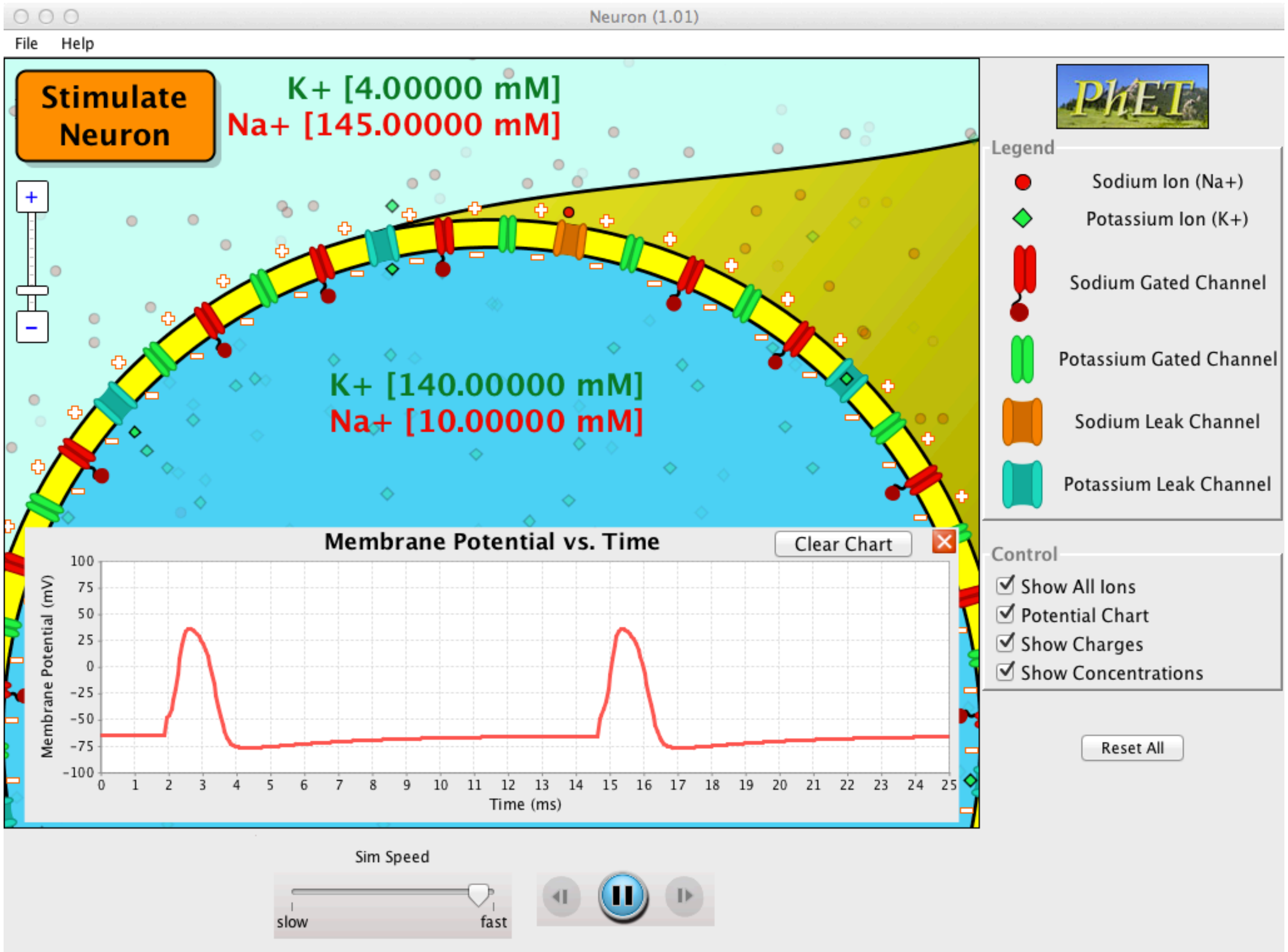
- Let’s begin by modeling <u>a single neuron</u>
- How?
  - An electrical circuit is a good starting model
- Why?
  - Because it <u>is</u> an (chemo)electrical circuit

From your past homework

The nervous system of the human body contains axons whose membranes act as small capacitors. A membrane is capable of storing 1.2×10^{-9} C of charge across a potential difference of 0.07 V before discharging nerve impulses through the body. What is the capacitance of one of these axon membranes?

→ neuron spike

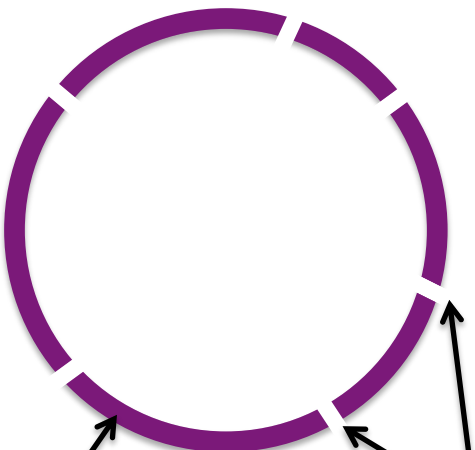
Single neuron simulation



http://phet.colorado.edu/en/simulation/neuron - play the simulation to see V flip/spike

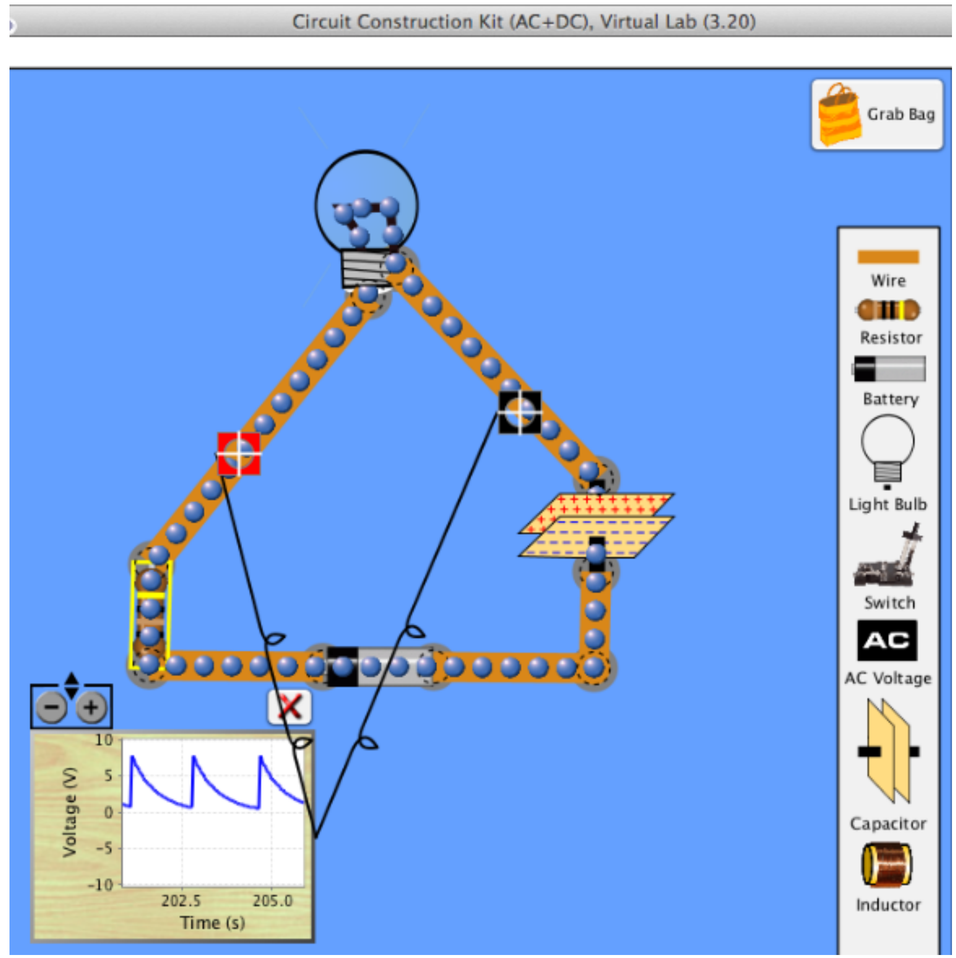
Simplified model of a neuron

RC circuit (Resistance-Capacitance)



Ion transports act as a resistor.

Cell membrane acts as a capacitor.



http://phet.colorado.edu/en/simulation/circuit-construction-kit-ac-virtual-lab

Leaky integrate-and-fire (LIF) model (#1)

$$\frac{dV}{dt} = \frac{1}{RC}(-V + I \cdot R)$$

Where variables refer to membrane's:
V = potential
R = resistance
I = current

if t > t_rest; otherwise = 0

- Note: for those who haven't taken Calculus (yet), dV/dt is a <u>derivative</u> (not division)
- This equation is a <u>differential equation</u>
- It can be solved numerically

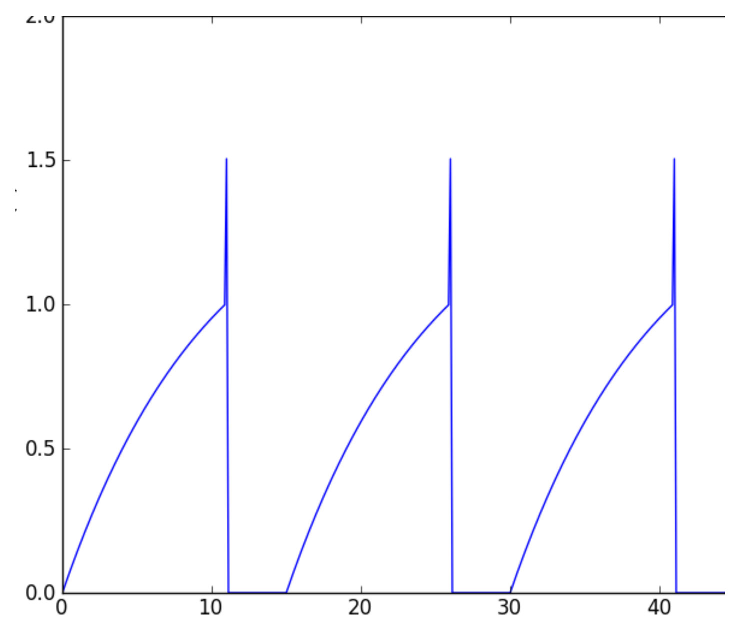
LIF in Python

$$\frac{dV}{dt} = \frac{1}{RC}(-V + I \cdot R)$$

```
#  initialize all variables
…

for i, t in enumerate(time):     # loop over desired time
    if t > t_rest:
        V[i] = V[i-1] + (-V[i-1] + I*R) / tau * dt
        if V[i] >= V_threshold:
            V[i] = V[i] + V_spike
            t_rest = t + tau_ref

plot(time,V)
```



Numerical integration via forward Euler method.

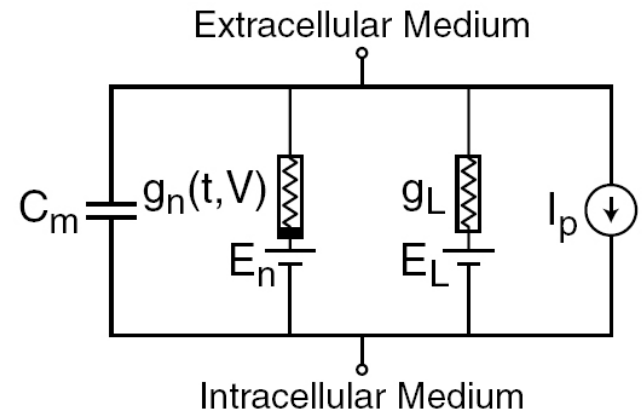
(Rf. www.neurdon.com/tag/spiking-neurons)

But it's not very realistic…

Hodgkin-Huxley model (#2)

- 1952 (Nobel Prize 1963)

Giant squid → measure voltages → Circuit model

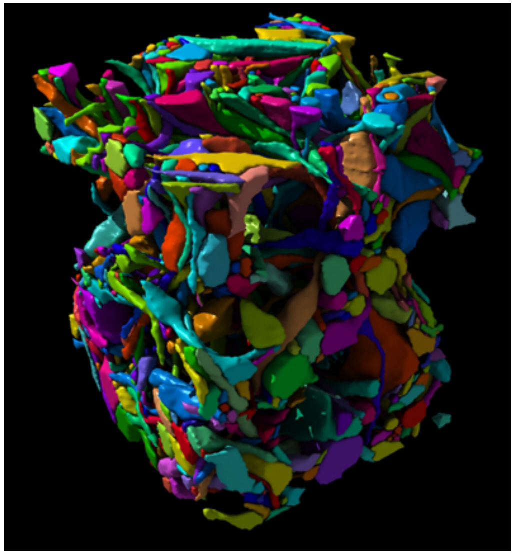


- Electrical circuit model
- A more complicated differential equation
  - has both linear and nonlinear components

What about modeling LOTS of neurons

- To model a brain, we want to model a network of neurons
- Need models of both the spiking behavior and the synapse (transmission between neurons)

In the human brain, each neuron is connected to several thousand other neurons.



http://connectomethebook.com/?page_id=58#all

Izhikevich model (#3)

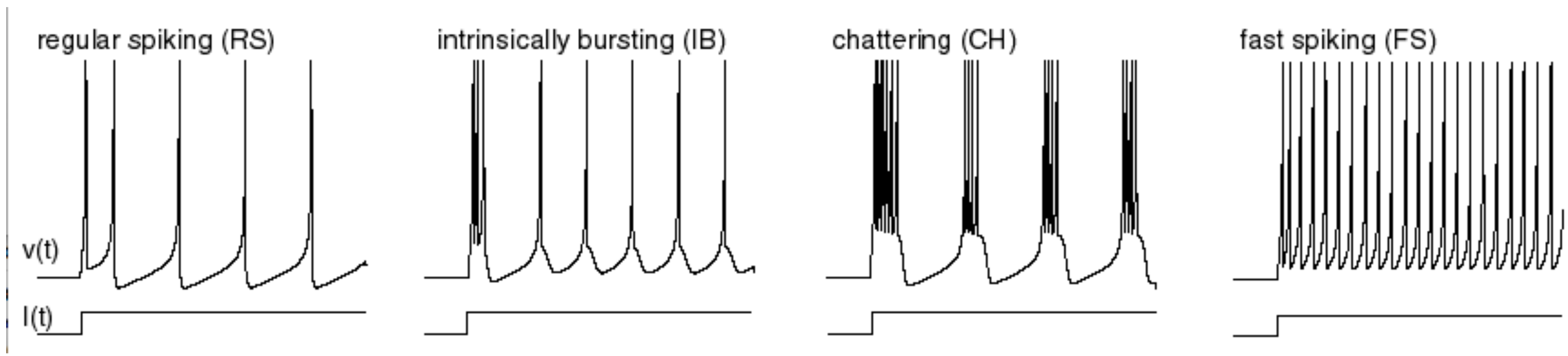
$$\frac{dv}{dt} = 0.04v^2 + 5v + 140 - u + I$$

$$\frac{du}{dt} = a(bv - u)$$

if v >= 30 mV then $\begin{cases} v = c \\ u = u + d \end{cases}$

- v=membrane potential; u=membrane recovery
- Captures multiple types of spiking behavior
- Computationally fast enough to do many neurons

Izhikevich model (cont'd)



(plus many more)

- Izhikevich E.M. (2003) **Simple Model of Spiking Neurons.** IEEE Transactions on Neural Networks, 14:1569- 1572

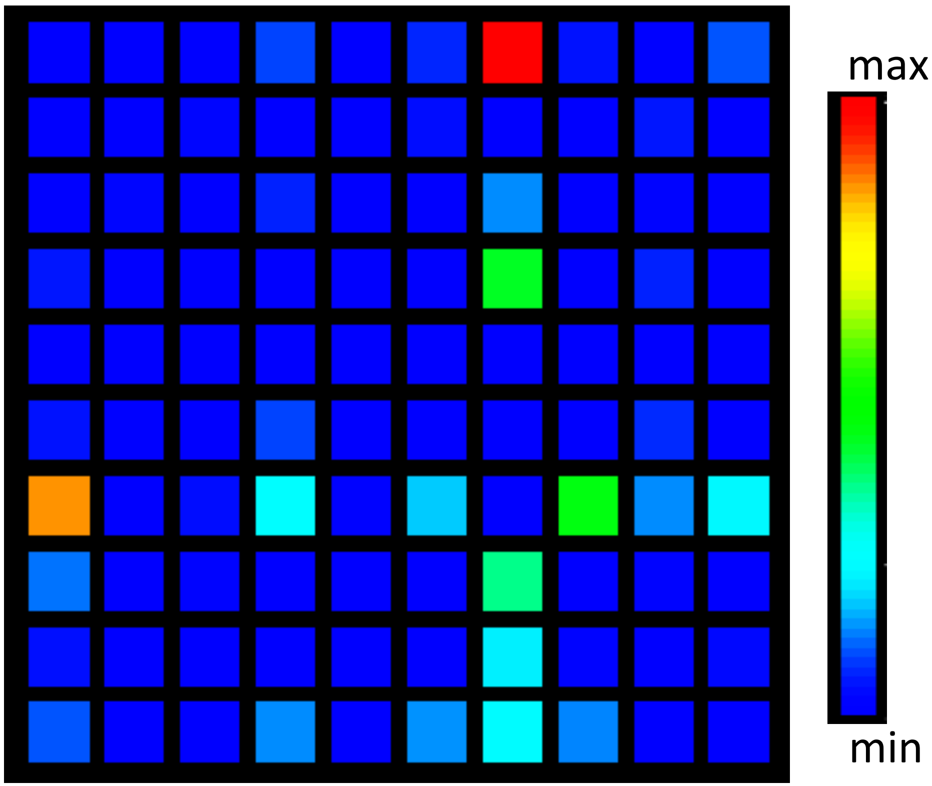
Analysis

- After you have a model and have run a simulation of the model, you need to analyze the resulting data. Similarly, data from an experiment needs to be analyzed.
  - *Transfer Entropy* is just one such analysis technique (next slide)

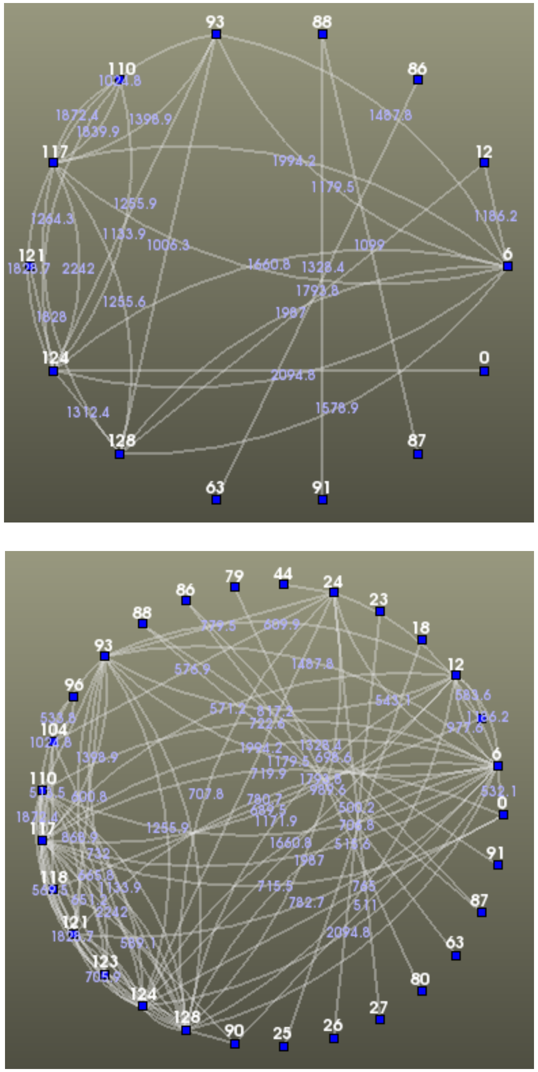
- The Fourth Paradigm: Data-Intensive Scientific Discovery (2009)
  - http://research.microsoft.com/en-us/collaboration/fourthparadigm

Visualization of analysis results

Transfer Entropy (TE) measures the effect that one neuron's spiking has on another neuron.



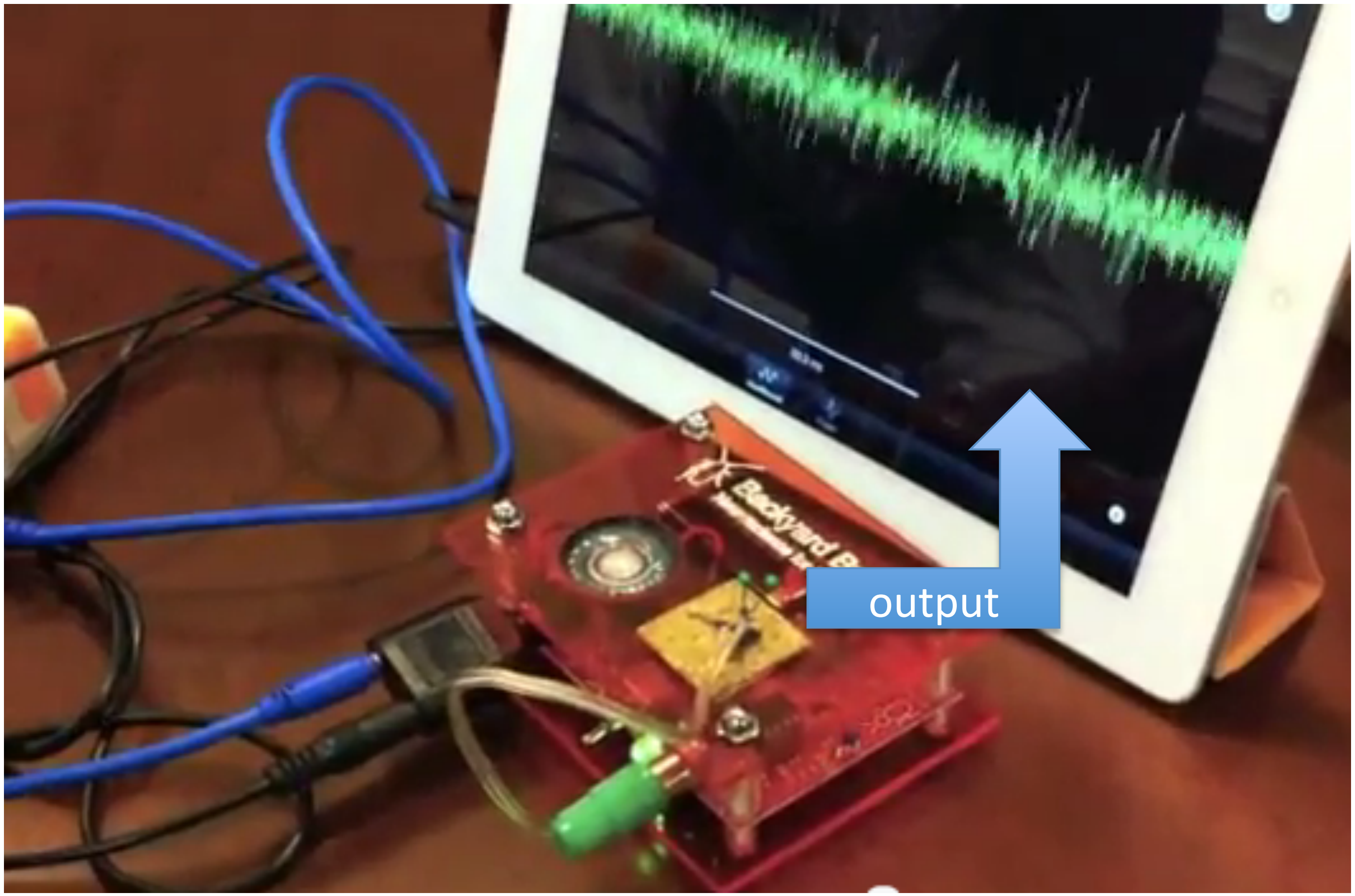
Part of much larger TE matrix



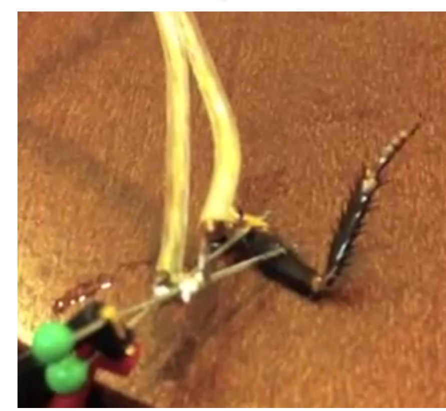
Graph displays of TE
(with different thresholds)

DIY neuroscience experiments

www.backyardbrains.com (SpikerBox: $50-$100)



input



http://www.youtube.com/watch?v=edEXKiOmPvE

Cockroach leg

Sampling of Research[ers]

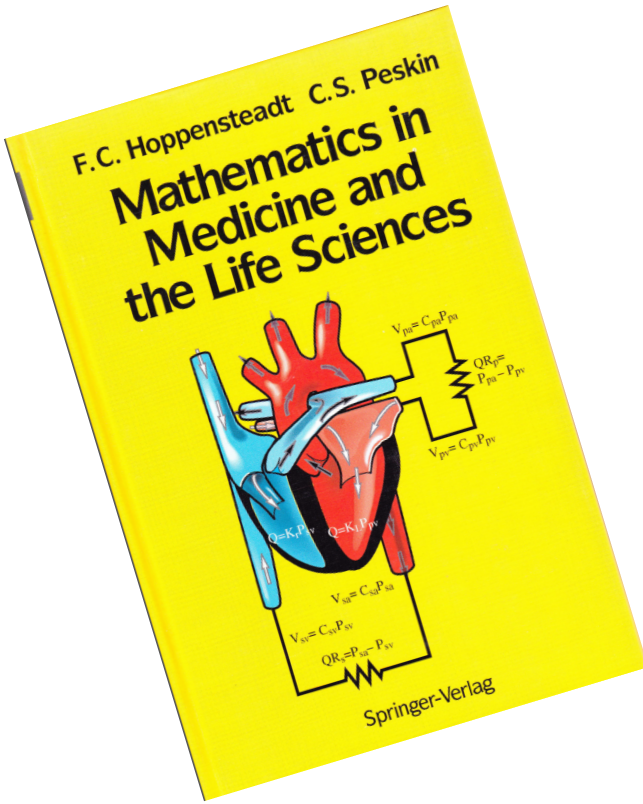
John Beggs, Physics,
Indiana U.
 - experimental research
("brains in a dish") and
analysis of experimental
and simulated data

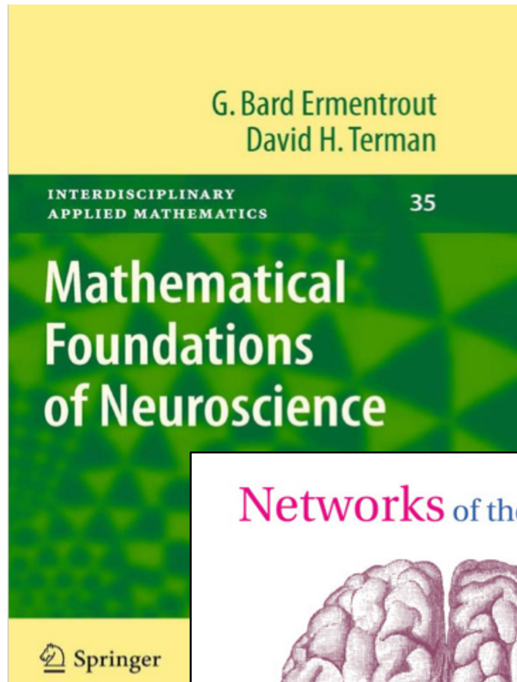
Susan Amara,
Neurobiology,
U. of Pittsburgh,
past President of Society
for Neuroscience.
- molecular & cellular
biology of transporters

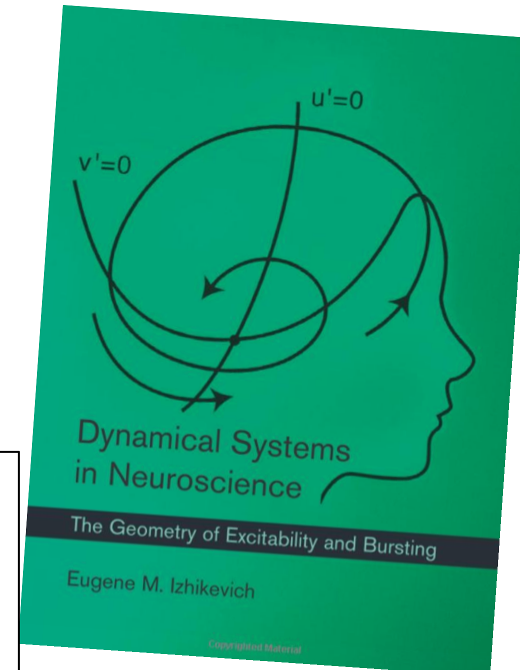
Nancy Kopell, Mathematics,
Boston U.
Co-Director of Center for
Biodynamics
- develops models for and
analysis of networks of
neurons, esp. rhythms and
oscillations.

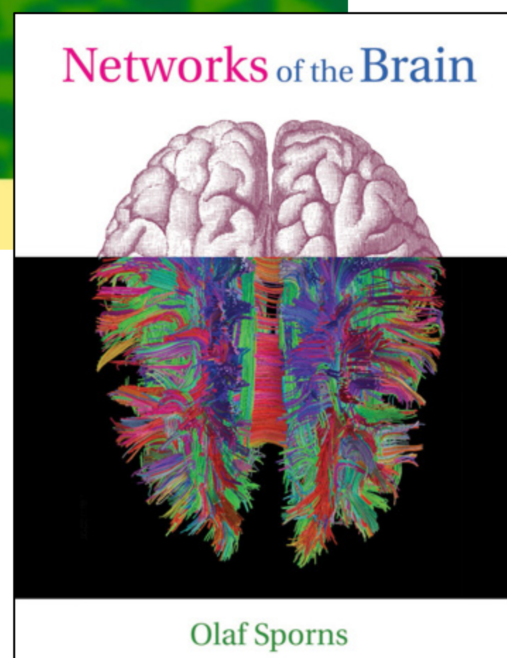
Olaf Sporns,
Psychological and Brain
Sciences, Indiana U.
 - computational
cognitive neuroscience;
neural networks; coined
"Connectome"

Some related textbooks









Summary

- Modeling uses math to approximate reality
- Modeling occurs at multiple scales
- Neuroscience: understand relationship between neural structures and functions
- Python lets you experiment with computational neuroscience (for free)

IU might be of interest to you

- Dept of Physics
  - Biophysics, Biocomplexity
- School of Informatics and Computing
  - Complex systems, computer science, data mining
- Dept of Pyschological and Brain Sciences
  - Learning, computational models of …
- Biology, Chemistry, …

Thanks!

Be curious. Be creative.
Be nice to your neurons.

Questions & short survey

Further reading/References

- http://www.neurdon.com/tag/spiking-neurons/
- http://connectomethebook.com/
- http://www.briansimulator.org/
- **Vase or Face? A Neural Correlate of Shape-Selective Grouping Processes in the Human Brain.** Journal of Cognitive Neuroscience, Aug 2001, pg 744-753
- http://www.scientificamerican.com/article.cfm?id=is-it-possible-to-use-more
- http://blogs.scientificamerican.com/streams-of-consciousness/2011/09/28/goldie-hawn-plunges-into-brain-science/
- http://faculty.washington.edu/chudler/what.html
- http://www.symmetrymagazine.org/cms/?pid=1000591 - From Eye to Sight, Alan Litke
- Craddock TJA , Tuszynski JA , Hameroff S (2012) Cytoskeletal Signaling: Is Memory Encoded in Microtubule Lattices by CaMKII Phosphorylation? PLoS Comput Biol 8(3): e1002421. doi:10.1371/journal.pcbi.1002421 http://www.ploscompbiol.org/article/info%3Adoi%2F10.1371%2Fjournal.pcbi.1002421