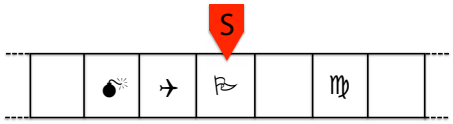


MCB 135 Lecture 3
Turing completeness in living systems
Self-replication and the role of tape

Recap: What is Turing completeness?



The ability to compute any function a Turing machine could compute, that is, anything that could be calculated by mechanical means*.

*as far as we know, see Church-Turing thesis.

Recap: proving Turing completeness

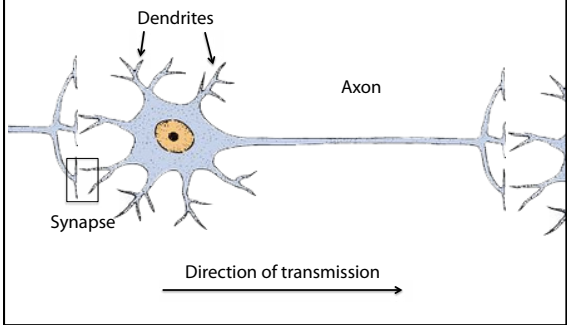
A system is Turing complete if:

- It can implement any Boolean function
  - This will be true if it can implement NAND gates
- It has unlimited memory

Today's Outline

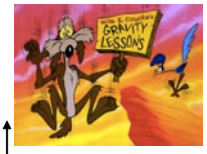
- Turing completeness of neurons
  - Signal transmission
  - The "artificial neuron" and Boolean functions
  - Memory storage
- The fundamental characteristics of life
  - von Neumann's "universal constructor"
- Turing completeness of gene regulation

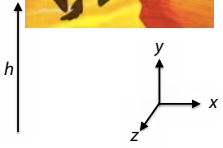
Anatomy of the neuron



Many forces have an associated potential

Example: Gravity



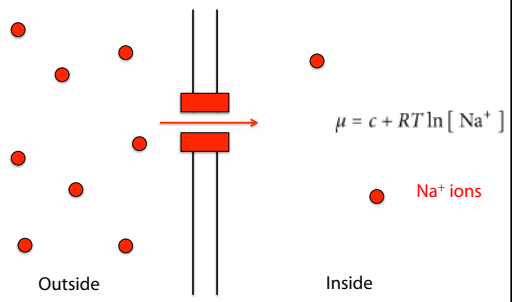


Gravitational potential (energy)

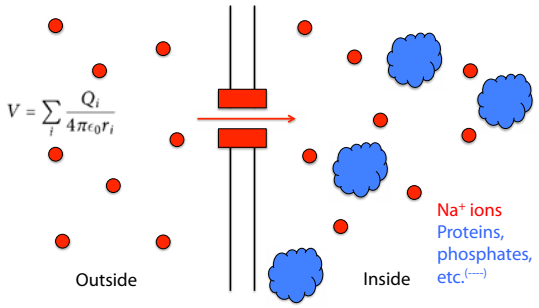
$$U = mgh = m \cdot 9.8\ \mathrm{m/s^2} \cdot h$$

Gravitational force

Chemical potential differences drive ions to regions of lower concentration

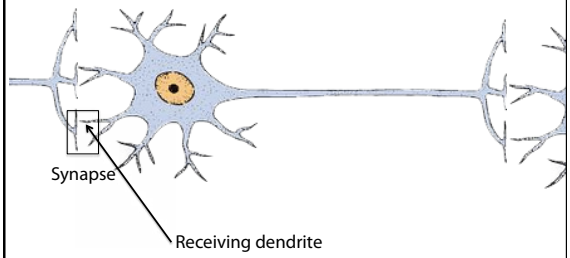


Electric potential differences drive ions toward opposite charges

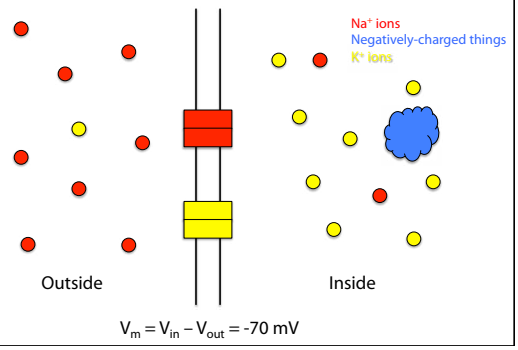


How neurons get excited

We'll focus in on the membrane of the receiving dendrite

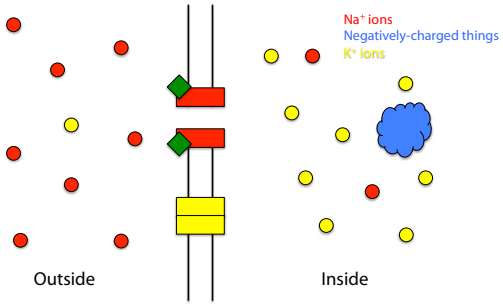


The neuron at rest

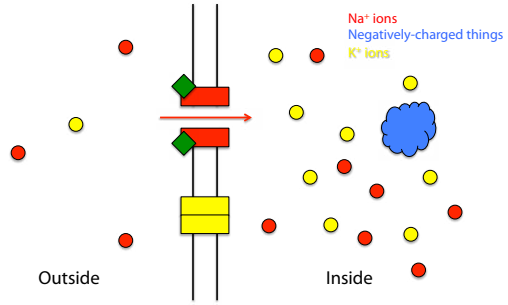


$V_m = V_{in} - V_{out} = -70$ mV

Excitatory neurotransmitter binding causes Na^+ channels to open

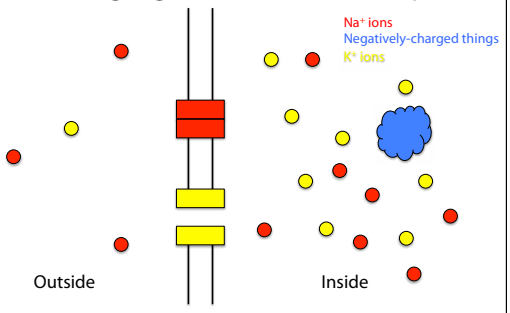


The neuron *depolarizes* as Na^+ flow in

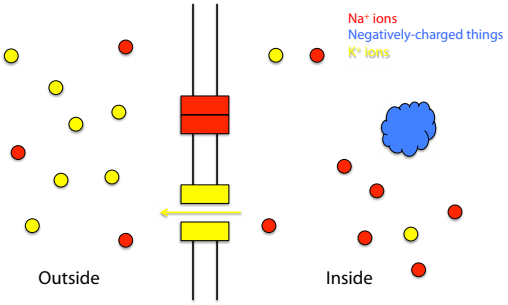


$V_m = V_{in} - V_{out} =$ + 30 mV

After a delay, Na^+ channels close and voltage-gated K^+ channels open

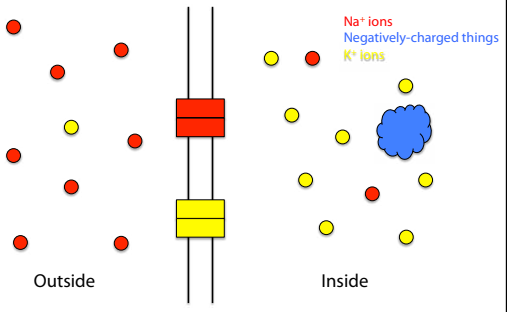


After a delay, Na^+ channels close and voltage-gated K^+ channels open



$V_m = V_{in} - V_{out} =$ -80 mV

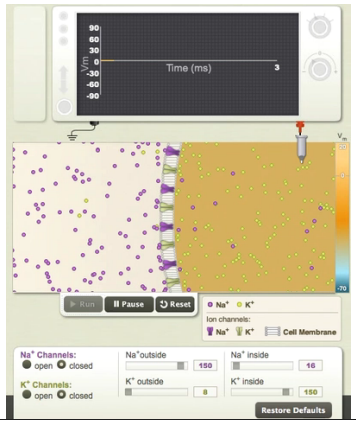
K^+ channels close and pumps (not shown) exchange Na^+ and K^+ to return the neuron to rest



$V_m = V_{in} - V_{out} =$ -70 mV

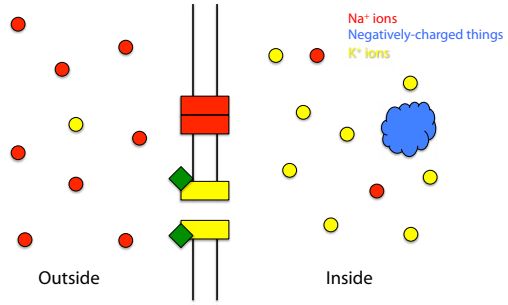
Recap: Excitation in neurons

- Na^+ channels bind neurotransmitter and Na^+ begins to flow in. V_m rises.
- Higher V_m triggers voltage-gated K^+ channels to open. K^+ begins to flow out.
- Around the same time, the neurotransmitter concentration decreases causing Na+ channels to close. V_m falls.
- K+ channels eventually close, and the original ion concentrations are restored by pumps.

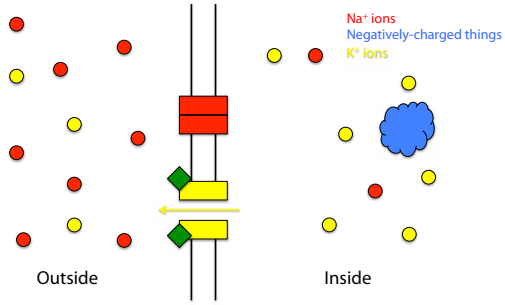


SimBio

Inhibitory signals lower V_m instead



Inhibitory signals lower V_m instead

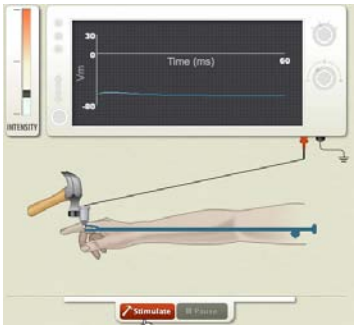


$V_m = V_{in} - V_{out} = -80$ mV

Excitatory and inhibitory signals alter V_m in the dendrites.

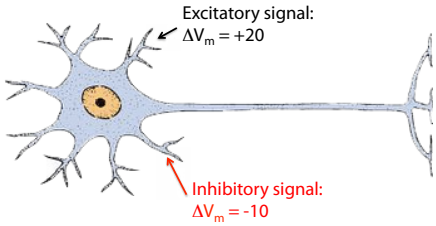
What determines whether the neuron "fires?"

A neuron "fires" when a change in V_m travels down the axon



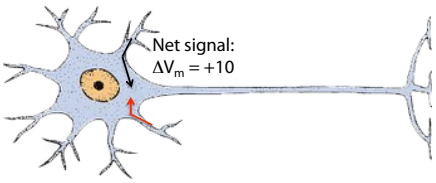
SimBio

Inhibitory and excitatory signals cause V_m changes in dendrites

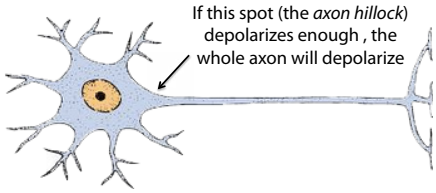


Each synapse may have a different strength (which can be regulated)

Ions diffuse down the dendrites, effectively "summing" membrane voltage changes near the base of the axon



The axon has voltage-gated Na^+ (and K^+) channels



If this spot (the *axon hillock*) depolarizes enough , the whole axon will depolarize

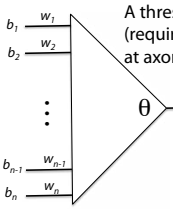
Neuronal firing is an all-or-none response

…and since inputs represent a previous neuron's firing, inputs are also all-or-none!

The "artificial neuron"

As many Boolean inputs as you like (correspond to synapses on dendrites)

Each input b_i has a weight, w_i (correspond to synapse strength and type)

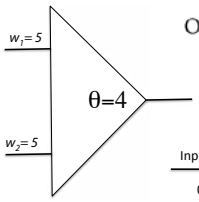


A threshold, θ (required depolarization at axon hillock for firing)

One Boolean output (axon firing)

$$\text{Output} = \begin{cases} 0, & \text{if } \theta > \sum_{i=1}^{n} b_i w_i \\ 1, & \text{otherwise} \end{cases}$$

Example: an OR gate

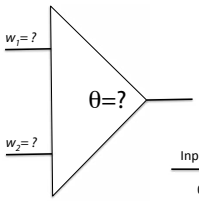


$$\text{Output} = \begin{cases} 0, & \text{if } 4 > 5b_1 + 5b_2 \\ 1, & \text{otherwise} \end{cases}$$

The "OR" gate

Input1	Input2	Weighted sum	Output
0	0		
1	0		
0	1		
1	1		

Your turn: a NAND gate



$$\text{Output} = \begin{cases} 0, & \text{if } \theta > \sum_{i=1}^{n} b_i w_i \\ 1, & \text{otherwise} \end{cases}$$

Input1	Input2	Weighted sum	Output
0	0	?	1
1	0	?	1
0	1	?	1
1	1	?	0

Neural systems can implement any Boolean function, since they can implement NAND gates.

But do they have memory?

Yes: the strength of each synapse can be modified through use or disuse.

Neural systems are Turing complete

We would need to prove Turing completeness in one of the fundamental qualities of living things

…but what are they?

According to Wikipedia

- Homeostasis
- (Cellular) organization
- Metabolism
- Growth
- Adaptation
- Response to stimuli
- Reproduction

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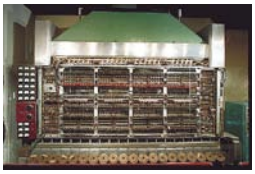
Self-reproduction with error is sufficient for adaptation

R. A. Fisher's 1930
Fundamental Theorem of Natural Selection:

"The rate of increase in fitness of any organism is equal to its genetic variance in fitness."

Johnny von Neumann

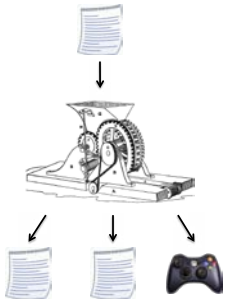


von Neumann's Universal Constructor

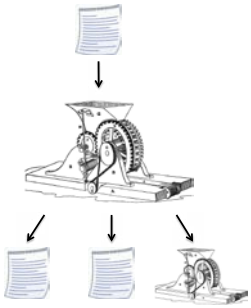
Stan Ulam

How would you design a constructor?

How would you design a constructor?

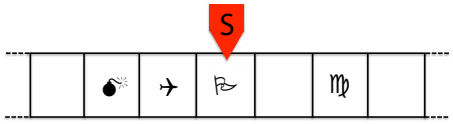


With the right instructions, a universal constructor is also a self-replicator



Some of von Neumann's inspiration

Turing machines (1936)



Avery, MacLeod, and McCarty (1941)

Showed that DNA was the hereditary material

Avery-MacLeod-McCarty experiment

Purified DNA

Try it at home!

What You Need:

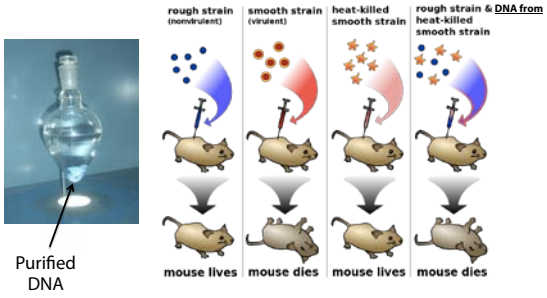
- **Small paper cups** (You want the smallest sized cups.)
- **1 bottle of colorless sports drink** (You can also use a strong salt water solution, but "Lemon Ice" flavored Gatorade tastes better — and you can use the leftovers for refreshments after the lab!)
- **Liquid dish soap** (You want to use the lightest color or colorless brand you can find!)
- **A few drops of pineapple juice** (You could also try using a quarter-teaspoon of meat tenderizer dissolved in a half-cup of water)
- **1 wood skewer** (You want the kind that looks like a very long toothpick. Look in the baking aisle at the grocery store — many people use them to test cakes for doneness.)
- **Alcohol** (You can use regular rubbing alcohol, but if you can find 91-percent isopropyl alcohol at the drugstore get that. The closer to 100 percent alcohol you use, the better this will work.)
- **Narrow container with a lid** (You can use a test tube with a stopper if you have one. You could also use a small jar like you buy spices in. Make sure it is clean and dry.)

Avery-MacLeod-McCarty experiment

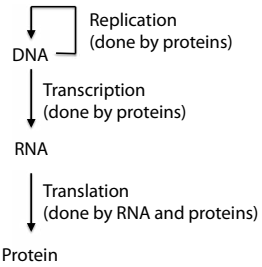
Purified DNA

Try it at home!

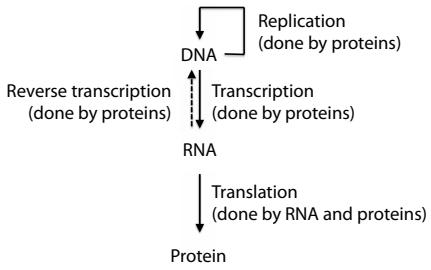
Avery-MacLeod-McCarty experiment



The Central Dogma



The Central Dogma: extended edition

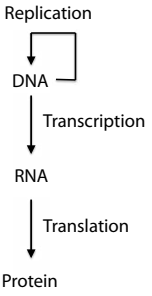


Self-reproduction requires interpreting instructions encoded in DNA (gene expression).

If we can show that gene expression is Turing complete, then all biological systems are Turing complete.

What you absolutely must know about regulation of gene expression

Gene regulation occurs at all levels



- How often gene transcription begins
- How long transcription takes
- How fast the mRNA gets degraded or diluted
- How often translation of the mRNA begins
- How long translation takes
- How often the protein folds into a functional form
- How often the protein is modified to activate or deactivate it
- How fast the protein gets degraded or diluted
- …even, how many copies of the encoding DNA are present

Gene regulation occurs at all levels

Replication
DNA
Transcription
RNA
Translation
Protein

- How often gene transcription begins
- How long transcription takes
- How fast the mRNA gets degraded or diluted
- How often translation of the mRNA begins
- How long translation takes
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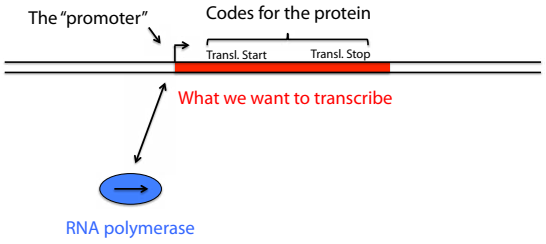
- …even, how many copies of the encoding DNA are present

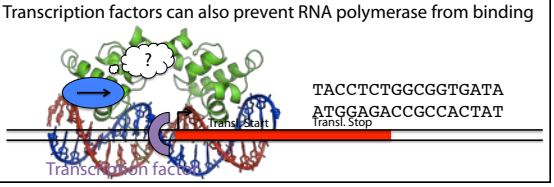
Regulation of transcription initiation



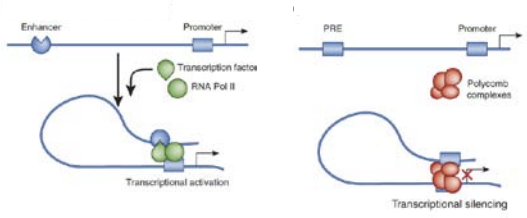
Transcription factors help position RNA polymerase

Transcription factors that bind RNA polymerase can help recruit it

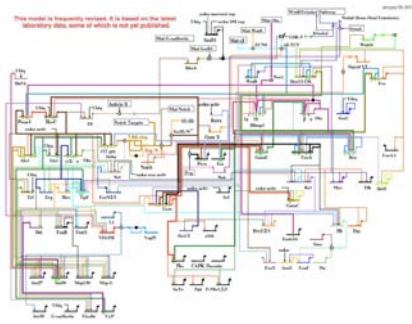
Transcription factors can also prevent RNA polymerase from binding



Transcription factors can also inhibit or promote transcription from a distance



Natural gene regulatory networks can be very complex



Can we make NAND gates?

First, need to define "ON" and "OFF" for gene regulation.

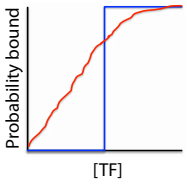
Try transcription factor concentration ([TF]):

- [TF] = 0 → binding site not occupied
- [TF] >> 0 → binding site occupied

Tempting to set a threshold in between to make quasi-continuous concentrations into Boolean variables.

Binding site occupancy is probabilistic

- The TF finds its binding site through a random search
  - A 1 nm protein in a >1 μm cell
  - A small site in 10^6-10^9 bp of DNA
  - # of copies of TF may be small
  - Time-consuming: similar DNA sequences are "almost as good"
- Once arrived, TF could fall off again
  - By chance, or
  - Pushed aside -- at least as often as DNA is replicated
- RNA polymerase faces related issues



What we want
What we (might) get

Can we make NAND gates?

First, need to define "ON" and "OFF" for gene regulation.

Try transcription factor concentration ([TF]):
- [TF] = 0 → binding site not occupied
- [TF] >> 0 → binding site occupied

Tempting to set a threshold in between to make quasi-continuous concentrations into Boolean variables.

Probabilistic binding at intermediate concentrations will cause noise: gene expression when there should not be, and vice versa.

Your computer encodes Boolean values as high and low voltages (often 5V and 0V).

Voltage is a continuous quantity.

To get from high to low, or vice versa, must go through every value in between.

Why don't the transitions cause problems for the computer?