Intro

- Explore how we can simulate electrical signals neurons use to communicate
- Don't worry if you don't know neuroscience—I'll explain

Baseball to Brain Science

- Before I talk about my project… something to think about while I talk.
- Have you ever been hit in your funny bone? That's your ulnar nerve.
- It feels like electricity shooting down your arm, then you have some tingling
- There's some pretty cool science there, very connected to my project

Nature's Split Second Decisions

- Speaking of split second reactions
- This plant has no brain, but can close in under 1/10th of a second

What is an Action Potential?

- Imagine you touch something hot. How does ur brain know to pull hand away?
- Info travels through nerves as a wave of electrical activity—an action potential
- An action potential Is ALL OR NOTHING: just how a domino falls completely or doesn't, an action potential happens completely or doesn't at all.
- Makes neural signaling reliable and very precise - **DISCUSS PARTS ON GRAPH**
- **Depolarization:**electrical potential becomes less negative, repolar is more negative

Basic Physics

- Neurons membrane is like a barrier separating two solutions
- Inside the cell we have different concentrations of ions (mainly potassium) compared to outside (mainly sodium)
- This creates an electrical voltage, like battery
- At rest, inside of neuron is negative compared to the outside
- When stimulated, proteins in the membrane open to let ions flow, changing voltage

Why Care About These Gates?

- Gates r proteins in the membrane that can change shape—open or closed like door
- It's like a dam with controllable gates - when you open gates, water (ions) flows.
- Probability of being open depends on voltage across membrane
- Three types:
  - N gates control potassium flow in the cell
  - M and h gates work together to control sodium flow in the cell
- Connection between these gates that create the action potential

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Hodgkin Huxley Model

- Leads to the Hodgkin Huxley model, published 1952
- Model exists of four coupled differential equations:
  - One for voltage, three for different gates
- Each term represents a different ion current thru membrane

The Math Behind It (SAME SLIDE)

- For each gate type we have lambda equation (on slide)
- X is prob of being open, alpha and beta are voltage-dependent rate contacts
- Solve this to find final probability of the gate being open at each voltage

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Equations part 1 **(sodium)**

- **capacitance:** ability of the neuronal membrane to store charge
- **V:** membrane potential, voltage diff across neuronal membrane (varies over time)
- **g_na**: maximum possible flow rate of sodium ions thru channel
- **Ionic currents:** sodium current, potassium current, leakage current
- **M, h:** gating variables for sodium channels, probability of them being open or closed
- **E_na**: equilibrium potential, aka the voltage where there is no flow of sodium ions across the membrane

Equations part 2 **(potassium)**

- **g_k** maximum flow rate of potassium thru flow channel
- **N** gating variable, influences opening of potassium channels
- **e_k** equilibrium, no flow of potassium
- **g_l and e_l** leakage, leakage channels allow sodium and potassium to "leak" back to their original places
- **Potassium only has one gate because potassium primarily functions to restore the membrane back to resting state, which requires a simpler opening mechanism**
- **Sodium has two because the rapid influx of sodium during action potential needs to be tightly controlled to ensure a brief depolarization**
- **I_EXTERNAL**: external current applied!

Project Goals / Implementation

- 1. Write program (python) to solve equations numerically (numpy, Matplotlib, seaborn were libraries used)
  - Different methods, Euler cromer, Adams bash forth
- 2. Verify steady state behavior - finding where nothing changes w/ time
- 3. Study dynamics, how system responds to different stimuli

Steady State

- First experiment: study system at rest
- We plot the steady-state values of n, m, and h versus membrane potential
- Tells us how the steady states of the model vary with different membrane potential values
- SECOND SLIDE: this is examining the model over time
- Notice how the potentials even out over time when the system balances out.

Single Spike

- Now, we apply a brief stimulus. The standard current for my experiment is 1-10 **microamp per square centimeter, with 1 being minimum**
- **Basically wanted to study what stimulus needed to trigger action potential**
- I was able to get action potentials as low as 1 microamps per square centimeter
- However, although the amplitude is smaller, notice the action potential still occurs!
- Notice here how the different gates respond in sequence, too.
- Notice all or nothing. Right side min threshold, top one is called a subthresold response. Means theres a small depolarization that doesn't result in action pot

Spike Trains

- here we consider what happens with continuous stimulation
- If we apply constant current: below threshold we get nothing, just above regular firing, high above threshold faster firing of action potentials
- This is a graph of a general point above the threshold. Notice the consistent spiking, each action potential looks the same.
- Here's a graph of the frequency based on current applied. As you can see, before the threshold there are no spikes, then it jumps up and increases

Step Response

- Final experiment involvers a two-phase current
- Initial current I1 for 20ms, then a step up to I2 after that.
- We're testing four cases here: SMALL intial, SMALL step, SMALL into, LARGE step
- LARGE initial, SMALL step, LARGE initial, LARGE step.
- Helps us understand how neurons respond to changing inputs
- Larger the input gets, the closer the action potentials become—remember our frequency graph from earlier

Putting it Together/Future Research

- Remember that funny bone? When you hit your ulnar nerve, you temporarily disrupt ion channels. Same ones we've been modeling.
- Tingling is them rapidly opening and closing
- When these channels are affected—your arm tingles, flytraps close, local anesthetics work… which brings us to where I'm headed—future research
- I've previously researched on Venus flytrap action potentials and affects of anesthesia
- We could potentially in the future create needle free local anesthetics that block ion channels without a needle.
- Studying something like this on Venus flytraps first—they model similar action potentials when hairs are triggered