Models of Cellular Electrical Activity
The Pioneers of Modern Neuroscience

Andrew Huxley (1917-2012)

Alan Hodgkin (1914-1998)

The cover of the 1963 Nobel Prize program
Neuronal Action Potential

First recording of a neuronal action potential. From Hodgkin & Huxley (1945)
The Hodgkin-Huxley equations were solved numerically using a Brunsviga 20 mechanical calculator, which used a hand crank. It took a few weeks (thousands of cranks) for Huxley to simulate the propagating action potential.
Impulses Occur in Many Tissues?
Sequential Opening and Closing of Different Ion Channels Drives the Impulse

1. Outside
2. 
3. Inside
4. 
5. 

Na⁺, K⁺
Electrodiffusion Across the Plasma Membrane

Red – K⁺ ions
Green – Cl⁻ ions
Circuitry Diagram for Voltage Clamp

- Intracellular electrode
- Axon
- Membrane potential amplifier
- Extracellular electrode
- Signal generator
- Feedback amplifier
- Current monitor
An Example of Voltage Clamp Recordings

Apply voltage pulses

Measure current
Action Potential Propagation Video

https://youtu.be/Sa1wM750Rvs
Morris-Lecar Phase Plane

Red: subthreshold response, Green: impulse
A Type-1 Neural Oscillator

Oscillation period approaches infinity near the homoclinic bifurcation
“On Relaxation-Oscillations”, *Philosophical Magazine* (1926)

Solution to the van der Pol equations with $\mu = 10$, from his 1926 paper.

Balthasar van der Pol
Relaxation Oscillations in an Electrical Circuit

Relaxation Oscillations in the Phase Plane

The trajectory follows the outer branches of the $x$ nullcline, except at jumps

Thanks to Josh Kimrey for animations
Motion on the Fast Timescale

The fast-nullcline becomes a bifurcation diagram, with parameter $y$.

Cyan circles are randomly-chosen initial conditions.
Motion on the Slow Timescale

The “parameter” $y$ is now the sole variable.

The phase points are constrained to the cubic curve.
Most Pioneering Work on Neuronal Electrophysiology was Done With Invertebrates

Eric Kandel wins Nobel Prize in Physiology or Medicine in 2000, for his studies of memory in invertebrate neurons
Parabolic Bursting in *Aplysia* Neuron R15
First Reported in 1968

Abdominal ganglion of *Aplysia*

Treistman and Levitan, 1976
Parabolic Bursting in a Hypothalamic Neuron

Bursting in a rodent GnRH neuron
(Chu et al., 2012)
Insulin is Secreted by β-cells in Pancreatic Islets

"Square-wave" bursting in an islet β-cell

- the pancreas
  - common bile duct
  - intestine
  - exocrine tissue
  - pancreatic duct

- the islet
  - endocrine tissue
  - α-cell
  - β-cell
  - δ-cell

- the β-cell
  - glucose
  - ATP
  - ADP
  - K^+_ATP
  - K^+
  - Ca^{2+}
  - mitochondria
  - repolarisation
  - VDCC
  - insulin

Voltage (mV)
- -80
- -60
- -40
- -20

2 min
John Rinzel Pioneers the Application of Fast-Slow Analysis to Bursting in 1985
Fast/Slow Analysis of Bursting

Analysis of bursting in the modified Morris-Lecar model
Fast/Slow Analysis of Bursting

Analysis of bursting with the average voltage curve (dark blue)
Effect of Glucose on β Cell Bursting
Aplysia, Also Known as the Sea Slug