Models of Cellular Electrical Activity
The Pioneers of Modern Neuroscience

The cover of the 1963 Nobel Prize program

Andrew Huxley (1917-2012)

Alan Hodgkin (1914-1998)
Squid Giant Axon
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?
Electrodiffusion Across the Plasma Membrane

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

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

Apply voltage pulses

Measure current
Sequential Opening and Closing of Different Ion Channels Drives the Impulse

1. Outside
2. Inside
3. Na⁺, K⁺
4. Na⁺, K⁺
5. Na⁺, K⁺
Action Potential Propagation Video

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

Red: subthreshold response, Green: impulse
Morris-Lecar Bifurcation Analysis

A Type-1 Neural Oscillator

Oscillation period approaches infinity near the homoclinic bifurcation
Deterministic Morris-Lecar Model

Deterministic Morris-Lecar with small-amplitude sinusoidal input

\( v_3 = 2, \; v_4 = 30, \; I_{\text{ic}} = 80 \text{ pA} \)
Stochastic Morris-Lecar Model

Stochastic Morris-Lecar (N=20) with small-amplitude sinusoidal input
Stochastic Morris-Lecar Model

Stochastic Morris-Lecar (N=100) with small-amplitude sinusoidal input. The spiking frequency is approximately that of the forcing frequency.
Stochastic Morris-Lecar Model

Stochastic Morris-Lecar (N=1000) with small-amplitude sinusoidal input. The cell rarely spikes.
Stochastic Morris-Lecar Model

Response is defined as correspondence between peaks of the input current and impulses.
Double-Well Potential
Stochastic Resonance with a Double-Well Potential

Sinusoidal signal (green) alters the shape of the potential function. The size of the circle reflects the probability that the particle is in a particular well.
Stochastic Resonance in PubMed

Stochastic resonance is catching on! Citation number of the topic according to PubMed
Some Titles of SR in Biology

“Stochastic and vibrational resonance in complex networks of neurons”, 2021

“Recurrence-mediated suprathreshold stochastic resonance”, 2021
(on feed-forward neural networks

“Stochastic resonance and sensory information processing: a tutorial and review of applications”, 2004

“Detection of single molecules using stochastic resonance of bistable oligomers”, 2020

”A review of methods for identifying stochastic resonance in simulations of single neuron models”, 2015

“Stochastic resonance and angry back syndrome: noisy skin”, 1996
“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

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
John Rinzel Pioneers the Application of Fast-Slow Analysis to Bursting in 1985
Major Role for Ca\textsuperscript{2+}-activated K\textsuperscript{+} Channels in \(\beta\)-cell Bursting
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

![Graph showing the effect of glucose on β cell bursting](image)

- **G3** to **G5**: Shows a change in potential voltage from -50 mV to -70 mV.
- **G7**: Indicating a plateau potential at -60 mV.
- **G10**: Highlighting threshold potential.
- **G15**: Demonstrating a lower voltage range.
- **G20**: At a higher voltage range with a plateau potential.

**1 min**