Neuronal Systems as Nonlinear Dynamical Systems

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References on Nonlinear Dynamics


References on Modeling Neuronal System Dynamics


Dynamics of Excitability and Oscillations

Cellular level
(spiking)

Network level
(firing rate)

Hodgkin-Huxley model

Wilson-Cowan model

Membrane currents

Activity functions

Activity dynamics in the phase plane

Onset of repetitive firing (Type I & II)
(bifurcations)
Nonlinear Dynamical Response Properties

Cellular: “HH”

Excitability

Repetitive activity

Bistability

Bursting

Network: Wilson-Cowan
(Mean field)
Take Home Messages

Excitability/Oscillations: fast autocatalysis + slower negative feedback

Value of reduced models

Time scales and dynamics

Phase space geometry

Different dynamic states – “Bifurcations”; concepts and methods are general.

XPP software: http://www.pitt.edu/~phase/ (Bard Ermentrout’s home page)
Synaptic input – many, $O(10^3 \text{ to } 10^4)$

“Classical” neuron

Dendrites, 0.1 to 1 mm long

Signals: $V_m \sim 100 \text{ mV}$ membrane potential

$O(\text{msec})$

Ionic currents

Membrane with ion channels –

variable density over surface.

Dendrites – graded potentials,

linear in classical view

Axon – characteristic impulses, propagation
Electrical Activity of Cells

- $V = V(x,t)$, distribution within cell
  - uniform or not?, propagation?
- Coupling to other cells
- Nonlinearities
- Time scales

Current balance equation for membrane:

$$C_m \frac{\partial V}{\partial t} + I_{ion}(V) = \frac{d}{4R_i} \frac{\partial^2 V}{\partial x^2} + I_{app} + \text{coupling}$$

*Capacitive channels cable properties other cells*

### Coupling:

- \( \sum_j g_{c,j}(V_j - V) \) “electrical” - gap junctions
- \( \sum_j g_{syn,j}(V_j(t)) (V_{syn} - V) \) chemical synapses

### Current balance equation:

- \( I_{ion} = I_{ion}(V, W) \) generally nonlinear
  - \( \sum_k g_k(V, W) (V - V_k) \) channel types

- \( \frac{\partial W}{\partial t} = G(V, W) \) gating dynamics
A QUANTITATIVE DESCRIPTION OF MEMBRANE CURRENT AND ITS APPLICATION TO CONDUCTION AND EXCITATION IN NERVE

BY A. L. HODGKIN AND A. F. HUXLEY

From the Physiological Laboratory, University of Cambridge

(Received 10 March 1953)

100mV

Action potential
squid axon

V_{rest}

1 msec

Nobel Prize, 1959
Current Balance:
(no coupling, no cable properties, “steady state”)

\[ 0 \approx g_K(V-V_K) + g_{Na}(V-V_{Na}) + g_L(V-V_L) \]

\[ V \approx \frac{g_K V_K + g_{Na} V_{Na} + g_L V_L}{g_K + g_{Na} + g_L} \]
HH Recipe:

V-clamp ➔ $I_{\text{ion}}$ components

Predict $I$-clamp behavior?

$I_K(t)$ is monotonic; activation gate, $n$
$I_{Na}(t)$ is transient; activation, $m$ and inactivation, $h$

e.g., $g_K(t) = I_K(t)/(V-V_K) = G_K n^4(t)$
with $V=V_{\text{clamp}}$
gating kinetics:
$$\frac{dn}{dt} = \frac{\alpha(V)\,(1-n) - \beta(V)\,n}{\tau_n(V)}$$
$$n_{\infty}(V) = \frac{n_{\infty}(V) - n}{\tau_n(V)}$$
n_{\infty}(V) increases with $V$.

mass action for “subunits” or HH-”particles”

OFF $\alpha(V)$ ON
$P \leftrightarrow P^*$
\begin{align*}
\beta(V) \\
I_{Na}(t) = G_{Na} m^3(t) h(t) (V-V_{Na})
\end{align*}
HH Equations

\[ C_m \frac{dV}{dt} + G_{Na} m^3 h (V-V_{Na}) + G_K n^4 (V-V_K) + G_L (V-V_L) = I_{app} \]

\[ \frac{dm}{dt} = \phi \left[ m_\infty(V) - m \right]/\tau_m(V) \]
\[ \frac{dh}{dt} = \phi \left[ h_\infty(V) - h \right]/\tau_h(V) \]
\[ \frac{dn}{dt} = \phi \left[ n_\infty(V) - n \right]/\tau_n(V) \]

\( \phi, \) temperature
\( \) correction factor
\( = Q_{10}^{**[(temp-temp_{ref})/10]} \)
\( \) HH: \( Q_{10} = 3 \)

Reconstruct action potential

Time course
Velocity
Threshold
Refractory period
Ion fluxes
Repetitive firing?

\[ E_{Na} \]
\[ E_M \]
\[ E_K \]
Biophysical Developments

Pharmacological Blockade

\[ TTX \rightarrow I_K \]
\[ TEA \rightarrow I_{Na} \]

Patch Clamp - Neher (1979)

Other channels
\[ I_{Ca} \rightarrow T, L, N \text{ types} \]
\[ I_A \rightarrow K^+ \text{ w/ inactivation} \]
\[ I_{K-Ca} \rightarrow K^+ \text{ activated by } V \text{ and } [Ca^{2+}]_{int} \]
$1 \mu m^2$ has about 100 Na$^+$ and K$^+$ channels.
Bullfrog sympathetic Ganglion “B” cell

Cell is “compact”, electrically … but not for diffusion Ca$^{2+}$

MODEL:

“HH” circuit
+ [Ca$^{2+}$]$_{\text{int}}$
+ [K$^+$]$_{\text{ext}}$

g$_c$ & g$_{\text{AHP}}$ depend on [Ca$^{2+}$]$_{\text{int}}$

Yamada, Koch, Adams ‘89
Cortical Pyramidal Neuron

Complex dendritic branching
Nonuniformly distributed channels

Pyramidal Neuron with axonal tree

Koch, Douglas, Wehmeier '90

Schwark & Jones, '89
I-V relations: $I_{SS}(V)$ steady state $I_{inst}(V)$ “instantaneous”

HH: $I_{SS}(V) = G_{Na} \, m_{\infty}^3(V) \, h_{\infty}(V) \, (V-V_{Na}) + G_{K} \, n_{\infty}^4(V) \, (V-V_{K}) + G_{L} \, (V-V_{L})$

$I_{inst}(V) = G_{Na} \, m_{\infty}^3(V) \, h \, (V-V_{Na}) + G_{K} \, n \, (V-V_{K}) + G_{L} \, (V-V_{L})$

fast slow, fixed at holding values e.g., rest
Dissection of HH Action Potential

Fast/Slow Analysis - based on time scale differences

h, n are slow relative to V,m

Idealize AP to 4 phases

h,n – constant during upstroke and downstroke

V,m – “slaved” during plateau and recovery
Repetitive Firing, HH model and others

Response to current step

nerve block

Subthreshold

![Graph showing frequency vs. applied current with different angles representing different conditions.](Image)
Repetitive firing in HH and squid axon
-- bistability near onset

Linear stability: eigenvalues of 4x4 matrix. For reduced model w/ $m=m_\infty(V)$: stability if
\[
\frac{\partial I_{\text{inst}}}{\partial V} + \frac{C_m}{\tau_n} > 0.
\]

HH eqns

Squid axon

Interval of bistability

Rinzel & Miller, '80

Guttman, Lewis & Rinzel, '80
Bistability in motoneurons
2-compartment model; plateau generator in dendrite

Booth & Rinzel, '95
Two-variable Model \( \rightarrow \) Phase Plane Analysis

\( I_{\text{Ca}} \) – fast, non-inactivating
\( I_K \) -- “delayed” rectifier, like HH’s \( I_K \)

Morris & Lecar, ’81 – barnacle muscle

\[
C \frac{dV}{dt} = -\overline{g}_{\text{Ca}} m_{\infty}(V) (V - V_{\text{Ca}}) - \overline{g}_K w(V - V_K) - \overline{g}_L (V - V_L) + I
\]

\[
\frac{dw}{dt} = \phi \frac{w_{\infty}(V) - w}{\tau_w(V)}
\]

\( m_{\infty}, w_{\infty} \)

\( V_K, V_L, V_{\text{rest}}, V_{\text{Ca}} \)
Phase Plane & Attractors

Effect of Perturbations

P.P. Analysis
Get the Nullclines

\[
\frac{dV}{dt} = -\ I_{\text{inst}}(V,w) + I_{\text{app}}
\]

\[
\frac{dw}{dt} = \phi \left[ w_\infty(V) - w \right] / \tau_w(V)
\]

\[
\frac{dV}{dt} = 0
\]

\[
I_{\text{inst}}(V,w) = I_{\text{app}}
\]

\[
\frac{dw}{dt} = 0
\]

\[
w = w_\infty(V)
\]
ML model - excitable regime

Case of small $\varphi$

traj hugs V-nullcline - except for up/down jumps.
Anode Break Excitation or Post-Inhibitory Rebound (PIR)

\[ i_{app} \]

\[ \dot{\varphi} = 0 \text{ for } t > 0 \]

\[ \dot{\varphi} = 0 \text{ for } t < 0 \]

\[ i_{app} < 0 \]

\[ I_K - \text{deactivated} \]
Repetitive Firing in phase plane for M-C model

$\frac{dv}{dt} = 0$

excitable

repetitive firing

$\frac{dv}{dt} = 0$

limit cycle

depolarization block

stable steady state of depolarization
Repetitive Activity in ML (& HH)

Onset is via Hopf bifurcation

"rest" - unstable
only if on middle branch (math)

"Type II" onset
Hodgkin '48

Condition for instability:
\[
\frac{1}{C_m} \frac{\partial i_{ion}}{\partial V} < -\frac{\Phi}{\ell_w}
\]

near "rest"
\[i_{ss} - monotone\]
Adjust param’s → changes nullclines: case of 3 “rest” states

3 states → $I_{ss}$

Stable or Unstable?

3 states – not necessarily:


$\Phi$ small enough, then both upper/middle unstable if on middle branch.
ML: $\phi$ large $\rightarrow$ 2 stable steady states

Neuron is bistable: plateau behavior.

Saddle point, with stable and unstable manifolds

<table>
<thead>
<tr>
<th>V</th>
<th>t</th>
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<tr>
<td>$I_{\text{app}}$ switching pulses</td>
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e.g., HH with $V_K = 24 \text{ mV}$
ML: $\varphi$ small $\rightarrow$ both upper states are unstable

Neuron is excitable with strict threshold.

$I_{ss}$ must be N-shaped.

$I_{K-A}$ can give long latency but not necessary.
Onset of Repetitive Firing – 3 rest states

SNIC- saddle-node on invariant circle

- excitable
- saddle-node
- limit cycle

emerge w/ large amplitude – zero frequency
ML: $\phi$ small

freq $\sim \sqrt{I-I_1}$

low freq but no conductances
very slow

$I_{K-A}$ ? (Connor et al '77)

"Type I" onset

Hodgkin ‘48
Wilson-Cowan Model

\[ \tau_e \frac{dP_{\text{ex}}}{dt} = -P_{\text{ex}} + S_e \left( a_{ee} P_{\text{ex}} - a_{ie} P_{\text{inh}} + J_e \right) \]
\[ \tau_i \frac{dP_{\text{inh}}}{dt} = -P_{\text{inh}} + S_i \left( a_{ei} P_{\text{ex}} - a_{ii} P_{\text{inh}} + J_i \right) \]

\( P_{\text{ex}}(t) \) and \( P_{\text{inh}}(t) \) are the relative (to max) activity or firing rate levels of the excitatory and inhibitory populations.

\( a_{jk} \) - effective weights for synaptic input from population j to population k.

\( S_e(x) \) and \( S_i(x) \) are the “sigmoidal” input/output functions of the two populations;
typically \( S(x) = \frac{1}{1+\exp((\theta-x)/k)} \) where
\( \theta \) is the activation threshold and \( k \) determines the sigmoid’s steepness (steeper for smaller \( k \)).

\( J_e, J_i \) -- inputs from external sources

Network has no spatial structure; cells are random and sparsely connected.

What are \( \tau_e \) and \( \tau_i \)?

**JR: recruitment time constants for the network.**

Wilson-Cowan Model
dynamics in the phase plane.

Phase plane, nullclines for range of $J_e$. 
Oscillator death

Regime of repetitive activity
"Oscillator Death" but cells are firing
ML: $\varphi$ intermediate

Upper state unstable, surrounded by stable oscill'n (via Hopf)

Response/bifur'cndiagram

bistability

Saddle-loop bifur'cn $T \sim \ln (1 - I_1)$
HH – N-shaped $I_{ss}$ for increased $[K^+]_{ext}$

Temperature 18.5° C

$V_K$ relative to “rest”, -65 mV
Transition from Excitable to Oscillatory

Type II, \( \text{min freq} \neq 0 \)
- \( I_{ss} \) monotonic
- subthreshold oscill’ns
- excitable w/o distinct threshold
- excitable w/ finite latency

Type I, \( \text{min freq} = 0 \)
- \( I_{ss} \) N-shaped – 3 steady states
- w/o subthreshold oscillations
- excitable w/ “all or none” (saddle) threshold
- excitable w/ infinite latency

Hodgkin ’48 – 2 classes of repetiitive firing;
Also - Class I less regular ISI near threshold
Threshold Firing Frequency–Current Relationships of Neurons in Rat Somatosensory Cortex: Type 1 and Type 2 Dynamics

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Tateno, T., A. Harsch, and H.P.C. Robinson. Threshold firing frequency–current relationships of neurons in rat somatosensory cortex: type 1 and type 2 dynamics. J Neurophysiol 92: 2283–2294, 2004; 10.1152/jn.00109.2004. Neurons and dynamical models of spike generation display two different types of threshold behavior, with steady current stimulation: type 1 [the firing frequency vs. current (f–I) relationship is continuous at threshold] and type 2 (discontinuous f–I). The dynamics at threshold can have profound effects on the encoding of input as spikes, the sensitivity of spike generation to input noise, and the coherence of population firing. We have examined the f–I and frequency–conductance (f–g) relationships of cells in layer 2/3 of slices of young (15–21 DIV) rat somatosensory cortex, focusing in detail on the nature of the threshold. Using white-noise stimulation, we also measured firing frequency and interspike interval variability as a function of noise amplitude. Regular-spiking (RS) pyramidal neurons show a type 1 threshold, consistent with their well-known ability to fire regularly at very low frequencies. In fast-spiking (FS) inhibitory interneurons, although regular firing is supported over a wide range of frequencies, there is a clear discontinuity in their f–I relationship at threshold (type 2), which has not previously been highlighted. FS neurons are unable to support maintained periodic firing below a critical frequency $f_c$, in the range of 10 to 30 Hz. Very close to threshold, FS cells switch irregularly between bursts of periodic firing and subthreshold oscillations. These characteristics mean that the dynamics of RS neurons are well suited to encoding inputs into low-frequency firing rates, whereas the dynamics of FS neurons are suited to maintaining and quickly synchronizing to gamma and higher-frequency input.

of these 2 types, which thus represent the behavior of a wide range of excitable membranes.

Even simple dynamical models of spike generation can exhibit both kinds of behavior, depending on their parameters (Morris and Lecar 1981; Rinzel and Ermentrout 1998). In these models, because of the different natures of dynamical bifurcation at threshold, type 1 behavior is associated with all-or-nothing spikes, whereas type 2 behavior is associated with graded spike amplitude and subthreshold oscillations. Recently, modeling studies have shown that the threshold type of the neuron profoundly affects the reliability of spike generation in the presence of noise (Gutkin and Ermentrout 1998; Robinson and Harsch 2002). Experimental classification of the responses of neurons in the cortex, however, has focused mostly on the form of the frequency vs. current (f–I) relationship in responses that are well above threshold (Connors and Gutnick 1990; Kawaguchi and Kubota 1997; Nowak et al. 2003); a clear classification of the continuity or discontinuity of the f–I relationship at threshold is lacking. Therefore in this paper we study the thresholds of 2 well-characterized types of cell—regular-spiking and fast-spiking neurons—and show that they follow type 1 and type 2 behaviors, respectively. We discuss what impact this could have on the roles of these 2 cell types in the cortical network.

METHODS
Noise smooths the f-I relation

frequency

Type II

Type I

I_{app}
Take Home Message

Excitability/Oscillations: fast autocatalysis + slower negative feedback

Value of reduced models

Time scales and dynamics

Phase space geometry

Different dynamic states – “Bifurcations”

XPP software: http://www.pitt.edu/~phase/ (Bard Ermentrout’s home page)