

CN510: Principles and Methods of Cognitive and Neural Modeling

Extensions and Simplifications of Hodgkin-Huxley Formalism

Lecture 6

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Hodgkin-Huxley or Conductance-Based Model

The general formalism is derived from the equivalent electrical circuit representing cell membrane

$$C_m \frac{dV_m}{dt} = \sum I \quad \text{or} \quad C_M \frac{dV_m}{dt} = \sum J$$

Hodgkin-Huxley is just a subcase

$$C_M \frac{dV_m}{dt} = g_K (V_m - E_K) + g_l (V_m - E_l) + g_{Na} (V_m - E_{Na})$$

Each conductance is a product of the maximal conductance \bar{g}_{ion} and a set of gating variables $\bar{g}_{ion} g_1^n g_2^k \dots$

where each gating variable $0 < g_i (V_m, t, \dots) < 1$ has opening and

$$\frac{dg_i}{dt} = \alpha (1 - g_i) - \beta g_i$$

closing functions determined experimentally

Assumptions of a Conductance-Based Model

The different ion channels in the cell membrane are independent from each other,

Activation and inactivation gating variables are voltage-dependent and independent of each other for a given ion channel type,

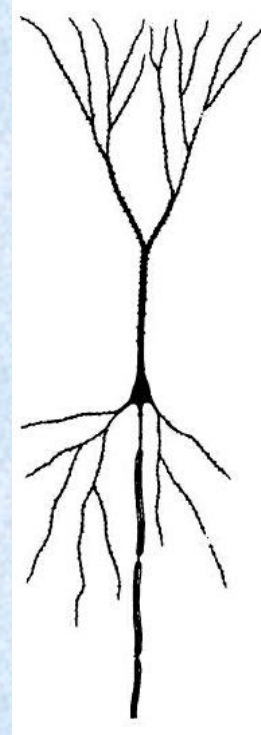
Each gating variable follows first-order kinetics

$$\frac{dg}{dt} = \alpha(1 - g) - \beta g$$

The model cell is isopotential: V_m is identical across the cell, cell is reduced to a point

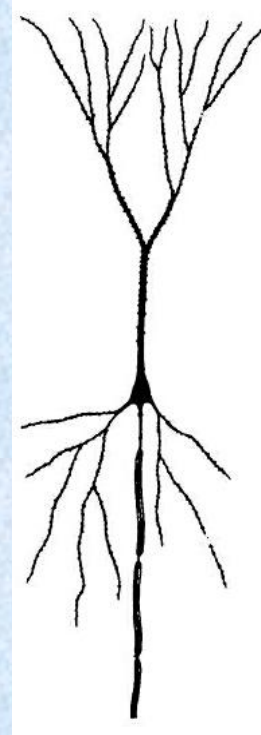
Hopefully such point neurons are as useful as point masses in physics

Moving to More Realistic Neurons



Spatial distribution of channels is largely unknown
Unless you have the data the model will be garbage
Blue Brain project is designed to build a database of these
distributions as well as cell geometries

Moving to More Realistic Neurons



Our differential equation for non-point neuron shall include space derivatives in addition to time derivatives

$$C_M \frac{\partial}{\partial t} V(x,t) = J_A + g_L(x)(E_L - V(x,t)) + \bar{g}_K n^4(x,t)(E_K - V(x,t)) \\ + \bar{g}_{Na} m^3(x,t)h(x,t)(E_{Na} - V(x,t))$$

Cable Equation

$$C_M \frac{\partial}{\partial t} V(x,t) = J_A + g_L(x)(E_L - V(x,t)) + \bar{g}_K n^4(x,t)(E_K - V(x,t)) \\ + \bar{g}_{Na} m^3(x,t)h(x,t)(E_{Na} - V(x,t))$$

Membrane
area

Since $I_A = \frac{\pi d^2}{4r_A} \frac{\partial V(x,t)}{\partial x}$ then

$$I_A = \frac{\pi d^2}{4r_A} \frac{\partial V(x,t)}{\partial x}$$

Area of
crosssection

Voltage
gradient

$$J_A = \frac{\pi d^2}{4r_A} \frac{\partial V(x,t)}{\partial x} \frac{1}{\pi d \Delta x} = \frac{d}{4r_A} \frac{\partial V(x,t)}{\partial x} \frac{1}{\Delta x}$$

$$\rightarrow \frac{d}{4r_A} \frac{\partial}{\partial x} \left(\frac{\partial V(x,t)}{\partial x} \right) = \frac{d}{4r_A} \frac{\partial^2 V(x,t)}{\partial x^2}$$

and

$$C_M \frac{\partial}{\partial t} V(x,t) = g_L(x)(E_L - V(x,t)) + \bar{g}_K n^4(x,t)(E_K - V(x,t)) \\ + \bar{g}_{Na} m^3(x,t)h(x,t)(E_{Na} - V(x,t)) + \frac{d}{4r_A} \frac{\partial^2 V(x,t)}{\partial x^2}$$

Simplification for a Passive Dendrite

Removing HH currents:
$$C_M \frac{\partial}{\partial t} V(x,t) = -g_L V(x,t) + \frac{d}{4r_A} \frac{\partial^2 V(x,t)}{\partial x^2}$$

And multiplying both sides by membrane resistance $R_M = 1/g_L$

$$\tau_m \frac{\partial}{\partial t} V(x,t) = -V(x,t) + \frac{dR_m}{4r_A} \frac{\partial^2 V(x,t)}{\partial x^2}$$

where $C_M R_M = \tau_m$ is a membrane time constant and defining

$$\lambda = \sqrt{\frac{dR_M}{4r_A}} \text{ electrotonic length} \quad \tau_m \frac{\partial}{\partial t} V(x,t) = -V(x,t) + \lambda^2 \frac{\partial^2 V(x,t)}{\partial x^2}$$

This can be solved analytically for various simple cases

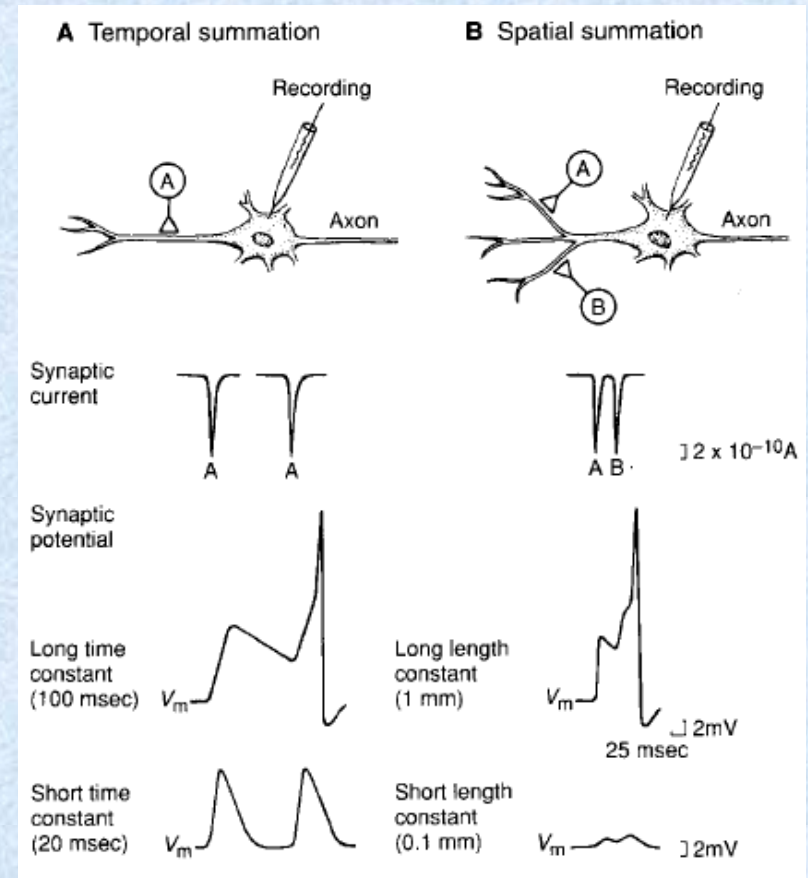
Length Constant and Time Constant

If we fix the voltage at one end of the cable

$$\lambda = \sqrt{\frac{dR_M}{4r_A}}$$

defines how long a cable shall be to attenuate the voltage by a factor of e

length constant determines the amount of degradation a postsynaptic potential undergoes per unit distance



Spatial summation is the process of summing PSPs from different synapses

Length Constant and Time Constant

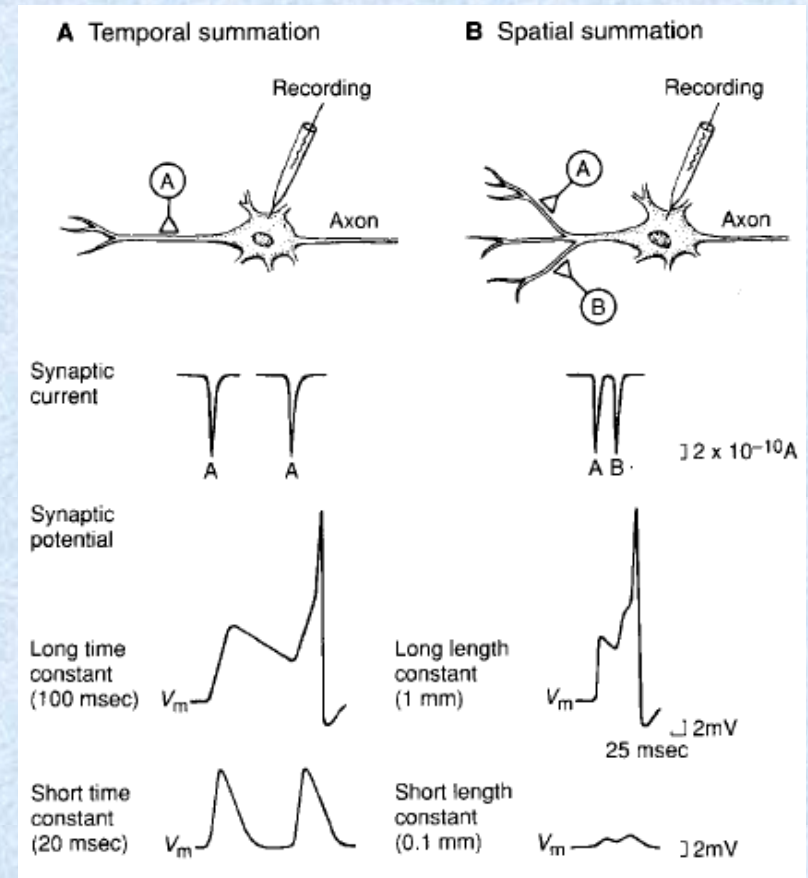
If we apply the current at a point (no cable here)

$$\tau_m = C_M R_M$$

determines how much time it will take to change the voltage by a factor of e

time constant determines how fast a postsynaptic potential decays

Temporal summation is the process of summing consecutive PSPs at the same synapse



Length Constant and Time Constant

From $\lambda = \sqrt{\frac{dR_M}{4r_A}}$ you can see that attenuation in thicker segments is less than in thinner segments

So signal decays more on the way from remote dendritic segment towards soma than on the way from soma towards dendrites

From $C_M R_M = \tau_m$ you can see that the lower the leakage the slower you can charge the cell

Same as in your homework: increase of A makes the exponent steeper

Thus, to accurately determine whether a neuron will fire an action potential in response to several synaptic inputs, we need to know:

- The firing threshold at the trigger zone
- Whether synaptic inputs are excitatory or inhibitory
- The strength of the synaptic inputs
- How far the synapses are from the trigger zone
- What the length constant of the cell is
- How close together in time PSPs occur
- What the time constant of the cell is
- ...

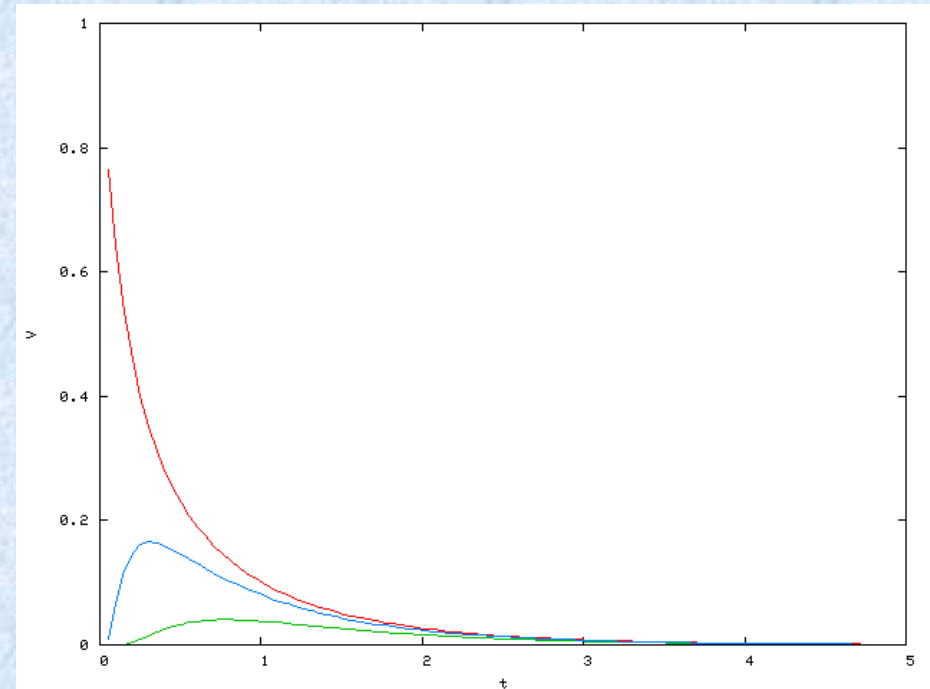
Not just the simple “weighted sum and threshold” process typically used in neural network models!

Combination of Spatial and Temporal Effect

Instantaneous current pulse is injected

In close proximity of injection the voltage goes up very fast and high, then decays (red)

Further away it takes time to build up, and spatial attenuation makes the peak not as high (blue)



Even further away both temporal delay and spatial attenuation become even more pronounced (green)

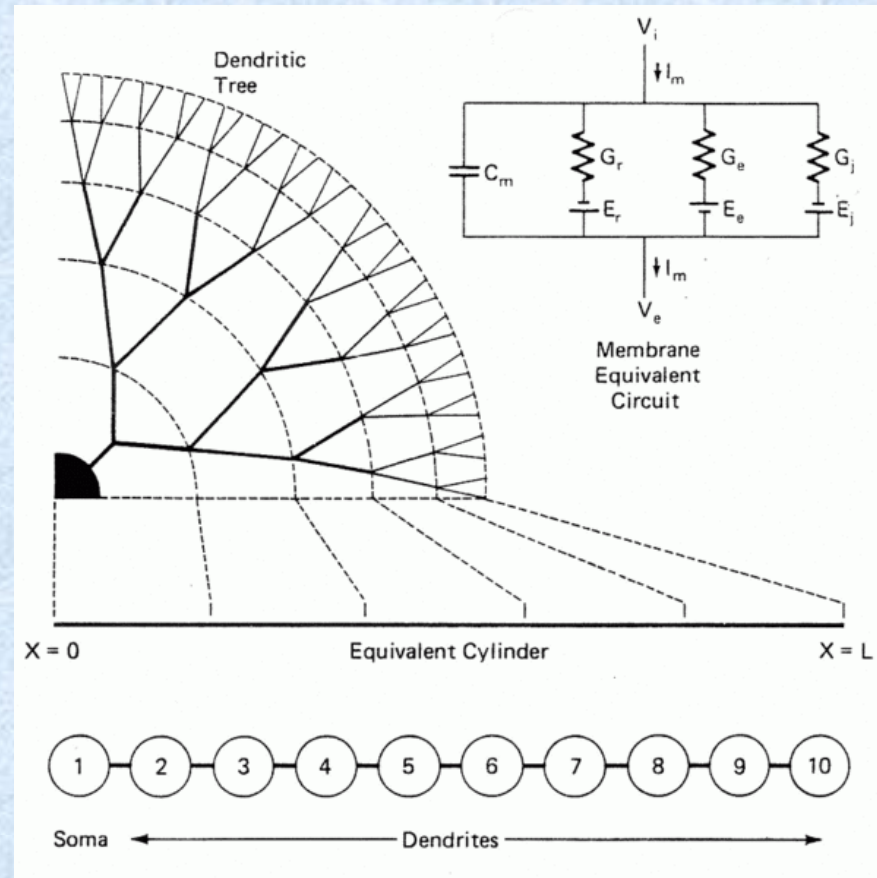
Rall Model

Cable equation simplifies neuronal geometry from 3D to 1D

Wilfrid Rall suggested that if a complicated dendritic tree follows a few rules, then it can be mapped to an equivalent 1D cylinder

- Branching is symmetric
- Each branch follows $d^{3/2}$ rule:

$$d_{parent}^{3/2} = d_{branch1}^{3/2} + d_{branch2}^{3/2}$$



$d^{3/2}$ rule does not hold for many cells including pyramidal cells, more general solution can be used to approximate these

Compartmental Model from Cable Equation

$$C_m \frac{\partial}{\partial t} V(x,t) = g_L(x)(E_L - V(x,t)) + \bar{g}_K n^4(x,t)(E_K - V(x,t)) + \bar{g}_{Na} m^3(x,t)h(x,t)(E_{Na} - V(x,t)) + \frac{d}{4r_A} \frac{\partial^2 V(x,t)}{\partial x^2}$$

Make space discret:

$$C_m \frac{d}{dt} V^i(t) = g_L^i (E_L^i - V^i(t)) + \bar{g}_K^i n_i^4(t) (E_K^i - V^i(t)) + \bar{g}_{Na}^i m_i^3(t) h_i(t) (E_{Na}^i - V^i(t)) + \frac{d_i}{4r_A^i} \frac{V^{i-1}(t) - 2V^i(t) + V^{i+1}(t)}{l_i^2}$$

Results in a system of ODEs – one (or more if conductances are HH) for each segment or compartment

Replacing Space Derivative with Diffusion

In the most general case $\frac{d_i}{4r_A^i} \frac{V^{i-1}(t) - 2V^i(t) + V^{i+1}(t)}{l_i^2}$

can be rewritten as two diffusion currents

$$g_- (V^{i-1}(t) - V^i(t)) + g_+ (V^{i+1}(t) - V^i(t))$$

where conductances are determined from the axial resistances between compartments, their lengths and diameters

Branching can be easily implemented by adding more currents like these above, so no need to collapse into a single cable

Problems with Conductance-based Models

As the number of currents included in the model expands, it becomes more difficult to

- understand and predict the resulting model dynamics
- numerically simulate the cell

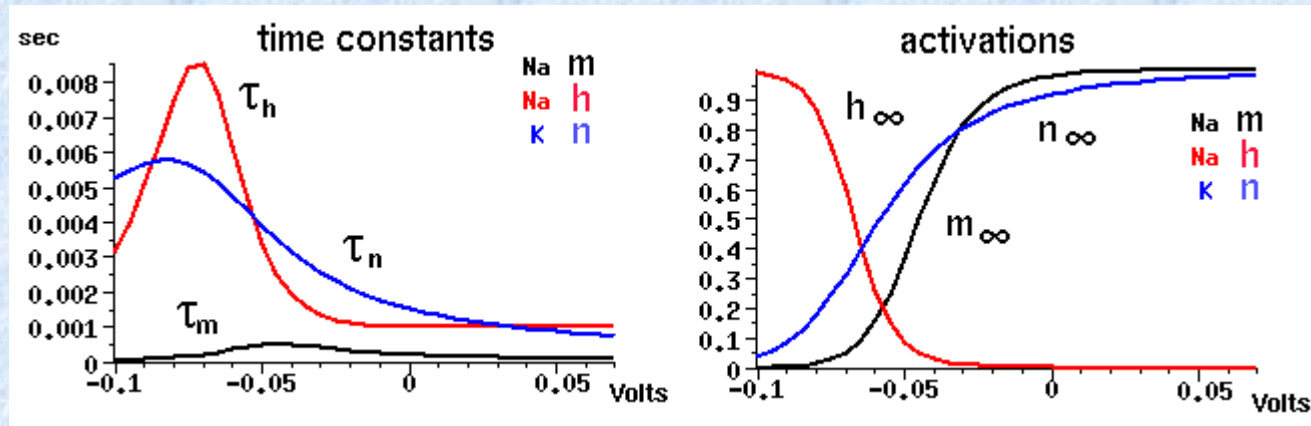
due to the increasing number of differential equations

Efforts have been made

- to capture the qualitative dynamics of conductance-based models with fewer variables
- mathematically analyze distinctions in conductance-based models using dynamical system and bifurcation analyses

These usually only consider spike-producing currents

Hodgkin Huxley Reduction



Assume the change in m as instantaneous: reasonable because m is very fast

Merge together the properties of slow closing Na and slow opening K channels (h and n): reasonable because both are slow and lead to decrease in positive current or increase in negative current

Substitute simple functions for $m(V_m)$ and $dn/dt=f(V_m)$

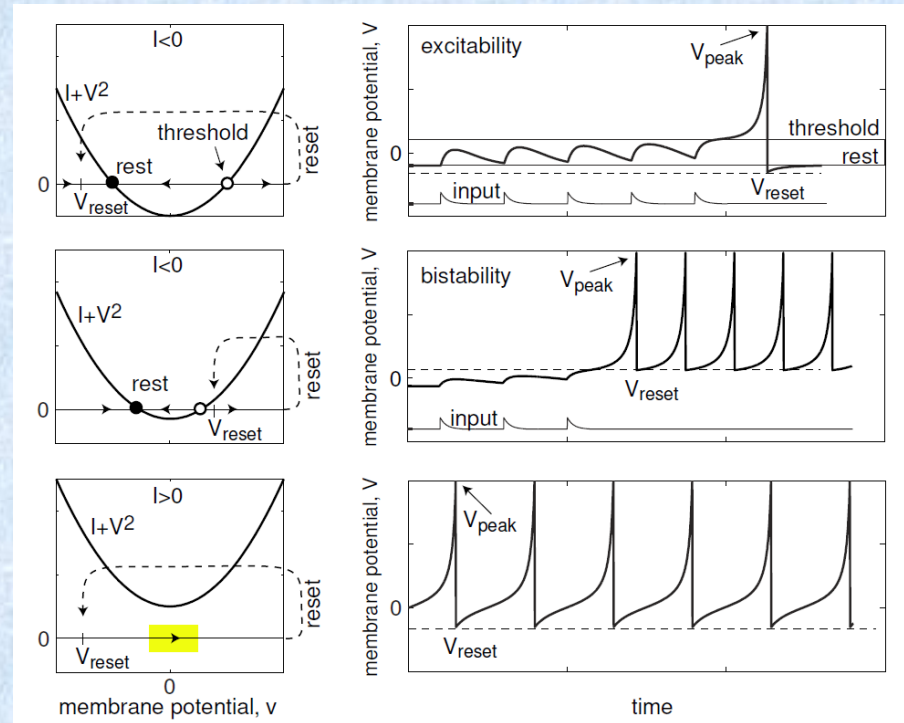
Quadratic Integrate-and-Fire

To mimic fast positive feedback of Na current we have quadratic term in the derivative:

$$\frac{dV}{dt} = aV^2 - b + I$$

With small pulse inputs – integrates them until passes the unstable critical point, then spikes and resets

With large constant input – fires continuously



Increasing the input current shifts the curve up until two critical points merge and disappear – saddle-node bifurcation

Ermentrout-Kopell Canonical Neuron

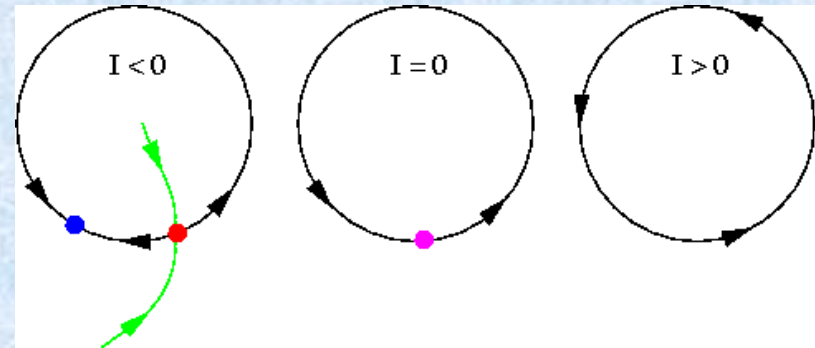
Also known as theta neuron

Basically quadratic integrate-and-fire transformed into polar coordinates ($V = \tan(\theta/2)$) to eliminate discontinuity and simplify the analysis

$$\frac{d\theta}{dt} = 1 - \cos \theta + (1 + \cos \theta)I(t)$$

Spike is produced when θ crosses π

Same regimes as in qIaF



Note that to do proper extensions of this model you need

- first create a modified version of qIaF
- and then apply a variable substitution $V = \tan(\theta/2)$

FitzHugh-Nagumo Model

Cubic nonlinearity for voltage
allows fast positive feedback

Linear recovery variable allows
slow negative feedback

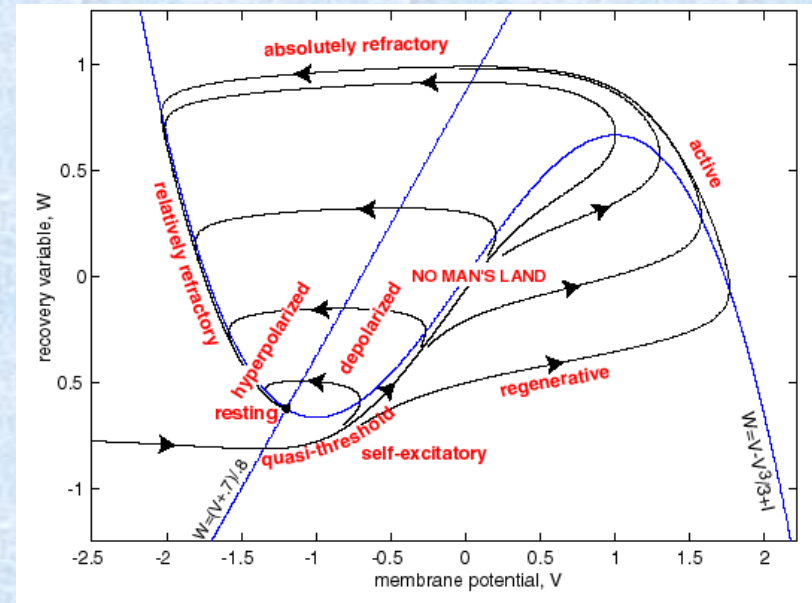
$$\frac{dV}{dt} = f(V) - u + I$$

$$\frac{du}{dt} = a(bV + c - u)$$

Condition on parameters: only
one critical point

$$\frac{dV}{dt} = V - \frac{V^3}{3} - u + I$$

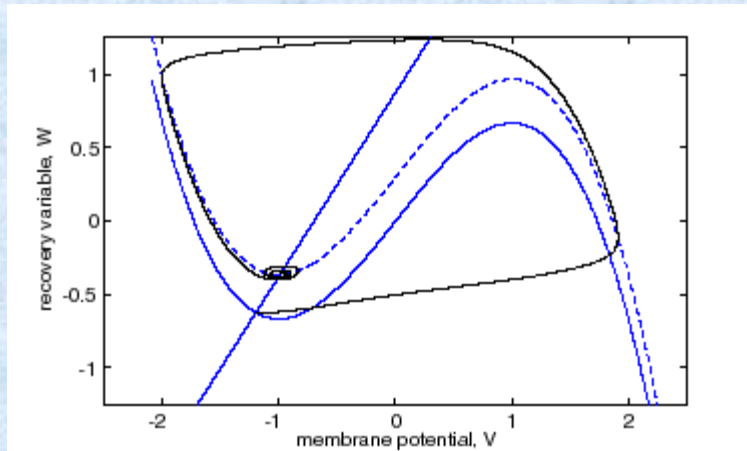
$$\frac{du}{dt} = 0.08(V + 0.7 - 0.8u)$$



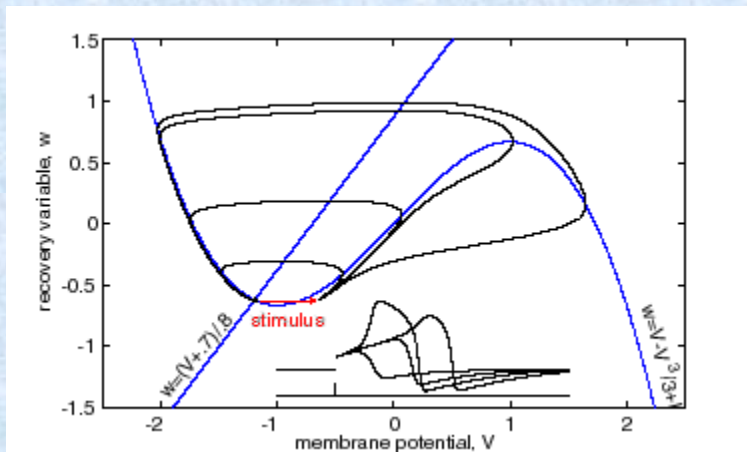
Below cubic nullcline
solution goes to the right,
above – to the left

To the left of linear nulcline
solution goes down, to the
right – up

FitzHugh-Nagumo Model



Injected current I shifts cubic nullcline up: slow shift – depolarization, fast or deep shift – spike



Model shows no fixed threshold, variable spike amplitude, release from inhibition spiking and other properties of HH model

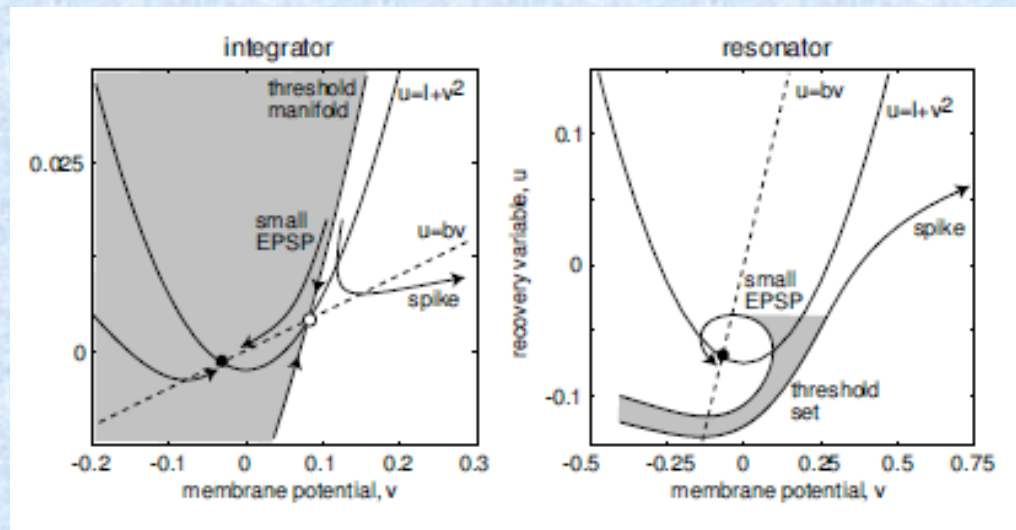
Izhikevich (Simple) Neuron

A combination of quadratic IaF and recovery variable similar to the one in FitzHugh-Nagumo

$$\frac{dV}{dt} = 0.04V^2 + 5V + 140 - u + I$$

$$\frac{du}{dt} = a(bV - u)$$

V has to be checked against peak spike amplitude and if needed reset to c , at this moment $u = u + d$

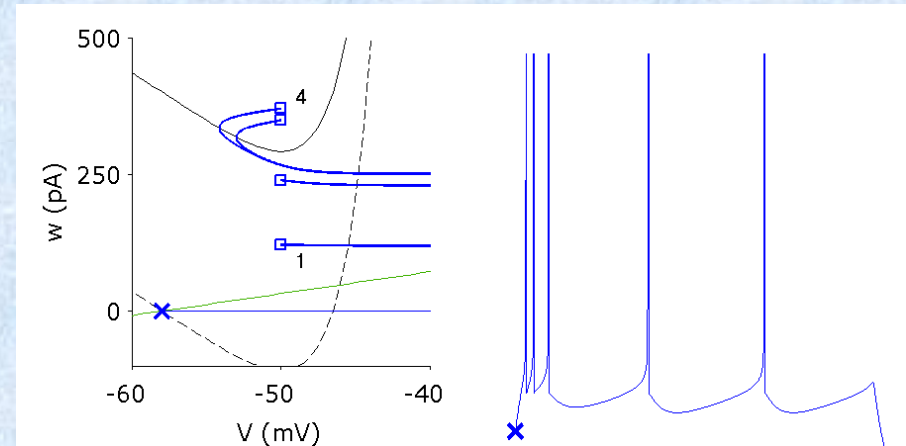


Adaptive Exponential IaF

Same bifurcation patterns as Izhikevich neuron

Both are easy to implement

Both account for a variety of firing patterns



Better quantitative fit

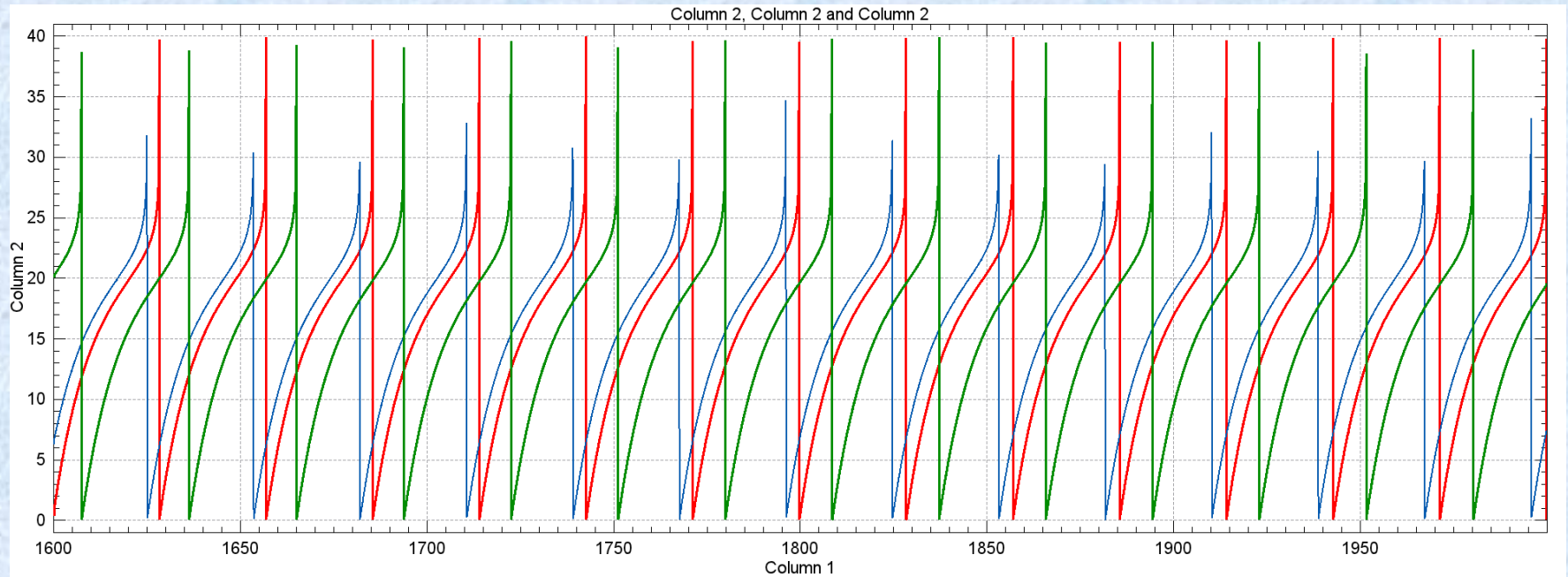
Better shape of the upswing of action potential

Higher requirements for integration method precision

$$\frac{dV}{dt} = g_L \Delta_T \exp\left(\frac{V - V_T}{\Delta_T}\right) - u + I$$

$$\frac{du}{dt} = a(bV - u)$$

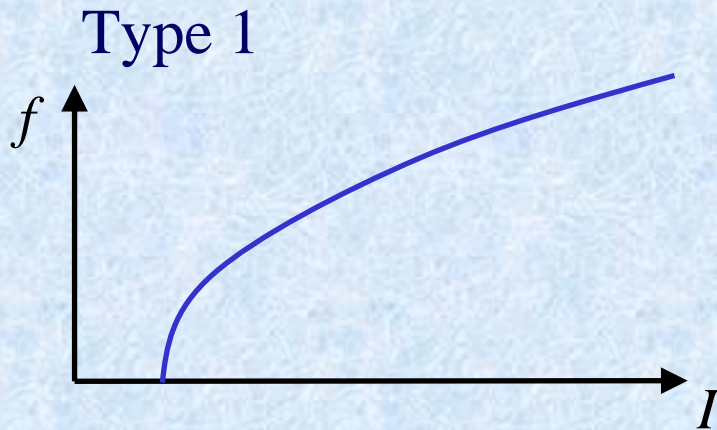
Quote from the Inventor



Me: I tried forward 4-th order Runge Kutta, and it is incredibly inefficient. It approaches the variable step solution with the decrease in step size, but these are very short steps (green plot 0.25 microseconds, red 0.125 us)

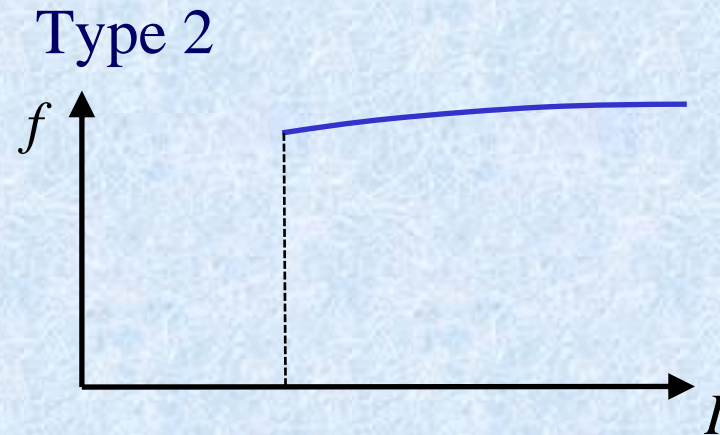
Romain Brette: ... it's normal that you get a drift in such a condition ... Anyway: personally I tend to use standard IF models, rather than AdEx.

Excitability Types



An arbitrary low firing frequency can be set by an appropriate input

The relationship between I and f does not saturate; square root type curve

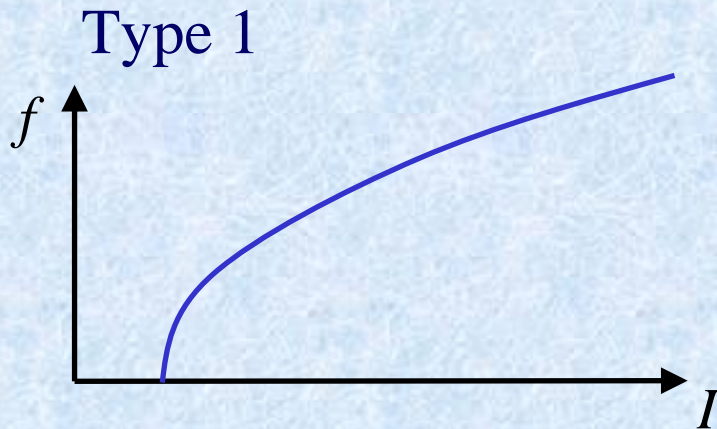


Lower frequencies are impossible

The relationship between I and f is almost flat

Basically, a neuron has an intrinsic frequency and fires close to it when input is strong enough

Excitability Types

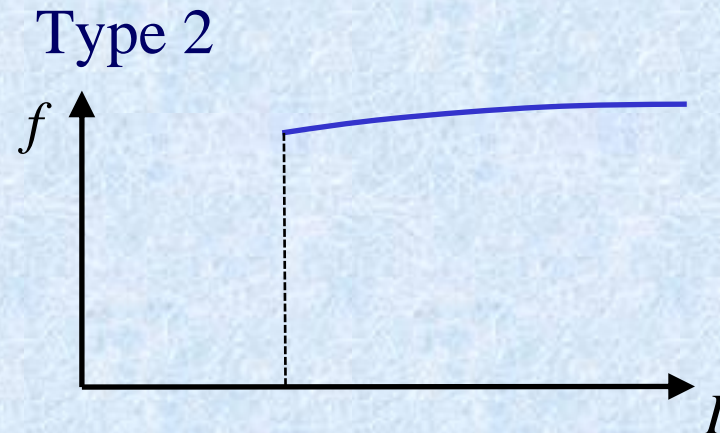


Quadratic IaF

Ermentrout-Kopell model

Some regimes of Izhikevich
and AdEx neurons

Some regimes of Morris-
Lecar model



Hodgkin-Huxley model

FitzHugh-Nagumo model

Resonate-and-Fire model by
Izhikevich

Some regimes of Izhikevich
and AdEx neurons

Some regimes of Morris-Lecar
model

Neuron Equation	Integration method	Runtime	RHS Evaluations	Step size/Tolerance
Reduced Hodgkin-Huxley 50s	Functional-Adams	3.54s	5193215	4.00E-07
	Functional-BDF	3.21s	5691091	2.00E-07
	Runge-Kutta 4	11.55s	50000000	0.008ms
Leaky Iaf 50s	Functional-Adams	0.13s	216104	8.00E-06
	Functional-BDF	0.18s	315843	4.00E-06
	Runge-Kutta 4	0.15s	2683232	0.15ms
Adaptive Leaky Iaf 50s	Functional-Adams	0.21s	330500	1.00E-05
	Functional-BDF	0.25s	411942	1.25E-05
	Runge-Kutta 4	>256.3s		<0.000125ms
FitzHugh-Nagumo 50s	Functional-Adams	0.70s	1181251	9.00E-07
	Functional-BDF	0.55s	1137532	8.00E-07
	Runge-Kutta 4	0.39s	4444448	0.09ms
Exponential Iaf 50s	Functional-Adams	0.66s	1360126	1.80E-07
	Functional-BDF	0.65s	1611657	1.80E-07
	Runge-Kutta 4	42.99s		0.00085ms
Adaptive Exponential Iaf 50s	Functional-Adams	0.67s	1198098	2.00E-07
	Functional-BDF	0.63s	1270166	2.90E-07
	Runge-Kutta 4	413.17s		0.00011ms
Quadratic Iaf 50s	Functional-Adams	0.29s	534948	8.10E-07
	Functional-BDF	0.33s	761431	5.10E-07
	Runge-Kutta 4	0.58s	8909584	0.045ms
Izhikevich (Adaptive Quadratic Iaf) 50s	Functional-Adams	0.26s	471770	2.80E-07
	Functional-BDF	0.33s	607503	2.00E-07
	Runge-Kutta 4	39.66s		0.00085ms

Optimal

Prohibitive

Next Time

Consideration of the need to factorize an input pattern from the total input energy leads to the shunting network

Feedforward shunting network properties of automatic gain control and activity normalization are addressed

Readings:

- Appendix C of Grossberg, S. (1980). How does the brain build a cognitive code? *Psychological Review*, **87**, pp. 1-51. [SMB Chapter 1; NFR Chapter 24.]

Homework due:

Numerical Integration of Leaky Integrator and Leaky IaF assignment is due before the class starts