Theoretical & computational Neuroscience:

Programming the Brain

(BM 6330)

3-credit

H-H model : A 4-variable model

- A case for simplification
- Lesser number of variables makes it easier to compute and visualize

Reduction by Rinzel in

- "On repetitive activity of nerve" , Rinzel, 1978

Hodgkin-Huxley equations
Which variables are redundant ? (Relatively)

$$
\begin{aligned}
I_{inj} &= C_m . \frac{dV}{dt} + I_{ion}(V,t) \\
I_{ion}(V,t) &= g_{Na}(V,t).(V - E_{Na}) + g_K(V,t).(V - E_K) + g_L.(V - E_L) \\
g_{Na}(V,t) &= m^3(V,t).h(V,t).\bar{g}_{Na}(V - E_{Na}) \\
g_K(V,t) &= n^4.(V,t).\bar{g}_K(V - E_K) \\
\frac{dm}{dt} &= \frac{m_\infty(V) - m}{\tau_m(V)} \\
\frac{dn}{dt} &= \frac{n_\infty(V) - n}{\tau_n(V)} \\
\frac{dh}{dt} &= \frac{h_\infty(V) - h}{\tau_h(V)}
\end{aligned}
$$

$$
where\ x_\infty = \frac{\alpha_x}{\alpha_x + \beta_x}\ and\ \tau_x = \frac{1}{\alpha_x + \beta_x}
$$

Note that $h_\infty < h_0$, $n_\infty > n_0$ and $m > m_0$

Class project:
Plot neuron trajectory on phase plane and find redundant dimensions ??

PCA ??

How do you make the system 2-dimensional ? Which dimensions should be eliminated ?

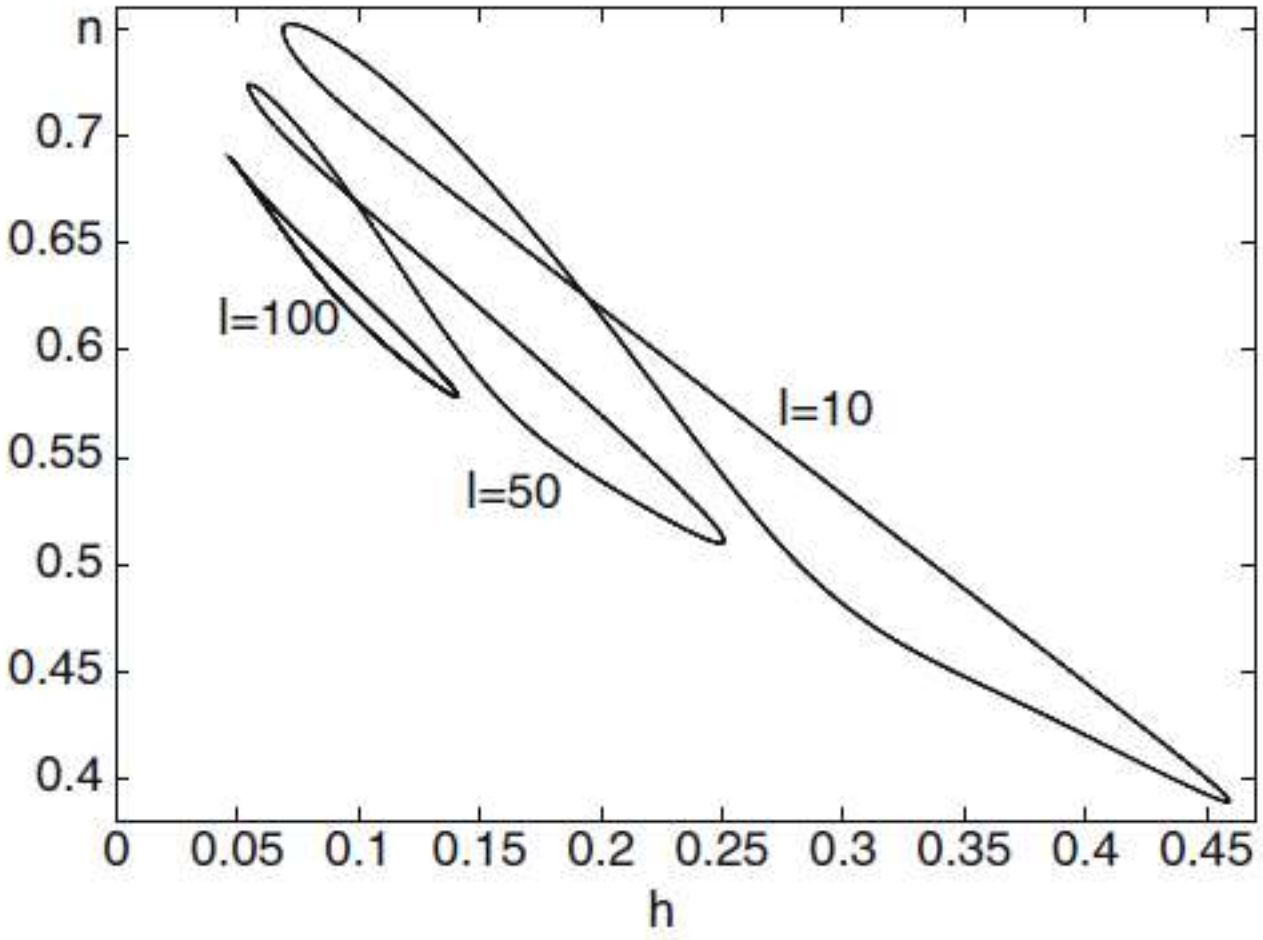
Entire dimension or combinations of elements ?

m is fast !

- Assume τ_m is very small, assume m = m_∞

(n,h) lies on a straight line

One of n and h (usually h) can be eliminated



Mathematical foundations of Neuroscience
Bard Ermentrout and Dave Terman

Variants

- This simplification leaves us with a 2-variable model.
- Many rearrangements of terms and approximations may be used to come up with different forms of 2-variable neuron model
- E.g:
- Fitzhugh-Nagumo
- Morris-Lecar
- Izhikevich

Phase planes

- Let $(x_1,x_2\ldots x_n)$ be the state of the system given by the system of equations

$$\frac{dx_i}{dt} = f_i(x_1,..x_n\,)$$

- Evolution of the system starting from (x_0,y_0) can be represented as a trajectory in the n-dimensional space :
- The vector $[\frac{dx_1}{dt},..\frac{dx_n}{dt}]$ gives the velocity of the at point $(x_1,x_2\ldots x_n)$ in phase space.

- This is easier visualized in a 2-d system : "Phase Plane" method

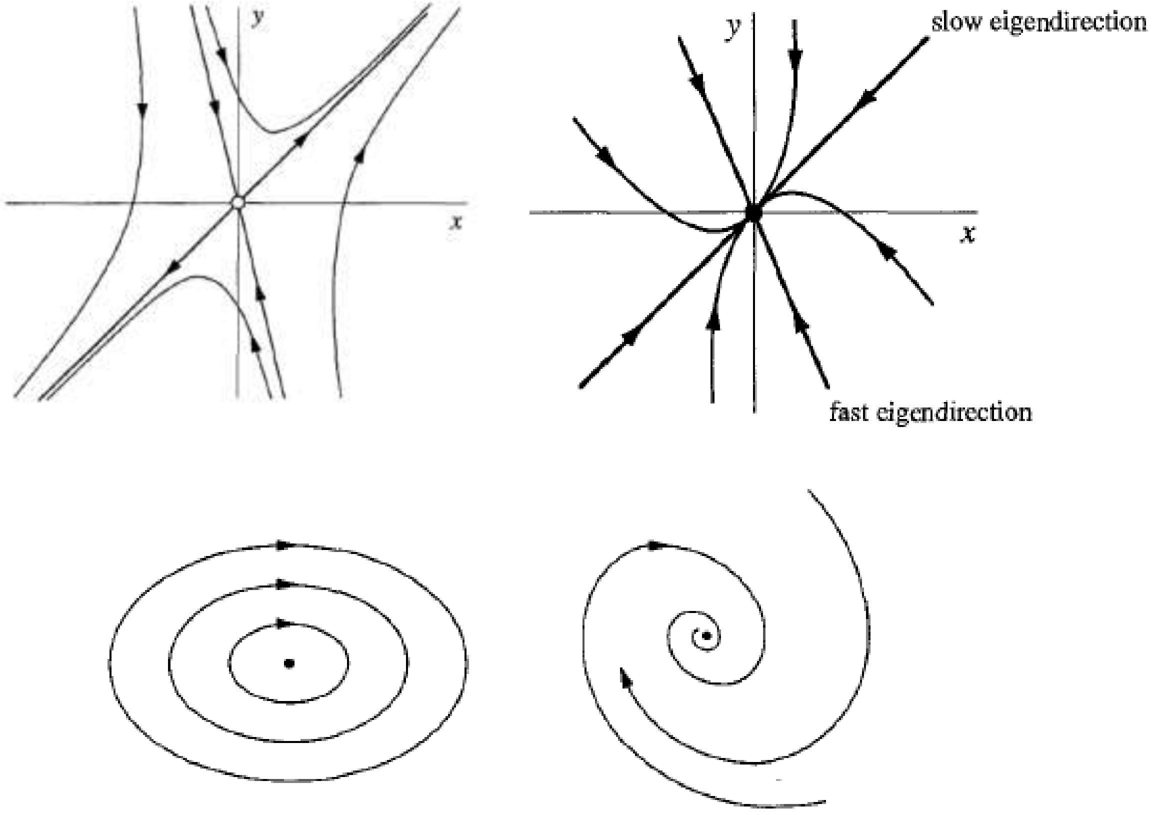
- One of the motivations for reducing 4-variable HH model to 2-variable models

Linear system

- If all functions f_i are linear in x_i , the system is linear and can be described in matrix notation as
- $\dot{x} = A.x$, $where\ x =$ $[x_1, x_2 \dots xn]^T$
- Solutions of $A.x = 0$ are fixed points {Velocity is zero}
- What do the eigen values and eigen vectors of A tell us ? Hint : compute trajectory starting from an eigen vector ?
-

Eigen values and vectors of system transformation matrix A

- Consider 2-variable system
- Both eigen values real , negative : stable
- One positive, other negative : saddle node
- complex eigen values : centres and spirals
- Stability of fixed points ? Perturb from fixed point and see if trajectory leads back.



(a) center (b) spiral

Non linear dynamics and chaos, Strogatz

In a non linear system

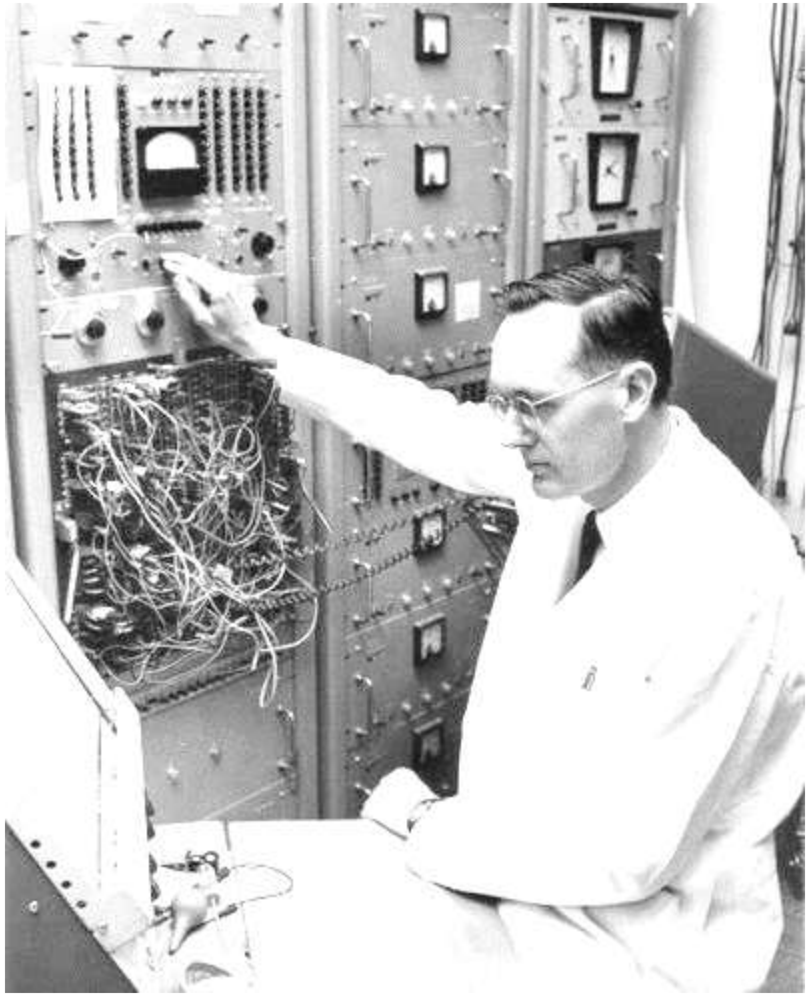
- No eigen value and vector !!
- Approximation : In the vicinity of a fixed point perform linearization (similar to Taylor series expansion)
- $\dot{x} = J.x$, where J is the Jacobian computed at the fixed point
- Can be used to analytically prove stability of fixed point provided linearization errors are negligible

Numerical simulation

Numerically compute $\dot{x}$ fields !!

Fitzhugh-Nagumo

$$v' = v - \frac{v^3}{3} - w + I$$
$$w' = \epsilon(b_o + b_1 v - w)$$



How do b0, b1 change the nullcline ?

How does I change nullcline

Where is the fixed point ?
Put states[0] at fp... What do you see?

Put states[0] small distance away from fp in all direct
What do you see ?

What property are you testing?

Stability!!

.

.

.

Do it for all fixed points

See phase plane with I =0 and I positive and then I=0

Change parameters so that you get only 1 spike...(no

Change parameters so neuron fires repeatedly ???
never stops....

How would you do it ?

Change parameters so neuron fires repeatedly ???
never stops....

How would you do it ?

Change parameters such that :

At small currents neuron is at rest

At larger currents, fires repeatedly

At large currents gets stuck at high depolarised poter

Keep w nullcline tangential to middle branch !

Now plot I vs the position of fp…

Morris-Lecar model

$$C_{\mathrm{M}}\frac{\mathrm{d}V}{\mathrm{d}t} = I_{\mathrm{app}} - g_{\mathrm{L}}(V - E_{\mathrm{L}}) - g_{\mathrm{K}}n(V - E_{\mathrm{K}}),$$
$$-g_{\mathrm{Ca}}m_{\infty}(V)(V - E_{\mathrm{Ca}}) \equiv I_{\mathrm{app}} - I_{\mathrm{ion}}(V, n),$$
$$\frac{\mathrm{d}n}{\mathrm{d}t} = \phi(n_{\infty}(V) - n)/\tau_n(V),$$

where

$$m_{\infty}(V) = \frac{1}{2}[1 + \tanh((V - V_1)/V_2)],$$
$$\tau_n(V) = 1/\cosh((V - V_3)/(2V_4)),$$
$$n_{\infty}(V) = \frac{1}{2}[1 + \tanh((V - V_3)/V_4)].$$

Parameter sets for Morris-Lecar neurons

Parameter	Hopf	SNLC
ϕ	0.04	0.067
g_{Ca}	4.4	4
V_3	2	12
V_4	30	17.4
E_{Ca}	120	120
E_{K}	−84	−84
E_{L}	−60	−60
g_{K}	8	8
g_{L}	2	2
V_1	−1.2	−1.2
V_2	18	18
C_{M}	20	20

SNLC saddle–node on a limit cycle

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Try Hopf parameter set...

Change I ($85<I<90$) and tabulate the number of spike

.

.

plot the f-I curve...

Try SNLC parameter set...

Change I (39<I<41) and tabulate the number of spike

.

.

plot the f-I curve...

What differences did you notice ?

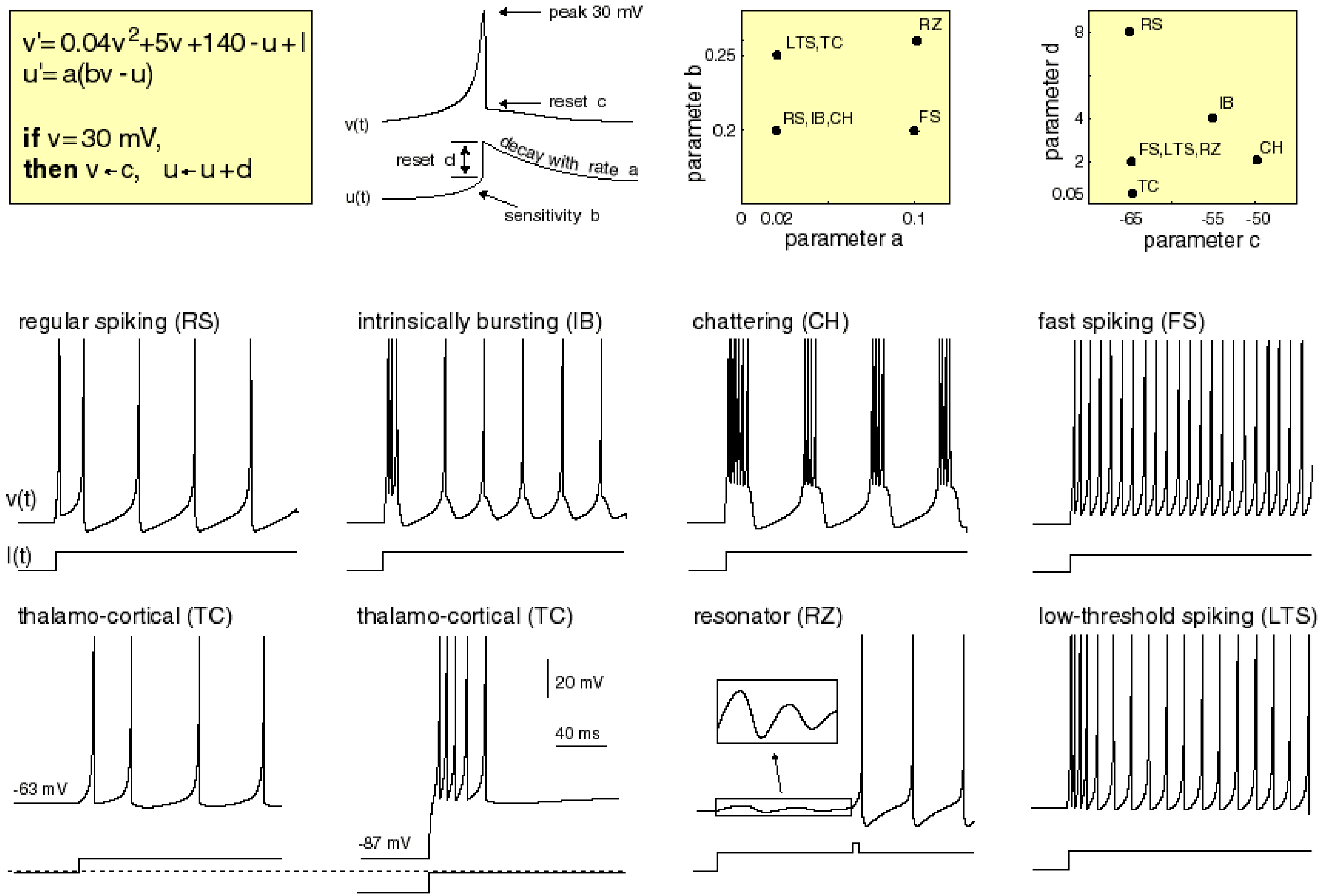
What causes the difference ?
Look at the nullclines carefully !!

Izhikevich model

$$v' = 0.04v^2 + 5v + 140 - u + I$$
$$u' = a(bv - u)$$

$$If v = 30mV,$$
$$then$$
$$v = c,$$
$$u = u + d$$

Izhikevich model



Assignment !!
Try out all parameter sets

Integrate and fire

$$v' = \frac{-(v - E_L)}{RC_M} + \frac{I}{C_M}$$
$$If v \geq \theta$$
$$then$$
$$firespike, resetv = v_{RMP}$$

Integrate-Fire

On your own ! You are at sea with the snakes... swim to survive !!

References

- Mathematical foundations of Neuroscience
- - Bard Ermentrout

Simple neuron models

- 4-variable model

–E.g.

Hodgkin-Huxley

- 2-variable models

–E.g.

Fitzhugh Nagumo

Morris-Lecar

Izhikevich

- 1-variable model

Integrate and Fire