10/19/04

real scientists ↓

Experimental observations → equations → solutions → predictions

easy numerical problem → solutions

predictions → Experimental observations: in an ideal world

Two things changed this view:

1. The open question is: how do low level eqns. (e.g. HH) describe high level behavior (e.g. people).

2. "Easy" numerical problem isn't. Often easy should be replaced by impossible.

So, people started studying equations and their solutions. (Dynamical systems a.k.a. chaos theory).

Questions:

1. Do equations fall into distinct classes, w/ each class having characteristic solutions? Sort of

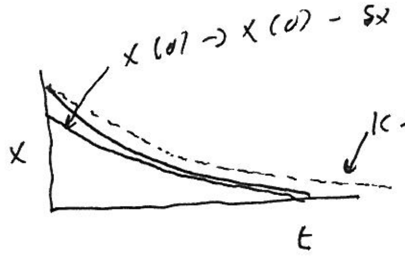
2. What equation can be solved? depends on (?)

3. What does question (2) mean? hard

4. Are solutions to equations sensitive to ~~usually~~ almost always
   a) initial conditions?
   b) parameters? ~~of eqn~~

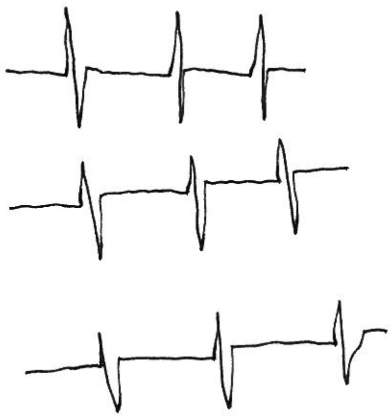
Examples:

$$\frac{dx}{dt} = -kx$$



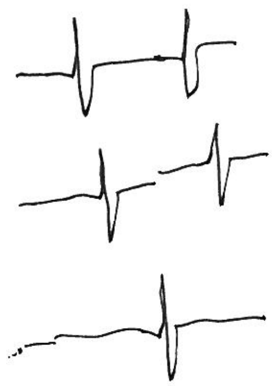

differ in I.C.

differ param

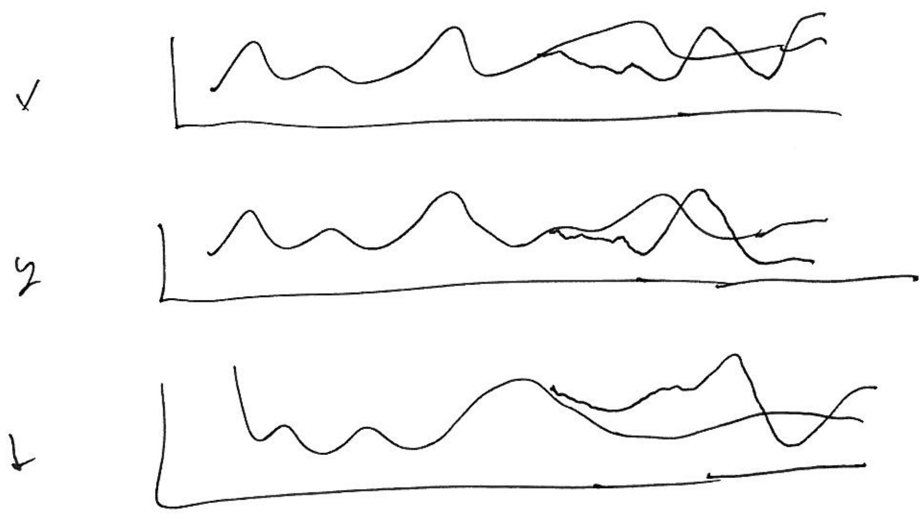


~~differ I.C.~~ - - -

~~differ~~



Edward Lorenz (~1960)




~~Ch~~

Birth of a field

We're going to use some of these techniques to examine spiking neurons, starting with HH.

$$\tau \frac{dV}{dt} = F(V,m,h,n) + I$$

$$F(V,m,h,n) = -(V-E_L) - \bar{\rho}_{Na}\, m^3 h\,(V-E_{Na}) - \bar{\rho}_K\, n^4 (V-E_K)$$

$$\tau = \frac{C_m}{\bar{g}_L} = C_m R_m$$

$$\bar{\rho}_{Na} = \frac{\bar{g}_{Na}}{\bar{g}_L} \qquad \bar{\rho}_K = \frac{\bar{g}_K}{\bar{g}_L}$$

$$\tau_m(V)\frac{dm}{dt} = m_\infty(V) - m$$

$$\tau_h(V)\frac{dh}{dt} = h_\infty(V) - h$$

$$\tau_n(V)\frac{dn}{dt} = n_\infty(V) - n$$

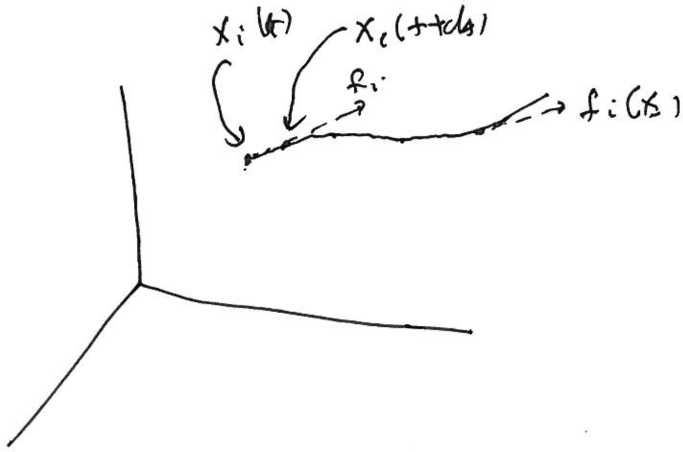
$\boxed{\text{4-D ODE!!!}}$

Aside on solutions to equations

$$\frac{dx_i}{dt} = f_i(\underline{x}) \quad \leftarrow x_1, x_2 \ldots$$

$$x_i(t+dt) \simeq x_i(t) + \frac{dx_i}{dt}\, dt$$

$$= x_i(t) + f_i(\underline{x})\, dt$$




- Solutions are trajectories
- $\underline{f}$ is vector field

Problem: go from vector field to trajectories

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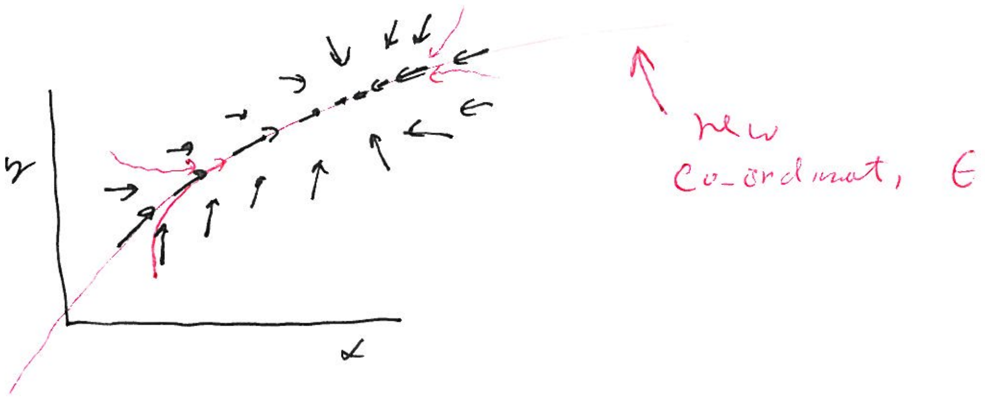
# Dimensionality reduction




$$\frac{dx}{dt} = f_x(x,y)$$

$$\frac{dy}{dt} = f_y(x,y)$$

$$\Rightarrow \quad \frac{d\theta}{dt} = F(\theta)$$

The plan: find ~~strongly attracting~~ attractors

$\infty$-dimensional ODE's (AKA PDE's) can have finite dimensional attractors!

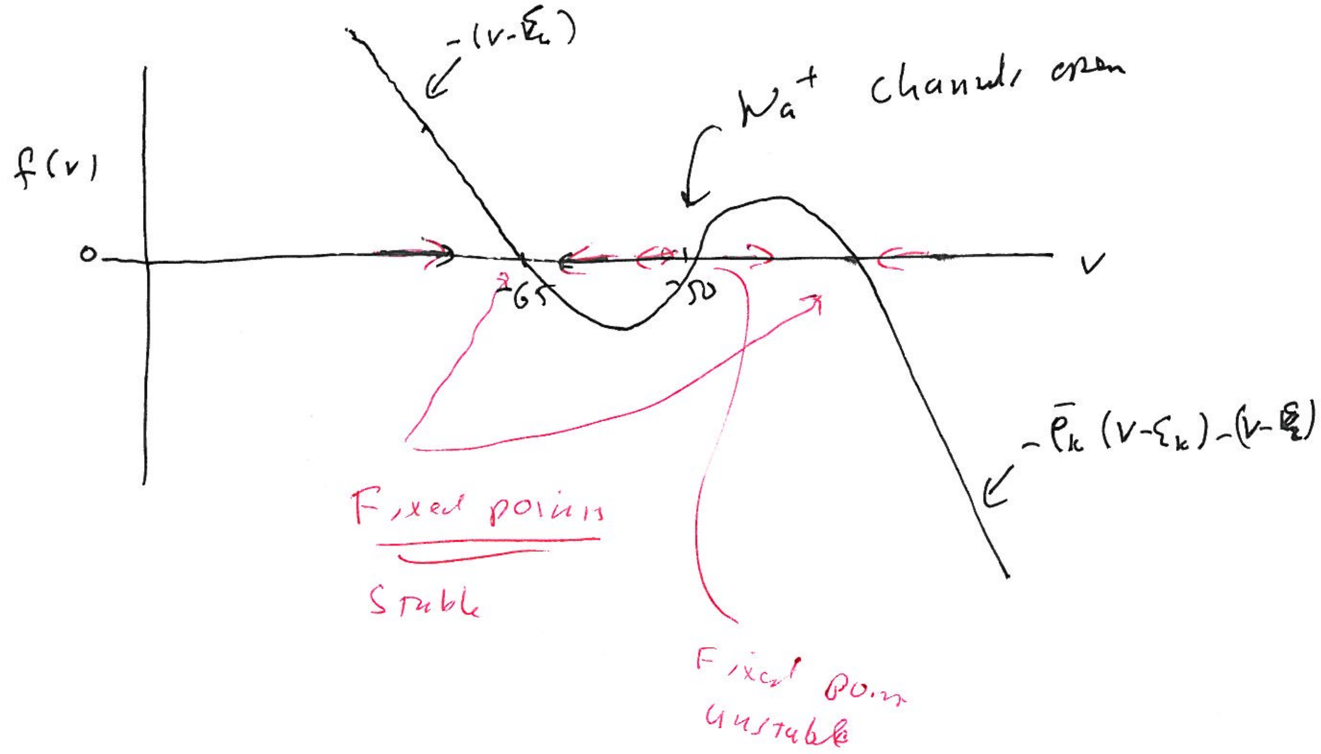
- reduce 4-D HH to 2-D

Approximation # 1 : $\tau \gg \tau_m, \tau_h, \tau_n$ (high resistance cell).

$$\Rightarrow \; m \simeq m_\infty(v)$$
$$n \simeq n_\infty(v)$$
$$h \simeq h_\infty(v)$$

$$\tau \frac{dv}{dt} = F(v, m_\infty(v), h_\infty(v), n_\infty(v)) + I$$
$$= f(v) + I$$

What does f(v) look like?



$$\tau \frac{dv}{dt} = f(v) + I$$

$$f(v_0) + I = 0 \qquad \text{(fixed point)}$$

$$v = v_0 + \delta v \quad , \quad \delta v \text{ small}$$

$$\tau \frac{d}{dt} V = \tau \frac{d}{dt}(V_0 + \delta v) = \tau \frac{d\delta v}{dt} = f(v_0 + \delta v) + I$$

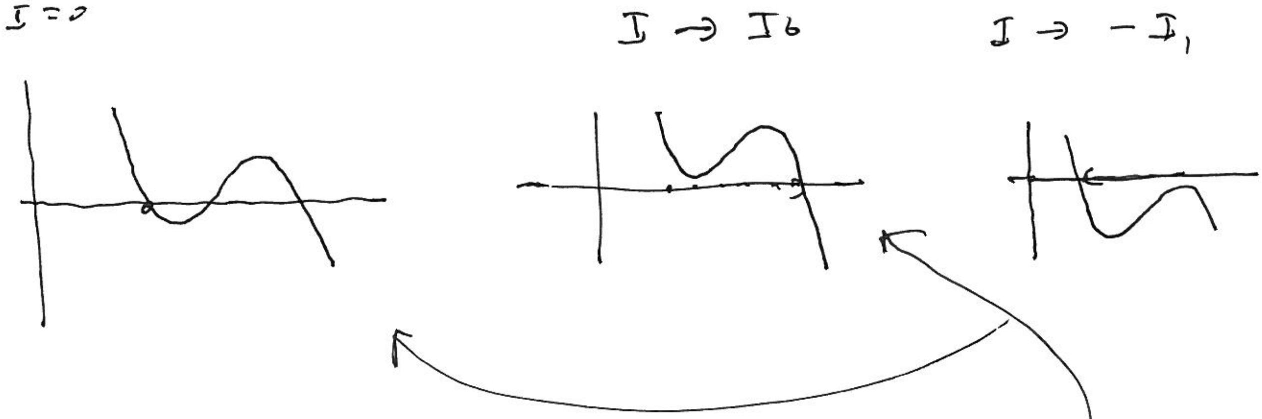
$$\simeq f(v_0) + \delta v \, f'(v_0) + I$$

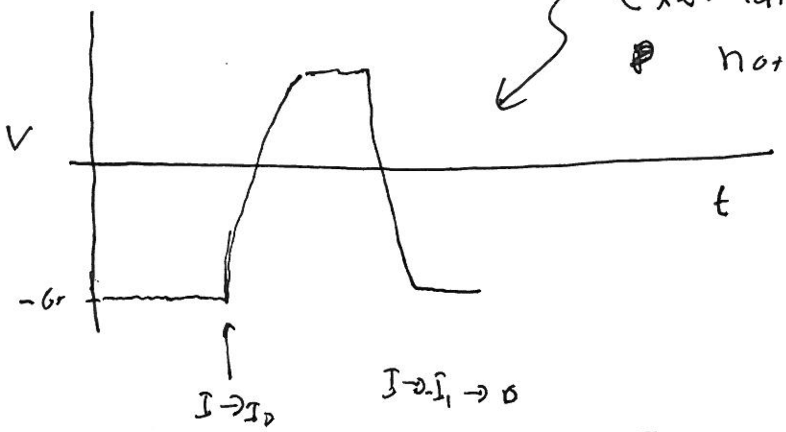
$$\tau \frac{d\delta v}{dt} = f'(v_0)\,\delta v \Rightarrow \boxed{\delta v(t) = \delta v(0)\, e^{f'(v_0) t/\tau}}$$

$$f'(v_0) < 0 \Rightarrow \text{stable}$$

$$f'(v_0) > 0 \Rightarrow \text{unstable}$$

No repetitive firing !!!!




externally caused AP.

not the way neurons work !!!

(Except this is called depolarization block)

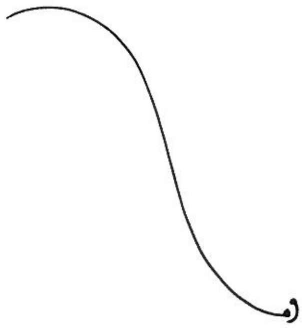
→ death.

Approx. # 1 was a good idea, but it didn't work !!

– that "explains" why $J \sim J_m, J_h, J_n \ldots$

Approx. # 2:

$m = m_\infty(v)$



$u = u'$

$h = h_\infty(u)$

$n = n_\infty(u')$

$$\frac{dh}{dt} = \frac{1}{\tau_h}\left(h_\infty(v) - h\right) = \frac{dh_\infty(u)}{du}\,\frac{du}{dt}$$

$$\frac{du}{dt} = \frac{\dfrac{h_\infty(v) - h_\infty(u)}{\tau_h(v)}}{\dfrac{dh_\infty(u)}{du}} \xrightarrow{v = u + v - u} \frac{v-u}{\tau_h(v)}$$

$$\frac{du'}{dt} = \frac{\dfrac{n_\infty(v) - n_\infty(u')}{\tau_n(v)}}{\dfrac{dn_\infty(u)}{du}} \longrightarrow \frac{v-u'}{\tau_n(v)}$$

$u, u'$ relaxes toward $v$ w/ time constants $\tau_h(v)$ $\tau_n(v)$.

one app

$$\frac{d}{dt}(u-u') = \frac{v}{\tau_h} - \frac{v}{\tau_n} - \left(\frac{u}{\tau_h} - \frac{u'}{\tau_n}\right)$$

$$\tau \frac{dv}{dt} = F(V, m_\infty(v), h_\infty(u), n_\infty(u)) + I$$

$$F_{true}(v, m_\infty(v), h, n) \longleftarrow \text{true}$$

~~Kepler~~ Abbott & Kepler:

$$\left.\frac{dF_{true}}{dt}\right|_{\substack{v \text{ fixed} \\ h=h_\infty, \\ v=v_\infty}} = \left.\frac{dF}{dt}\right|_{v \text{ fixed}}$$

$$= \frac{\partial F}{\partial h}\frac{dh}{dt} + \frac{\partial F}{\partial n}\frac{dn}{dt} = \left[\frac{\partial F}{\partial h_\infty}\frac{dh_\infty}{du} + \frac{\partial F}{\partial n_\infty}\frac{dn_\infty}{du}\right]\frac{du}{dt}$$

$$\frac{du}{dt} = \frac{\frac{\partial F}{\partial h_\infty(u)}\frac{h_\infty(v) - h_\infty(u)}{T_h(v)} + \frac{\partial F}{\partial n_\infty(u)}\frac{n_\infty(v) - n_\infty(u)}{T_n(v)}}{\frac{\partial F}{\partial h_\infty}\frac{dh_\infty}{du} + \frac{\partial F}{\partial n_\infty}\frac{dn_\infty}{du}}$$

$$\frac{du}{dt} = g(v, u)$$

$$\tau \frac{dv}{dt} = f(v,u) + I$$

$$\frac{du}{dt} = g(v,u) \qquad g(0,0)=0 \quad v=u \text{ is equilibrium.}$$

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nullcline analysis:

$1^{st}$ question: what are the fixed points???

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

nullclines: $\left.\begin{aligned} \frac{dv}{dt} &= 0 \\ \frac{du}{dt} &= 0 \end{aligned}\right\}$ define curves in 2-D space; intersection are fixed points.

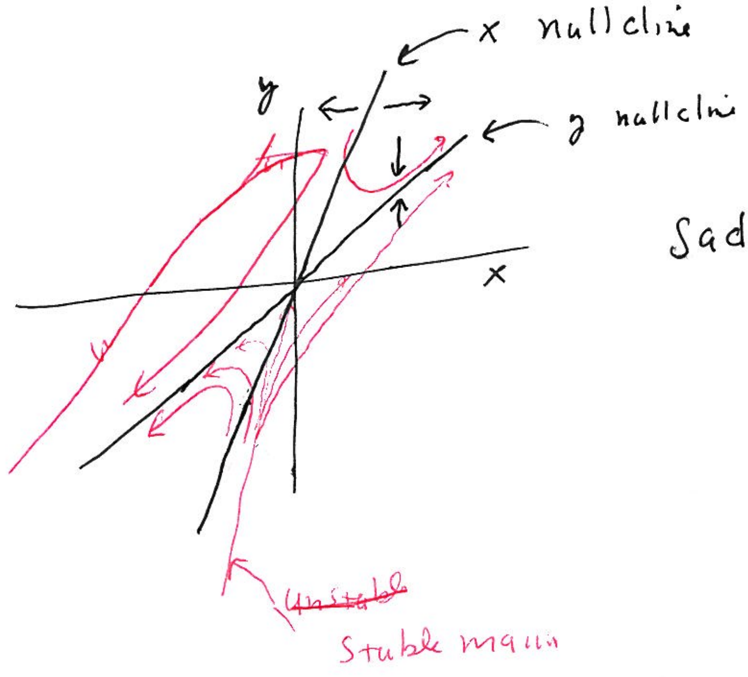
Example

$$\frac{dx}{dt} = ax - by$$

$$\frac{dy}{dt} = cx - dy$$

$$\frac{dx}{dt} = 0 \Rightarrow y = \frac{a}{b} x$$

$$\frac{dy}{dt} = 0 \Rightarrow y = \frac{c}{d} x$$




Saddle point

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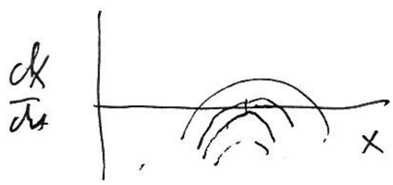
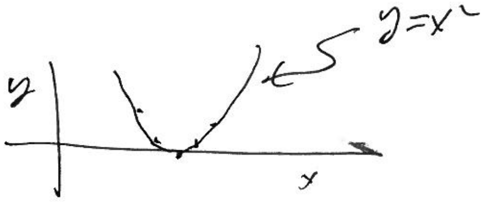
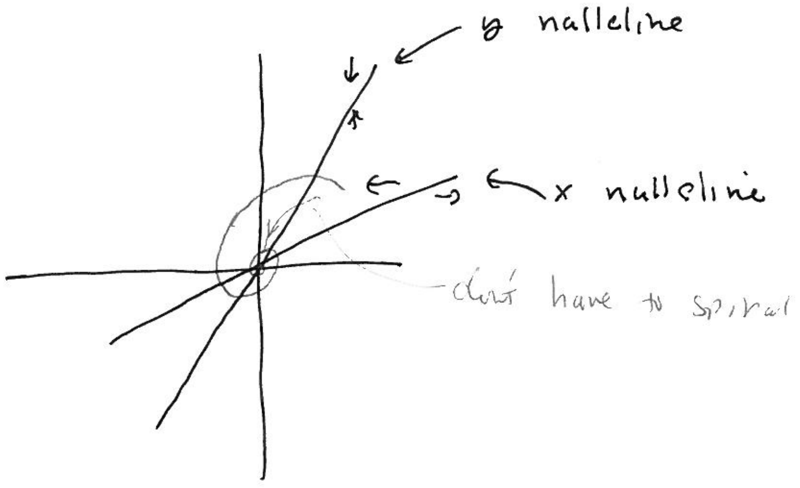
$$\frac{dx}{dt} = y - x^2$$

$$\frac{dy}{dt} = x - y$$



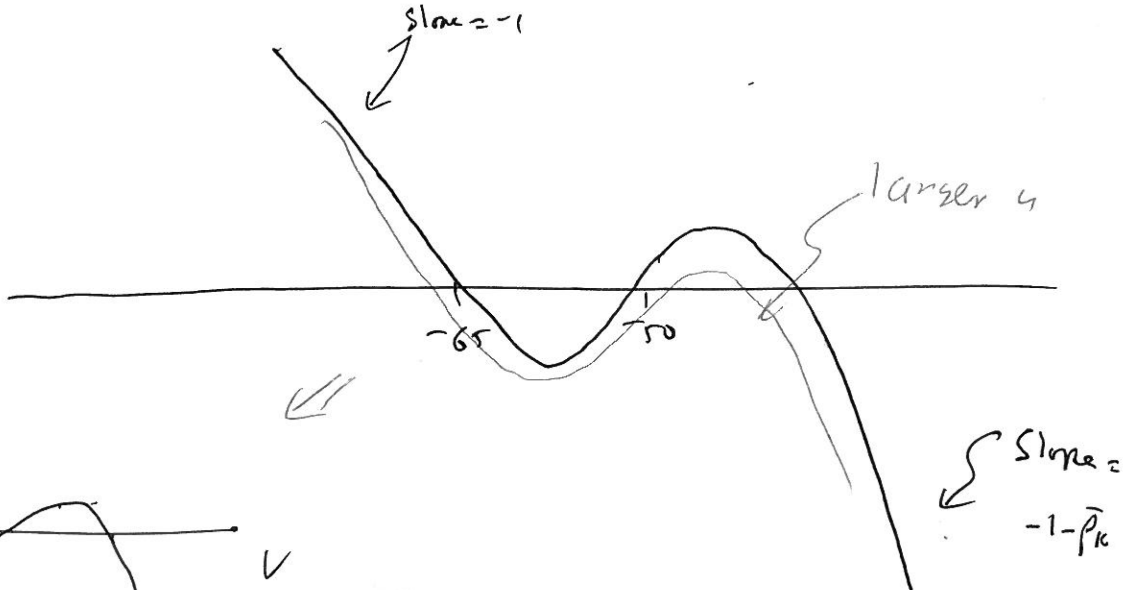

main approach

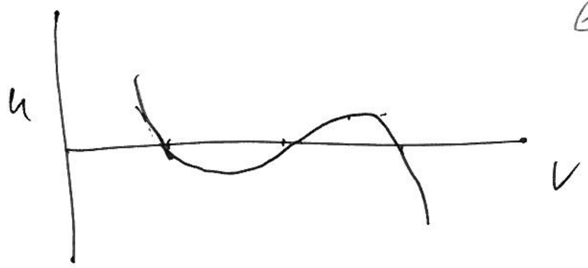




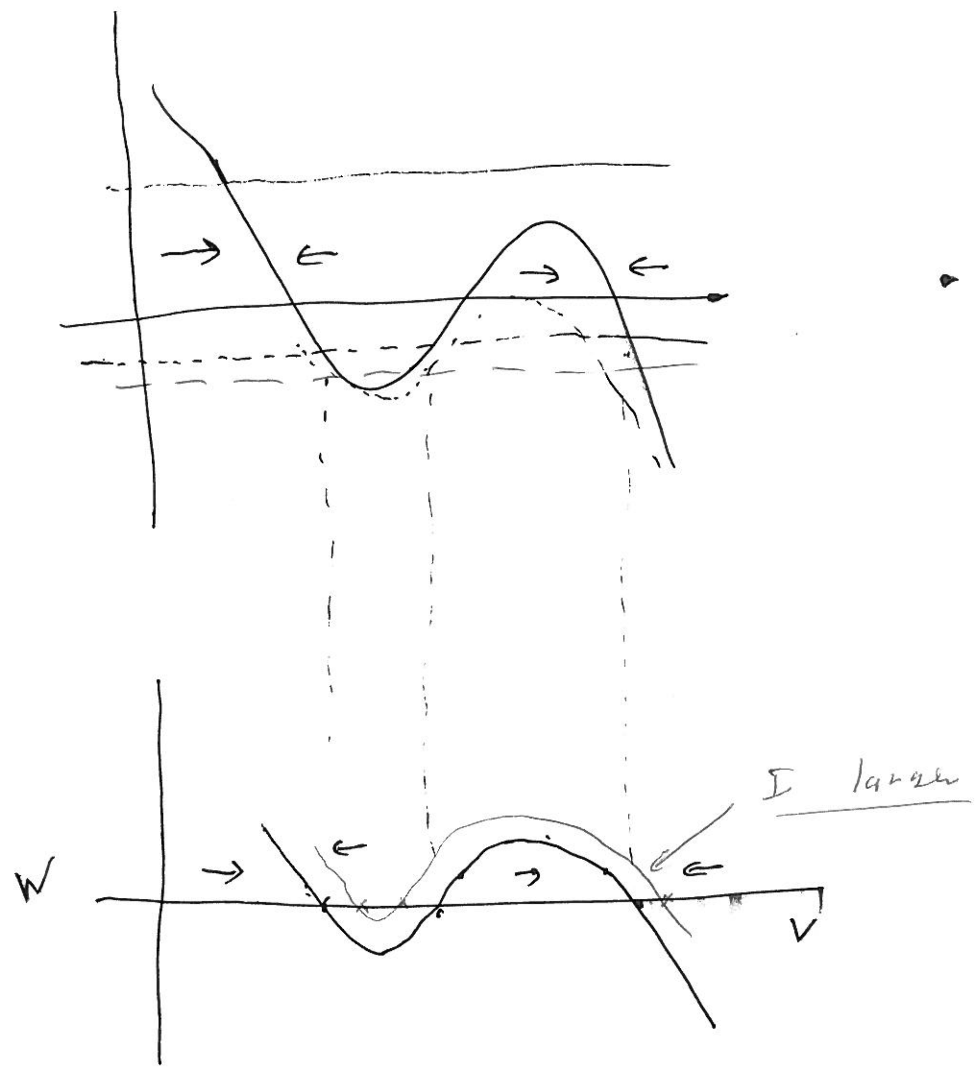

What does $f(V, u)$ look like?

$$f(v,u) = -(v-\Sigma_L) - \bar{\rho}_{Na} m_\infty^3(v) h_\infty(u)(V-\Sigma_{Na}) \; \bar{\rho}_K n_\infty^4(u)(V-\Sigma_K)$$



$$\frac{dV}{dt} = 0 \Rightarrow f(V, w) \pm I = 0$$



FitzHugh - Nagumo:

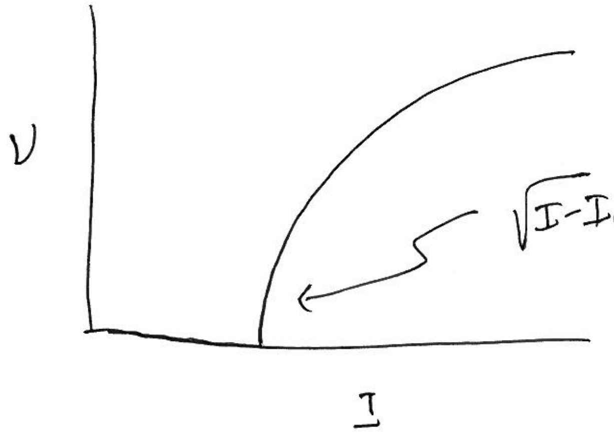
$$\dot{V} = V - \frac{V^3}{3} - w + I$$

$$\dot{w} = \phi (V + a - bw)$$

Morris - Lecar

$$C_m \frac{dV}{dt} = - \bar{g}_{Ca} m_\infty(V)(V - E_{Ca}) - \bar{g}_K w (V - E_K) - \bar{g}_L (V - E_L) + I$$

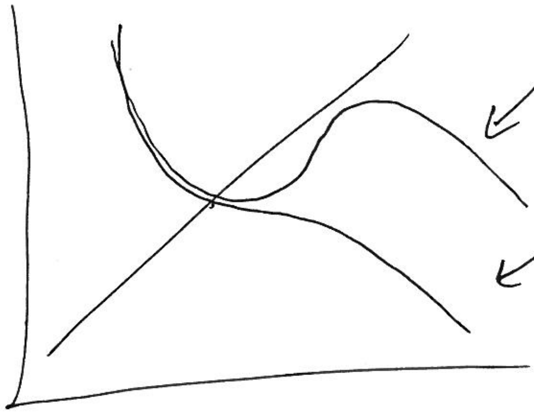
$$\tau_w(V) \frac{dw}{dt} = \frac{w_\infty(V) - w}{\tau_w(V)}$$


$\sqrt{I - I_0}$ (we'll show this later)

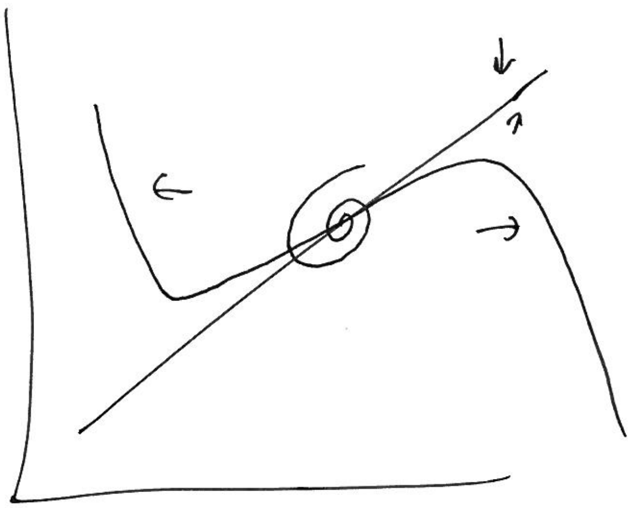
$\boxed{\text{Type I!!}}$

<u>all-or-none</u>



not enough $Na^{++}$ channels –

no spikes!!!
(at least no
all-or-none)



Hopf - eigenvalues - subcritical