3/19/2020

HH eqs.

$$C\frac{dV}{dt} = g_{Na} m^3 h (V - V_{Na}) + g_K n^4 (V - V_K) + g_l (V - V_l) + I$$

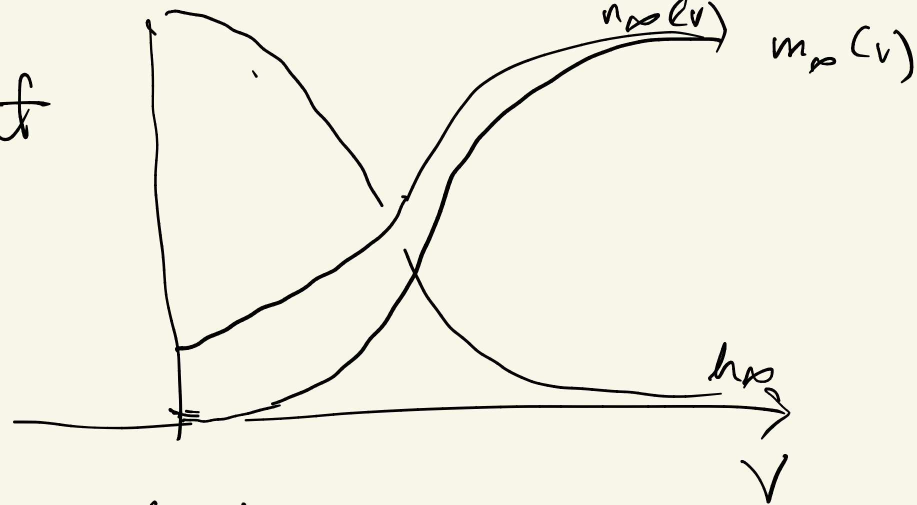
m, n, h.

$$\frac{dj}{dt} = \alpha(1-j) - \beta j \qquad j = m, n, h$$

$$\alpha, \beta = f(V)$$

$j_\infty(V)$, τ_j time constant

$n_\infty + h_\infty \sim$ constant



low V

m is fast

h is slow

m, n off , h on

low

Reduced HH model

Because $\tau_m \ll 1$ (fast) take $m \to m_\infty$

take $h + n \sim n_0$

$h = n_0 - n.$

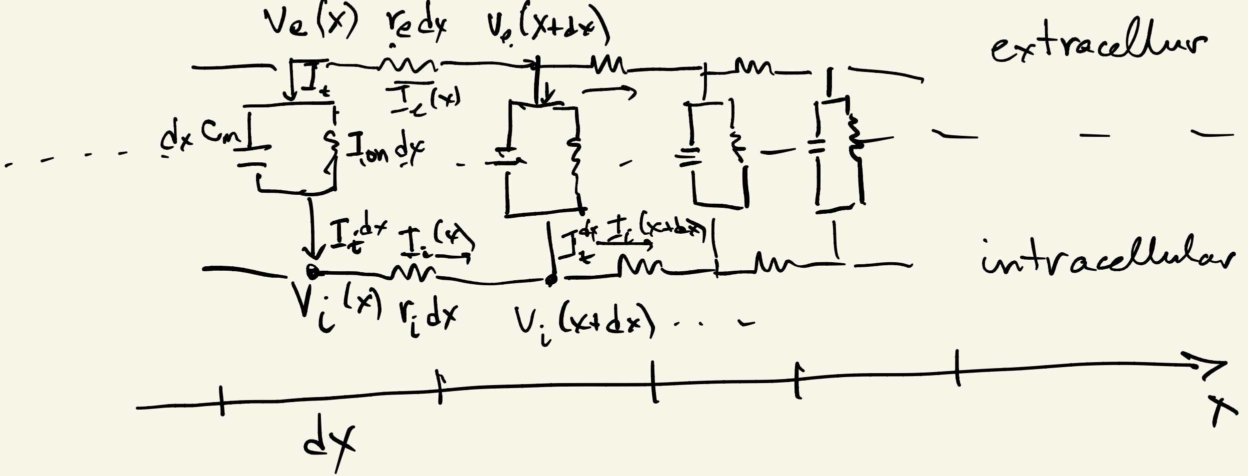
$$\begin{cases} C\dfrac{dV}{dt} = g_n m_\infty^3 (V - V_n)\, g_K n^4 (V - V_K) + g_l (V - V_l) + I \\[2ex] \dfrac{dn}{dt} = \alpha_n (1-n) - \beta_n (n) \end{cases}$$

Morris Lecar   barnacle muscle fibers

$$\begin{cases} C\dfrac{dV}{dt} = g_{Ca}\, m_\infty(V)(V - V_{Ca}) + g_K w (V - V_K) + g_L (V - V_L) \\[2ex] \tau_w \dfrac{dw}{dt} = w_\infty(V) - w \end{cases}$$

voltage reg calcium (sodium)   gated potassium

3/24/2020



$$V_i(x+dx) - V_i(x) = r_i\, dx\, I_i(x)$$ Ohm's law.

$$V_e(x+dx) - V_e(x) = r_e\, dx\, I_e(x)$$

$\lim_{dx \to 0}$

$$\frac{\partial V_i}{\partial x} = r_i I_i, \quad \frac{\partial V_e}{\partial x} = r_e I_i$$

$$I_t = \partial I_i / \partial x$$

$$\begin{cases} I_i(x) + I_i\, dx = I_i(x+dx) \\ I_e(x) = I_e(x+dx) + I_t\, dx \end{cases} \Rightarrow \lim_{dx \to 0} \; -I_t = \frac{\partial I_e}{\partial x}$$

$$\frac{\partial I_i}{\partial x} + \frac{\partial I_e}{\partial x} = 0$$

$$I_i + I_e = I_T$$

$$dx\, I_t = \underbrace{\left(C_m \frac{dV}{dt} + I_{ion}\right)}_{} dx \qquad V = V_i - V_e$$

transmembrane element/circuit.

$$I_t = C_m \frac{dV}{dt} + I_{on.} = \frac{\partial I_i}{\partial x} = -\frac{\partial I_e}{\partial x}$$

$$I_T = I_i + I_e = \frac{1}{r_i}\frac{\partial V_i}{\partial x} + \frac{1}{r_e}\frac{\partial V_e}{\partial x}$$

$$= \frac{1}{r_i}\frac{\partial V_i}{\partial x} + \frac{1}{r_e}\frac{\partial}{\partial x}(V_i - V)$$

$$= \left(\frac{1}{r_i} + \frac{1}{r_e}\right)\frac{\partial V_i}{\partial x} - \frac{1}{r_e}\frac{\partial V}{\partial x}$$

$$\left(\frac{1}{r_i}+\frac{1}{r_e}\right)\frac{\partial V_i}{\partial x} = I_T + \frac{1}{r_e}\frac{\partial V}{\partial x}$$

$$\frac{r_i+r_e}{r_i r_e}\left(r_i I_i\right) = I_T + \frac{1}{r_e}\frac{\partial V}{\partial x}$$

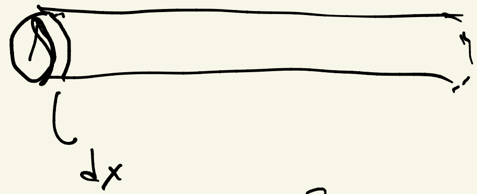
$$I_i = \frac{r_e}{r_i+r_e}\left(I_T + \frac{1}{r_e}\frac{\partial V}{\partial x}\right)$$

$$P\left(C_m\frac{\partial V}{\partial t} + I_{ion}\right) = \frac{\partial}{\partial x}\left(\frac{r_e}{r_i+r_e}I_T + \frac{1}{r_i+r_e}\frac{\partial V}{\partial x}\right)$$

$$\boxed{\frac{1}{C_m(r_i+r_e)}} \sim D \qquad \frac{\partial^2 V}{\partial x^2}$$

$$C_m \sim F/A \qquad r_i \qquad \sim \ell^2/t \qquad D = \frac{1}{P\, C_m (r_i+r_e)}$$

TBI



pde $\frac{\partial V}{\partial t} = D \frac{\partial^2 V}{\partial x^2} - (\ )\underbrace{I_{ion}}$ — H,H, rHH, ML
— . .

diffusion reaction Eqn.

de' ... gating variables.

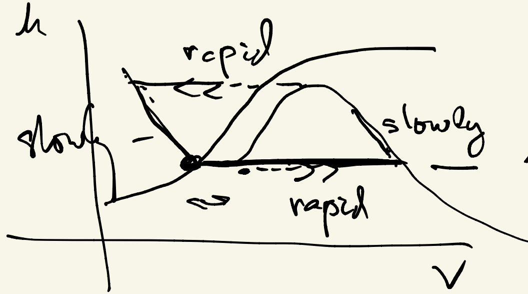
+

3 ode's (

$\frac{\partial}{\partial t} =$ variable (x,t)

Traveling Waves.

rHH



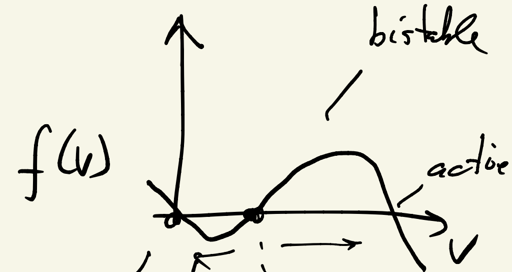
keep gating variable fixed

front = upstroke.

What is behavior of front.

rHH : keep n, h fixed

$$\frac{\partial V}{\partial t} = D\frac{\partial^2 V}{\partial x^2} + f(V) \quad (*)$$



① Does eqn (*) have traveling wave solution?

② If so, how fast does it travel?

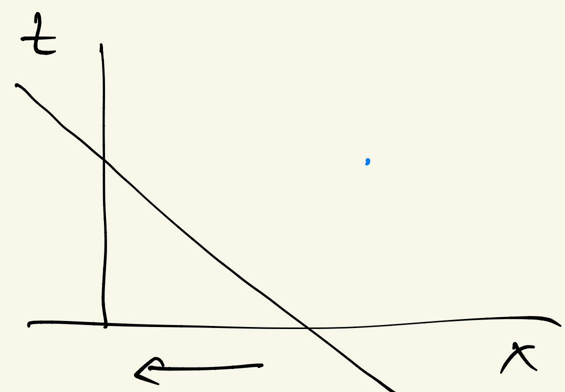
3) What can stop it? How?

$$V = V(x+ct) \qquad \xi = x+ct, \quad c>0\,?$$

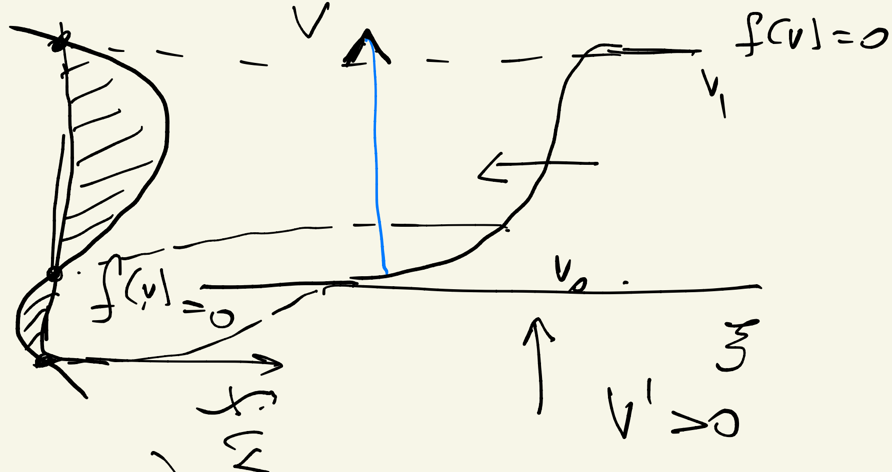
$$\Rightarrow \quad cV' = V'' + f(V)$$

Change scale so $D = 1$.

$V(x+ct)$ travels to left.



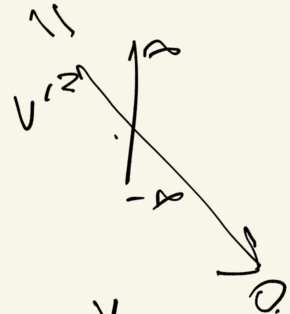
4 $c>0$



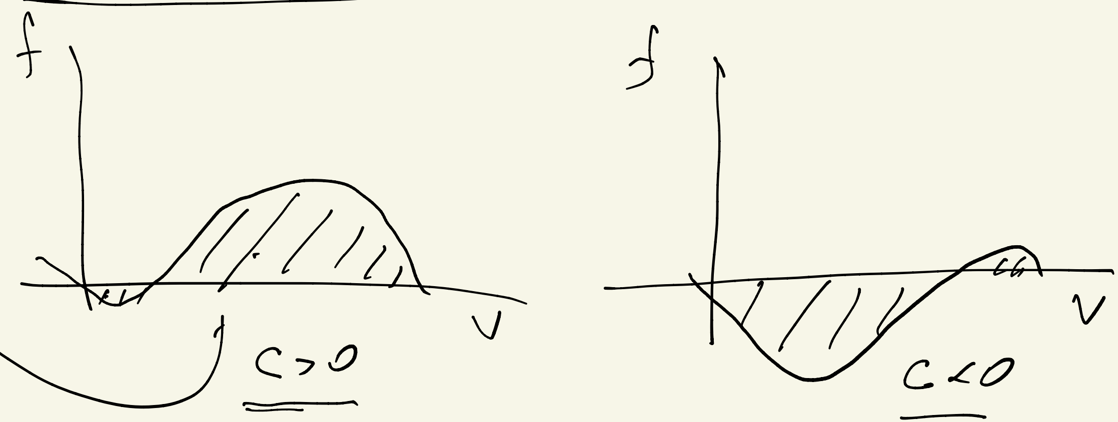
$$\int_{-\infty}^{\infty} V'\left(cV' = V'' + f(V)\right) d\xi.$$

$$c\underbrace{\int_{-\infty}^{\infty} V'^2\, d\xi}_{>0} = \int_{-\infty}^{\infty} V'V''\, d\xi + \int_{-\infty}^{\infty} f(V)\, V'\, d\xi$$

$$= \int_{-\infty}^{\infty} \frac{1}{2}\frac{d(V'^2)}{d\xi}\, d\xi \qquad \int_{V_0}^{V_1} f(V)\, dV$$

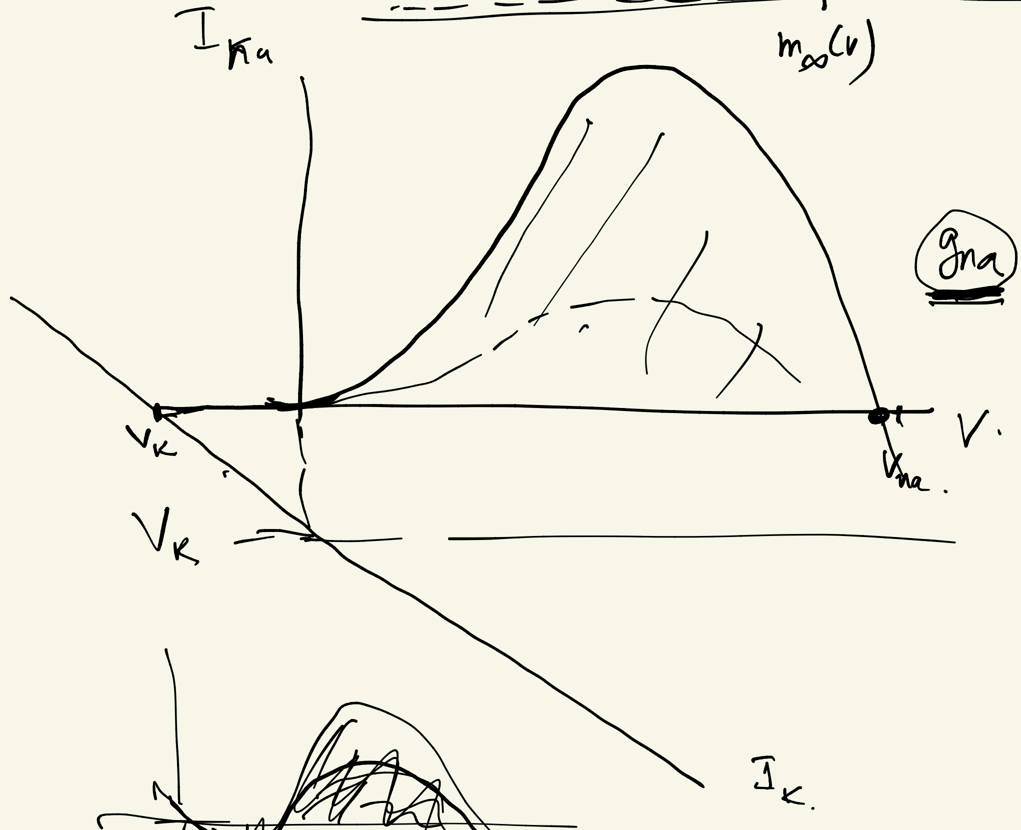


$$c\int_{-\infty}^{\infty} v'^2\, d\xi = \int_{v_0}^{v_1} f(v)\,dv.$$



HH: $I_{ion} = g_K n^4 (V - V_K) + g_{Na} m^3 h (V - V_{Na}) + g_L (V - V_L)$

$m_\infty(V)$



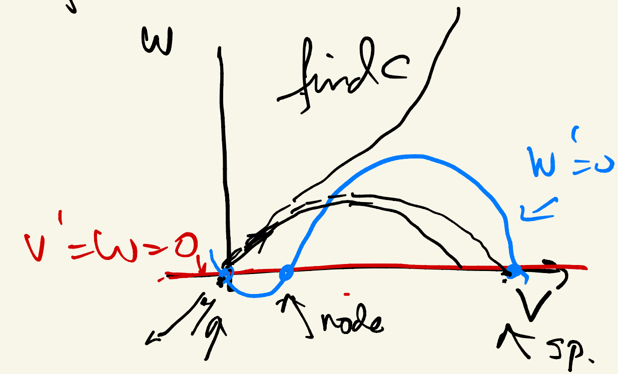
3/26/20

Prove that $\exists$ heteroclinic solution of

$$cV' = V'' + f(V)$$

how? look at V-V' phase plane

$$\Rightarrow \begin{cases} V' = w \\ w' = cw - f(V) \end{cases}$$



$$\frac{dw}{dV} = \frac{cw - f(V)}{w} \qquad w = \frac{1}{c} f(V)$$

$$\begin{pmatrix} V' \\ w' \end{pmatrix} = \begin{pmatrix} 0 & 1 \\ -f'(V^*) & c \end{pmatrix} \begin{matrix} V \\ W \end{matrix}$$

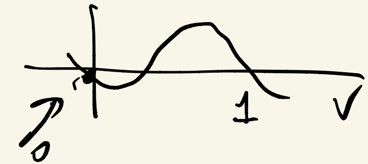
$$\lambda^2 - c\lambda + f'(V^*) = 0$$

$$\lambda = \frac{c}{2} \pm \frac{1}{2}\sqrt{c^2 - 4f'}$$

$f' < 0$

$f' < 0 \Rightarrow$ saddle pt

Try different c value.



1) $\underline{c=0}$

$$v' = w$$
$$w' = -f(v)$$

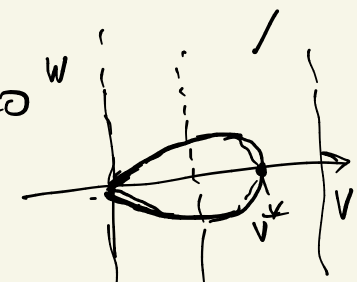
$$\frac{dw}{dv} = -\frac{f(v)}{w}$$

$$w\,dw = -f(v)\,dv$$

$$F'(v) = f(v)$$
$$F = \int_0^v f(u)\,du$$

$$w^2/2 = -F(v)$$

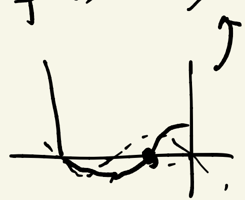
$$w^2/2 + F(v) = K = 0$$



$$\int_0^1 f(u)\,du > 0$$

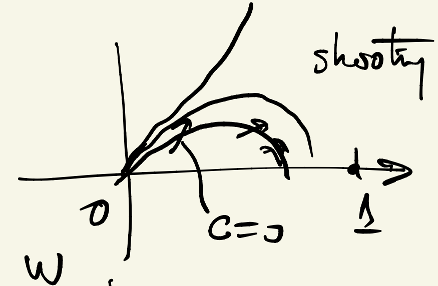
$$\int_0^{v^*} f(u)\,du = 0$$

$F(v) =$



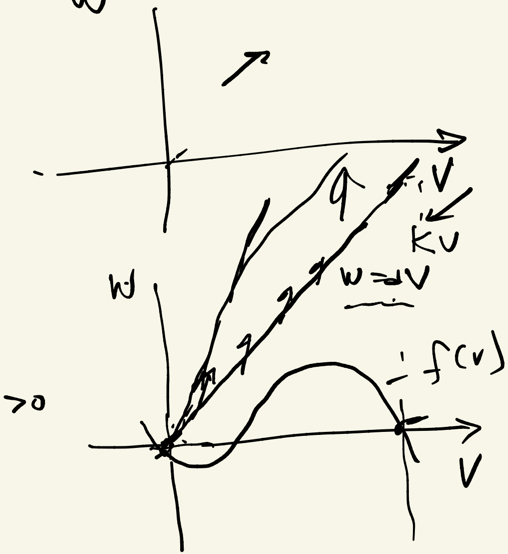
$\Rightarrow$ for $c=0$ the unstable mfld of $v=0$

fails to reach $v=1$



$$\frac{dw}{dv} = \frac{cw - f(v)}{w}$$

$$\frac{dw}{dv} = c - \frac{f(v)}{w}$$ monotone increasing in c



If c is large what happens?

$\exists$ K so that $\frac{f(v)}{v} \leq K$ $v>0$

$$f(v) \leq Kv$$

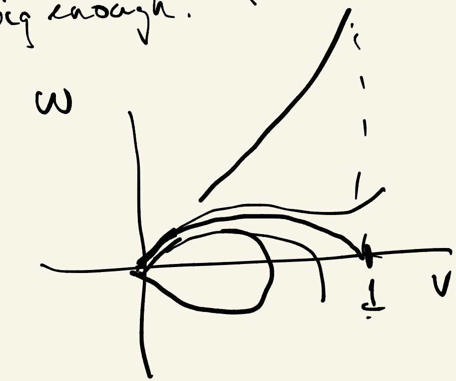
$$\frac{dw}{dv} = c - \frac{f(v)}{\sigma v} \geq \boxed{c - \frac{K}{\sigma}}$$

Pick

$w = \sigma v$

$c - K/\sigma > \sigma$ $\quad c > \sigma + K/\sigma$

Pick c big enough.



$\exists$ unique $c \ni$

$V(-\infty) = 0$

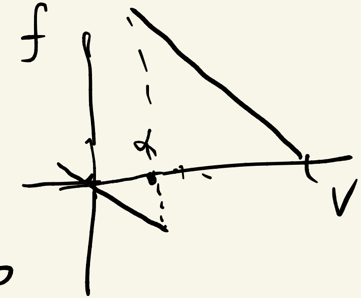
$V(+\infty) = 1$

$\Rightarrow$ done

What is c?

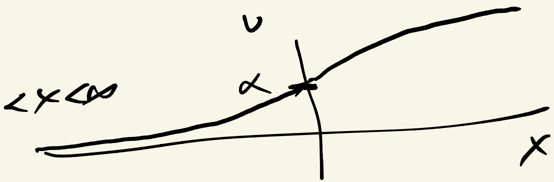
For particular f

① piecewise linear f



$$f(v) = \begin{cases} -v & 0<v<\alpha \\ 1-v & \alpha<v<1 \end{cases}$$

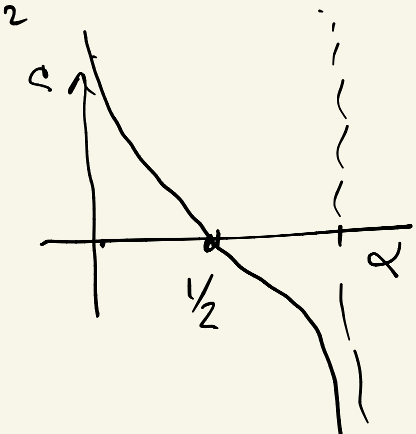
$$v'' + cv' - v = 0 \quad \text{on } -\infty<x<0$$



$$v'' + cv' + 1 - v = 0 \quad \text{on } 0<x<\infty$$

v cont^s, v' cont^s.

$v(0)=\alpha \Rightarrow \quad c = \dfrac{1-2\alpha}{\sqrt{\alpha-\alpha^2}}$



② cubic polynomial:

$$f = v(v-\alpha)(1-v)$$

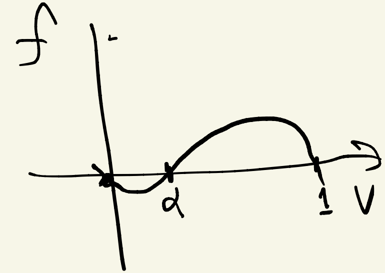
Try to solve

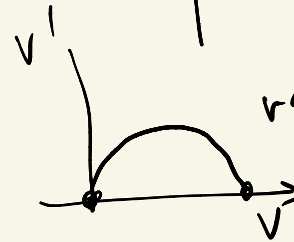
$$v'' + cv' + f = 0$$

Try $v' = \underset{?}{A}\, v(1-v)$

$$v'' = Av'(1-v) - Avv'$$

$$Av'(1-2v)$$





right form.

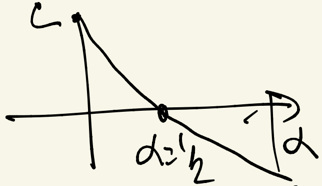
$$Av'(1-2v) + cv' + v(v-\alpha)(1-v) = 0$$

$$[A(1-2v)+c]A\cancel{v}\cancel{(1-v)} + \cancel{v}(v-\alpha)\cancel{(1-v)} = 0$$

$$[A(1-2v)+c]A + v - \alpha = 0 \quad \text{linear in } v$$

$$\begin{cases} A^2 + cA - \alpha = 0 \\ -2A + 1 = 0 \end{cases}$$

$A = \frac{1}{2}$, $\quad \frac{1}{4} + c\,\frac{1}{2} - \alpha = 0$

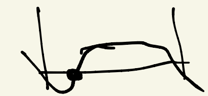


$\frac{c}{2} = \alpha - \frac{1}{4} \qquad c = \frac{A}{\sqrt{2}}\underbrace{(1-2\alpha)}$

$\Rightarrow 0 \quad \alpha = 1/2$

$f = v(v-1)(\alpha - v)$

β



dimensionless.

$v_t = v_{xx} + f(v)$

$v_t = D\, v_{xx} + \beta\, f(v)$

3 effects $\underbrace{D, \alpha, \beta}$

How do D & β affect speed c.

Let $\quad t = \tau/\beta \qquad v_\tau = \frac{D}{\beta} v_{xx} + f(v)$

$x = \xi \sqrt{D/\beta} \qquad v_\tau = v_{\xi\xi} + f(v)$

$$v = V(\xi - c\tau)$$

$$= V\left(\sqrt{\tfrac{\beta}{D}}\,x - c\beta t\right)$$

$$= V\left(\sqrt{\tfrac{\beta}{D}}\left(x - \boxed{c\,\beta\sqrt{\tfrac{D}{\beta}}}\,t\right)\right)$$

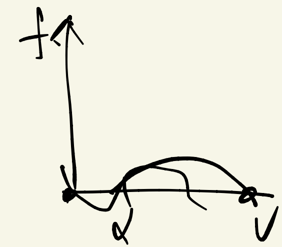
Speed $= \sqrt{D\beta}\;\underline{c}$

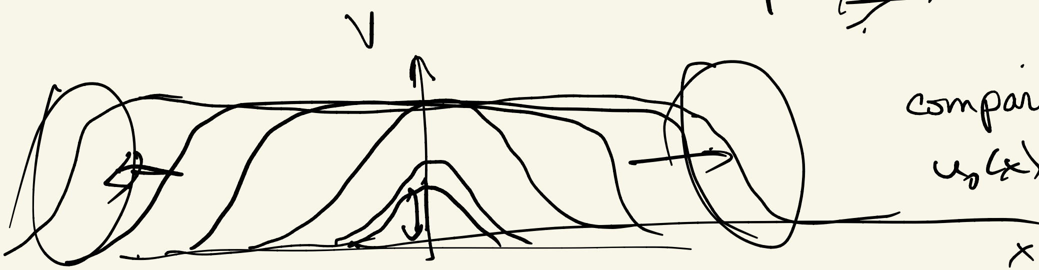
$$\frac{\quad}{\tau}$$

$x -$

Speed $= \sqrt{D\beta}\;c(\alpha)$

f





comparison theorem

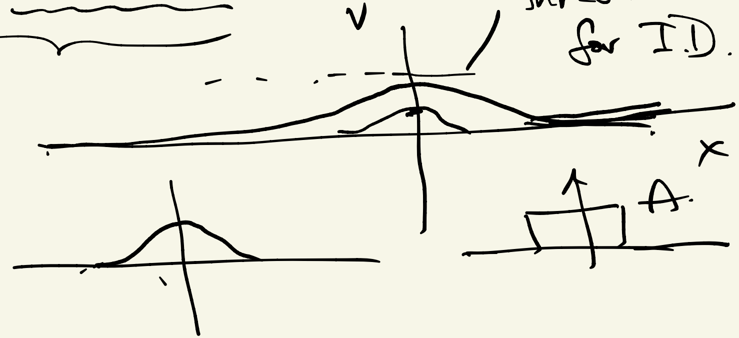
$u_0(x) \le v_0(x)$

then $u(x,t) \le v(x,t)$ for all t.

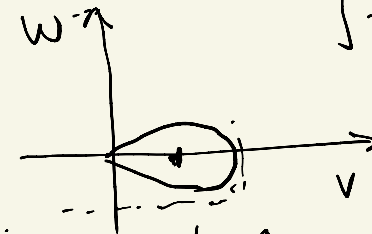
$c = 0$

$$v_t = \underbrace{\underline{v''} + f(v)}_{} = 0$$

threshold for I.D.



$\int f > 0$



standing solution

blocking solution

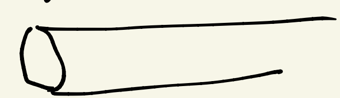
3/31/2020

Dimensional Analysis

$v_t = v_{xx} + f(v)$ bistable

$v = V(x-ct)$ $c \sim f$

perimeter

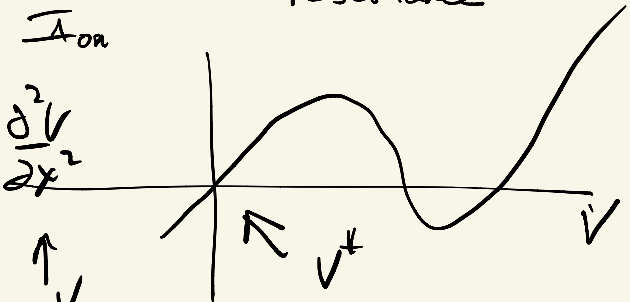


in dimensional units

$$p\left(C_m \frac{dV}{dt} + I_{on}\right) = \frac{1}{r_i + r_e}\frac{\partial^2 V}{\partial x^2}$$

$$\frac{1}{R_m} = \frac{\partial I_{ion}}{\partial V}\bigg|_{V=V^*}$$

R_m membrane resistance



$$\Big(\underbrace{R_m C_m}_{\tau_m} \underset{\uparrow_V}{\frac{\partial V}{\partial t}} + \underset{|_V}{R_m I_{ion}} \Big) = \underbrace{\frac{R_m}{p(r_e+r_i)}}_{\lambda_m^2} \underset{\uparrow_V}{\frac{\partial^2 V}{\partial x^2}}$$

$$R_m C_m = \tau_m$$

$$\frac{R_m}{p(r_e+r_i)} = \lambda_m^2$$

$$\underline{s} = \underset{n.d}{\cancel{c}} \left(\frac{\lambda_m}{\tau_m} \right) = c \sqrt{\frac{R_m}{p(r_e+r_i)}} \frac{1}{C_m R_m}$$

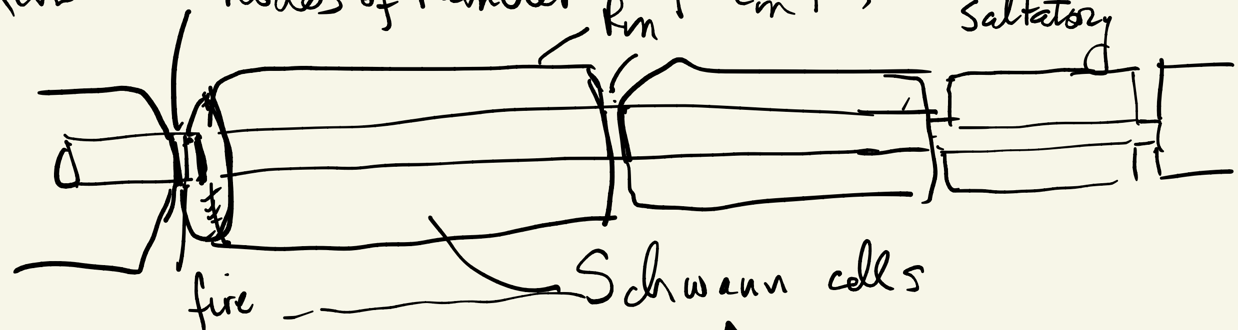
$$r_i = \frac{R_c}{A_i}$$ resistivity

A_i - Area

$$s = c \sqrt{\frac{R_m A_i}{p R_c}} \frac{1}{R_m C_m} = \underline{\frac{c}{C_m} \sqrt{\frac{d}{4 R_c R_m}}}$$

diameter

myelination



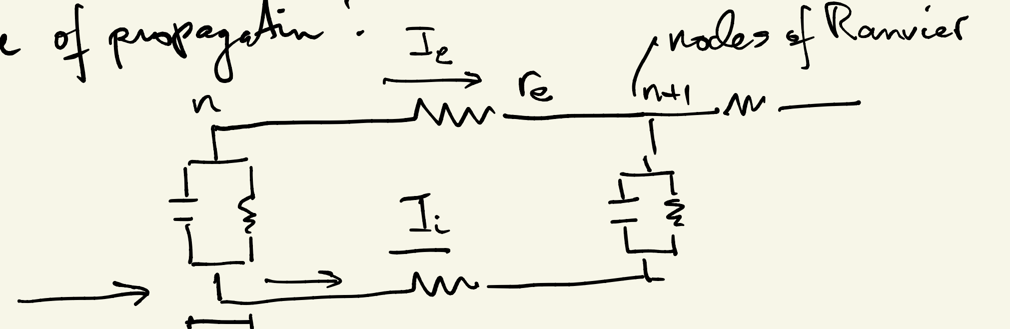
MS - autoimmune disease attacks

Speed slow

Is speed increased for myelinated fibers?

failure of propagation?

Model



$$\underbrace{\qquad}_{L}$$

$$I_e = \frac{-1}{L r_e}\left(V_{e,n+1} - V_{e,n}\right)$$

$$I_i = -\frac{1}{L r_i}\left(V_{i,n+1} - V_{i,n}\right)$$

at n^{th} node

$$\mu p\left(C_m^{R_m}\frac{\partial V_n}{\partial t} + \overset{R_m}{I_{ion}}\right) = \underbrace{I_{i,n} - I_{i,n+1}}_{} = \frac{R_m}{L(r_i+r_e)}\underbrace{\left(V_{n+1} - 2V_n + V_{n-1}\right)}_{}$$

transmemb--

Discrete Cable equation

$$\underbrace{\frac{R_m C_m}{\tau_m}}\frac{\partial V_n}{\partial t} + \underbrace{\frac{R_m I_{ion}}{V}} = \underbrace{\frac{R_m}{\mu p L(r_i+r_e)}}_{D}\underbrace{\left(V_{n+1} - 2V_n + V_{n-1}\right)}_{V}$$

D coupling coefficient

$$\underline{\frac{\partial V_n}{\partial \tau} + f(V_n) = D\left(V_{n+1} - 2V_n + V_{n-1}\right)}$$

What have we learned?

cont^s cable $$\frac{\partial V}{\partial t} + f(V) = D_c \frac{\partial V^2}{\partial x^2}$$

$$s \sim \sqrt{D_c}$$

discrete cable $$\frac{\partial V_n}{\partial t} + f(V_n) = D\left(V_{n+1} - 2V_n + V_{n-1}\right)$$

there is no scaling law, small $D \to$ failure.

Traveling waves? yes but proof is hard

$$V_n = U(\tau)$$

$$V_{n+1} = U(\tau - \tau_d) \qquad V_{n-1} = U(\tau + \tau_d)$$

$$\frac{dU}{dt} + f(U) = D\left(\underbrace{U(t - \tau_d) - 2U(t) + U(t + \tau_d)}\right)$$

t

However, suppose τ_d is small (fast)

$$\circledast \quad \underbrace{D\tau_d^2 V_{\tau\tau} - V_\tau + f(u) = 0.}$$

τ_d small. $\tau_d = ?$

$$\boxed{-cU_\xi + U_{\xi\xi} + f(u) = 0}$$

bistable eqn $\Longleftarrow$

$U(\xi)$

$$V(\tau) \sim U(\xi)$$

$$V(\tau) = U(\alpha\tau)$$

$$V_\tau = \alpha U'(\alpha\tau)$$

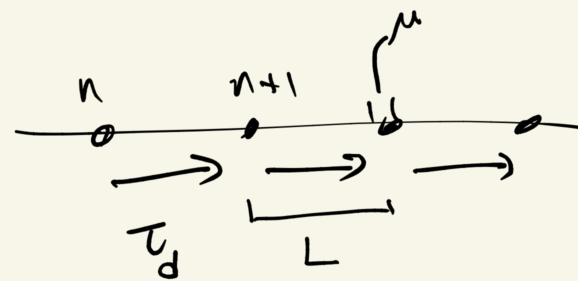
$$V_{\tau\tau} = \alpha^2 U''$$

$$D\tau_d^2\alpha^2 U'' - \alpha U' + f(u) \stackrel{?}{=} 0$$

$$U'' - cU' + f(u) = 0$$

$$\alpha = c \qquad D\tau_d^2 c^2 = 1$$

$$D\tau_d^2 = \frac{1}{c^2} \qquad \underline{\tau_d = \frac{1}{c}\sqrt{D}}$$



Speed

$$\frac{\mu+L}{\tau_d} = \boxed{\frac{c(\mu+L)}{\sqrt{D}}}$$

$$D = \frac{R_m}{\mu L p (r_i + r_e)} \Bigg|_{r_e \to 0}$$

$$\frac{L+\mu}{\sqrt{\mu L}} \underbrace{\frac{c}{2C_m}\sqrt{\frac{d}{R_m R_c}}}_{\text{cable speed}}$$

discrete factor enhancement

$$10 \quad \frac{L+\mu}{\sqrt{\mu L}}$$

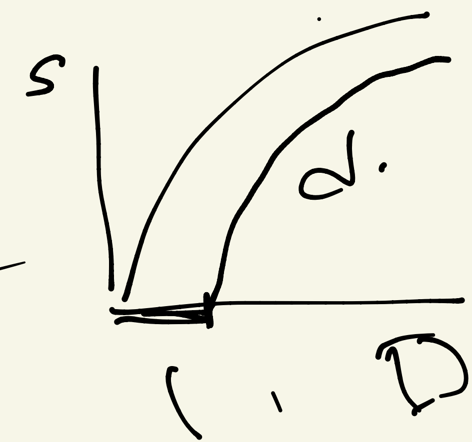
6

$L \sim 100\,\mu m$

$\mu \sim 1\,\mu m$

Why / How does decreasing $\underline{\underline{D}}$ affect speed?

Show that for D small $\Rightarrow$ failure.



$$\underbrace{v_t - f(v_n) = D\left(v_{n+1} - 2v_n + v_{n-1}\right)}$$

look for standing solution. v_n

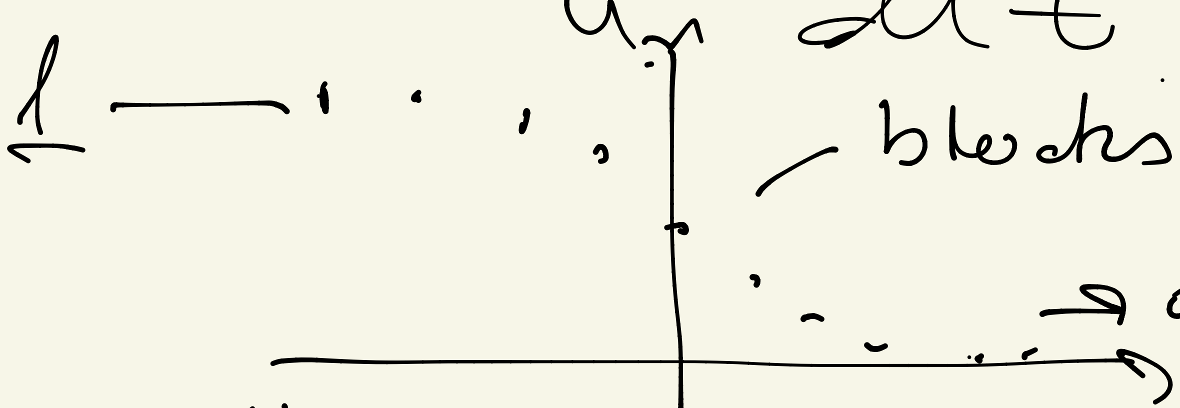
3/2/20

cf. JTK SIAM J. AM 1987. failure

Ordering. Solutions are order

$u_n(0) < v_n(0)$

$\Rightarrow u_n(t) < v_n(t)$ for all t



$$u_{n+1} - 2u_n + u_{n-1} = f(u_n)$$

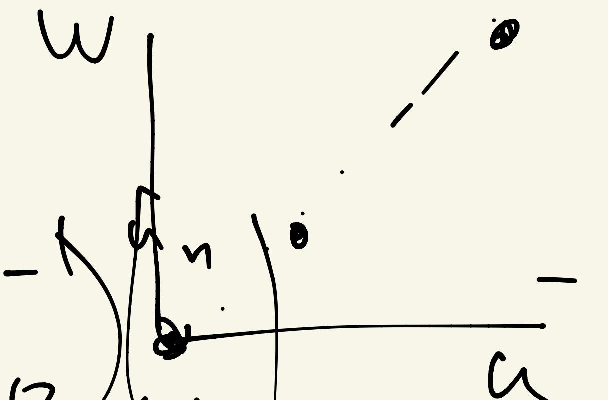
$$w_{n+1} = u_n \qquad D \sim d/\Delta x$$

$$\phi \begin{cases} u_{n+1} = 2u_n - w_n + \dfrac{f(u_n)}{D} \\ w_{n+1} = u_n \end{cases}$$

$$0 = f(0) = f(\alpha) = f(1)$$

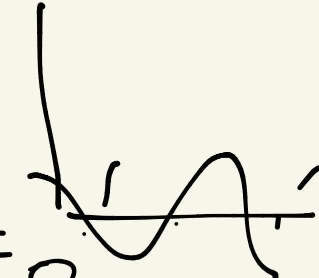
$$\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} 1 \\ 1 \end{pmatrix}, \begin{pmatrix} \alpha \\ \alpha \end{pmatrix}$$

$$\begin{pmatrix} u_{n+1} \\ w_{n+1} \end{pmatrix} = \begin{pmatrix} 2+f' & -1 \\ 1 & 0 \end{pmatrix} \begin{pmatrix} u_n \\ w_n \end{pmatrix}$$



$$(2+f'-\lambda)(-\lambda)+1=0$$

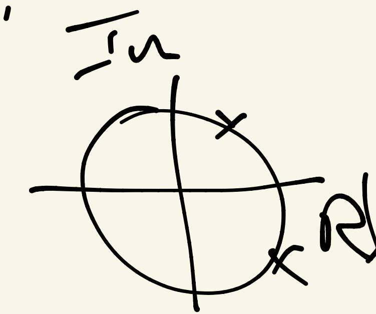
$$\lambda^2-\lambda(2+f')+1=0$$



$$\lambda=\frac{(2+f')\pm\sqrt{(2+f')^2-4}}{2}$$

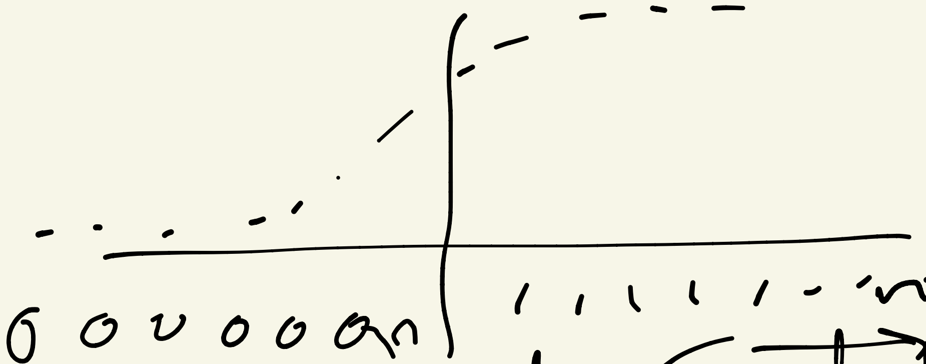
$f'<0 \Rightarrow$ Re, <1, >1

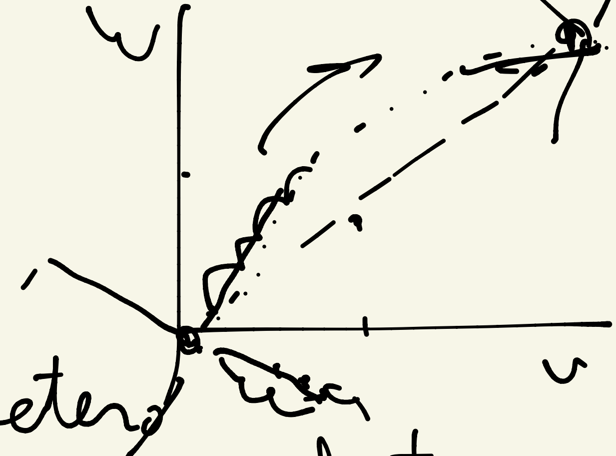
Saddle pt.



$f'>0$ $\mathbb{I}$ ev.

center.

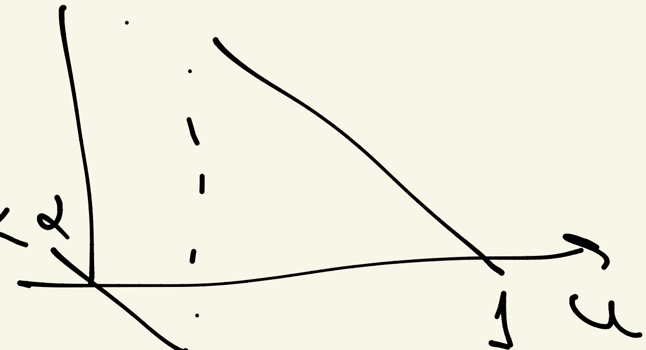




Goal: Find heteroclinic orbit

Ex: $f =$

$$= \begin{cases} -u, & u<\alpha \\ 1-u, & u>\alpha \end{cases}$$

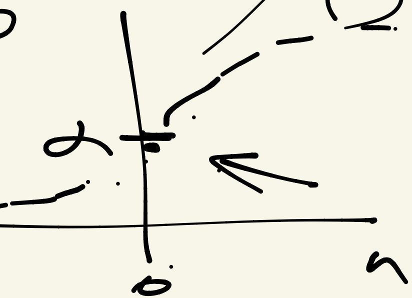


$$u_{n+1} - 2u_n + u_{n-1} = -f/D$$

$$A\lambda^n \quad < 0$$

$$u_n = $$

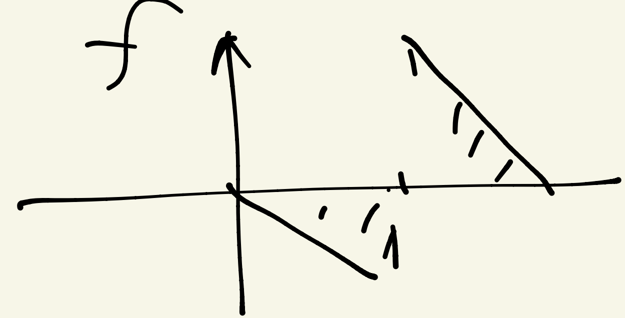
$$1 + \lambda^{-n}$$



If D small enough it works

$$D < D^* = \frac{\alpha(1-\alpha)}{(2\alpha-1)^2}$$

fant?



chaos.

Moser / Smale - horseshoe map

to show that map is equiv to shift on sequence space

$$\phi(x_n) = x_{n+1} \in \mathbb{R}^2$$

$$\sigma \in \{0,1\}^{\mathbb{Z}}$$

$$\{s_{?}\} = s_n \in \{0,1\}$$

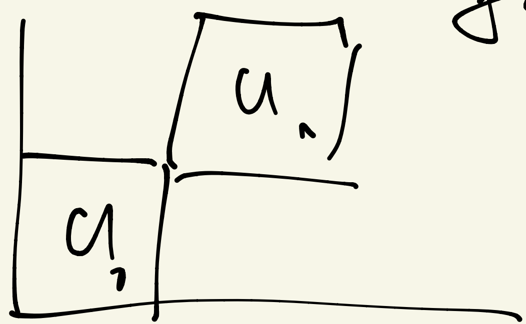
$$1$$

$$\ldots\ 0,\ 1,\ 0\ 0\ 0,\ 1,\ 1,\ 0\ \ldots$$

$$U_0,\ U_1$$

$$\sigma(s_n) \to s_{n+1}$$

For any $\{s_n\}$ $\exists$ $x_n \in U_{s_n}$ for all n



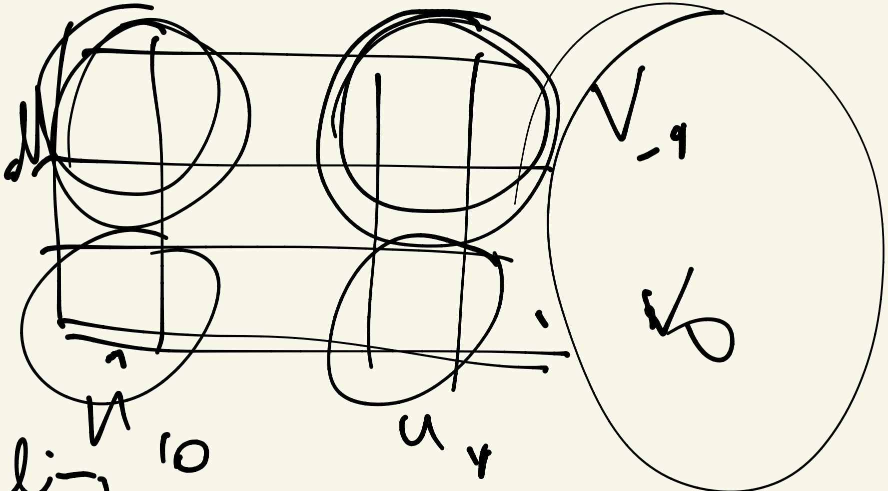
$s_n \Leftrightarrow x_n$

0 0 0 0 1 1 1 1

chaotic

Moser.

If D small



$\Rightarrow$ Thm applies

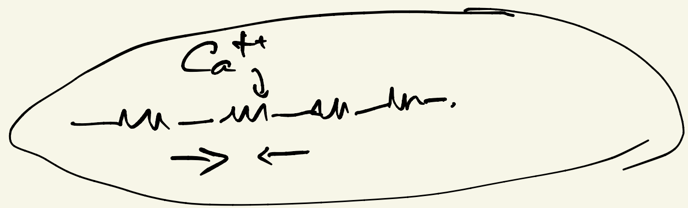
$\Rightarrow$ prop failure!

$\phi(U_i) = V_i$ U vertical
V horiz

4/7/20 Calcium Signalling

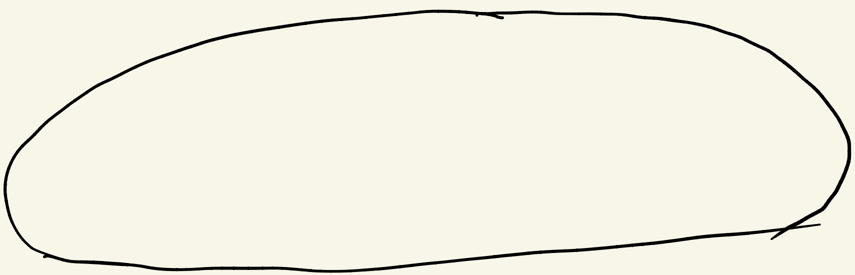
Control of muscle, of vesicle release, insulin release
hormone control, ...

example: Calcium is highly, in muscle



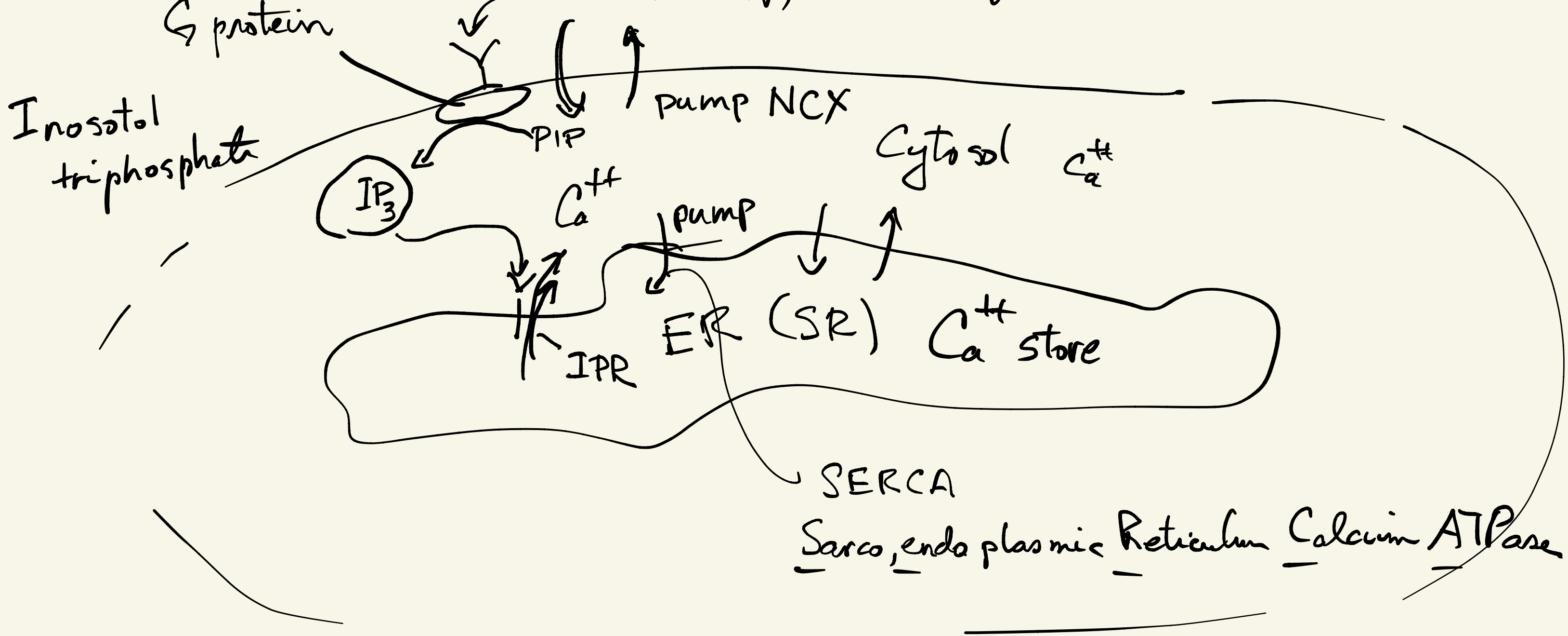
rigor mortis
failure to pump calcium out of cytosol.

1) IP_3 receptors



2) Ryanodine receptors / $\sim 1000 \times Ca^{++}_{cyt}$

$Ca^{++} >> Ca^{++}_{cyt}$



Endoplasmic reticulum
Sarcoplasmic " = cardiac cells

$$\frac{dc}{dt} = \underbrace{J_{IPR} + J_{L\text{-}T} - J_{serca} - J_{ncx} \cdots}_{\text{conservation}}$$

J_{serca} : ATPase model

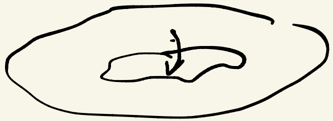
$$\begin{tikzcd}
E_1 \arrow[r, shift left, "k_1 c^2"] \arrow[d, shift left] & E_1 C_2 \arrow[l, shift left] \arrow[r, shift left] & E_1 C_2 - P \arrow[l, shift left] \arrow[d, shift left] \\
E_2 \arrow[u, shift left] \arrow[r, shift left] & E_2 - P \arrow[l, shift left] \arrow[r, shift left, "k_4 c^2"] & E_2 C_2 - P \arrow[l, shift left] \arrow[u, shift left]
\end{tikzcd}$$

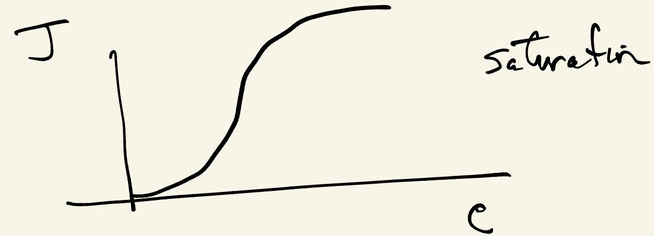
c_e

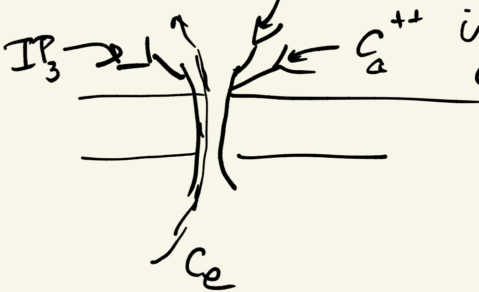
$$J = \frac{c^2 - K_1 K_2 K_3 K_4 K_5 c_e^2}{(\cdots \cdots)}$$

1 $J_{serca} = \dfrac{V_p\, c^2}{K_p^2 + c^2}$ usual "simple" model for J_{serca}

c — $c_{cyt.}$



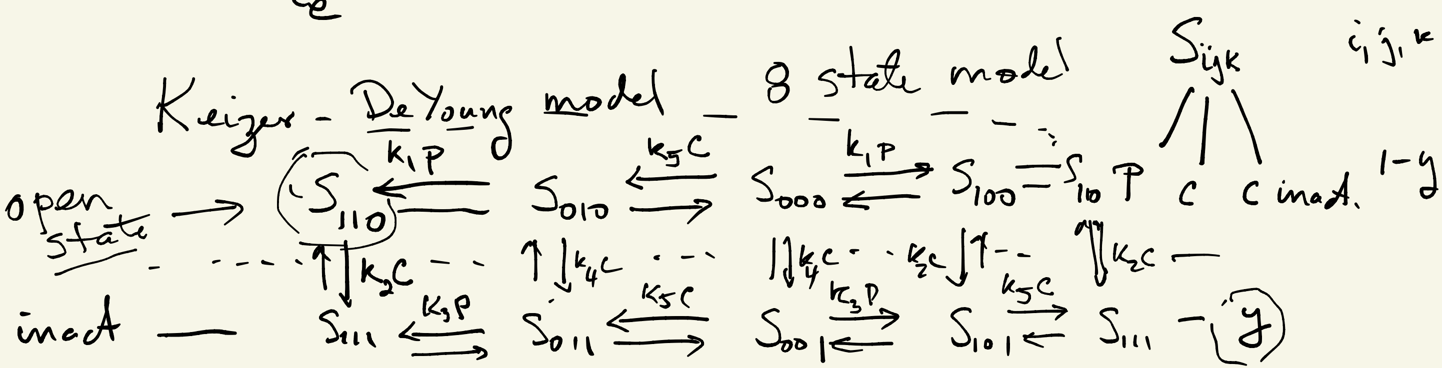


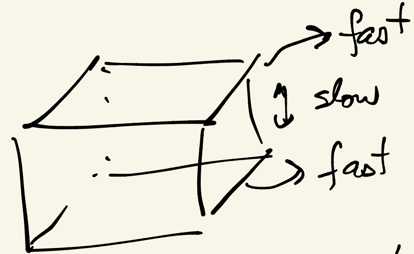


CICR

Calcium Induced Calcium Release

Keizer - DeYoung model — 8 state model S_{ijk} $i,j,k \in \{0,1\}$





$$\frac{dy}{dt} = \underline{\left(\frac{(\quad p\quad)c}{\cdot\,(p+K_1)}\right)}(1-y) - \underline{\left(\frac{p\cdots}{p+K_3}\right)}y$$

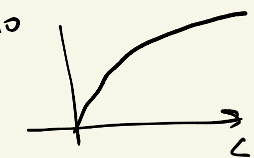
no c

getting

$c=0 \quad y \to 0$

$c \gg 1 \quad y \to 1$

y inactivate



model

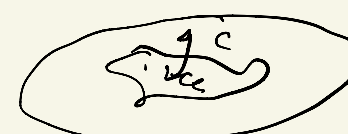
$$\left\{ \quad x_{110} = \frac{pc(1-y)}{(p+K)(c+K)} \right.$$

$y \to 1 \quad \underline{\underline{x_{110}}} \to 0$ conducting state

Full model

leak (stochastic leak)

$$\frac{dc}{dt} = \left(k_f P_o + J_{er}\right)\left(\bar{c}_e - c\right) - J_{serca}$$



$$P_o = (x_{110})^3 \quad \text{cooperativity (3 subunits)}$$

$$V_{cy} C + V_{er} c_e = c_T$$

$$h = 1 - y$$

$$\frac{dh}{dt} = (\quad)(1-h) - (\quad) h.$$

$$\boxed{c + \frac{c_e}{\gamma} = c_t}$$

parameter in K&S.

xpp phase plane

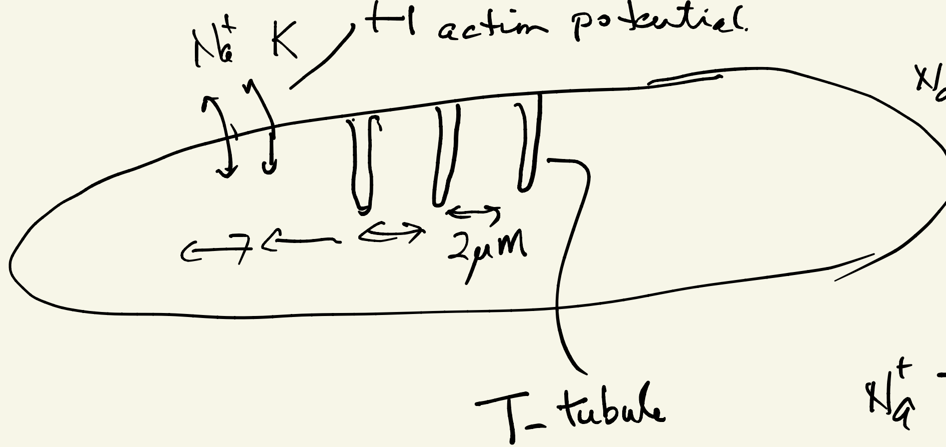
maple :

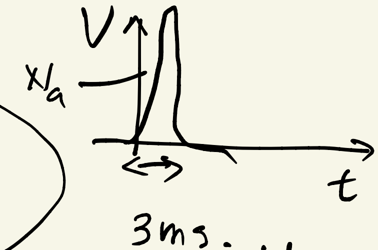
$\Rightarrow$ CICR

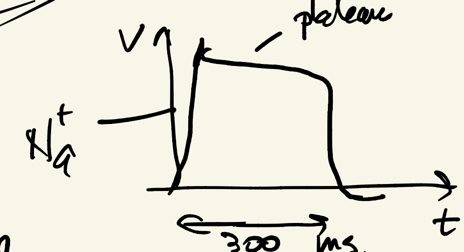
cardiac cells. contract in response to electrical signal

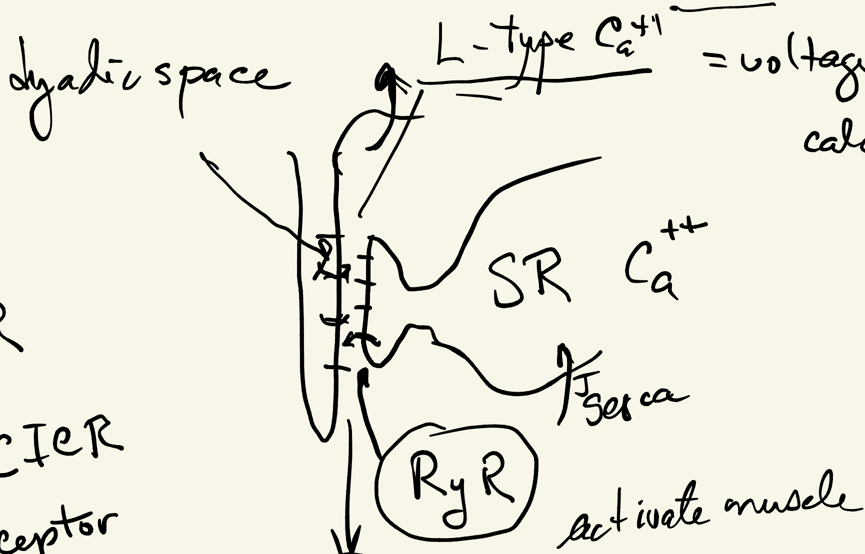
excitation – contraction coupling.

similar to nerves







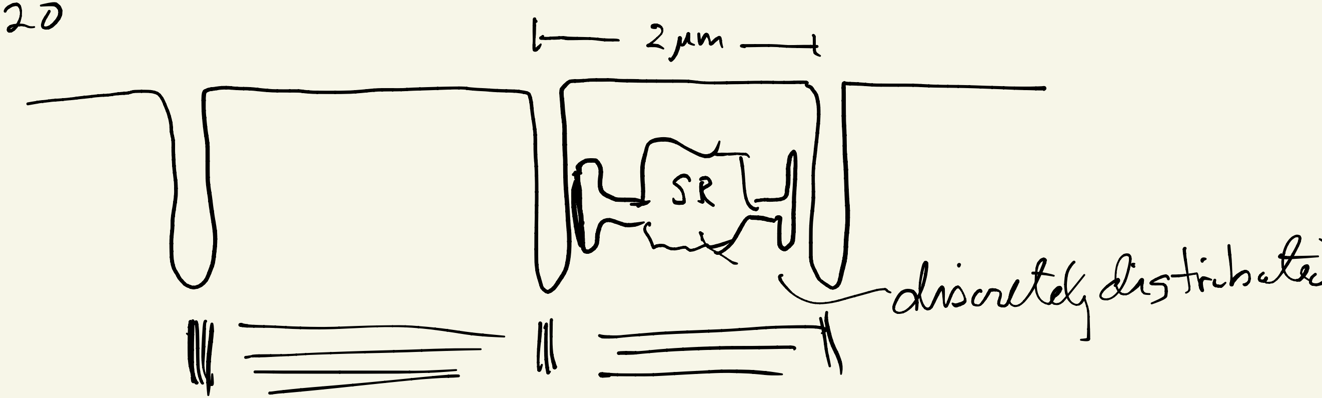


= voltage gated calcium channel

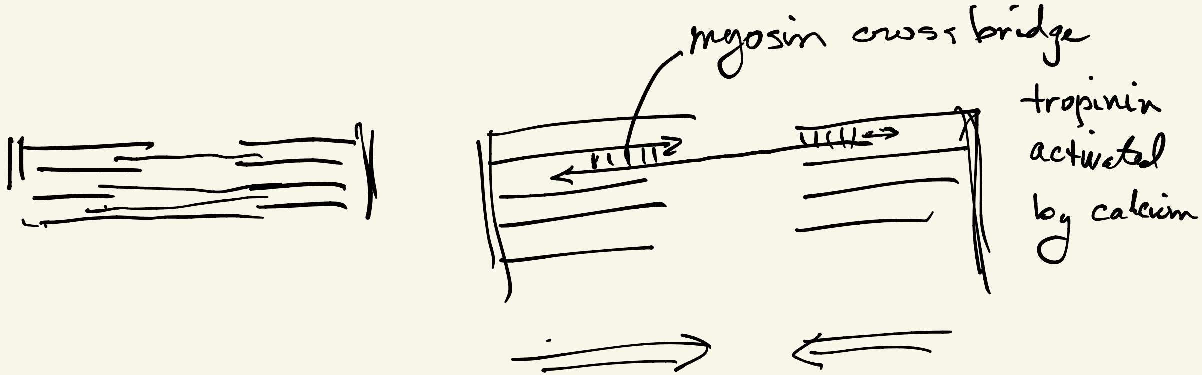
traveling waves?

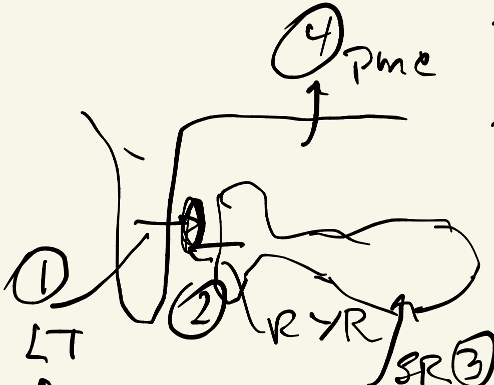
RyR are CICR receptor

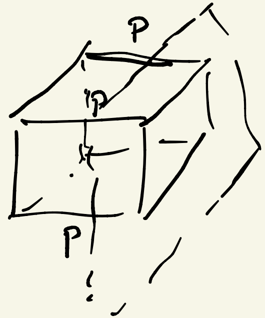
4|9|2020

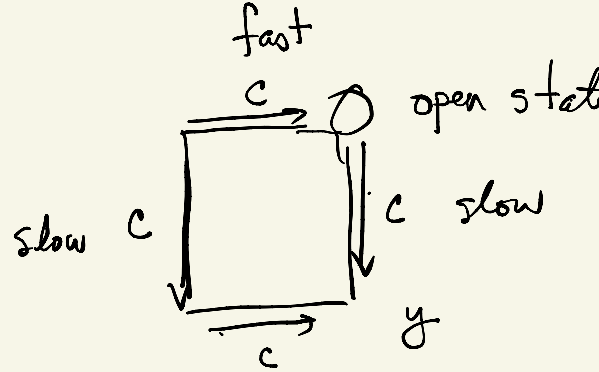


Z band





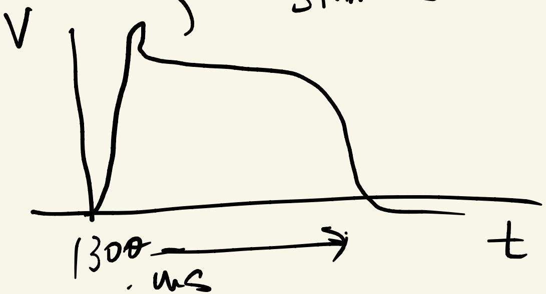


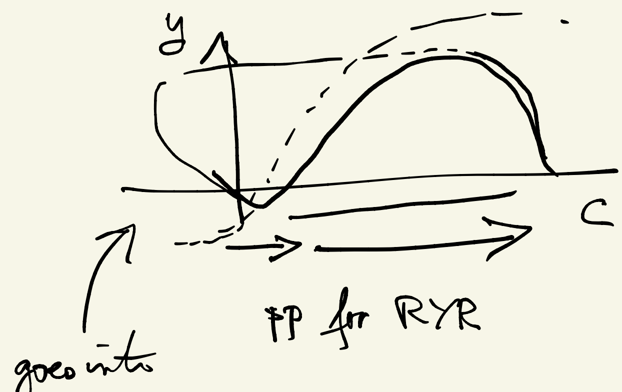


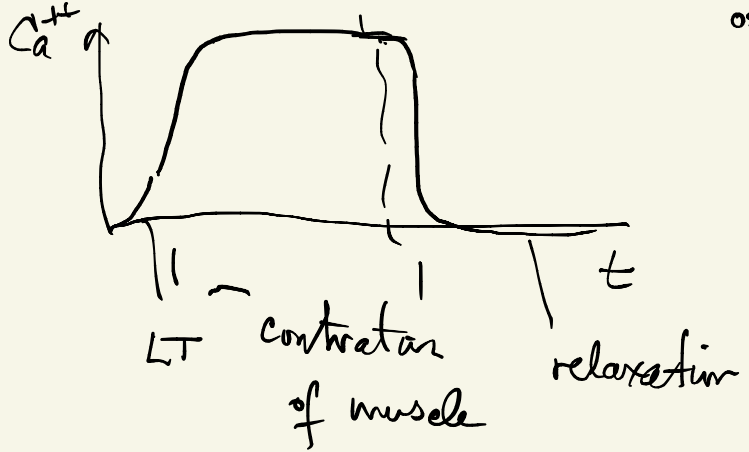
fast

$$\frac{dc}{dt} = \underline{\underline{J_{LT}}} + \underline{J_{RyR}} - \underline{J_{serca}} - \underline{J_{PMC}}$$

stimulus







oscillation.

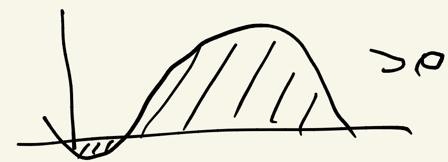
calcium overload.

$C_T \uparrow$ too much calcium in SR

$\Longrightarrow$ explanation for spontaneous contraction of heart arrhythmia.

include spatial.

$$\underbrace{\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + f(c)}_{\text{not good}}$$



$\Rightarrow$ traveling waves.

Excitable

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + \sum f(c)\,\underbrace{\delta(x-x_i)}_{\text{sites of release}}$$

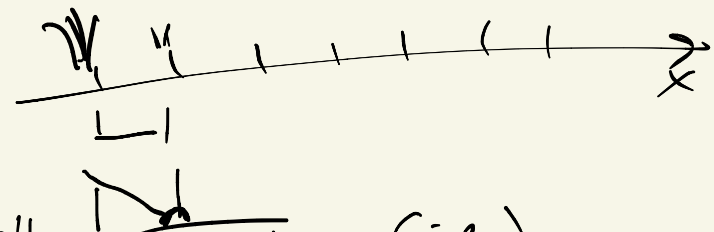
What space is discrete

$$\frac{\partial c_n}{\partial t} = D\left(c_{n+1} - 2c_n + c_{n-1}\right) + f(c)$$

$\Rightarrow$ propagation failure

Standing waves?

$$0 = D\frac{\partial^2 c}{\partial x^2} + \underline{\sum_{i=-\infty}^{\infty} f(c)\,\delta(x-x_i)} = 0$$



$$\frac{\partial^2 c}{\partial x^2} = 0$$

$\Rightarrow$ solving a difference equation. (idea)

Fire diffuse fire model

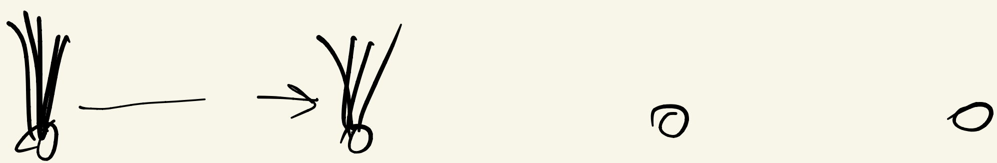
$$-k_s c$$

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + \sum_i \underbrace{\sigma\,\delta(x-x_i)\,\delta(t-t_i)}$$

large instantaneous release event

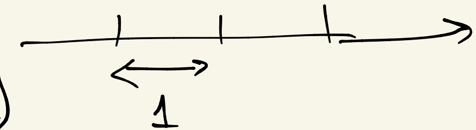
$t_i \doteq$ time at which $c = \underline{\theta}$ threshold.

firing event $\Rightarrow$ diffuses until next firing event



model this between firing events solution is diffusion

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} - k_s c + \sum_i \sigma\, \delta(x-x_i)\,\delta(t-t_i)$$



$$\frac{\partial c}{\partial t} = \beta\frac{\partial^2 c}{\partial x^2} - c + \sigma\sum \delta(x-i)\,\delta(\tau-\tau_i)$$

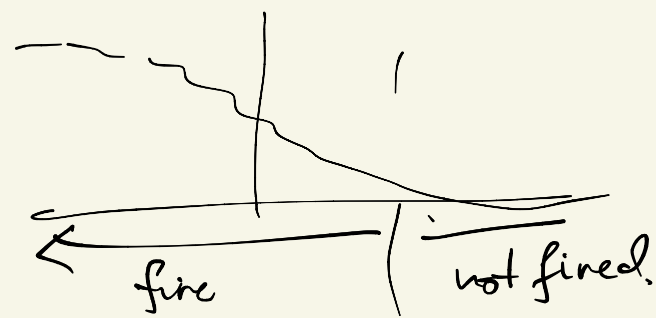
$$\overset{\circ}{c}(x,t) = \frac{\sigma H(t)}{\sqrt{4\pi\beta t}} \exp\left(-\frac{x^2}{4\beta t} - t\right)$$

fundamental solution of diffusion equation.

$c_i = \overset{\circ}{c}(x-x_i,\, t-t_i)$ $\qquad x_i, t_i$

$$c(x,t) = \sum_i \overset{\circ}{c}(x-x_i,\, t-t_i)$$

where firing has occurred



Are there traveling waves?

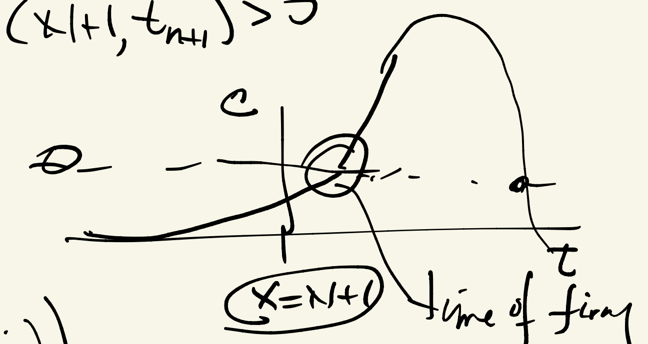
$$x_i = i\delta, \quad t_i = t_{i-1} + \Delta\tau$$ fixed delay

velocity $\dfrac{\delta}{\Delta\tau}$ $\begin{matrix}\text{distance traveled} \\ \text{time it takes.}\end{matrix}$

When does firing occur?

When $\underline{c = \theta}$ at time of firing

$$c(N+1, t_{n+1}) = \theta \qquad c'(N+1, t_{n+1}) > 0$$



$$\theta = \sum c^0(N+1-i, t_{N+1} - t_i)$$

$$\theta = \sum c^0(N+1-i, \Delta\tau(N+1-i))$$

$$\frac{\theta L}{\sigma} = \sum_{n=1}^{\infty} \frac{1}{\sqrt{4\pi n \eta}} \exp\left(-\frac{n}{4\eta} - \beta^2 \eta\right) = g_\beta(\eta)$$

$$\eta = \frac{\beta \, \Delta\tau}{L^2}$$

Find η so that

$$\eta = \eta\left(\frac{\theta L}{\sigma}\right)$$

Plot $g_\beta(\eta)$ vs θ.

reverse axes

Plots: Use Matlab code fdf_plots.m