Mathematical Physiology Weeks 5-8, Michaelmes Fern 2025

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4.2 wave propagation c = v-ke-F two pool model: $C_{\mathbf{s}} = F$ intracellular + diffusion of sarcoplam calcium mortrix fluid bec = r-kc-F + Daxc 06Cs = F upon nondimensionalisation t = t/k $X = \ell \widetilde{x}$ and the lengthscale l is fixed by diffusion: DOXC = De-2 DXC Ot C = k Ot C in particular, space gives one additional degree of freedom 80 we can set l'such that: $\mathcal{D}\ell^{-2}\mathcal{E}^{-1}=1$ l = /D/k diffusion-to-decay laythocale

hence, the model becomes: $(u+vv)_{t} = \mu-\mu+\mu\times\times$ $\varepsilon v_{t} = \varepsilon(\mu,v)$ next we look for travelling wave volutions: Ne = N(S) where $S = x + \sigma t$ σ in TW wordinates () = d d\$ $\int o(u+vv)' = \mu - u + u''$ $\int e \sigma v' = f(u,v)$ f(u,v)=0 W1 = 0 sketch of the nave in (M,v)-plane

the vave would look something like recoll E~ k, so smaller & means slower deay of sarcoplasm concentration, which will lead to a faster mave. El => 07 D > A Wave speed celebron this occurs over a thin region: $3 = \epsilon^a t$ [σε-α (μ+ γν) = μ- μ + ε-2α μ" of to the first 1 0 E 1 - a (u+ Yv) = E (p - u) + E 1 - 2a u 11 $\int \sigma \varepsilon^{1-\alpha} \sigma' = f(u,v)$ these can be balanced if $a = \frac{1}{2}$, $\sigma = \frac{1}{\sqrt{\epsilon}}$ (moteunote ~ TE!)

) S (u+ v) = E(u-u) + u" to give:] sv' = f(u,v) which at zeroth order in E, gives: $\int S(u+vv)' = u''$ $\int Sv' = f(u,v)$ 0(4) thua: s(u+Yv) - s(u0+Yv0) = u'-10 now simply define $U = u - u_D$ to eget . W = 0-50 U' = F(U, V) v_{saddle} v_{saddle} v_{saddle} v_{saddle} v_{saddle} v_{saddle} | W = s (W + Y V) u'=0

does a heteroclinic sol. from D to A

exist? (saddle
$$\rightarrow$$
 caddle)

only for a specific value of s!

assuming monotonicity of V:

$$\frac{dV}{dU} = \frac{1}{s^2} \frac{F(U,U)}{U+TU}$$

war $U = 0$, and on the stable soddle

seperatrix $U \sim k$ at while k satisfies!

$$k = \lim_{s \to 0} \frac{dU}{du}$$

$$U \Rightarrow 0$$

$$V + F(0) + F(0)U + F(0)U + C(0)U + C(0$$

determinant = $\Delta = [8^2 + |Fv|]^2 + 4Fu8s^2$ which is > 0 => one positive not $k = \frac{1}{2Ys^2} \left[-(s^2 + |Fv|) + \sqrt{\Delta} \right]$ Sto IFVI until O (stelle mode) -> V ~ O 57+10 formally 8=+00 $34\nu=0\Rightarrow V=0$ $42\nu=0\Rightarrow V=0$ so by continuity 3s > 0 s.t Theteroclimac is it unique? if trajectories variations were monotone, then yes! (see lecture notes) => s (and hence or) is selected by the front! end of D-A

4-3B this a clow phase, reall nee had: $\int \sigma(u+v\sigma)'=\mu-u+u'$ $\int \sigma \varepsilon \sigma' = f(u, \sigma) \quad \text{with } \sigma = \frac{s}{\sqrt{\varepsilon}}$ D -> A occured on 3 ~ TE D B 1 2 NE 2 6 2 0 what about A = D? here o'~ 0 and we look for possible balances 3 = 8 5 1 5 E 1/2+b (u+ yor) = u-u+ E 2b u 11 S & 1/2 + b y = f (M , y) which can be balanced if $b = \frac{1}{2}$

ther the wave has a width $\sim \frac{1}{\sqrt{\epsilon}} + O(\sqrt{\epsilon})$ and we obtain: 1 s(u+ &v) = m- u + Eu' $\int SEV = f(M,V)$ so at 200th order in E: 0(4) | f(u,v) = 0 = > 0 = g(u) $u's(1+8g'(u)) = \mu - \mu$ su' = u-u 4 + Y g'(n) 11 > 11 and gl > 0 in this region so. and in decreases from 1/4 to 1/8

this region is similar to A-D, and also has width VE, to order O(1) in E we get:

 $|u'=s[u-uB+\gamma(v-v_B)]$ |sv'=f(u,v)

UB is determined by a similar argument to

S, connecting B -> C. See Learne notes

for more describe

NOTE: The nondimensional diffusion coefficient in the leature notes is $\nu = \varepsilon$. I've chosen this value to 1, and discussed the dependance of each region's width and of the speed on ε . These two approachs are equivalent, with $S = \sqrt{\varepsilon} \ \sigma = O(1)$.

in higher dimensions

two main type of : target pattens & spirel wave can occur

Common framework:

$$\mu(\vec{x},t) = \mu(r,o,t)$$

mo = 4(r)
spiral waves have been observed in frog developing eggs.

5. the heart (dectrocherical action) two main parts to the heart function: (1) electrochemical action: creates muscle contraction to pump blood around the (2) mechanical action: evables unidirectional circulation via a system of volves we begin studying (1) RA LA

the luart has four chambers

RA: right atnium

LA: left atrium

RV: right ventricle

LV: left ventricle

· blood flows into the RA from the venous system (superior and inferior vena cava), then flows

to the RV and from these perfuses through the luys to gain exygen. o blood returns to the heart into the LA, there to the LV and the LV pumps oxygenated blood out to the body through the acrta. · Cardial cells are electrically active: -> Sino-atrial mode cells, located at the RA, act as pacemakers with a periodic action potential. - three are also other types of cells that are excitable / extrio-ventricular mode cells, rentricular myocytes, Pirkinje pières) but with a different action potential.) compose the muscle of the ventricles the ventrales contract when all the myoghts

electrocardiogram (ECG): body surface measurement of the electrical signols that stimulate the contraction of cardiac cell membranes and cause the depolarisation of the membrane potential, and the subsequent repolarisation. (cell membrus ore electrically polerised) - different electrical synals can come the mentione to dyplane. ECG meanues there · a second electrical signal repolaries the Amembrane ECG P = depolerisation of the otria QRS = depolarisation of the ventricles Goddnotes = repolarisation of the ventricles

thre are ~20 waves propagating through the heart from the sino-atrial mode (RA). the heart is not 1d! blockage of conduction paths can lead to "re-entrant spairal waver, which cycle wand the diseased tissue this can cause ventoicular tachyeordia or if they secome chastic verticuler fi brillation our goal: study the action potential of cordiac cells in particuler: ventriculer myoujtes and SA node cells. Goodventrollar myocytes SA node cells

The Noble model (1962) · Early model for the action potential of neutricular myocytes o similar to Hodgkin - Huxley but more variables due to the greater number of currents involved. conic current = Na + K + leakage wests Noble model is largely based $C_{\rm m} \frac{dV}{dt} = -I_{\rm i}$ on experimental T: = INa + Ix + I results. INa = [qo + gramile] (V-VNa) suitching gate off IK = (PK + gkn4) (V - VK) indiant long lasting cond. of K

in the Noble () madel g is very & constant lockese conductivity Small and the gate variables satisfy: in fact with Cm m = m ps - m, gr = 0, the model shows Thh = 100 - 12 call-sutained perodic behavior This = no -n Cm ~ 0.25 ms 2h ~ 8 ms Th ~ 500 ms ! much layer - Mis Nos 1 remember graph for 10 50 1 Corpernats! mo, hos, nos depend on VI

for egs. to solve (V, n, m, h) · to reduce the system we observe that Tn>> Zh >> Zm Lo successive relaxation of the · We further aissure gl ~ 0 so trat the reduces to: (amy to) Thh = ho(V)-h \ CmV = - \[(go + g Na min (V) h) (V - VNa) + f(V) (V - VK) \]) fort phene of Noble model, timescale ~ En where f(v) = f(v) + g(v) + g(v)on this phase n ~ constant real to ~ 500ms) then we could look in the phase plane for a trajectory winnerry two fixed equations

the phere plane looks like: vode logh / v = 0 show these are the stable of t 12-80 mV (or send me an email if you don't see it!) more formelly, we would V_{Na} rescale time by $Zh: t = Zh\bar{t}$ to get: $\frac{Zm}{Zh}\dot{m} = mu - m , \frac{Zm}{Zh} < < 1$ h = h - h $\frac{Zn}{Zh} \dot{n} = no - n \qquad \frac{Zn}{Zh} = \frac{1}{\varepsilon} >> 1$ L) n = ε (n - n) on the forst phase n ~ n w we also nondimensionalise V -> V

the full equation for T would become: T = - G(V, h, n) (see Lecture Notes for full wondin. Whe:

6 = - [80 + 8 wa ma (7) h] (Vwa - V) + \$ (V+1) + YL (V+VL) U Noble took 8L = 0 to / (V)+ 1xn1 begin with. (leaker part) -> slow variations in n $n = \varepsilon (np - n)$ solutions storts at the left fixed point, where V is low => nu is low => n goes down => & goes down => mildine gass down the two steedy states more and

become unstable so we jump to the right stedy state from here, no is now high so no-n >0 =) M goes up so the nullchine (v=0) goes back up again until the left steady state reappears and we jump back there again. [the two fixed points on the niht " drawy from lette! waves in two or three dimensions waves propagate though the heart in ~ two spatial dimensions · Wort muscle is compared of billions of interconnected ells in practice, homogenisetor techiques allow us to

desire continuum effective descriptions of electrical activity in the tissue. We will consider the simplest possible model where we Rn is a vector of reactants e.g. w = (V, m, n, h) and the reaction kinetics are siven by f(w), where f: IR" -> IR", and spatial transmission is modeled via liner diffuin: Dtw = f(w) + E Dw · all reactants have saw liferinity: & , f(w) is such that in = f(w) has a Stable limit cycle behavior with priod -> we call this sol. W = Wo(t) · spatial transmission occurs on a slow the slow time is $z = \varepsilon t$

idea: becoure E is small, diffrent cells will oscillate with the same pood, but with different place. Also, control vonations
cef the place will evolve on a slow timescale
(z = et)! method of multiple scales. we seek a solution $W = W(x,t,\epsilon t) = w(x,t,\epsilon)$ then the reaction - diffusion eq. becomes: D+w + E D=w = f(w) + E Dw we seek a perturbative sol: W = Wo + & W, +... at order zero: h θewo = f(wo) limit eycle oscilletion > W. = W. (t + 4(x,z)) period cloudy varying phase Sawo = (at = t + c'(x,z)

atorder 0/E) we have: 2+ W1 + 2- w0 = Df(w.)ω, + Δω. $\partial t w_i - D f(w_0) w_i = - \partial z w_0 + \Delta w_0$ in tens of wo = Wo (t+4 (x,z)) J = Df (W.) 8 = 8 = 4 Wo $\Delta W_0 = \nabla \cdot [\nabla \mathcal{V} W_0'] = \Delta \mathcal{V} W_0' + |\nabla \mathcal{V}|^2 W_0'$ so putting everyteing to settler: 2001 - Jw, = (-0=4+ by) Wo+10412wo" non-homogeners equation this is a (remember DES II)

now use Fredholm's alternative; u is a solution of Lu = f if \VE noll(2) (i.e. 4v = 0) we have < \$1, v > = 0 $\int \mathcal{L} V = 0$ in our case we need the integral one one period $S^{T} = 0$.

So, take v such that $\partial_{t}v - Jv = 0$.

and then: and then: 0= \(\bigv \bigv \warphi' \left(- \dagger \psi + \dagger \psi \right) + \warphi'' \sqrt{2} dt = (- 2=4+A4) \vwo'dt + |\v\4|\frac{1}{2}\vwo''dt

so we obtain the solvebility condition: $(\partial_z 4 - \Delta 4) \int_0^1 V W_0' = |\nabla 4|^2 / V W_0''$ define: $\alpha = \frac{\int_0^T v w'' dt}{\int_0^T v w'' dt}$ D=4 = A4 + 217412 which gives the eq. for the phase Summery: Dtw = f(w) + & Dw to order zero we get: $W(x_1t) \sim W_0(t+\psi(x_1z))$ where $\partial_z \psi = \Delta \psi + x |\nabla \psi|^2$ and Wolt) is the limit apple of 2+w= f(w).

some notes on: $0z4 = \Delta4 + x17412$. both spirel and target patterns! · integrated form of Burgers | equation set u = - Y-1 - 4 and then 8 = (V 4) = V A V + Q V | V 4 | 2 · note V. u = -r Dy 80 7 (V·u) = - Y VA Y and this is related to the vector Laplacian (note different from scalar Leplecian) $\Delta u = \nabla(\nabla u) - \nabla \times (\nabla \times u)$ for ud VV gradient field Txu=0 80 V (V. U) = AU.) Hersian of 4 · also V | V 4 | = 2D 4 V 4 =282 (Ju)U =272 (u.V) u (convective for w

so we get: Y 0 = u +2 x Y2 (u. v)u = YAu choose 8 = 22 $\partial z u + (u \cdot \nabla) u = \Delta u$ Viscous Burgers' equation, which is known to develop "shocks" (only for small diffusion)

=> jumps of the phase gradient target patterns and spiral waves We focus on $\partial_{\overline{L}} \psi = \Delta \psi + \overline{a} |\nabla \psi|^2$ relevant situation for the lunt: SA cell acting as a preewaker located at the origin

these originate target patterns

80 assume (as a result of cells mor ~0)

 $4(z_i x) = z$ if |x| = r = b

there are BCS coordinates

We look for a solution that decays radially:

 $\gamma(z, x) = \gamma(z, r) = z - \varphi(r)$ with $\varphi(b) = 0$ and $\lim_{r \to +\infty} \varphi(r) = 0$

 $\Rightarrow f'' + \frac{1}{r} f' - \kappa (f')^2 + 1 = 0$

this resembles some sort of Bessel eq. but not quite yet! Denote q = e of, then. g = - af g 9"=(a?f')2-af")9 $= \alpha q \left(\alpha (\beta')^2 - \beta''\right)$ $= \alpha q \left(\frac{1}{r} + 1 \right)$ = 29 - 31 L> 9"+ 9 - 29 = 0 and set $r = s/\sqrt{x}$ so: xg'' + xg' - xg = 0=> g 1 + 1 g 1 - g = 0 Modified Benel equation: g(s) = A Io (s) + B Ko(s)

To (s) ->+>> ax s ->+>0 hence $f \sim -\frac{\Delta}{\alpha} \log (I_0)$ is not admissible A = 0and $f(n) = -\frac{1}{\alpha} log[BKo(/\alpha r)]$ B = ko ((a b) - 1 for BC at r = 6. $\Rightarrow f(r) = -\frac{1}{\alpha} log \left[\frac{K_0(\sqrt{\alpha}r)}{K_0(\sqrt{\alpha}b)} \right]$ Q: what happens if a < 0? r>> => 4~ Z - F $= -\frac{1}{12} \left(r - \sqrt{\alpha} z \right)$ => propagation speed = VX

spirel waves also exist, but are associated with a core which allows the maintenance of a travelling wave eirculating (this makes it slightly less assure BC at the core is given by: r=b => 4 = 2= + mo now use the auset 2: 4 = 22 + mo - g(r) to find the solution. $g = -\frac{1}{\alpha} \log \left[\frac{k_0(\sqrt{\alpha} n)}{\kappa_0(\sqrt{\alpha} n'b)} \right]$ 80 Y~ Slz+m0-/slrasr>+10. this is an Archivedean spiral!

in general, there arise when electrical signals proposate unevenly through huart tissue due to heterogeneity. (atricl or ventricular) curved front propagation consider a wave in which the phase of the potential varies rapidly within a thin region (wave front) which curs more lightly in other directions 450 we will work with the general eguction: 0= V = f(v) + DV (*) assuming that it has a ID travelling were solection V=V(3), 3 = ct-x, c>0, V(w)= 4, V(-w)=0

 \Rightarrow eV' = f(V) + V''let of denote the phase of the wave and the location of the nave front is given as $\psi(x,t) = 0$ x = 1Rd, d = 2, 3. We want to describe the evolution of the front, which is slowly verying in the directions transvere to the direction of propagation. curvilineer coordinate, so that 3 muarres distance along the normals of 4(x,t) = ct proximel is $\vec{u} = -\frac{\nabla \psi}{|\nabla \psi|}$ $\psi = ct$ look for a solution to (*) of the form V = V(Y(x(t))) so that V 2+ 4 = A4V + 104/2V" + f(V)

next we take a "quari" ID approximation arouning the front is thin two, in the curviliner coordinate I we have: 8 = V'(4) 1741 this follows from. VV = V'(4) V4 and BV is the anichive of Vinthu & direction So $0 \vee -\vec{n} \cdot \nabla V = V'(4)\vec{n} \cdot \nabla V$ Airection

Airection $= V'(4)|\nabla Y|$ then we also have 0= V = V"(4) | V4| + V'(4) 0= | V4) so we obtain

and we already know: cosV = f(v) + osV 80 we obtain 1041 = 1741 + C - 021741 or equivalently: DEY = AY + C1541 - 081541 remember 95 9 = 56. n por 6 = 6(x) 80 VA - 08 10 A1 = A. (AA) - A (12A1) AA $= |\nabla \mathcal{V}| \nabla \cdot \left(\frac{\nabla \mathcal{V}}{|\nabla \mathcal{V}|} \right)$ $= -|\nabla \mathcal{V}| \nabla \cdot \vec{\mathcal{V}} = -\vec{\mathcal{V}}$ so we could rewritte it as: $V_n := \frac{\partial_t \psi}{|\nabla \psi|} = C - \nabla \cdot \vec{n}$ eikonal equation Goodnotes C normal velocity of the surface

this equation relates on, the normal velocity of the surface, to the curveture V. vi why is V. it related to the curvature? if it is flat (prefet front) then n = ct and v = 0 if 4 = ct looks like concentric rigs of ~ circular shape R ~ (×ix) and V. n = 1 = conduce mean curveture ~ ST. ndV (dS