Mathematical Physiology

Weeks 5 – 8, Michaelmas Term 2025

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4.2 wave propagation

two pool model:

$$\dot{c} = r - kc - F$$

$$\dot{c}_s = F$$

intracellular matrix fluid

+ diffusion of sarcoplasm calcium

$$\partial_t c = r - kc - F + D\partial_x^2 c$$

$$\partial_t c_s = F$$

upon nondimensionalisation $t = \tilde{t}/k$

$$x = \ell \tilde{x}$$

and the lengthscale ℓ is fixed by diffusion:

$$D\partial_x^2 c = D\ell^{-2}\partial_{\tilde{x}}^2 c$$

$$\partial_t c = k\partial_{\tilde{t}} c$$

in particular, space gives one additional degree of freedom so we can set ℓ such that:

$$D\ell^{-2}k^{-1} = 1$$

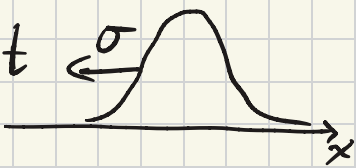
$$\ell = \sqrt{D/k}$$ diffusion-to-decay lengthscale

hence, the model becomes:

$$\begin{cases} (u+\gamma v)_t = \mu - u + u_{xx} \\ \varepsilon v_t = f(u,v) \end{cases}$$

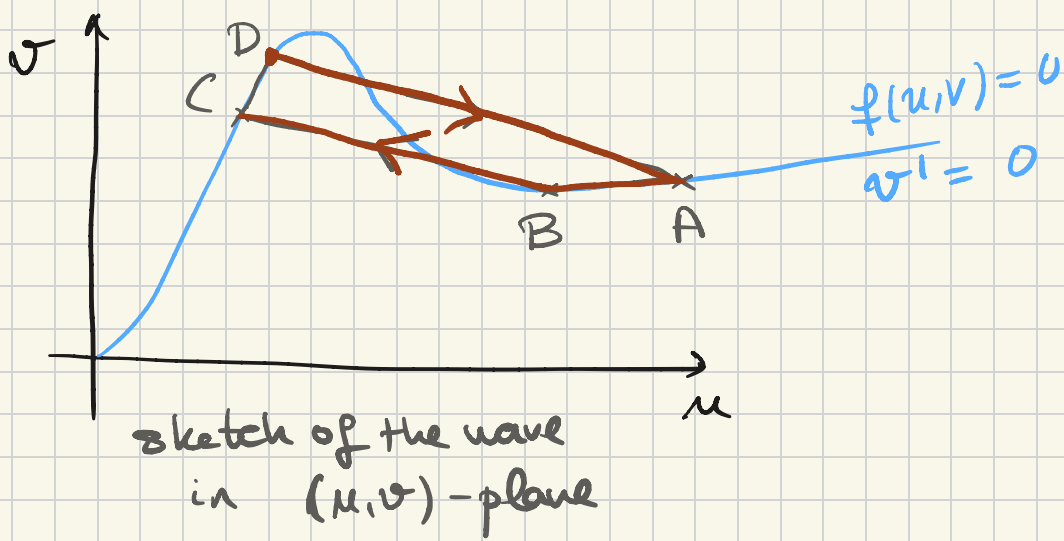
next we look for travelling wave solutions:

$u = u(\xi)$
$v = v(\xi)$ where $\xi = x + \sigma t$



in TW coordinates $(\,)' = \dfrac{d}{d\xi}$

$$\begin{cases} \sigma(u+\gamma v)' = \mu - u + u'' \\ \varepsilon \sigma v' = f(u,v) \end{cases}$$



sketch of the wave in (u,v)-plane

the wave would look something like

recall $\varepsilon \sim k$, so smaller ε means slower decay of sarcoplasm concentration, which will lead to a faster wave. $\varepsilon \downarrow \Rightarrow \sigma \uparrow$

D → A Wave speed selection

this occurs over a thin region: $\xi = \varepsilon^a \eta$

$$\begin{cases} \sigma \varepsilon^{-a}(u+v)' = \mu - u + \varepsilon^{-2a} u'' \\ \sigma \varepsilon^{1-a} v' = f(u,v) \end{cases}$$ (we still need to find $\sigma = \sigma(\varepsilon)$!)

$$\Downarrow$$

$$\begin{cases} \sigma \varepsilon^{1-a}(u+v)' = \varepsilon(\mu - u) + \varepsilon^{1-2a} u'' \\ \sigma \varepsilon^{1-a} v' = f(u,v) \end{cases}$$

these can be balanced if $\boxed{a = \frac{1}{2},\ \sigma = \frac{s}{\sqrt{\varepsilon}}}$

(note $\sigma \sim \frac{1}{\sqrt{\varepsilon}}$!)

to give: $\begin{cases} s(u+\gamma v)' = \varepsilon(\mu - u) + u'' \\ s v' = f(u, v) \end{cases}$

which at zeroth order in ε, gives:

$$\begin{cases} s(u+\gamma v)' = u'' \\ s v' = f(u, v) \end{cases} \qquad O(1)$$

then: $s(u+\gamma v) - s(u_D + \gamma v_D) = u' - u_D'^{\,0}$

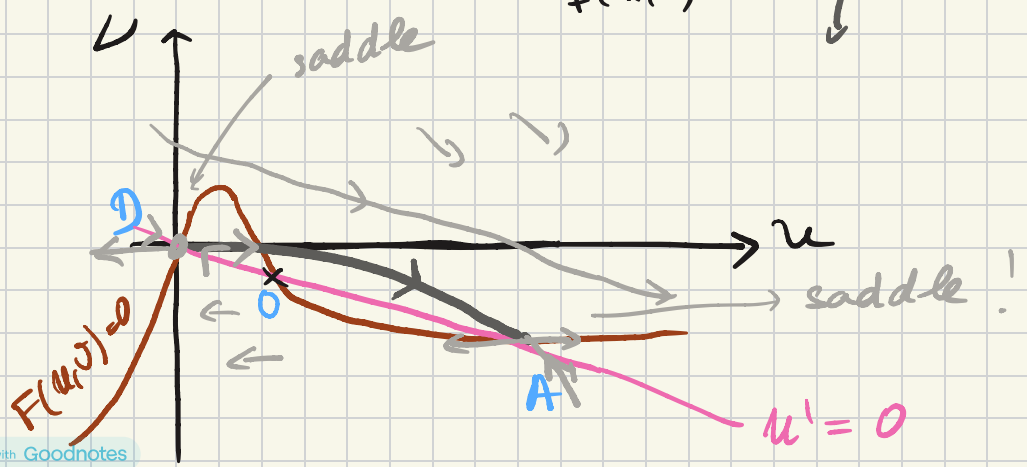
now simply define $\mathcal{U} = u - u_D$

$\mathcal{V} = v - v_D$

to get:

$$\begin{cases} \mathcal{U}' = s(\mathcal{U} + \gamma \mathcal{V}) \\ \mathcal{V}' = F(\mathcal{U}, \mathcal{V}) \end{cases} \quad \text{"} f(u,v) \text{"}$$

2D system!



does a heteroclinic sol. from D to A exist? (saddle → saddle)

only for a specific value of s!

assuming monotonicity of V:

$$\frac{dV}{du} = \frac{1}{s^2} \frac{F(u,V)}{u+\gamma V}$$

near $u=0$, and on the stable saddle seperatrix $V \sim k u$ where k satisfies:

$$k = \lim_{u\to 0} \frac{dV}{du}$$

$$= \frac{1}{s^2} \lim_{u\to 0} \frac{F(0) + F_u(0)u + F_v(0)ku + O(u^2)}{u + \gamma k u}$$

$$= \frac{1}{s^2} \frac{F_u + F_v k}{1+\gamma k}$$

$F_v(0) < 0$ so:

$$s^2 k(1+\gamma k) = F_u - |F_v| k$$

$$s^2 \gamma k^2 + k(s^2 + |F_v|) - F_u = 0$$

determinant $= \Delta = \left[s^2 + |F_v| \right]^2 + 4 F_u \gamma s^2$

which is > 0 $\Rightarrow$ one positive root

$$k = \frac{1}{2\gamma s^2} \left[-(s^2 + |F_v|) + \sqrt{\Delta} \right]$$

$s \downarrow 0 \longrightarrow \dfrac{F_u}{|F_v|}$ → motion along V-nullcline until 0 (stable node)

$s \uparrow +\infty \longrightarrow 0$ → $V \sim 0$

formally $s = +\infty$

$\Rightarrow \dfrac{dv}{du} = 0 \Rightarrow V = 0$

so by continuity $\exists s > 0$ s.t heteroclinic orbit

is it unique? if trajectories variations were monotonic, then yes! (see lecture notes)

$\Rightarrow$ s (and hence σ) is selected by the front!

end of $\mathcal{D} \to A$

A → B

this a slow phase, recall we had:

$$\begin{cases} \sigma (u+\gamma v)' = \mu - u + u'' \\ \sigma \varepsilon v' = f(u,v) \end{cases}$$

recall! with $\sigma = \frac{s}{\sqrt{\varepsilon}}$

D → A occured on $\xi \sim \sqrt{\varepsilon}$

$\sqrt{\varepsilon}$? $\sim \varepsilon^b$? $b \geq 0$

what about A → B ? here $v' \sim 0$

and we look for possible balances

$$\xi = \varepsilon^{-b} s$$

$$\begin{cases} s\,\varepsilon^{-1/2+b}(u+\gamma v)' = \mu - u + \varepsilon^{2b} u'' \\ s\,\varepsilon^{1/2+b} v' = f(u,v) \end{cases}$$

which can be balanced if $\boxed{b = \frac{1}{2}}$

then the wave has a width $\sim \frac{1}{\sqrt{\varepsilon}} + O(\sqrt{\varepsilon})$

and we obtain:

$$\begin{cases} s(u+\gamma v)' = \mu - u + \varepsilon u'' \\ s\varepsilon v' = f(u,v) \end{cases}$$

so at zeroth order in ε:

$O(1)$

$$\begin{cases} f(u,v) = 0 \Rightarrow v = g(u) \\ u' s\left(1+\gamma g'(u)\right) = \mu - u \end{cases}$$

$$s u' = \frac{\mu - u}{1+\gamma g'(u)}$$

$u > \mu$ and $g' > 0$ in this region so:

$$u' < 0$$

and u decreases from u_A to u_B

B → C

this region is similar to A → D, and also has width $\sqrt{\varepsilon}$, to order $O(1)$ in ε we get:

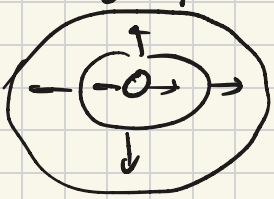
$$\begin{cases} u' = s\left[u - u_B + \gamma(v - v_B)\right] \\ sv' = f(u, v) \end{cases}$$

u_B is determined by a similar argument to s, connecting $B \to C$. See Lecture notes for more details.

NOTE: The nondimensional diffusion coefficient in the lecture 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 approaches are equivalent, with $s = \sqrt{\varepsilon}\sigma = O(1)$.

Waves in higher dimensions

two main types of wave can occur : target patterns & spiral waves



common framework:

$$u(\vec{x},t) = u(r,\theta,t)$$

$$= u(-\Omega t + m\theta - \psi(r))$$

$m = 0$, target pattern $\rightarrow \psi' > 0$, $\Omega > 0$

$m \neq 0$, spiral wave

$$\downarrow$$

$$m\theta = \psi(r)$$

spiral waves have been observed in frog developing eggs.

5. the heart (electrochemical action)

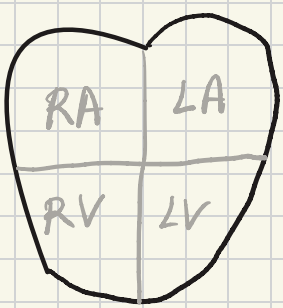
two main parts to the heart function:

(1) **electrochemical action**: creates muscle contraction to pump blood around the body

(2) **mechanical action**: enables unidirectional circulation via a system of valves

we begin studying (1)

the heart has four chambers



RA: right atrium
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 there perfuses through the lungs to gain oxygen.

- blood returns to the heart into the LA, then to the LV and the LV pumps oxygenated blood out to the body through the aorta.

- Cardiac cells are electrically active:

→ Sino-atrial node cells, located at the RA, act as pacemakers with a periodic action potential.

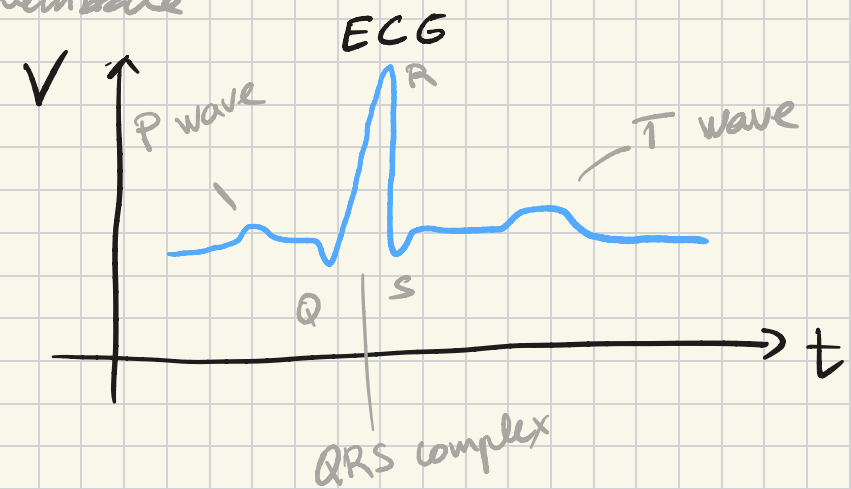
→ there are also other types of cells that are excitable (atrio-ventricular node cells, ventricular myocytes, Purkinje fibres) but with a different action potential.

→ compose the muscle of the ventricles
the ventricles contract when all the myocytes contract simultaneously.

electrocardiogram (ECG): body surface measurement of the electrical signals that stimulate the contraction of cardiac cell membranes and cause the depolarisation of the membrane potential, and the subsequent repolarisation.

(cell membranes are electrically polarised)

- different electrical signals can cause the membrane to depolarise. ECG measures these
- a second electrical signal repolarises the membrane



P = depolarisation of the atria

QRS = depolarisation of the ventricles

T = repolarisation of the ventricles

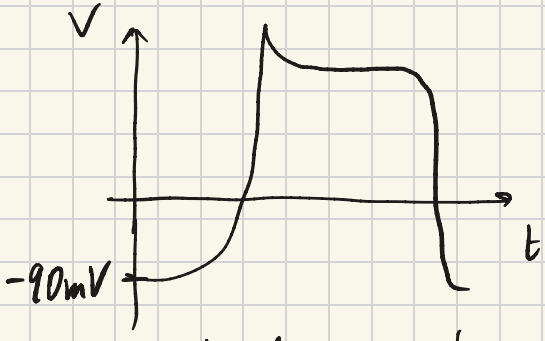
there are ~20 waves propagating through the heart from the sino-atrial node (RA).

the heart is not 1d! blockage of conduction paths can lead to "re-entrant" spiral waves, which cycle around the diseased tissue

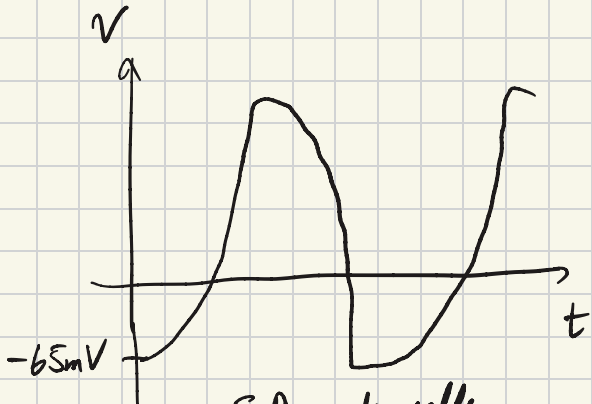
this can cause ventricular tachycardia.

or if they become chaotic ventricular fibrillation

our goal: study the action potential of cardiac cells. in particular: ventricular myocytes and SA node cells.



ventricular myocytes



SA node cells

The Noble model (1962)

- Early model for the action potential of ventricular myocytes
- similar to Hodgkin-Huxley but more variables due to the greater number of currents involved.

ionic current = Na + K + leakage currents

$$C_m \frac{dV}{dt} = -I_i$$

$$I_i = I_{Na} + I_K + I_L$$

$$I_{Na} = \left[g_0 + g_{Na} m^3 h \right] (V - V_{Na})$$

g_0: residual; $g_{Na} m^3 h$: HH; m: switching on gate; h: switching off gate

$$I_K = (f_K + g_K n^4)(V - V_K)$$

f_K: instant; $g_K n^4$: long-lasting; cond. of K

(!) Noble model is largely based on experimental results.

$$I_L = g_L (V - V_L)$$

in the Noble model, g_L is very small

↳ constant leakage conductivity

and the gate variables satisfy:

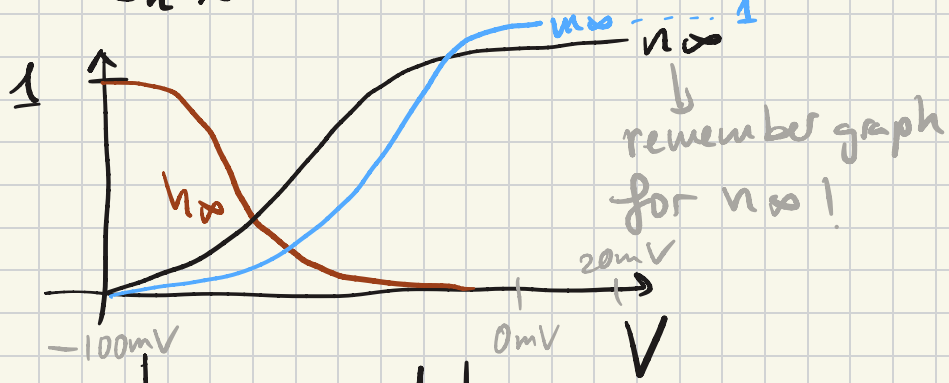
in fact with $g_L = 0$, the model shows self-sustained periodic behaviour

$$\tau_m \dot{m} = m_\infty - m,$$
$$\tau_h \dot{h} = h_\infty - h$$
$$\tau_n \dot{n} = n_\infty - n$$

where $\tau_m \sim 0.25\,ms$

$\tau_h \sim 8\,ms$

$\tau_n \sim 500\,ms$! much larger



↳ remember graph for n_∞!

↳ experiments!

$m_\infty, h_\infty, n_\infty$ depend on V!

four eqs. to solve (V, n, m, h)

- to reduce the system we observe that $\tau_n >> \tau_h >> \tau_m$

  ↳ successive relaxation of the gates.

- we further assume $g_L \sim 0$ so that the model reduces to: (assume $\tau_m \to 0$)

$$\begin{cases} \tau_n \dot{h} = h_\infty(V) - h \\ C_m \dot{V} = -\left[\left(g_0 + g_{Na} m_\infty^3(V) h \right)(V - V_{Na}) + f(V)(V - V_K) \right] \end{cases}$$

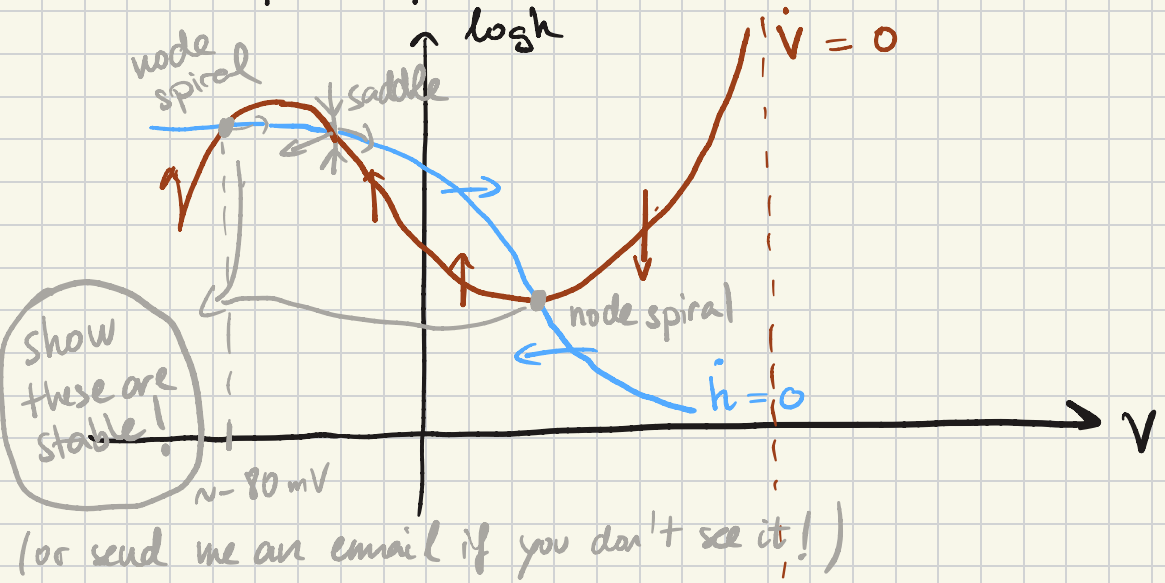
↳ fast phase of Noble model, timescale $\sim \tau_h$

where $f(V) = f_K(V) + g_K n^4$

on this phase $n \sim$ constant (recall $\tau_n \sim 500ms$)

then we could look in the phase plane for a trajectory connecting two fixed equations

the phase plane looks like:



(or send me an email if you don't see it!)

more formally, we would rescale time by τ_h: $t = \tau_h \tilde{t}$ to get:

$$\begin{cases} \frac{\tau_m}{\tau_h} \dot{m} = m_\infty - m \quad , \quad \frac{\tau_m}{\tau_h} << 1 \\ \dot{h} = h_\infty - h \\ \frac{\tau_n}{\tau_h} \dot{n} = n_\infty - n \qquad \frac{\tau_n}{\tau_h} = \frac{1}{\varepsilon} >> 1 \end{cases}$$

$$\hookrightarrow \dot{n} = \varepsilon (n_\infty - n)$$

on the fast phase $n \approx n_\infty$

we also nondimensionalise $V \longrightarrow \tilde{V}$

the *full* equation for $\dot{V}$ would become:

$$\dot{V} = -G(V, h, n)$$

(see Lecture Notes for full nondim.)

where:

$$G = -\left[\gamma_0 + \gamma_{Na} m_\infty^3(V) h\right](V_{Na} - V) + \phi(V+1) + \gamma_L(V + V_L)$$

$\phi(V+1) = \phi_K(V) + \gamma_K n^4$

Noble took $\gamma_L = 0$ to begin with. (leakage part)

→ slow variations in n $\quad \dot{n} = \varepsilon(n_\infty - n)$

solutions starts at the **left** fixed point, where

V is low ⇒ n_∞ is low ⇒ n goes down

⇒ ϕ goes down ⇒ nullcline goes down

the two steady states merge and

become unstable so we jump to the right steady state

from here, n_∞ is now high so $n_\infty - n > 0$

$\Rightarrow n$ goes up so the nullcline ($\dot{v} = 0$) goes back up again until the left steady state reappears and we jump back there again.

[the two fixed points on the right hand side merge as well!]

* drawing from lecture!

waves in two or three dimensions

waves propagate through the heart in ~ two spatial dimensions

- heart muscle is composed of billions of interconnected VMs
- gap junctions form electrical connections between cells

in practice, homogenisation techniques allow us to

derive continuum effective descriptions of electrical activity in the tissue.

We will consider the simplest possible model where $w \in \mathbb{R}^n$ is a vector of reactants

e.g. $w = (V, m, n, h)$

and the reaction kinetics are given by $f(w)$, where $f: \mathbb{R}^n \to \mathbb{R}^n$, and spatial transmission is modeled via linear diffusion:

$$\partial_t w = f(w) + \varepsilon \Delta w$$

- all reactants have same diffusivity: ε
- $f(w)$ is such that $\dot{w} = f(w)$ has a stable limit cycle behavior with period T → we call this sol. $w = W_0(t)$
- spatial transmission occurs on a slow timescale

the slow time is $\tau = \varepsilon t$

idea: because ε is small, different cells will oscillate with the same period, but with different phase. Also, spatial variations of the phase will evolve on a slow timescale ($\tau = \varepsilon t$)!

↳ method of multiple scales.

we seek a solution $w = w(x, t, \varepsilon t) = w(x, t, \tau)$

then the reaction-diffusion eq. becomes:

$$\partial_t w + \varepsilon \partial_\tau w = f(w) + \varepsilon \Delta w$$

we seek a perturbative sol: $w = w_0 + \varepsilon w_1 + \dots$

at order zero:

↳ $\partial_t w_0 = f(w_0)$ limit cycle oscillations

$$w_0 = W_0(t + \psi(x, \tau))$$

W_0: period T!

ψ: slowly varying phase

, this is a constant of integration

$$\int \frac{dw_0}{f(w_0)} = \int dt = t + C'(x, \tau)$$

at order $O(\varepsilon)$ we have:

$$\partial_t w_1 + \partial_z w_0 = Df(w_0) w_1 + \Delta w_0$$

$$\Rightarrow$$

$$\partial_t w_1 - Df(w_0) w_1 = -\partial_z w_0 + \Delta w_0$$

in terms of $w_0 = \bar{W}_0(t + \psi(x, z))$

we have:

$$J = Df(\bar{W}_0)$$

$$\partial_z w_0 = \partial_z \psi \bar{W}_0'$$

$$\Delta w_0 = \nabla \cdot [\nabla \psi w_0'] = \Delta \psi w_0' + |\nabla \psi|^2 w_0''$$

so putting everything together:

$$\partial_t w_1 - J w_1 = \left(-\partial_z \psi + \Delta \psi\right) w_0' + |\nabla \psi|^2 w_0''$$

this is a non-homogeneous equation!
(remember DEs II)

now use Fredholm's alternative:

u is a solution of $\mathcal{L}u = f$ if $\forall v \in \text{null}(\mathcal{L})$ (i.e. $\mathcal{L}v = 0$) we have $\langle f, v \rangle = 0$

$$\int_\Omega f v = 0.$$

in our case we need the integral over one period $\int_0^T = 0$.

so, take v such that $\partial_t v - \mathcal{J} v = 0$.

and then:

$$0 = \int_0^T v \left[W_0'(-\partial_z \psi + \Delta\psi) + W_0'' |\nabla \psi|^2 \right] dt$$

$$= (-\partial_z \psi + \Delta\psi) \int_0^T v W_0' \, dt + |\nabla \psi|^2 \int_0^T v W_0'' \, dt$$

so we obtain the solvability condition:

$$(\partial_\tau \psi - \Delta \psi) \int_0^T v W_0' = |\nabla \psi|^2 \int_0^T v W_0''$$

define: $\bar{\alpha} = \dfrac{\int_0^T v W_0'' dt}{\int_0^T v W_0' dt}$ so:

$$\partial_\tau \psi = \Delta \psi + \bar{\alpha} |\nabla \psi|^2$$

which gives the eq. for the phase

Summary: $\partial_t W = f(W) + \varepsilon \Delta W$.

to order zero we get:

$$W(x,t) \sim W_0(t + \psi(x,\tau))$$
$$\tau = \varepsilon t$$

where

$$\partial_\tau \psi = \Delta \psi + \bar{\alpha} |\nabla \psi|^2$$

and $W_0(t)$ is the limit cycle of $\partial_t W = f(W)$.

some notes on: $\partial_z \psi = \Delta\psi + \bar{\alpha}|\nabla\psi|^2$

- both spiral and target patterns!
- integrated form of Burgers' equation

set $u = -\gamma^{-1}\nabla\psi$ and then

$$\partial_z(\nabla\psi) = \nabla\Delta\psi + \bar{\alpha}\nabla|\nabla\psi|^2$$

- note $\nabla\cdot u = -\gamma^{-1}\Delta\psi$

so $\nabla(\nabla\cdot u) = -\gamma^{-1}\nabla\Delta\psi$

and this is related to the vector Laplacian (note different from scalar Laplacian)

$$\Delta u = \nabla(\nabla\cdot u) - \nabla\times(\nabla\times u)$$

for $u \propto \nabla\psi$ gradient field $\nabla\times u = 0$

so $\nabla(\nabla\cdot u) = \Delta u$ → Hessian of ψ

- also $\nabla|\nabla\psi|^2 = 2D^2\psi\nabla\psi$

$$= 2\gamma^2(\nabla u)u$$

$$= 2\gamma^2(u\cdot\nabla)u$$ (convective form)

so we get:

$$\gamma \partial_t u + 2\bar{\alpha}\gamma^2 (u\cdot\nabla)u = \gamma \Delta u$$

choose $\gamma = \frac{1}{2\bar{\alpha}}$

$$\partial_t u + (u\cdot\nabla)u = \Delta u .$$

viscous Burgers' equation, which is known to develop "shocks" (only for small diffusion)

$\Rightarrow$ jumps of the phase gradient

target patterns and spiral waves

we focus on $\partial_t \psi = \Delta\psi + \bar{\alpha}|\nabla\psi|^2$

relevant situation for the heart:

SA cell acting as a pacemaker located at the origin

these originate target patterns

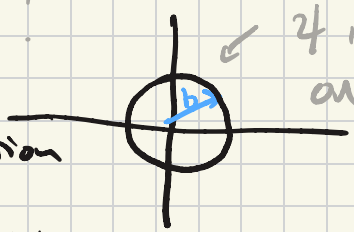
so assume (as a result of cells near ~ 0)

$$\psi(\tau, x) = \tau$$

$$\text{if} \quad |x| = r = b$$

↑ radius in polar coordinates

these are BC's!



↙ ψ is prescribed on $|x| = b$.

We look for a solution that decays radially:

$$\psi(\tau, x) = \psi(\tau, r) = \tau - f(r)$$

with $f(b) = 0$ and $\lim_{r \to +\infty} f(r) = 0$

we obtain

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

$$\Leftrightarrow \quad f'' + \frac{1}{r} f' - \alpha (f')^2 + 1 = 0$$

this resembles some sort of Bessel eq.

but not quite yet!

Denote $g = e^{-\alpha f}$, then:

$$g' = -\alpha f' g$$

$$g'' = (\alpha^2 (f')^2 - \alpha f'') g$$

$$= \alpha g \left(\alpha (f')^2 - f'' \right)$$

$$= \alpha g \left(\frac{1}{r} f' + 1 \right)$$

$$= \alpha g - \frac{g'}{r}$$

$$\Rightarrow \quad g'' + \frac{g'}{r} - \alpha g = 0$$

and set $r = s/\sqrt{\alpha}$ so: $\alpha g'' + \frac{\alpha g'}{s} - \alpha g = 0$

$$\Rightarrow g'' + \frac{1}{s} g' - g = 0$$ Modified Bessel equation:

$$g(s) = A I_0(s) + B K_0(s)$$

$$I_0(s) \to +\infty \quad \text{as} \quad s \to +\infty$$

hence $f \sim -\frac{1}{\alpha}\log(I_0)$ is not admissible

$A = 0$

and $$f(r) = -\frac{1}{\alpha}\log\left[B K_0(\sqrt{\alpha}\, r)\right]$$

$B = K_0(\sqrt{\alpha}\, b)^{-1}$ for BC at $r = b$.

$$\Rightarrow f(r) = -\frac{1}{\alpha}\log\left[\frac{K_0(\sqrt{\alpha}\, r)}{K_0(\sqrt{\alpha}\, b)}\right]$$

Q: what happens if $\alpha < 0$?

$$r >> \frac{1}{\sqrt{\alpha}} \Rightarrow \psi \sim \tau - \frac{r}{\sqrt{\alpha}}$$

$$= -\frac{1}{\sqrt{\alpha}}\left(r - \sqrt{\alpha}\,\tau\right)$$

$\Rightarrow$ propagation speed $= \sqrt{\alpha}$

Spiral waves also exist, but are associated with a core which allows the maintenance of a travelling wave circulating (this makes it slightly less excitty ?!)

assume BC at the core is given by:

$$r = b \Rightarrow \psi = \Omega z + m\theta$$

now use the ansatz:

$$\psi = \Omega z + m\theta - g(r)$$

to find the solution: $\nu = im\alpha$!

$$g = -\frac{1}{\alpha} \log\left[\frac{K_\nu(\sqrt{\alpha\Omega}\, r)}{K_\nu(\sqrt{\alpha\Omega}\, b)}\right]$$

so $\psi \sim \Omega z + m\theta - \sqrt{\frac{\Omega}{\alpha}}\, r$ as $r \to +\infty$.

this is an Archimedean spiral!

in general, these arise when electrical signals propagate unevenly through heart tissue due to heterogeneity.
(atrial or ventricular fibrilation)

curved front propagation

Consider a wave in which the phase ψ of the potential varies rapidly within a thin region (wave front) which curves more slightly in other directions

we will work with the general equation:

$$\partial_t V = f(V) + \Delta V \quad (*)$$

assuming that it has a 1D travelling wave solution

$V = V(\xi)$, $\xi = ct - x$, $c > 0$, $V(\infty) = 1$, $V(-\infty) = 0$

$$\Rightarrow \quad c\bar{V}' = f(\bar{V}) + \bar{V}''$$

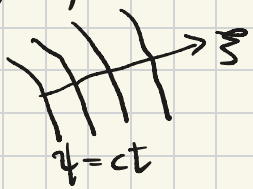
let ψ denote the phase of the wave and the location of the wave front is given as $\psi(x,t) = 0$

$x \in \mathbb{R}^d$, $d = 2, 3$.

We want to describe the evolution of the front, which is slowly varying in the directions transverse to the direction of propagation.

curvilinear coordinate, so that ξ measures distance along the normals of $\psi(x,t) = ct$

normal is $\vec{n} = -\dfrac{\nabla\psi}{|\nabla\psi|}$



we look for a solution to (*) of the form of $v = \bar{V}(\psi(x,t))$ so that

$$\bar{V}'\partial_t\psi = \Delta\psi\bar{V}' + |\nabla\psi|^2\bar{V}'' + f(\bar{V})$$

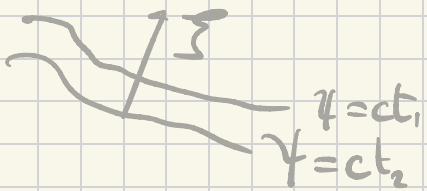
next we take a "quasi" 1D approximation

assuming the front is thin

thus, in the curvilinear coordinate ξ we have:

$$\frac{\partial \bar{V}}{\partial \xi} = V'(\psi)\,|\nabla \psi|$$

this follows from:



$$\nabla V = V'(\psi)\nabla\psi$$

and $\frac{\partial V}{\partial \xi}$ is the derivative of V in the ξ direction

so $\frac{\partial V}{\partial \xi} = \vec{n}\cdot\nabla V = V'(\psi)\vec{n}\cdot\nabla\psi$

↑ directional derivative

$= V'(\psi)|\nabla\psi|$

$\frac{\partial_\xi V}{|\nabla\psi|}$

then we also have

$$\partial_\xi^2 \bar{V} = V''(\psi)|\nabla\psi|^2 + V'(\psi)\,\partial_\xi|\nabla\psi|$$

so we obtain

$$\frac{\partial_t \psi}{|\nabla\psi|}\partial_\xi V = \frac{\Delta\psi}{|\nabla\psi|}\partial_\xi V + \partial_\xi^2 V - \frac{\partial_\xi V}{|\nabla\psi|}\partial_\xi|\nabla\psi| + f(V)$$

and we already know:

$$c\partial_\xi V = f(V) + \partial_\xi^2 V$$

so we obtain

$$\frac{\partial_t \psi}{|\nabla \psi|} = \frac{\Delta \psi}{|\nabla \psi|} + c - \frac{\partial_\xi |\nabla \psi|}{|\nabla \psi|}$$

or equivalently:

$$\partial_t \psi = \Delta \psi + c|\nabla \psi| - \partial_\xi |\nabla \psi|$$

remember $\partial_\xi \varphi = \nabla \varphi \cdot n$ for $\varphi = \varphi(x)$

so $\Delta \psi - \partial_\xi |\nabla \psi| = \nabla \cdot (\nabla \psi) - \nabla \left(|\nabla \psi| \frac{\nabla \psi}{|\nabla \psi|} \right)$

$$= |\nabla \psi| \nabla \cdot \left(\frac{\nabla \psi}{|\nabla \psi|} \right)$$

$$= -|\nabla \psi| \nabla \cdot \vec{n}$$

so we could rewritte it as:

$$V_n := \frac{\partial_t \psi}{|\nabla \psi|} = c - \nabla \cdot \vec{n}$$

eikonal equation

V_n: normal velocity of the surface

this equation relates v_n, the normal velocity of the surface, to the curvature $\nabla \cdot \vec{n}$

why is $\nabla \cdot \vec{n}$ related to the curvature ?

if ψ is flat (perfect front)

then $\vec{n} = \vec{ct}$ and $\nabla \cdot \vec{n} = 0$

if $\psi = ct$ looks like concentric rings

of ~ circular shape

$$\vec{n} \sim \frac{(x,y)}{R}$$

and $\nabla \cdot \vec{n} = \frac{1}{R}$ = curvature

or in 3D:

$$\text{mean curvature} \sim \frac{\int_V \nabla \cdot \vec{n}\, dV}{V} = \frac{\int_{\partial V} dS}{V}$$

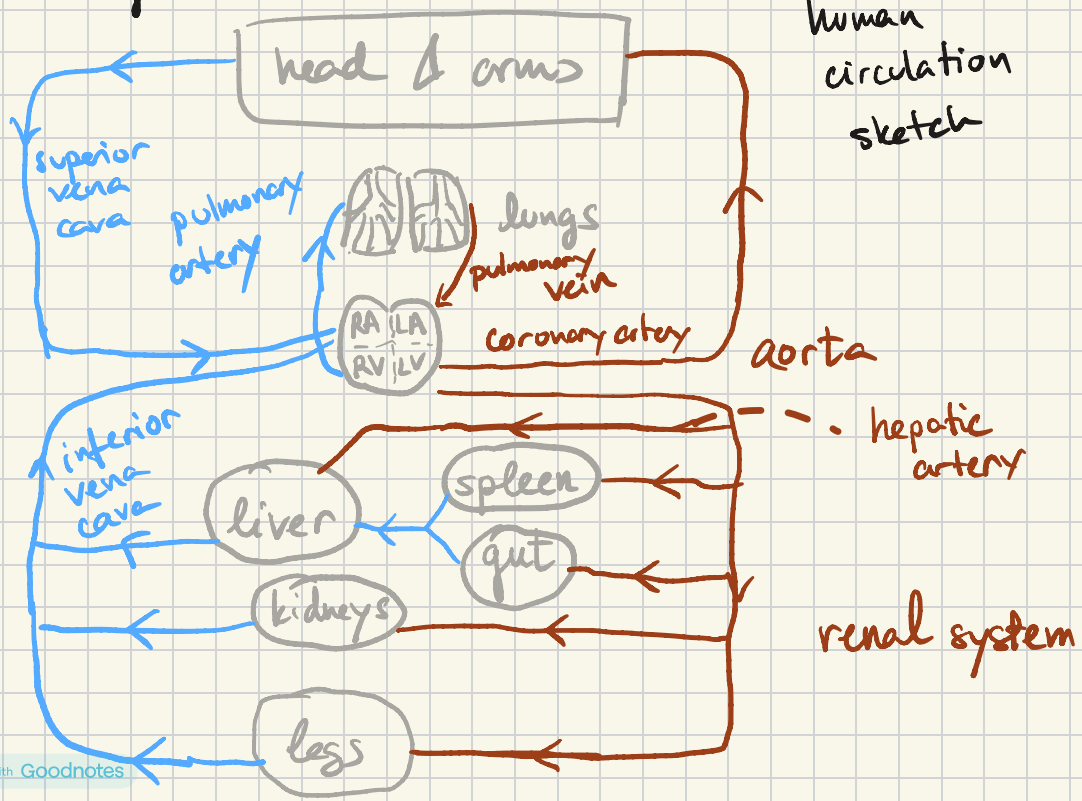
$$= \frac{S}{V} \sim \frac{R^2}{R^3} = \frac{1}{R}.$$

6. The heart as a pump

We looked at the electrochemical action of the heart. Next we move to the mechanical action of it.

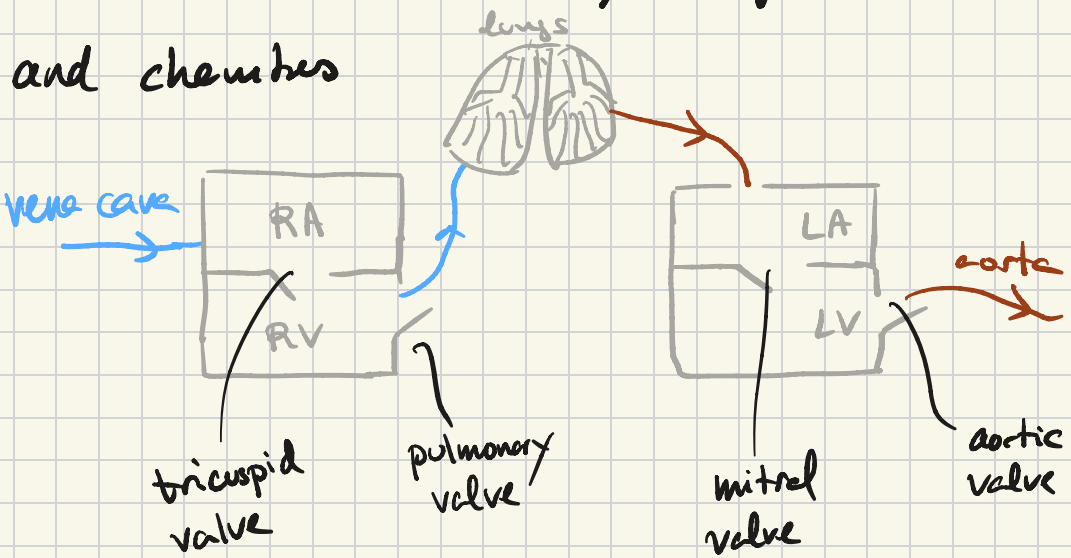
veins, heart, & arteries form a closed system of about five litres in volume!

a system of valves is necessary to effect a one way flow, and in order to prevent back flow.



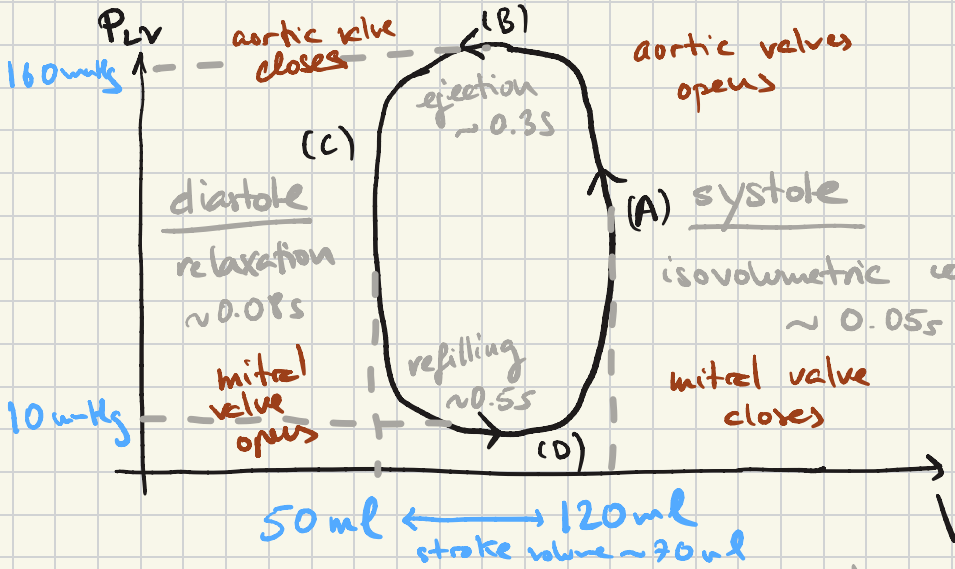
Blood collects oxygen (O_2) from the lungs and delivers this to the tissues, then collects CO_2 from tissues and dumps this to lungs (from which this is exhaled)

the heart works as a system of valves and chambers

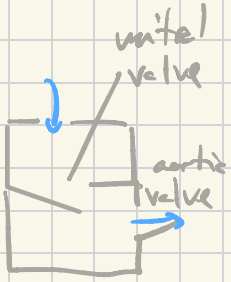


fluid flow is driven by a pressure gradient but the system is closed so there must be regions of negative gradient! valves are essential to avoid back circulation

Pressure – volume cycle of the left ventricle



(right ventricle acts almost synchronously)

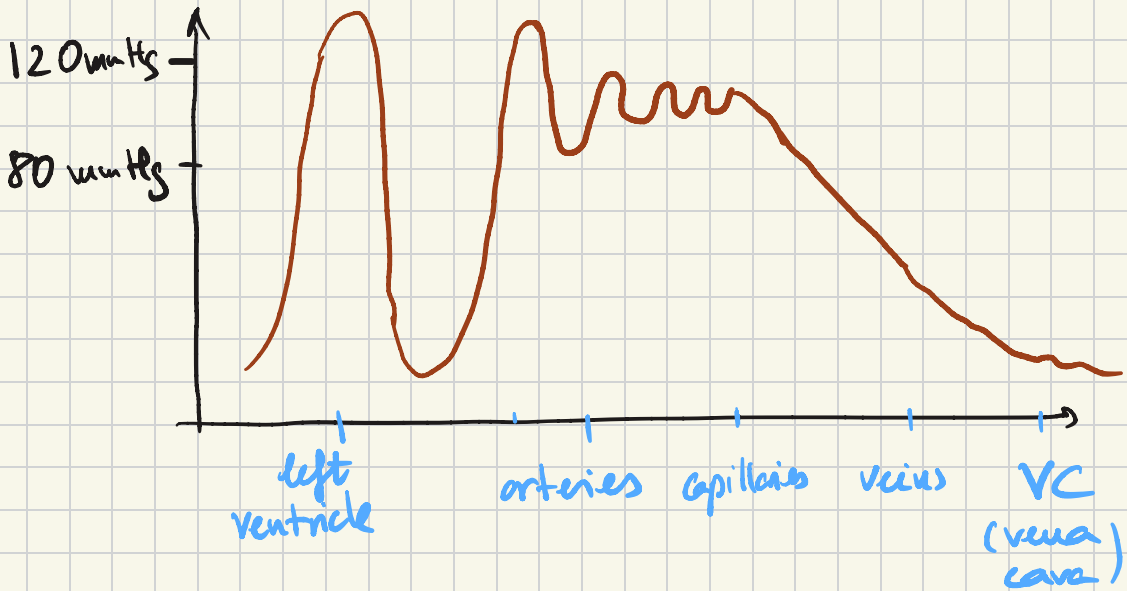


Systole: contraction phase – P rises

Diastole: relaxation phase – P falls

$$\text{Heart rate} \sim \frac{1}{\text{period SA node cells}}$$

Variation of pressure with arterial distance from the heart

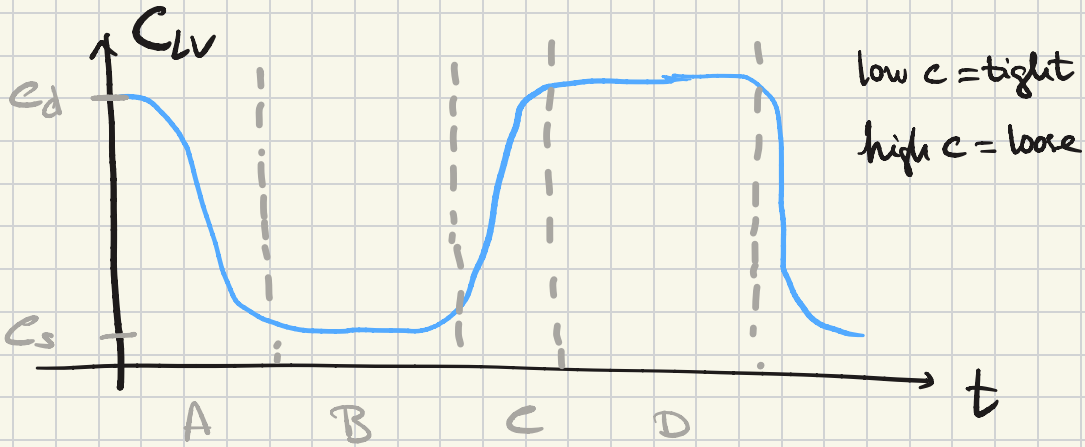


→ Changes in mechanical properties of the heart

- compliance (C): measure of the ability of an organ to increase / decrease volume with changes in pressure.

$$C = \frac{1}{\text{elastance}} \sim \frac{dV}{dP}$$

elastance ↓ ability to recoil to original shape upon removal of applied force



A. The Systole: isovolumetric contraction.
Compliance falls as the heart tightens

B. Ejection. constant low compliance, C_d, (tight)
pushes blood out

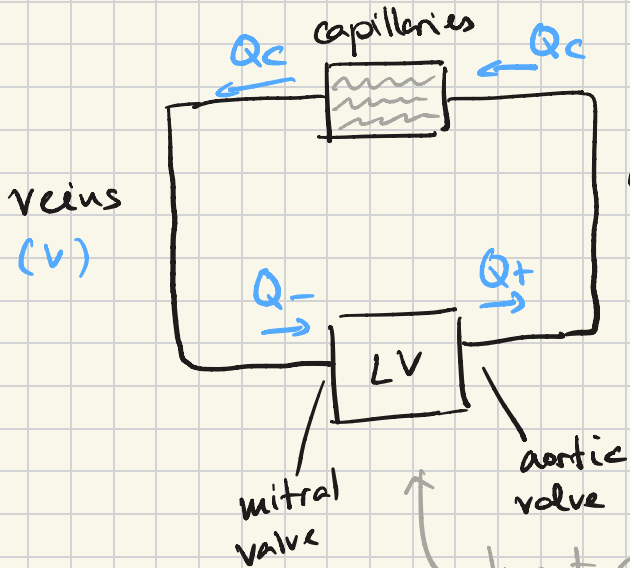
increase pressure at constant volume

C. Diastole: Isovolumetric contraction. Compliance rises as the heart loosens.

D. Refilling: constant high compliance; C_s, (loose)
allows blood in.

• a simple mechanical model of circulation

→ compartment model ignoring pulmonary circulation



Q_+, Q_-, Q_c = blood flows

V_a, V_v, V_{LC} = volumes of each compartment

heart as one single compartment! (LV)

- the model tracks volumes, pressures, and flows in the different compartments, which offer resistance to the flow
- → we assume capillary volume ~ 0 (but offers resistance!)

conservation of blood:

$$\begin{cases} \dot{V}_a = Q_+ - Q_- \\ \dot{V}_v = Q_c - Q_- \\ \dot{V}_{LV} = Q_- - Q_+ \end{cases}$$

Capillary resistance R_c:

$$Q_c = \frac{P_a - P_v}{R_c}$$

similarly, there are resistances associated with the flow to and from the left ventricle: R_v, R_a; so that:

$$Q_+ = \frac{[P_{LV} - P_a]_+}{R_a}, \quad Q_- = \frac{[P_v - P_{LV}]_+}{R_v}$$

$[x]_+ = \max(x, 0)$, $[\,]_+$ represents the valves!

no flow if pressure gradient is 0!

blood is incompressible but blood vessels and LV are compliant, which means their volumes are increased by pressure:

$$\left.\begin{aligned} V_a &= V_{a,0} + C_a P_a \\ V_v &= V_{v,0} + C_v P_v \\ V_{LV} &= V_{LV,0} + C_{LV} P_{LV} \end{aligned}\right\}$$ (needed to close the system!)

let's write the model in term of pressures:

$$(1)\quad C_a \frac{dp_a}{dt} = \frac{[P_{LV} - p_a]_+}{R_a} - \frac{p_a - p_v}{R_c}$$

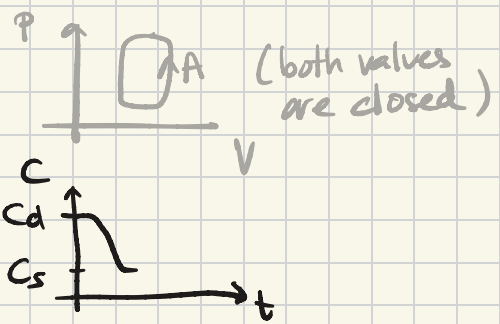
$$(2)\quad C_v \frac{dp_v}{dt} = \frac{p_a - p_v}{R_c} - \frac{[p_v - P_{LV}]_+}{R_v}$$

$$(3)\quad \frac{d}{dt}(C_{LV} P_v) = \frac{[P_v - P_{LV}]_+}{R_v} - \frac{[P_{LV} - p_a]_+}{R_a}$$

remember this oscillates!

main goal: does this model allows us to recreate the PV-cycle of the LV?

A. Isovolumetric contraction



initial conditions:

$P_{LV} < P_v << p_a$ heart is full!

then: $C_a \frac{dp_a}{dt} \sim -\frac{p_a}{R_c}$

we have $C_a R_c \sim 1.8\,s$

and time of contraction $\sim 0.05\,s$

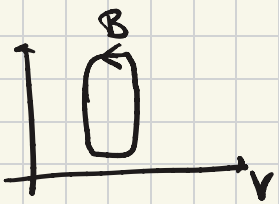
$\Rightarrow p_a \simeq$ constant on this phase

similarly $P_V \approx$ constant

and: $$\frac{d}{dt}(C_{LV} P_{LV}) = 0$$

so as C_{LV} falls P_{LV} rises !

B. Ejection



Atrial valve opens

$C_{LV} \sim$ constant $= C_S$

~ 0.3 s

$P_V << P_a < P_{LV}$

(1) becomes:

$$\underbrace{\frac{dP_a}{dt}}_{0.3\,s} = \frac{P_{LV} - P_a}{\underbrace{R_a C_a}_{0.095\,s}} - \frac{P_a - P_V}{\underbrace{R_c C_a}_{1.8\,s}}$$

↓ much smaller!

$$\Rightarrow P_{LV} \approx P_a$$

$$(2) \Rightarrow \frac{dP_V}{dt} = \frac{P_a - P_V}{\underbrace{R_c C_V}_{60\,s}} \Rightarrow P_V \sim \text{constant}$$

(3) $\frac{d}{dt}\left(C_{LV} P_{LV}\right) = -\frac{P_{LV} - P_a}{R_a}$

$C_{LV} = C_s$ constant

(recall from (1): $\frac{dP_a}{dt} = \frac{P_{LV} - P_a}{R_a C_a} - \frac{P_a - P_v}{R_c C_a}$)

so: $C_s \frac{dP_{LV}}{dt} = -C_a \frac{dP_a}{dt} - \frac{P_a - P_v}{R_c}$

and using $P_{LV} \propto P_a$: $(C_s + C_a)\frac{dP_a}{dt} = -\frac{P_a - P_v}{R_c}$

with $P_v << P_a$ so:

$$P_a \propto \exp\left(-\frac{t}{\underbrace{R_c(C_a + C_s)}_{2.2\,s}}\right) \quad t \approx 0.3\,s$$

so P_a falls by ~ 0.87 in this phase.

this argument can be made more rigorous using a perturbative expansion

$$(1)\quad \frac{dp_a}{dt} = \frac{1}{R_a C_a}(p_{LV} - p_a) - \frac{p_a - p_v}{R_c C_a}$$

$$(3)\quad C_s \frac{dp_{LV}}{dt} = -\frac{p_{LV} - p_a}{R_a}$$

so in general we always have:

$$C_s \frac{dp_{LV}}{dt} + C_a \frac{dp_a}{dt} = -\frac{p_a - p_v}{R_c}$$

now if $R_a C_a \ll$ phase duration $\ll R_c C_a$ we can write (1) as:

$$\frac{dp_a}{dt} = \frac{1}{\varepsilon}(p_{LV} - p_a) - \frac{p_a - p_v}{R_c C_a}$$

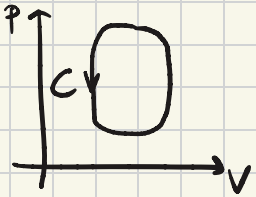
$$\Rightarrow p_{LV} \simeq p_a + O(\varepsilon)$$

and the final expression that we derived, i.e:

$$(C_s + C_a)\frac{dp_a}{dt} \sim -\frac{p_a}{R_c} \sim 0.095$$

is true to order $O\left(\frac{R_a C_a}{0.3\,s}\right)$

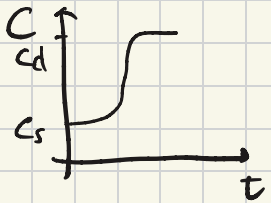
C. Isovolumetric relaxation



$P_V < P_{LV} < P_a$

both valves are closed

similar to the contraction phase



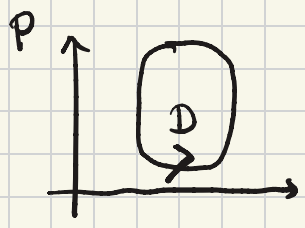
P_a, P_V ≈ constant

and $\frac{d}{dt}(C_{LV} P_{LV}) = 0$

so as C_{LV} rises, P_{LV} falls

until $P_{LV} = P_L$ when the mitral valve opens to begin filling

D. Refilling



mitral valve opens (0.5 s)

and C_{LV} ~ constant = C_d

$P_{LV} < P_V \ll P_a$

(1) $\Rightarrow \frac{dP_a}{dt} \approx -\frac{P_a}{C_a R_c}$ since $P_a >> P_V$

(2) $\Rightarrow \frac{dP_V}{dt} = \frac{P_a - P_V}{R_c C_V} - \frac{P_V - P_{LV}}{R_V C_V}$

$R_c C_V \sim 60$s

$R_V C_V \sim 0.8$s

$(3) \Rightarrow \frac{d}{dt} P_{LV} = \frac{P_V - P_{LV}}{C_d R_V}$

these give: $P_a \propto \exp\left(-\frac{t}{R_c C_d}\right)$

$\Rightarrow$ P_a falls by ~ 0.76 in this phase

So total fall in P_a is $0.76 \times 0.87 = 0.66$

note $0.66 \times (120\,\text{mmHg}) \sim 80\,\text{mmHg}$!

Nervous control of the heart

heart output = stroke vol. $\times$ HR

$\left(Q = \frac{\text{V of blood}}{\text{time}}\right)$ (HR: $\frac{1}{\text{time}}$)

the control of these two quantities controls blood flow

- stroke volume is controlled by the pumping mechanism of the heart, and also pressure (recall PV cycle)

- HR is controlled by the period of the firing of SA node cells and this is mainly controlled by the nervous system

two parts of the nervous system which control cardiac output: sympathetic & parasympathetic systems, and each consists of afferent nerves (to the brain), and efferent nerves (from the brain)

Sympathetic system: releases noradrenaline, adrenaline, and other neurotransmitters

for instance, noradrenaline functions in the brain to increase attention, vigilance (or produce anxiety!), and when it is released into the bloodstream it causes rapid increase in HR and pressure, constricts vessels and redirects flow to important muscles, dilates pupils to improve vision etc.

two parts of the sympathetic system

→ α-sympathetic (peripheral vessels): release of neurotransmitters to increase blood pressure (vasoconstriction)

→ β-sympathetic (ventricular muscle): release of transmitters to increase firing of the SA node cells (i.e. increase HR)

the sympathetic system acts slowly (~10 s)

Parasympathetic system: releases acetylcholine, another neurotransmitter, which has an immediate effect on HR, causing it to decrease, and also vasodilation. This system acts much quicker. ↳ so pressure decreases

both systems are determined by signals transmitted along afferent nerves.

For the control of blood flow, ↳ and pressure! the most important are the baroreceptors. These nerves

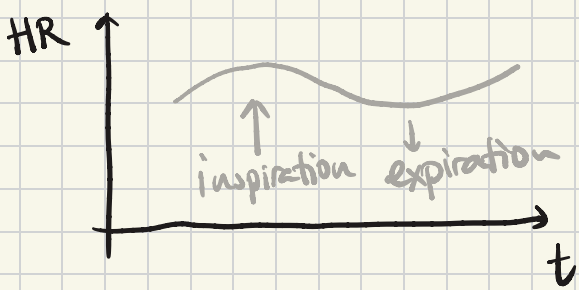
are located in the aortic arch of the chest and the carotid sinus in the neck. The control response is called the baroflex (baroreceptor reflex)

Oscillatory pattern>

HR oscillates on different timescales

→ respiratory sinus arrhythmia (RSA)

frequency ~ 0.2-0.4 Hz due to coupling between HR and respiration



this occurs because inspiration leads to low pressure which increases the HR because it's "easier" to flow.

→ Mayer waves frequency ≈ 0.1 Hz
(so period = 10 s)

↳ makes us believe that they're linked with the action of the sympathetic system

→ thermo-regulatory control ≲ 0.1 Hz freq.

Mathematical models of the baroflex

Ottesen model Three variables: average arterial and venous pressures P_a and P_v, and the HR → H

this aims to model long term sympathetic control by assuming P_a & P_v vary slowly under the influence of the slow sympathetic system

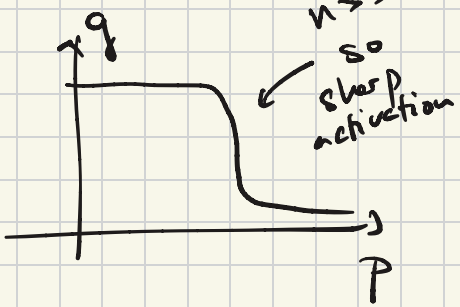
↳ this will lead to DDEs (T = delay) because the response takes time to be observed.

Model: Control is given by sympathetic and parasympathetic tones (T_s, T_p):

← arterial pressure time $t - \tau$

(sym.) $$T_s(t) = g(p_a(t-\tau))$$

(para) $$T_p(t) = 1 - g(p_a(t))$$



where g is a Hill function:

$$g(p) = \frac{1}{1 + (p/p_0)^n}$$

H response to T_s and T_p:

→ sympathetic response raises H

$$\dot{H} = \frac{\lambda_H T_s}{1 + \gamma T_p} - \mu_H T_p$$

↑ parasympathetic response lowers H

↓ vagal response: inhibiting effect on sympathetic response

one caveat: $T_s = T_p = 0$ sets no prefered H. In reality, H should stabilise $\underbrace{\sim 100\ s^{-1}}_{H_0}$. natural rest freq.

We thus modify the model to:

$$\dot{H} = \delta_H(H_0 - H) + \frac{\lambda_H T_s}{1+\gamma T_p} - \mu_H T_p$$

↳ simplest way to provide relaxation to H_0

the model is closed by assuming the two blood pressure eqns:

conservation of arterial blood

$$C_a \dot{p}_a = -\frac{p_a - p_v}{R_c} + \underbrace{H\Delta V}_{\text{cardiac output}} \quad (\square)$$

↳ stroke vol. ~constant

conservation of venous blood

$$C_v \dot{p}_v = \frac{p_a - p_v}{R_c} - \frac{p_v}{R_v}$$

to make analytical progress we realise that $p_v << p_a$ so that $(\square)$ becomes:

$$C_a \dot{p}_a \simeq -\frac{p_a}{R_c} + H\Delta V$$

So essentially we're neglecting p_v to get:

$$\begin{cases} \dot{H} = \delta_H (H_0 - H) + \dfrac{\lambda_H T_s}{1+\gamma T_p} - \mu_H T_p \\ R_c C_a \dot{p}_a = -p_a + R_c \Delta V H \end{cases}$$

non-dimensionalize:

$$\lambda = \frac{\lambda_H}{H_0^2} \sim 0.3 \qquad \delta = \frac{\delta_H}{H_0} \sim 1$$

$$\mu = \frac{\mu_H}{H_0^2} \sim 0.4$$

$$\Rightarrow \begin{cases} \dot{p} = k(-p + vh) \\ \varepsilon \dot{h} = \delta(1-h) + \dfrac{\lambda g(p_d)}{1+\gamma(1-g(p))} - \mu(1-g(p)) \\ \hookrightarrow \varepsilon \ll 1. \end{cases}$$

where $p_d = p(\hat{t} - 1)$, delay has been rescaled to 1.

For illustrative purposes (and simplicity) we will set $\gamma = 0$ and $\delta = 1$, but the same idea holds for arbitrary γ, δ.

to leading order in ε we have:

$$N = 1 + \lambda g(P_1) - \mu(1 - g(P))$$

substituting into the eq for $\dot{P}$ we get:

$$\dot{P} = k\left[-P - V - V\lambda g(P(t-1)) - \mu(1-g(P))\right]$$

which is a DDE for P.

the steady state satisfies:

$$g(P^+) = \frac{P^+ - V(1-\mu)}{V(\lambda+\mu)}$$

which is a transcendental eq.

to study the linear stability we set $P = P^+ + \mathcal{P}$ so:

$$\dot{\mathcal{P}} = k\left[-\mathcal{P} - V\left|g'(P^+)\right|\left(\lambda \mathcal{P}_1 + \mu \mathcal{P}\right)\right]$$

which is linear, so sols. are of the form

$\alpha e^{\sigma t}$ where:

$$\sigma = -B - Ge^{-\sigma}, \quad \sigma \in \mathbb{C}$$

where $B = k(1 + v|g'(p^*)|\mu) > 0$

$$G = kv|g'(p^*)|\lambda > 0$$

system is unstable if $\mathrm{Re}\,\sigma > 0$.

Note that if $\sigma \in \mathbb{R}$ then $B, G > 0 \Rightarrow \sigma < 0$

Generally for our parameter values the model is linearly stable.

It can become unstable if $\lambda > \mu$, and can predict waves period = 10s waves if the delay is chosen ~ 5s (see Lecture Notes for more details!)