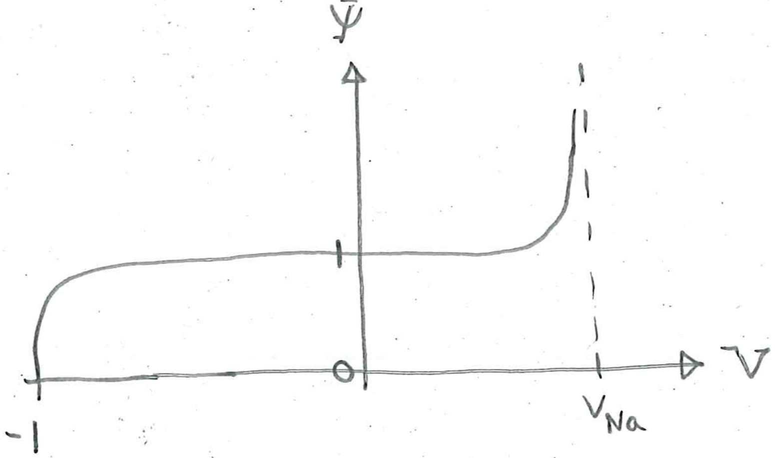
Problem Sheet 4

1). First there is fast motion on the $O(\frac{1}{\delta})$ timescale which takes w onto the V nullcline, $h = h_0(V)$.

Then on the $O(1)$ timescale, $h \to h_\infty(V)$

Then on the slow $O(\frac{1}{\varepsilon})$ timescale, $n \to n_\infty(V)$



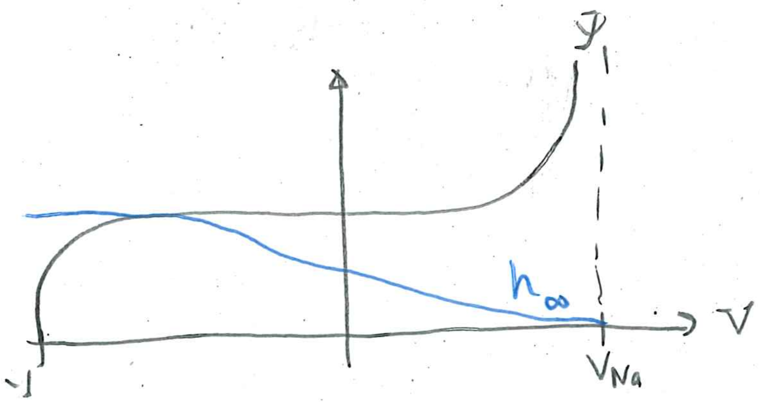
$$\bar{\Psi} = \frac{1 - e^{-(V+1)/\delta}}{1 - e^{-(V_{Na}-V)/\delta}}$$

$\delta << 1$.

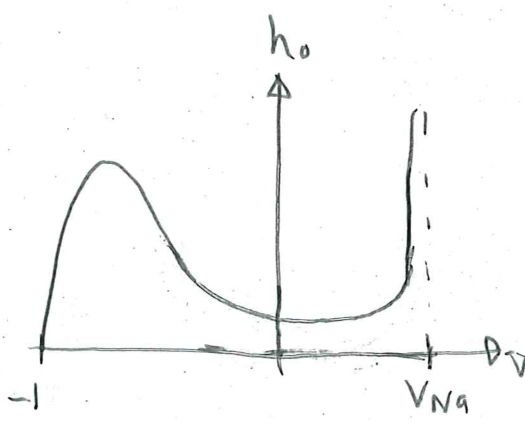
When $-1 < V < V_{Na}$, exponentials are small so $\bar{\psi} \sim 1$

As $V \to V_{Na}$, $\bar{\psi} \to \infty$

As $V \to -1$, $\psi \to 0$.



$\Rightarrow$



At the fixed point,

$$n = n_\infty \quad ①$$
$$h = h_\infty \quad ②$$
$$h = h_0 \quad ③$$

Now $h_0 = (1+\lambda)\,\bar{\psi}(V)\,h_\infty$ so ② and ③ $\Rightarrow$ $(1+\lambda)\,\bar{\psi}(V) = 1$ (*)

But $\bar{\psi}(V)$ is monotonic so there is a unique fixed point.

Since $\lambda \ll 1$, (*) $\Rightarrow$ $\bar{\psi}(V) \lesssim 1$,

so V is close to -1

Set $V = -1 + v$, $v \ll 1$.

In (*), $$(1+\lambda)\,\frac{1 - e^{-v/\delta}}{1 - \underbrace{e^{-(V_{NA}+1-v)/\delta}}_{\text{exponentially small}}} = 1$$

$$(1+\lambda)(1 - e^{-v/\delta}) \approx 1$$

$$1 - e^{-v/\delta} \approx \frac{1}{1+\lambda}$$

$$e^{-v/\delta} \approx 1 - \frac{1}{1+\lambda}$$

$$e^{-v/\delta} \approx 1 - (1-\lambda) \quad \text{since } \lambda \ll 1$$

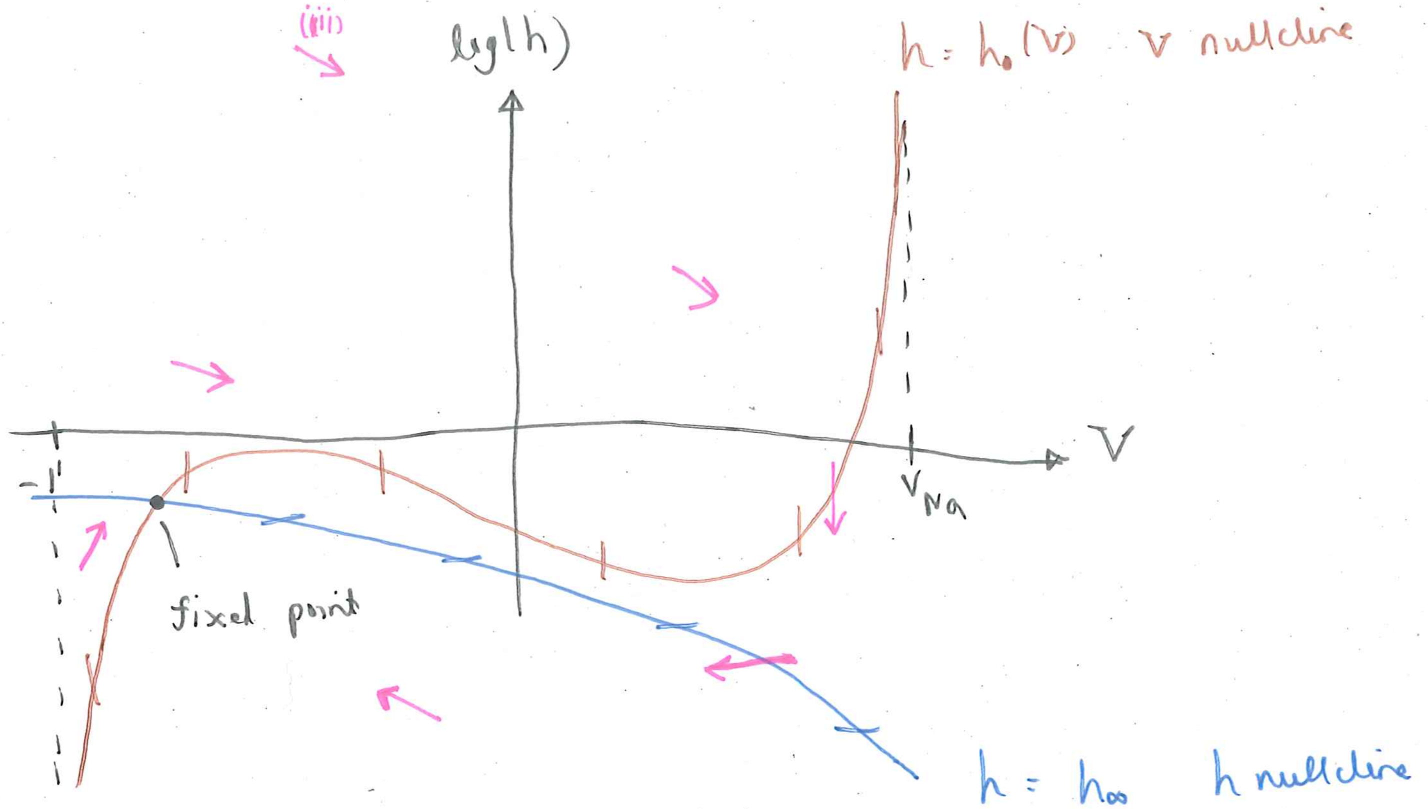
$$e^{-v/\delta} \approx \lambda$$

$$v \approx -\delta \log(\lambda)$$

$$v \approx \delta \log\left(\tfrac{1}{\lambda}\right)$$

So $V \approx -1 + \delta \log\left(\frac{1}{\lambda}\right)$

To visualize the phase plane it is helpful to use log(h) as the vertical axis:



Construct phase plane by following steps:

i) PLA nullclines

ii) Fixed point where nullclines cross

iii). For large h, $\dot{V} > 0$ and $\dot{h} < 0$.

iv). Fill in the other directions

Stability of the fixed point

Associated stability matrix $\underline{\underline{M}} = \begin{bmatrix} -1 & h_\infty' \\ \gamma & -\gamma h_0' \end{bmatrix}$

$$\text{trace}(\underline{\underline{M}}) = -1 - \gamma h_0'$$

So stable if $-1-\gamma h_0' < 0$

$$-1 < \gamma h_0'$$

$$-\frac{1}{\gamma} < h_0'$$

Since $\gamma \gg 1$, $\Rightarrow$ stability for $h_0'(V^*) \gtrsim 0$

Now $h_0(V) \doteq (1+\lambda)\,\psi(V)\,h_\infty(V)$

Near V^*, $\psi(V) \approx 1 - e^{-(V+1)/\delta}$

So $h_0'(V) \approx \left((1+\lambda)(1-e^{-(V+1)/\delta})\,h_\infty(V)\right)'$ near V^*

$$= \frac{(1+\lambda)}{\delta} e^{-(V+1)/\delta} h_\infty(V) + (1+\lambda)(1-e^{-(V+1)/\delta})h_\infty'$$

$$= \frac{(1+\lambda)}{\delta}\lambda h_\infty(V) + (1+\lambda)(1-\lambda)h_\infty'(V)$$

since $e^{-\frac{(V+1)}{\delta}} \simeq \lambda$ found earlier

$$\approx \frac{\lambda}{\delta} h_\infty(V) + h_\infty'(V)$$

since $\lambda \ll 1$.

fixed point is stable if $\boxed{\frac{\lambda}{\delta} h_\infty(V^*) + h_\infty'(V) \gtrsim 0}$

2) $V_n = \dfrac{-\psi_t}{|\nabla\psi|}$, $\underline{n} = -\dfrac{\nabla\psi}{|\nabla\psi|}$

So $v_n + \nabla \cdot \underline{n} = c$

$$\Rightarrow \boxed{\frac{\psi_t}{|\nabla\psi|} + \nabla \cdot \left(\frac{\nabla\psi}{|\nabla\psi|} \right) + c = 0}$$

Seek a solution of the form $\psi = -ct + f(r)$ for a target wave with $f' > 0$ for an outgoing wave

Then $\nabla\psi = +f'\,\underline{e}_r$

$$|\nabla\psi| = f'$$

$$V_n = \frac{-\psi_t}{|\nabla\psi|} = \frac{c}{f'}$$

$$\underline{n} = -\underline{e}_r$$

$$\nabla\cdot\underline{n} = \frac{1}{r}\frac{\partial}{\partial r}(r.1) = \frac{-1}{r}$$

So $\quad V_n = c - \nabla\cdot\underline{n} \Rightarrow \dfrac{c}{f'} = c - \dfrac{1}{r}$

$$\Rightarrow f' = 1 + \frac{1}{cr-1}$$

$$f = r + \frac{1}{c}\log(cr-1)$$

So $\psi = ct - f$

$$\boxed{\psi = ct - r - \frac{1}{c}\log(cr-1) \quad \text{for } r > \frac{1}{c}}$$

2D waves

If $\psi = -r + R(\theta, t)) = 0$ denotes the front (choose signs so $\psi > 0$ when $r < 0$).

then $\nabla\psi = \frac{\partial}{\partial r}(\psi)\,\underline{e}_r + \frac{1}{r}\frac{\partial \psi}{\partial \theta}\,\underline{e}_\theta$

$= -\underline{e}_r + \frac{1}{r} R_\theta\, \underline{e}_\theta$

$$v_n = \frac{\psi_t}{|\nabla\psi|} = \frac{R R_t}{\sqrt{R^2 + R_\theta^2}}$$

$$|\nabla\psi| = \sqrt{1 + \frac{R_\theta^2}{r^2}}$$

$$\underline{n} = -\frac{\nabla\psi}{|\nabla\psi|} = \frac{\left(1, -\frac{R_\theta}{r}\right)}{\sqrt{1 + \frac{R_\theta^2}{r^2}}}$$

$$\psi_t = R_t$$

So in (x),

$$R_t = \sqrt{1 + \frac{R_\theta^2}{r^2}}\left(c - \nabla \cdot \left(\frac{-\underline{e}_r + \frac{1}{r} R_\theta\, \underline{e}_\theta}{\sqrt{1 + \frac{R_\theta^2}{r^2}}}\right)\right)$$

$$= \frac{1}{r}\frac{\partial}{\partial r}\left(\frac{-r}{\sqrt{1 + \frac{R_\theta^2}{r^2}}}\right) + \frac{1}{r}\frac{\partial}{\partial \theta}\left(\frac{+\frac{1}{r}R_\theta}{\sqrt{1 + \frac{R_\theta^2}{r^2}}}\right)$$

$$= \frac{r^2 + 2R_\theta^2 - R R_{\theta\theta}}{\frac{1}{r}\left(r^2 + R_\theta^2\right)^{3/2}}$$

So $$\boxed{R_t = \frac{c\sqrt{R^2 + R_\theta^2}}{R} - \frac{R^2 + 2R_\theta^2 - R R_{\theta\theta}}{R(R^2 + R_\theta^2)}}$$

Target pattern: $R = R(t)$ only

$$\Rightarrow \boxed{\dot{R} = c - \frac{1}{R}}$$

$\Rightarrow$ If $R(0) < c$ then the patch will shrink. This is curvature blocking.

If $R(0) > c$ then the wave will propagate outwards indefinitely

Spiral waves $R = R(\eta)$, $\eta = \omega t - \theta$

$$\Rightarrow \omega R' = c\left(1 + \frac{(R')^2}{R^2}\right)^{1/2} - \frac{1}{R}\,\frac{\left[1 + \frac{2(R')^2}{R^2} - \frac{R''}{R}\right]}{1 + \frac{(R')^2}{R^2}}$$

For large time, $\eta >> 1$, $R >> 1$ set $\eta = \lambda \xi$, $R = \lambda f$ $\lambda >> 1$

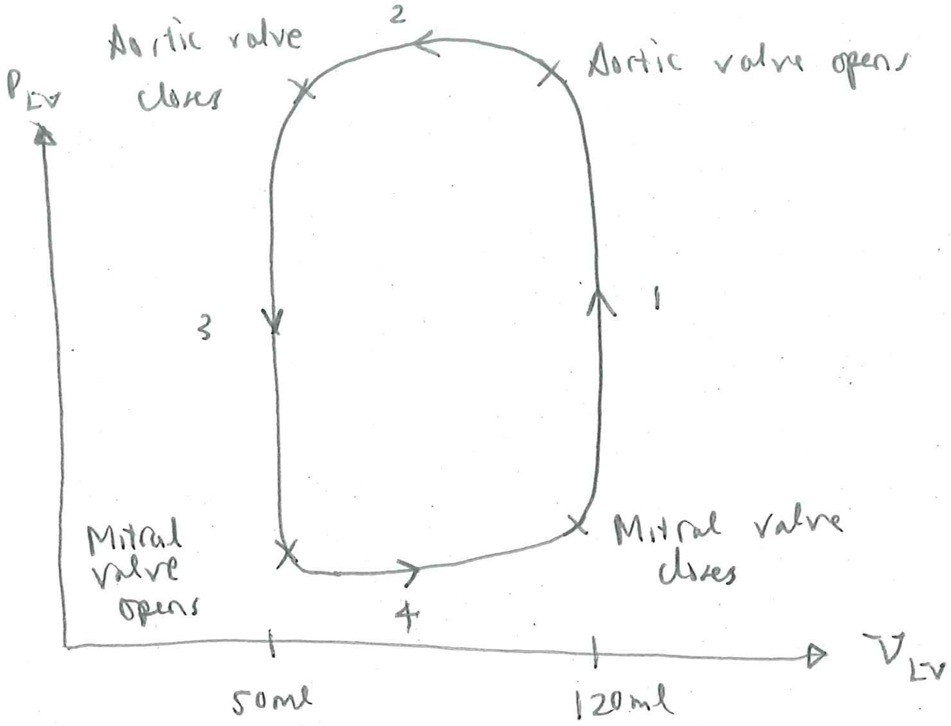
$$\omega f_\xi = c\left(1 + \frac{1}{\lambda^2}\frac{f_\xi^2}{f^2}\right)^{1/2} - \frac{1}{\lambda f}\,\frac{\left(1 + \frac{2 f_\xi^2}{\lambda^2 f^2} - \frac{f_{\xi\xi}}{\lambda^2 f}\right)}{1 + \frac{f_\xi^2}{\lambda^2 f^2}}$$

$$\Rightarrow f_\xi = \frac{c}{\omega} + O\left(\frac{1}{\lambda}\right)$$

$$\Rightarrow f = \frac{c\xi}{\omega}$$

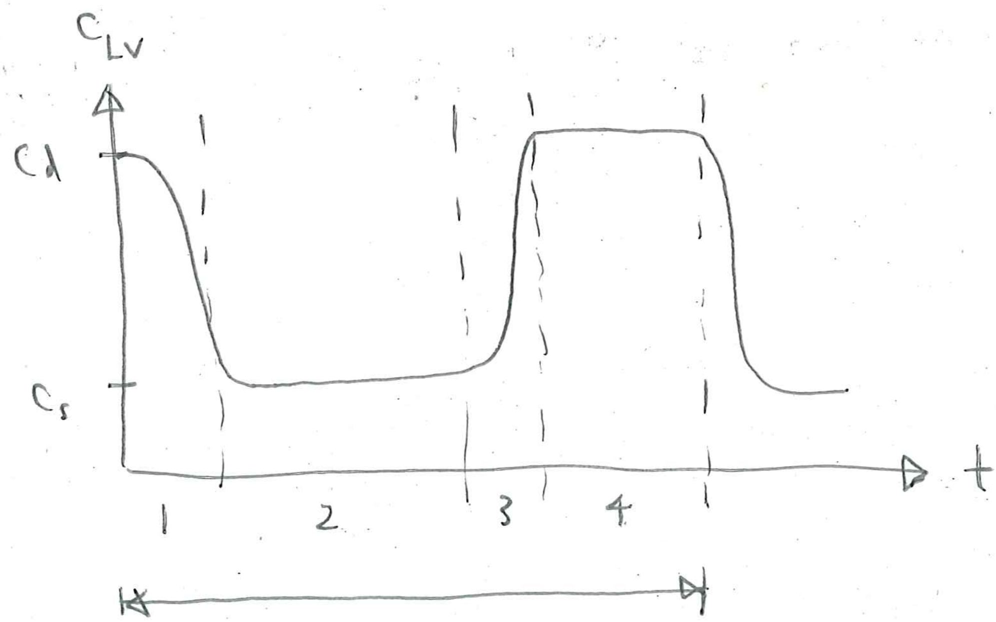
$$\boxed{R = \frac{c\eta}{\omega}}$$

3).



Stroke volume = 70ml.
= change in left ventricular volume on contraction

Left ventricle compliance.



T, time period of the sino atrial cells.

Heart rate $= \frac{1}{T}$.

3.2

1. The systole. Isovolumetric contraction. Both valves closed
The compliance falls as the heart tightens

2. Ejection. Aortic valve open. Constant low compliance C_s
(tight) pushes blood out.

3. The diastole. Isovolumetric contraction. Both valves closed.
The compliance rises as the heart loosens.

4. Refilling. Mitral valve open. Constant high compliance C_d
(loose) allows blood in.

5) a) Contraction. Isovolumetric because both valves are closed in this phase. Blood is incompressible so the volume cannot change.

In this phase the compliance C_{LV} falls from C_d to C_s. as the heart tightens.

Ejection. The aortic valve opens. The compliance C_{LV} is constant $=$ C_s. (low - tight). This ejects blood from the heart.

Relaxation. The aortic valve closes so this is isovolumetric. The compliance rises from C_s to C_d.

Refilling. The mitral valve opens. The compliance is constant $=$ C_d (high - loose). This allows blood to enter the heart.

$$\dot{p}_a = -\frac{(p_a - p_v)}{R_c C_a} + \frac{[p_{LV} - p_a]_+}{R_a C_a} \quad ①$$

$R_c C_a$ 1.85 s, $R_a C_a$ 0.09 s

$$\dot{p}_v = \frac{(p_a - p_v)}{R_c C_v} - \frac{[p_v - p_{LV}]_+}{R_v C_v} \quad ②$$

$R_c C_v$ 60 s, $R_v C_v$ 0.8 s

$$\dot{V}_{LV} = \frac{[p_v - p_{LV}]_+}{R_v} - \frac{[p_{LV} - p_a]_+}{R_a} \quad ③, \quad V_{LV} = V_0 + C_{LV} p_{LV}.$$

b) The contraction is isovolumetric because both valves are closed in this phase. Blood is incompressible so the volume cannot change.

Isovolumetric means V_{LV} = constant

$\Rightarrow$ $V_0 + C_{LV} p_{LV}$ = constant

$\Rightarrow$ $C_{LV} p_{LV}$ = constant since V_0 = constant

$p_{LV}^a < p_a^0$ so ① $\Rightarrow$ $\dot{p}_a = -\frac{p_a - p_v}{R_c C_a}$

Contraction $\approx 0.05\,s$ (given in question)

1.85 s

$\Rightarrow$ p_a approximately constant on this timescale

Similarly, in ②, this gives p_v approximately constant on this timescale.

$$C_a \times ① + ③ \Rightarrow \quad \frac{d}{dt}\left(C_a p_a + C_{LV} p_{LV} \right) = -\frac{p_a - p_v}{R_c} \quad Ⓐ$$

If C_{LV} very quickly goes from C_d to C_s, on this timescale,

$$\frac{d}{dt}\left(C_a p_a + C_{LV} p_{LV} \right) \approx 0$$

(could show this more rigorously by assuming that this happens on a timescale $O(\delta)$ $\delta \ll 1$ then rescaling $t = \delta T$ and considering the equation to leading order in δ)

So $C_a p_a + C_{LV} p_{LV} =$ const and

But C_a, p_a are constant in this phase, and C_{LV} goes from C_d to C_s to p_{LV} goes from p_{LV}^0 to $\boxed{\frac{C_d p_{LV}^0}{C_s}}$ (higher than p_{LV}^0).

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c) Now $$\frac{dp_a}{dt} = \frac{p_{LV} - p_a}{\underset{0.09\,s}{R_a C_a}} - \frac{p_a - p_v}{\underset{1.85\,s}{R_c C_a}}$$

and the ejection phase occurs over a time of 0.3 s, so the $\frac{p_{LV} - p_a}{R_a C_a}$ term dominates and so $p_{LV} \approx p_a$ in the ejection phase.

In the ejection phase, $C_{LV} = C_s$ and $p_a = p_{LV}$ so in (a),

$$(C_a + C_s)\frac{dp_a}{dt} = -\frac{p_a - p_v}{R_c}$$

$$\boxed{(C_a + C_s)\frac{dp_a}{dt} \approx -\frac{p_a}{R_c}}$$ since $p_a >> p_v$

Solving this subject to $p_a = p_a^0$ at $t = 0$ (where this corresponds to the start of the ejection phase) gives

$$\boxed{p_a = p_a^0 \exp\left[-\frac{t}{R_c(C_a + C_s)}\right]}$$

Since the ejection phase has duration Δt_F, at the end of this phase,

$$\boxed{p_a = p_a^0 \exp\left[-\frac{\Delta t_F}{R_c(C_a + C_s)}\right] \stackrel{\text{def}}{=} p_a^+}$$

And in (2), $\dot{p}_v \approx \frac{p_a}{R_c C_v}$ since $p_v < p_{LV}$ and $p_a >> p_v$

so $\dot{p}_v = \frac{p_a^0}{R_c C_v} \exp\left[-\frac{t}{R_c(C_a + C_s)}\right]$

$$\boxed{p_v = p_v^0 - \frac{p_a^0 R_c(C_a + C_s)}{R_c C_v}\left[\exp\left[-\frac{t}{R_c(C_a + C_s)}\right] - 1\right]}$$

So at the end of the ejection phase,

$$\boxed{p_v = p_v^0 - \frac{R_c(C_a + C_s)}{R_c C_v}\left[\exp\left[-\frac{\Delta t_F}{R_c(C_a + C_s)}\right] - 1\right] \stackrel{\text{def}}{=} p_v^*}$$

d) In the relaxation phase, $p_{LV} < p_a$ so in ① and ②,

$$\frac{dp_a}{dt} = -\frac{p_a - p_v}{R_c C_a} \qquad \frac{dp_v}{dt} = \frac{p_a - p_v}{R_c C_v} - \frac{[p_v - p_{LV}]_+}{R_v C_v}$$

0.08 s (given in question) 1.8 s 0.08 s 60 s 0.8 s

0.08 s is fast compared with the other timescales, so

$p_a \simeq$ constant and $p_v \simeq$ constant.

Again, since both valves are closed in the relaxation phase, this process is isovolumetric so V_{LV} = constant

$C_{LV} P_{LV}$ = constant.

In the contraction phase, C_{LV} goes from C_s to C_d $(C_s < C_d)$ so P_{LV} goes from P_{LV}^{start} to P_{LV}^{end} where

$$C_s P_{LV}^{start} = C_d P_{LV}^{end}$$

$$\text{so} \quad P_{LV}^{end} = \frac{C_s}{C_d} P_{LV}^{start}$$

But $P_{LV}^{start} = P_a^{start}$ because in the previous (ejection) phase we had $P_{LV} = P_a$. And $P_a^{start} = P^+$ (the value at the end of the ejection phase).

$$\text{so} \quad \boxed{P_{LV}^{end} = \frac{C_s}{C_d} P^+}$$

In the refilling phase,

① $\Rightarrow$ $\dot{p}_a = -\frac{p_a - p_v}{R_c C_a}$ since $p_{LV} < p_a$

$\simeq -\frac{p_a}{R_c C_a}$ Ⓒ since $p_a >> p_v$

② $\Rightarrow$ $\dot{p}_v = \frac{p_a}{R_c C_v} - \frac{p_v - p_{LV}}{R_v C_v}$ Ⓓ

③ $\Rightarrow$ $\dot{p}_{LV} = \frac{p_v - p_{LV}}{R_v C_d}$ Ⓔ since C_{LV} : constant $= C_d$ in this phase

Ⓒ with $p_a = p_a^+$ at $t = 0$ (denoting the start of the refilling phase) gives

$$\boxed{p_a = p_a^+ \exp\left[-\frac{t}{R_c C_a}\right]}$$

$C_a \times$ Ⓒ $+$ $C_v \times$ Ⓓ $+$ $C_d \times$ Ⓔ $\Rightarrow$

$$\frac{d}{dt}(C_a p_a + C_v p_v + C_d p_{LV}) = 0$$

$$C_a p_a + C_v p_v + C_d p_{LV} = \text{constant}$$

$$\boxed{C_a p_a + C_v p_v + C_d p_{LV} = C_a p_a^+ + C_v p^* + C_d p^+}$$

using values at the end of the previous phase

$$\textcircled{D} - \textcircled{E} : \quad \frac{d}{dt}(p_V - p_{LV}) = \frac{p_a}{R_c C_V} - \left(\frac{1}{R_V C_V} + \frac{1}{R_V C_d}\right)(p_V - p_{LF})$$

$$\Rightarrow \quad \frac{d}{dt}\left[(p_V - p_{LV})\exp[\alpha t]\right] = \frac{p^t}{R_c C_V}\exp\left[-\frac{t}{R_c C_a}\right]\exp[\alpha t]$$

$$\boxed{\alpha = \frac{1}{R_V C_V} + \frac{1}{R_V C_d}}$$

$$\Rightarrow \quad (p_V - p_{LV})\exp(\alpha t) = \frac{p^t}{R_c C_V(\alpha - \lambda)}\left(\exp[(\alpha-\lambda)t] - 1\right) + \left(p^* + \frac{C_s}{C_d}p^t\right)$$

$$\boxed{\lambda = \frac{1}{R_c C_a}}$$

$$p_V - p_{LV} = \frac{p^t}{R_c C_V(\alpha - \lambda)}\left(e^{-\lambda t} - e^{-\alpha t}\right) + \left(p^* + \frac{C_s}{C_d}p^t\right)e^{-\alpha t}$$

So at the end of this phase,

$$\boxed{p_V - p_{LV} = \frac{p^t}{R_c C_V(\alpha - \lambda)}\left(e^{-\lambda \Delta t_R} - e^{-\alpha \Delta t_R}\right) + \left(p^* + \frac{C_s}{C_d}p^t\right)e^{-\alpha \Delta t_R}}$$