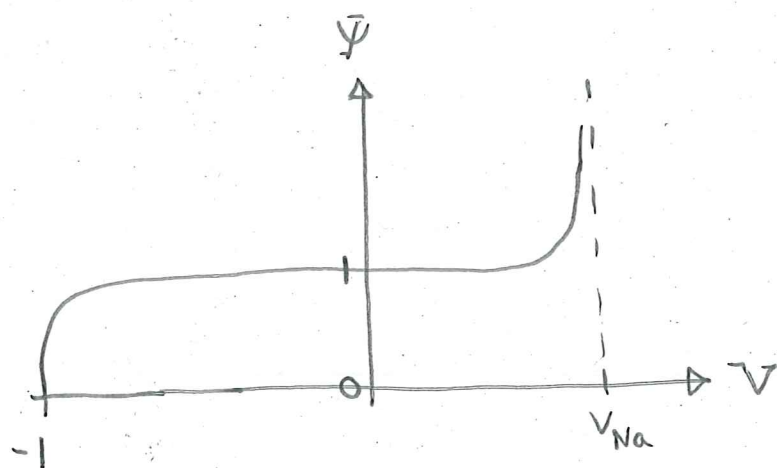


1). First there is fast motion on the  $O(\frac{1}{\delta})$  timescale which takes  $w$  onto the  $V$  nullcline,  $h = h_0(V)$

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

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



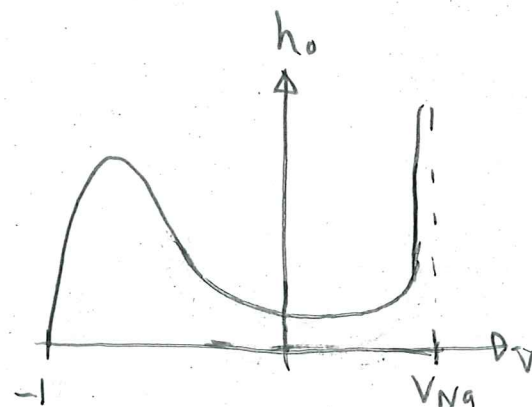
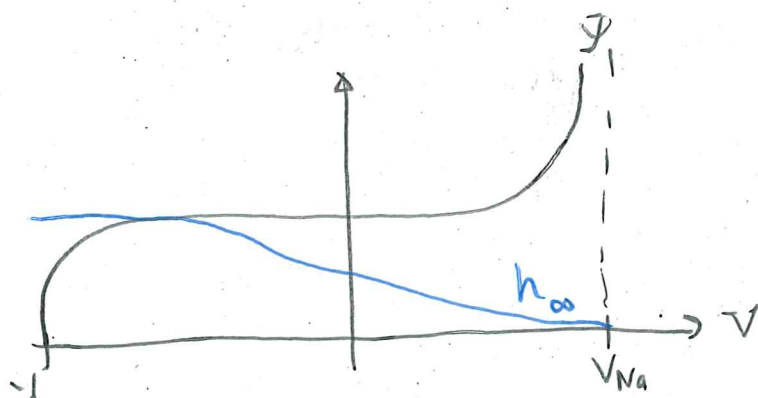
$$\bar{y} = \frac{1 - e^{-(V+1)/\delta}}{1 - e^{-(V_{Na}-V)/\delta}}$$

$$\delta \ll 1$$

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

As  $V \rightarrow V_{Na}$ ,  $\bar{y} \rightarrow \infty$

As  $V \rightarrow -1$ ,  $\bar{y} \rightarrow 0$ .



At the fixed point,  $n = n_\infty$  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  $\lambda \ll 1$ , (\*)  $\Rightarrow \bar{\psi}(V) \approx 1$ ,

so  $V$  is close to  $-1$ .

$$\text{Set } V = -1 + v, \quad v \ll 1.$$

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

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

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

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

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

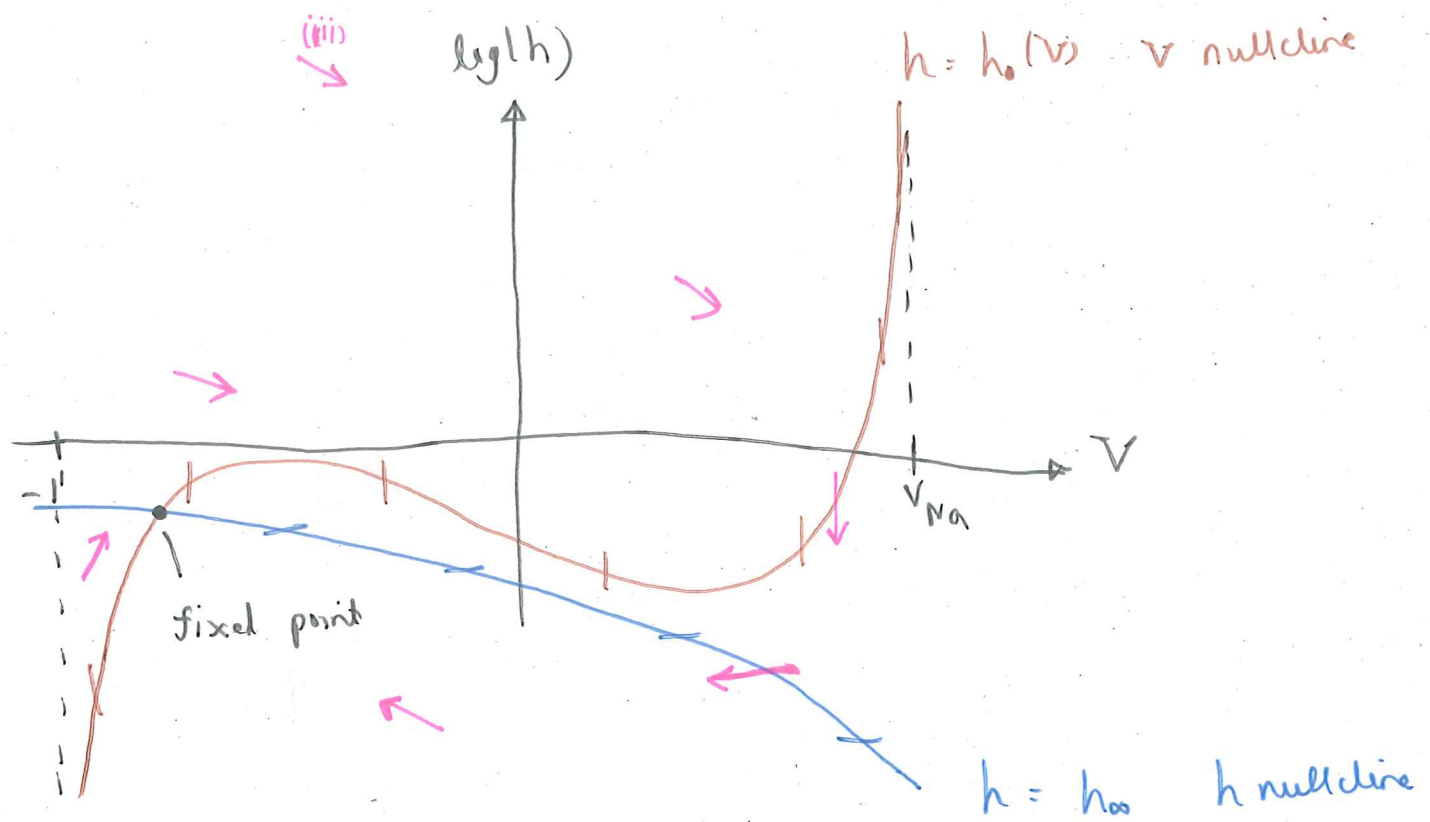
$$e^{-v/\delta} \approx \lambda$$

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

$$v = \delta \log\left(\frac{1}{\lambda}\right)$$

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

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



Construct phase plane by following step-:

- i) Plot 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

1.4

Associated stability matrix

$$\underline{M} = \begin{pmatrix} -1 & h_0' \\ \delta & -\delta h_0' \end{pmatrix}$$

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

so stable if  $-1 - \delta h_0' < 0$

$$-1 < \delta h_0'$$

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

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

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

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

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

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

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

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

found earlier

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

since  $\lambda \ll 1$ .

fixed point is stable if

$$\boxed{\frac{\lambda}{\delta} h_\infty(V^*) + h_\infty'(V) \gtrsim 0}$$

$$2) \quad v_n = \frac{-\psi_t}{|\nabla \psi|}, \quad \eta = -\frac{\nabla \psi}{|\nabla \psi|}$$

$$\text{So } v_n + \nabla \cdot \eta = c$$

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

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

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

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

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

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

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

So  $v_n = c - \nabla \cdot \underline{n} \Rightarrow \frac{c}{f'} = c - \frac{1}{r}$

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

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

So  $\psi = ct - f$

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

2D waves

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

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

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

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

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

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

$$\psi_t = R_t$$

So in (x),

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

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

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

So

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

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

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

$\Rightarrow$  If  $R(0) < 1/c$  then the patch will shrink. This is curvature blocking.  
 If  $R(0) > 1/c$  then the wave will propagate outwards indefinitely

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

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

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

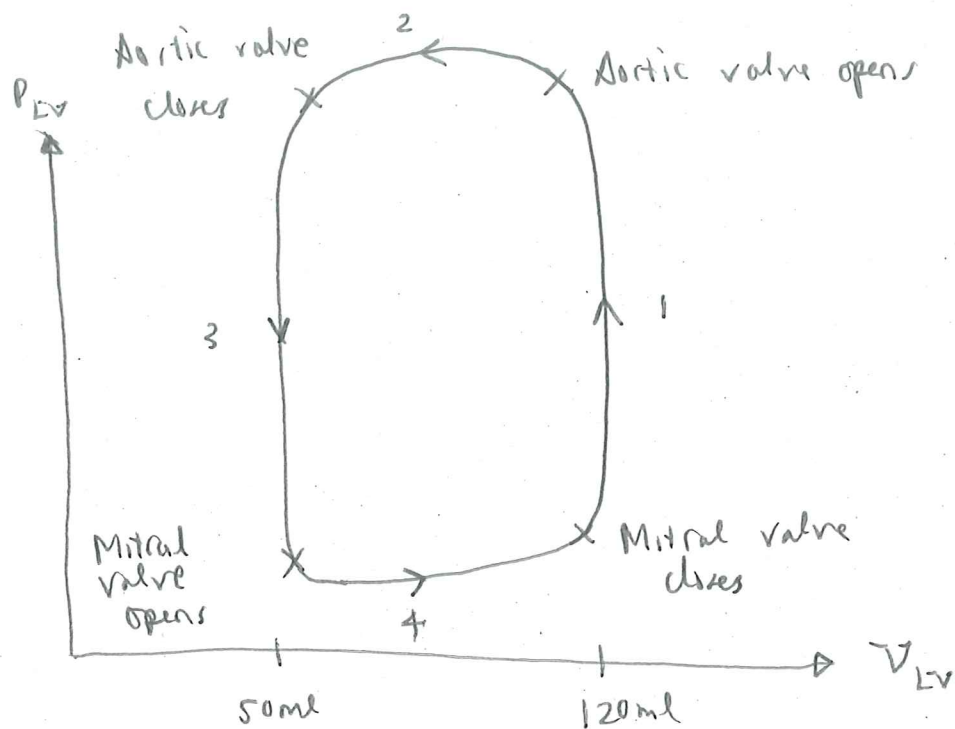
$$\omega f_{\eta} = c \left( 1 + \frac{1}{\lambda^2} \frac{f_{\eta}^2}{f^2} \right)^{1/2} - \frac{1}{\lambda f} \left( 1 + \frac{2 f_{\eta}^2}{\lambda^2 f^2} - \frac{f_{\eta\eta}}{\lambda^2 f^2} \right)$$

$$\Rightarrow f_{\eta} = \frac{c}{\lambda} + o\left(\frac{1}{\lambda}\right)$$

$$\Rightarrow f = \frac{c}{\lambda^2}$$

$$\boxed{R = \frac{c \lambda}{\epsilon^{1/3}}}$$

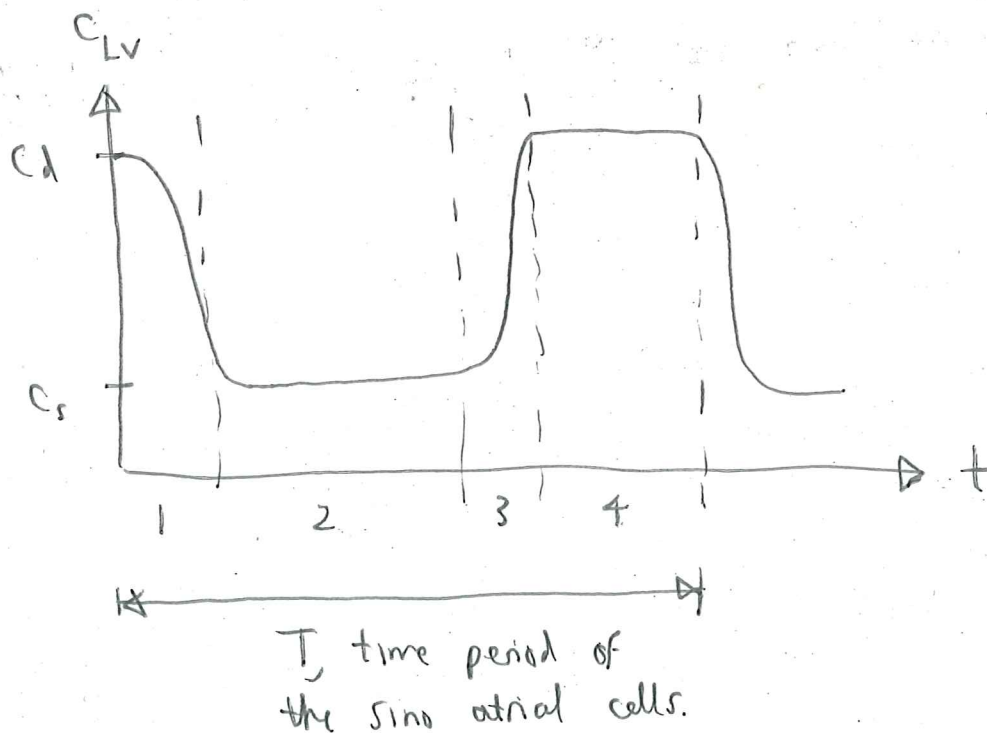
3).



Stroke volume = 70ml.

= change in left ventricular volume on contraction

Left ventricle compliance.



$$\text{Heart rate} = \frac{1}{T_s}$$

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.

4.1.  
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  $C_v$  falls from  $C_d$  to  $C_s$  as the heart tightens.

Ejection. The aortic valve opens. The compliance  $C_v$  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.

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

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

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

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

Isovolumetric means  $V_{LV} = \text{constant}$

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

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

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

Contraction  
= 0.05s  
(given in question)

$$\Rightarrow p_a \text{ approximately constant on this timescale}$$

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

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

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

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

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

So  $C_a p_a + C_{LV} p_{LV} = \text{constant}$

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  $p_{LV}^0$ ).

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

and the ejection phase occurs over a time of  $0.3s$ , 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), 4.4

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

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

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  $\Delta t_F$ , 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 (B),  $p_v \approx \frac{p_a}{R_c C_v}$  since  $p_v < p_{LV}$  and  $p_a \gg p_v$

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

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

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,

$$\frac{dp_a}{dt} = - \frac{p_a - p_v}{R_c C_a} \quad \frac{dp_v}{dt} = \frac{p_a - p_v}{R_c C_v} - \frac{[p_v - P_{Lv}]_+}{R_v C_v}$$

$0.05s$ 
 $0.05s$ 
 $60s$ 
 $0.8s$

$1.8s$ 
 $0.8s$

(given in question)

$0.08s$  is fast compared with the other timescales, so

$p_a \approx \text{constant}$  and  $p_v \approx \text{constant}$

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

$$C_{LV} P_{LV} = \text{constant}$$

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

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

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

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

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

In the refilling phase,

$$\textcircled{1} \Rightarrow \dot{p}_a = - \frac{p_a - p_v}{R_c C_a}$$

since  $p_{Lv} < p_a$

$$\approx - \frac{p_a}{R_c C_a} \textcircled{C} \text{ since } p_a \gg p_v$$

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

$$\textcircled{3} \Rightarrow \dot{p}_{Lv} = \frac{p_v - p_{Lv}}{R_v C_d} \textcircled{E}$$

since  $C_{Lv} = \text{constant}$   
 $= C_d$  in  
 this phase

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

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

$$C_a \times \textcircled{C} + C_v \times \textcircled{D} + C_d \times \textcircled{E} \Rightarrow$$

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

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

$$C_a p_a + C_v p_v + C_d p_{Lv} = C_a p_a^+ + C_v p_v^* + C_d p_{Lv}^+$$

using values at the end  
 of the previous phase

4.8

$$\textcircled{D} - \textcircled{E} : \quad \frac{d}{dt}(p_v - p_{Lv}) = \frac{p_a}{R_c c_v} - \left( \frac{1}{R_v c_v} + \frac{1}{R_v c_d} \right) (p_v - p_{Lv})$$

$$\Rightarrow \frac{d}{dt} \left[ (p_v - p_{Lv}) \exp[\alpha t] \right] = \frac{p^+}{R_c c_v} \exp \left[ -\frac{t}{R_c c_a} \right] \exp[\alpha t]$$

$$\alpha = \frac{1}{R_v c_v} + \frac{1}{R_v c_d}$$

$$\Rightarrow (p_v - p_{Lv}) \exp(\alpha t) = \frac{p^+}{R_c c_v (\alpha - \lambda)} \left( \exp[(\alpha - \lambda)t] - 1 \right) + \left( p^* - \frac{c_s}{c_d} p^+ \right)$$

$$\lambda = \frac{1}{R_c c_a}$$

$$p_v - p_{Lv} = \frac{p^+}{R_c c_v (\alpha - \lambda)} \left( e^{-\lambda t} - e^{-\alpha t} \right) + \left( p^* - \frac{c_s}{c_d} p^+ \right) e^{-\alpha t}$$

So at the end of this phase,

$$p_v - p_{Lv} = \frac{p^+}{R_c c_v (\alpha - \lambda)} \left( e^{-\lambda \Delta t_R} - e^{-\alpha \Delta t_R} \right) + \left( p^* - \frac{c_s}{c_d} p^+ \right) e^{-\alpha \Delta t_R}$$