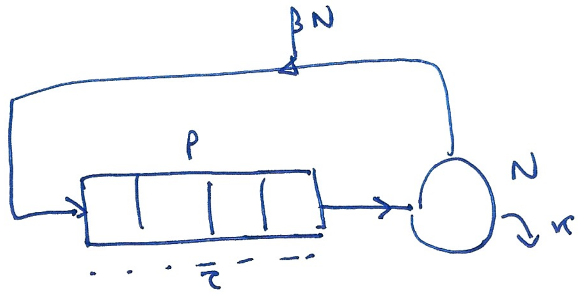
C5·12 Math Physiol 2014 q3

3)



$$\dot{p} = -\gamma p + \beta(N)N - e^{-\gamma\tau}\beta(N_\tau)N_\tau$$

$$\dot{N} = -\beta(N)N - \kappa N + 2e^{-\gamma\tau}\beta(N_\tau)N_\tau$$

$$\beta = \beta_0 \exp\left[-N/\beta_1\right]$$

(a) γ apoptosis rate

κ rate of recruitment to maturation

$e^{-\gamma\tau}\beta(N_\tau)N_\tau$ loss to resting phase after passage through mitotic cycle (with delay τ)

$2e^{-\gamma\tau}\beta(N_\tau)N_\tau$ 2× above through cell division

specific recruitment rate to mitosis decreases with increasing N

(b) evidently $t \sim \tau$: scale $P \sim P_0$, $N \sim \beta_1$

$$\Rightarrow \frac{P_0}{\tau}\dot{p} = -\gamma P_0 p + \beta_0\beta_1 e^{-n} n - e^{-\gamma\tau}\beta_0\beta_1 e^{-n_1} n_1$$

$$\Rightarrow \dot{p} = -\gamma\tau p + \frac{\beta_0\beta_1\tau}{P_0} n e^{-n} - \beta_0\beta_1 e^{-\gamma\tau}\frac{\tau}{P_0} n_1 e^{-n_1}$$

$$\frac{\beta_1}{\tau}\dot{n} = -\beta_0\beta_1 n e^{-n} - \kappa\beta_1 n + 2e^{-\gamma\tau}\beta_0\beta_1 n_1 e^{-n_1}$$

$$\Rightarrow \dot{n} = -\beta_0\tau n e^{-n} - \kappa\tau n + 2\beta_0 \cancel{\beta_1} \tau e^{-\gamma\tau} n_1 e^{-n_1}$$

and with $b = e^{-n}$ this is of the requested form if

$$c_0 = \gamma\tau$$

$$b_0 = \frac{\beta_0 \beta_1 \tau}{p_0}$$

$$b_0 e^{-c_0} = \frac{\beta_0 \beta_1 e^{-\gamma\tau} \tau}{p_0} = b_0 e^{-\gamma\tau}$$

and $b_0 = \beta_0 \tau$

$$k_0 = \kappa\tau$$

$$2 e^{-c_0} b_0 = 2\beta_0 \tau e^{-\gamma\tau}$$

so $\underline{c_0 = \gamma\tau}$, $\underline{b_0 = \beta_0 \tau}$, $\underline{p_0 = \beta_1}$

$\underline{k_0 = \kappa\tau}$

equilibrium $\dot{n} = -b_0 n e^{-n} - k_0 n + 2 b_0 e^{-c_0} n_1 e^{-n_1}$

$n = 0 \sim \quad k_0 = e^{-n}(2 b_0 e^{-c_0} - b_0)$

$\Rightarrow \quad e^{n} = (2e^{-c_0} - 1)\frac{b_0}{k_0}$

$\Rightarrow n_*$ if RHS > 1 ie $\underline{(2e^{-c_0} - 1) b_0 > k_0}$

(c)

$$n = n^* + m$$

linearise $\dot{n} = -b_0 n e^{-n} - k_0 n + 2b_0 e^{-c_0} n_1 e^{-n_1}$

Define $g(n) = ne^{-n}$

$$\dot{m} = -b_0 g' m - k_0 m + 2b_0 e^{-c_0} g' m_1$$

where $g' = g'(n^*) = (1-n^*)e^{-n^*}$

$$\Rightarrow \dot{m} = \alpha_1 m - \alpha_2 m_1$$

$$\alpha_1 = -b_0 g' - k_0$$
$$\alpha_2 = -2b_0 e^{-c_0} g'$$

$k_0 = 0.1 \quad b_0 = 4 \quad e^{-c_0} = 0.6$

equilibrium $\quad e^{n^*} = (1.2-1)\dfrac{4}{0.1} = 8 \qquad n^* = \ln 8 \simeq 2$

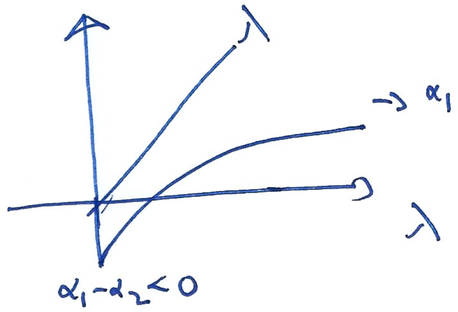
$$g' \simeq -0.125$$

$$\begin{cases} \alpha_1 \simeq 0.4 \\ \alpha_2 \simeq 0.6 \end{cases}$$

(d) $m = e^{\lambda t}$

(i) $\Rightarrow \lambda = \alpha_1 - \alpha_2 e^{-\lambda}$ $\qquad \alpha_1 = 0.4$, $\alpha_2 = 0.6$

I. +ve root?



slope of RHS $= \alpha_2 e^{-\lambda} < \alpha_2 < 1$ for $\lambda > 0$

& $\alpha_1 - \alpha_2 < 0 \Rightarrow$ no +ve root.

II. +ve real part?

$$\lambda = \alpha_1 - \alpha_2 e^{-\lambda}$$

Since $\alpha_1 < \alpha_2$, usual approach doesn't work

[$\mathrm{Re}\,\lambda > 0 \Rightarrow |\alpha_2 e^{-\lambda}| < \alpha_2$, no good]

If $\lambda = \lambda_R + i\lambda_I$ then

$$\lambda_R = \alpha_1 - \alpha_2 e^{-\lambda_R} \cos \lambda_I$$
$$\lambda_I = \alpha_2 e^{-\lambda_R} \sin \lambda_I$$

but $\dfrac{\sin \lambda_I}{\lambda_I} < 1 \;\; \forall \lambda_I$ So $1 = \alpha_2 \dfrac{\sin \lambda_I}{\lambda_I} e^{-\lambda_R}$

$\Rightarrow \lambda_R < 0$ as $\alpha_2 < 1$ $\square$.

(5

ii $k_0\downarrow$ $b_0\downarrow$ $\frac{k_0}{b_0}$ fixed.

$$e^{n^*} = (2e^{-c_0}-1)\frac{b_0}{4k_0} \quad \text{is fixed}$$

$\Rightarrow |g'|$ is fixed

$$\alpha_1 = b_0\left[|g'| - \frac{k_0}{b_0}\right]$$

$$\alpha_2 = 2b_0 e^{-c_0}|g'|$$

So $\alpha_1\downarrow$ $\alpha_2\downarrow$ with $\frac{\alpha_1}{\alpha_2}$ fixed

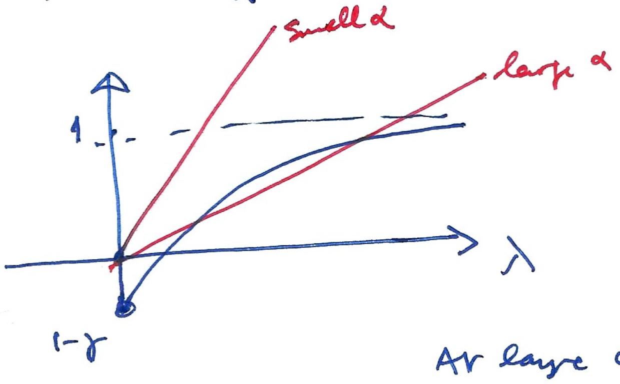
write $\alpha_1 = \alpha$, $\gamma = \cancel{\frac{\alpha_1}{\alpha_2}}$ $\frac{\alpha_2}{\alpha_1}$

$$\lambda = \alpha\left[1-\gamma e^{-\lambda}\right]$$

for $\gamma>1$, $\lambda = \lambda(\alpha)$. For $\alpha = 0.4$ $Re\lambda < 0$ ($\gamma = 1.5$).

The argument of part II above shows that $\lambda_R < 0$ if λ is complex

$$1-\gamma e^{-\lambda} = \frac{\lambda}{\alpha}, \quad \lambda \text{ real}, \quad \gamma > 1$$



~~[illegible]~~

~~[illegible]~~

??

∴ λ never crosses zero

At large α, 2 +ve roots but via two complex roots becoming real

$\Rightarrow$ Hopf bifurcation at earlier (large α)

Hopf bifurcation?

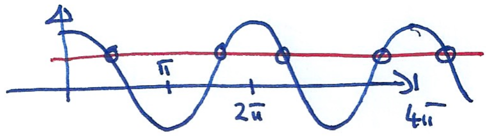
$$\lambda = \alpha\left[1 - \gamma e^{-\lambda}\right]$$

vary α $\quad \lambda = i\theta$

$$i\theta = \alpha\left[1-\gamma e^{-i\theta}\right]$$

$$0 = 1 - \gamma\cos\theta$$

$$\theta = \alpha\gamma\sin\theta$$



$\theta = \cos^{-1}\frac{1}{\gamma}$ for $\gamma > 1$

or with $\phi = \cos^{-1}\frac{1}{\gamma} \in (0, \pi/2)$

$\theta = 2n\pi \pm \phi \qquad n = 0, 1 \ldots$

& $\alpha = \dfrac{\theta}{\gamma\sin\theta}$ gives sequence of increasing +ve values

$$\alpha_n = \frac{2n\pi + \phi}{\gamma\sin\phi} = \frac{2n\pi+\phi}{(\gamma^2-1)^{1/2}}$$

first is $\alpha_0 = \dfrac{\cos^{-1}\frac{1}{\gamma}}{\sqrt{\gamma^2-1}}$ with $\gamma = 1.5$

$\alpha_0 \simeq 0.75$

Transversality $\lambda(\alpha)$

$$\lambda' = 1 - \gamma e^{-\lambda} + \alpha\gamma e^{-\lambda}\lambda'$$

$$= \frac{\lambda}{\alpha} + (\alpha - \lambda)\lambda'$$

so $\lambda' = \dfrac{\lambda}{\alpha(1-\alpha+\lambda)}$, at $\lambda = i\theta$, $\lambda' = \dfrac{i\theta\left[1-\alpha-i\theta\right]}{\alpha\left[(1-\alpha)^2+\theta^2\right]}$

$\Rightarrow \mathrm{Re}\,\lambda' = \dfrac{\theta^2}{\alpha\left[(1-\alpha)^2+\theta^2\right]} > 0$ so Hopf as α increases through

$\dfrac{\cos^{-1}\frac{1}{\gamma}}{\sqrt{\gamma^2-1}} \simeq 0.75$ not as $\alpha\downarrow$.