C5.12 Math Physiol 2016 q3 (1

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$$\dot{E} = F(E_\tau) - \gamma E$$

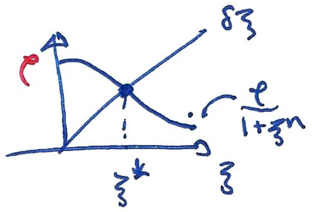
(a) E circulating erythrocytes, γ loss term (life time ~ 100 d)
F production from pluripotential stem cells with a delay τ
due to maturation time

(b) $F(E) = \dfrac{F_0 \theta^n}{E^n + \theta^n}$

(i) $E = \theta \xi \quad t = \tau T$

$$\Rightarrow \frac{\theta}{\tau} \dot{\xi} = \frac{F_0}{1+\xi_1^n} - \gamma \theta \xi$$

$$\Rightarrow \dot{\xi} = \frac{\rho}{1+\xi_1^n} - \delta \xi \qquad \rho = \frac{F_0 \tau}{\theta}, \quad \delta = \gamma \tau$$

(ii) 

clearly unique steady state

(iii) linearise : write $h = \dfrac{\rho}{1+\xi^n}$

$\xi = \xi^* + \eta$

$$\dot{\eta} = h'(\xi^*) \eta_1 - \delta \eta$$

Define $\alpha = -h'(\xi^*) = \dfrac{\rho}{(1+\xi^n)^2} \cdot n\xi^{n-1}$. Note $1+\xi^n = \dfrac{\rho}{\delta \xi}$

$$\Rightarrow \alpha = \frac{\rho\, \delta^2 \xi^2 \cdot n \xi^{n-1}}{\rho^2} = \frac{\delta^2 n}{\rho} \xi \left(\frac{\rho}{\delta\xi} - 1 \right)$$

$$= \delta n \left[1 - \frac{\delta \xi^*}{\rho} \right] > 0$$

$$\dot\eta = -\alpha\eta_1 - \delta\eta$$

$$\eta = e^{\sigma t}$$

$$\sigma = -\delta - \alpha e^{-\sigma}$$

Question does not define ω !!

If α is small $\operatorname{Re}\sigma < 0$ (certainly if $\alpha < \delta$)

Fix δ, $\sigma(\alpha)$ has derivative

$$\sigma' = -e^{-\sigma} + \alpha e^{-\sigma}\sigma'$$

$$\Rightarrow \sigma' = \frac{e^{-\sigma}}{\alpha e^{-\sigma} - 1}, \quad \alpha e^{-\sigma} = -\sigma - \delta$$

$$\text{so } \sigma' = \frac{1}{\alpha}\left[\frac{-\sigma-\delta}{-\sigma-\delta-1}\right] = \frac{\sigma+\delta}{\alpha(\sigma+\delta+1)}$$

Suppose $\sigma = i\theta$ at some value of α

$$\text{then} \quad i\theta = -\delta - \alpha e^{-i\theta}$$

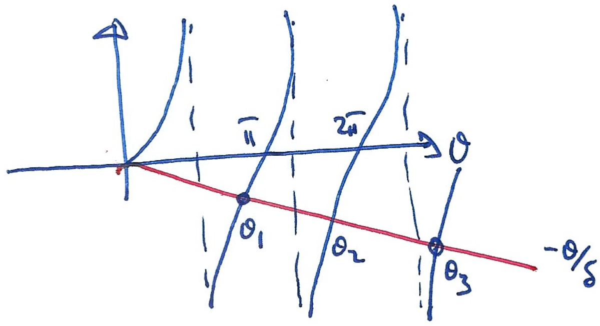
$$\Rightarrow 0 = -\delta - \alpha\cos\theta$$

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

$$-\delta = +\alpha\cos\theta$$

$$\Rightarrow \tan\theta = -\frac{\theta}{\delta}$$

$$\& \quad \alpha = \frac{\theta}{\sin\theta}$$



There are roots θ_i as shown

with $\theta_1 \in (\pi/2, \pi)$, $\theta_3 \in (5\pi/2, 3\pi)$ etc

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& corresponding positive $\alpha_1 = \frac{\theta_1}{\sin\theta_1}$, $\alpha_3 = \frac{\theta_3}{\sin\theta_3}$ etc

& $\alpha_1 < \alpha_3 <$.

[the latter because also $\alpha = -\frac{\delta}{\cos\theta}$ & from the graph we

see $\theta_r = r\pi - \phi_r$ where $\phi \in (0, \pi/2)$ is increasing with r

So $\theta_{2n-1} = (2n-1)\pi - \phi_{2n-1}$

$$\alpha = \frac{-\delta}{\cos\theta_{2n-1}} = \frac{\delta}{\cos\phi_{2n-1}}$$

$$\phi\uparrow \Rightarrow \cos\phi \downarrow \Rightarrow \frac{\delta}{\cos\phi}\uparrow$$]

Transversality: $$\sigma'\big|_{i\theta} = \frac{\delta + i\theta}{\alpha(1+\delta+i\theta)} = \frac{(\delta+i\theta)(1+\delta-i\theta)}{\alpha[(1+\delta)^2+\theta^2]}$$

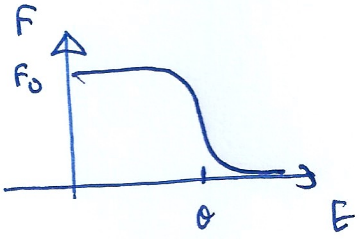
$$= \frac{\delta + i\theta + \delta^2 + \theta^2}{\alpha[(1+\delta)^2+\theta^2]}$$

So $\mathrm{Re}\,\sigma'\big|_{\sigma=i\theta} > 0$.

Therefore at $\alpha_1 = -\frac{\delta}{\cos\theta_1}$ instability occurs for $\alpha > \alpha_1$

So I suppose $\theta_1 = \omega^*$ not sure what A is about - seems to be upside down

(c) $n \to \infty$.



$$F = \frac{F_0}{1 + \left(\frac{E}{\theta}\right)^n}$$

$E < \theta \quad F \to F_0$

$E > \theta \quad F \to 0$

oops question has $\leq \theta$ &

$\leq E_\tau$

Should be $<$

$t = 0 \quad E = E_0 > \theta \quad , \quad E > \theta \quad -\tau \leq t \leq 0$

method of steps $\quad \dot{E} = F - \gamma E \quad$ $F = 0$ if $E_\tau > \theta$

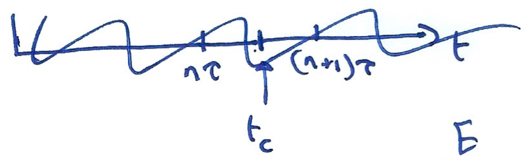
$F = F_0$ if $E_\tau < \theta$

(i) $0 < t < \tau$: $\quad \dot{E} = -\gamma E \Rightarrow E = E_0 e^{-\gamma t}$

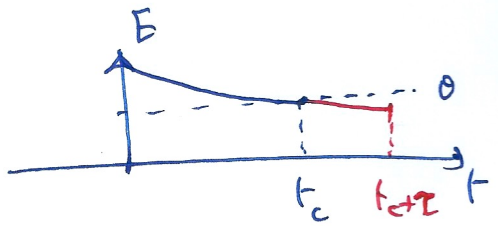
~~Ab~~ As long as $E_0 e^{-\gamma t} > \theta$ this solution carries on

~~Suppose $E_0 e^{-\gamma t}$~~ At $t = t_c = \frac{1}{\gamma} \ln \frac{E_0}{\theta}$

$E = E_0 e^{-\gamma t} = \theta$



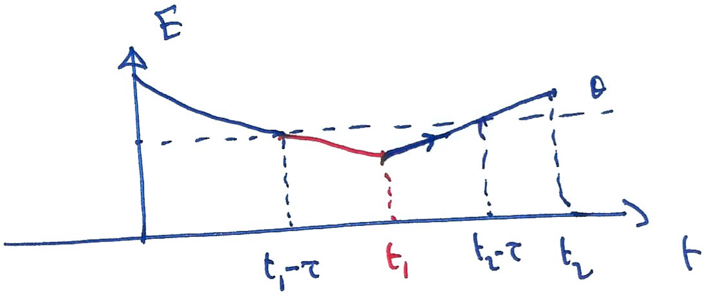
~~If $n\tau \leq t_c \leq (n+1)\tau$~~



For $t_c < t < t_c + \tau$ we still have $E_\tau > \theta$

so $E = E_0 e^{-\gamma t}$ till $t = t_c + \tau = \tau + \frac{1}{\gamma} \ln \frac{E_0}{\theta} = t_1$

$\Delta \; E_1 = \theta e^{-\gamma \tau}$



Now for $t > t_1$, $E_\tau < \theta$ so $F = F_0$

& $\dot{E} = F_0 - \gamma E$ $\quad E = E_1$ at $t = t_1$

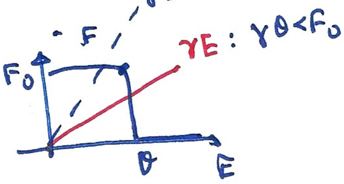
$$E - \frac{F_0}{\gamma} = \left(E_1 - \frac{F_0}{\gamma}\right) e^{-\gamma(t-t_1)}$$

and this will carry on till $t = t_2$

where $E(t_2 - \tau) = \theta$

ie $$\theta - \frac{F_0}{\gamma} = \left(E_1 - \frac{F_0}{\gamma}\right) e^{-\gamma[t_2 - t_1 - \tau]}$$

$$\Rightarrow \frac{\gamma\theta - F_0}{\gamma E_1 - F_0} = e^{-\gamma(t_2 - t_1 - \tau)}$$

[note: 

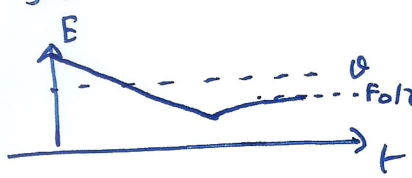
so ...

$$t_2 = t_1 + \tau + \frac{1}{\gamma} \ln\left[\frac{\gamma E_1 - F_0}{\gamma\theta - F_0}\right]$$

Looking back at stability result – oscillations if $\alpha = -h'$ large enough $\Rightarrow$ oscillations for $\gamma < \frac{F_0}{\theta}$, stable if $\gamma > \frac{F_0}{\theta}$]

The sketch above (ie E becomes $> \theta$ again) only applies if $\frac{F_0}{\gamma}$ (where E is heading) is $> \theta$

ie if $\gamma < \frac{F_0}{\theta}$ $\qquad$ If $\gamma < \frac{F_0}{\theta}$ then



In fact for $t > t_1$, $\dot{E} = F_0 - \gamma E$

& if $\gamma E_1 > F_0$ solution will continue to decrease

& will approach $\frac{F_0}{\gamma}$ monotonically

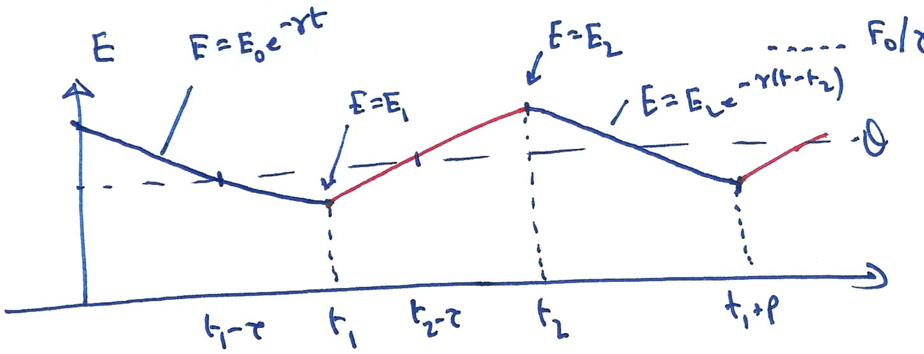
So $\gamma \theta e^{-\gamma\tau} > F_0$ solution decreases for ever

$F_0 < \gamma \theta e^{-\gamma\tau}$ decreases for ever, $t_1 = \infty$ $\left(E \to \frac{F_0}{\gamma} \right)$

$\gamma\theta e^{-\gamma\tau} < F_0 < \gamma\theta$ decreases till t_1, increases for ever after
$t_2 = \infty$ $\left(E \to F_0/\gamma \right)$

& if $F_0 > \gamma\theta$ oscillations. [I think]

$F_0 > \gamma\theta$



At t_2, $E = E_2 = \frac{F_0}{\gamma} + \left(E_1 - \frac{F_0}{\gamma}\right)\left(\frac{F_0 - \gamma\theta}{F_0 - \gamma E_1}\right) e^{-\gamma\tau}$

thereafter $E = E_2 e^{-\gamma(t-t_2)}$ and the solution is periodic with period P

where $E_2 e^{-\gamma(t_1 + P - t_2)} = E_1$, note $e^{-\gamma(t_1 - t_2)} = e^{\gamma\tau}\left(\frac{F_0 - \gamma E_1}{F_0 - \gamma\theta}\right)$

So $e^{\gamma P} = \frac{E_2}{E_1} e^{\gamma\tau}\left(\frac{F_0 - \gamma E_1}{F_0 - \gamma\theta}\right) = \frac{1}{E_1}\left[\frac{F_0}{\gamma}\left(\frac{F_0 - \gamma E_1}{F_0 - \gamma\theta}\right) e^{\gamma\tau} + E_1 - \frac{F_0}{\gamma}\right]$

$\Rightarrow P \ldots$

Question needed to state that $F_0 > \gamma\theta$.