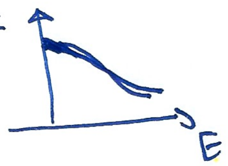
C5.12 Math Physiol q3

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

(a) E : erythrocytes produced at rate F which depends on E via feedback (eg. via EPO) to stemcells which take time τ to mature : γ represents death rate of blood cells in circulation

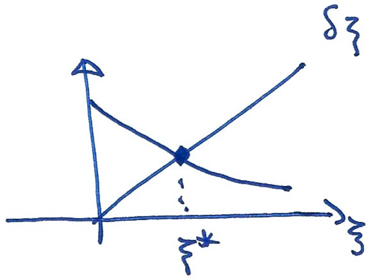
(b) 

production is reduced as E increases which acts to control numbers

(c) (i) $t \sim \tau \quad E = \theta \xi \quad , F = \dfrac{F_0 \theta^n}{(E_\tau + \theta)^n}$

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

$$\Rightarrow \dot{\xi} = \frac{\rho}{(1+\xi_1)^n} - \delta \xi \qquad \left\{ \begin{array}{l} \rho = \dfrac{F_0 \tau}{\theta} \\ \delta = \gamma \tau \end{array} \right.$$

(ii) 

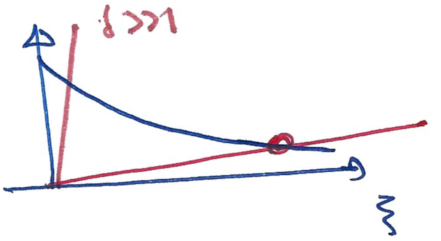
steady $\underbrace{\dfrac{\rho}{(1+\xi)^n}}_{\text{decreasing}} = \underbrace{\delta \xi}_{\text{increasing}}$

$\Rightarrow$ unique steady state

$$f(\xi) = \frac{1}{(1+\xi)^n}$$

so $\dot{\xi} = \rho f(\xi_1) - \delta \xi$

$\delta \ll 1$



ξ^* is large

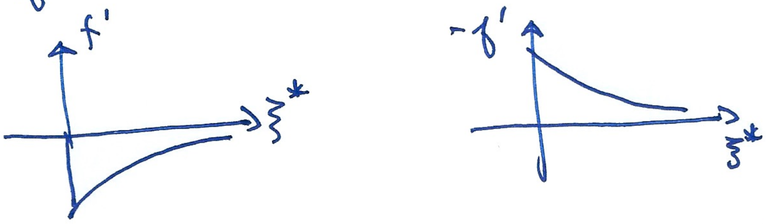
$$\frac{\rho}{(1+\xi)^n} = \delta \xi \quad \Rightarrow \quad \xi^* \approx \left(\frac{\rho}{\delta}\right)^{\frac{1}{n+1}} \qquad \delta \ll 1$$

if $\delta \gg 1$, $\xi \ll 1$, $\xi^* \approx \frac{\rho}{\delta}$ $\qquad \delta \gg 1$

So $f' = \left(\frac{1}{(1+\xi)^n}\right)' = -\frac{n}{(1+\xi)^{n+1}} \approx -\frac{n\delta}{\rho} \qquad \delta \ll 1$

$\approx -n \qquad \delta \gg 1$

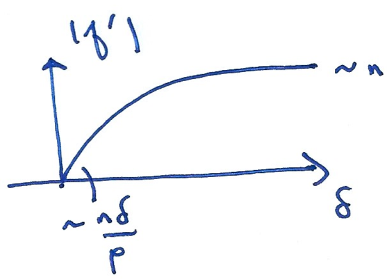
Clearly f' is monotonic in ξ



& ξ^* increases monotonically as δ decreases

$\Rightarrow |f'|$ increases with δ

$\Rightarrow$



(iii) $\delta \ll 1$

& perturb steady state $\xi = \xi^* + X$

$\Rightarrow \quad \dot{X} = -p|f'(\xi^*)| X_1 - \delta X$

$X = e^{\sigma t} \qquad \sigma = -p|f'| e^{-\sigma} - \delta$ ← note this is fine

$\delta \ll 1 \quad , \; p|f'| \simeq n\delta$ ← but this is misguided - see bottom p5

$\Rightarrow \sigma \simeq -\delta n e^{-\sigma} - \delta$

Clearly for $n<1$ all roots have $\mathrm{Re}\,\sigma < 0$

σ varies smoothly with n

If instability occurs then $\sigma = i\theta$ for some n

$\Rightarrow i\theta = -\delta n [\cos\theta - i\sin\theta] - \delta$

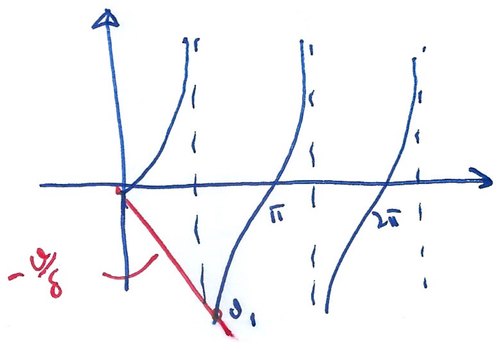
$\Rightarrow \theta = \delta n \sin\theta$

& $n\cos\theta + 1 = 0$

or $-1 = n\cos\theta$

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

& then $n = \frac{-1}{\cos\theta}$



Note when $\delta \ll 1$

roots are $\theta_1 = \pi/2 + \phi_1 \qquad \phi_1 \ll 1$

$\theta_2 = 3\pi/2 + \phi_2 \qquad \phi_2 \ll 1$

$\vdots$

$\theta_m = (m - \tfrac{1}{2})\pi + \phi_m \quad$ & ϕ_m decreases with m

so $$-\frac{1}{\cos\theta_m} = \frac{-1}{(-1)^m \cos(-\tfrac{1}{2}\pi + \phi_m)}$$

$$= \frac{(-1)^{m+1}}{\sin\phi_m}$$

only interested in m odd

corresponding $n_m = \dfrac{1}{\sin\phi_m} \quad m$ odd

ϕ_m decreases with m

so does $\sin\phi_m \ (\simeq \phi_m)$

so n_m increases with m

So $\displaystyle\min_{m \text{ odd}} n_m = n_1$.

We have $-\dfrac{\theta}{\delta} \simeq \tan\theta \quad$ & $\theta_1 = \pi/2 + \phi_1$

$$-\frac{\pi}{2\delta} \simeq \frac{\cos\phi_1}{-\sin\phi_1} \simeq -\frac{1}{\phi_1} \Rightarrow \phi_1 \simeq \frac{2\delta}{\pi}$$

$$\Rightarrow n_1 \simeq -\frac{1}{\cos\theta_1} = \frac{1}{\sin\phi_1} \simeq \frac{\pi}{2\delta}$$

So the steady state is unstable for $n \gtrsim \frac{\pi}{2\delta}$

(assuming some approximation works).

Transversality $\sigma(n)$

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

$$\sigma' = -\delta e^{-\sigma} + \delta n e^{-\sigma}\sigma'$$

$$= \frac{\sigma+\delta}{n} - (\sigma+\delta)\sigma'$$

$$\Rightarrow \sigma' = \frac{1}{n}\left[\frac{\sigma+\delta}{\sigma+\delta+1}\right]$$

at $\sigma = i\theta$ $\quad \sigma' = \frac{1}{n}\left[\frac{(1+\delta-i\theta)(\delta+i\theta)}{(1+\delta)^2+\theta^2}\right]$

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

$\Rightarrow \operatorname{Re}\sigma' > 0$ transversality.

[Actually the part ii is a bit off-putting. Linear stability is $\sigma = -\rho|f'|e^{-\sigma} - \delta = -\beta e^{-\sigma} - \delta$ say in any case so all the above, replacing δn by $\rho|f'| = \beta$ still works, so the condition is $\rho|f'| \gtrsim \pi/2$ — independently of whether the approximation for f' still works. In fact if you put $\rho|f'| = \pi/2$ you find $\xi^* = \frac{1}{\frac{2n\delta}{\pi}-1}$ which is $O(1)$ if $n\delta = O(1)$ so (ii) seems irrelevant]