C5.12 Math Physiol 2017 q2 answer

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

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

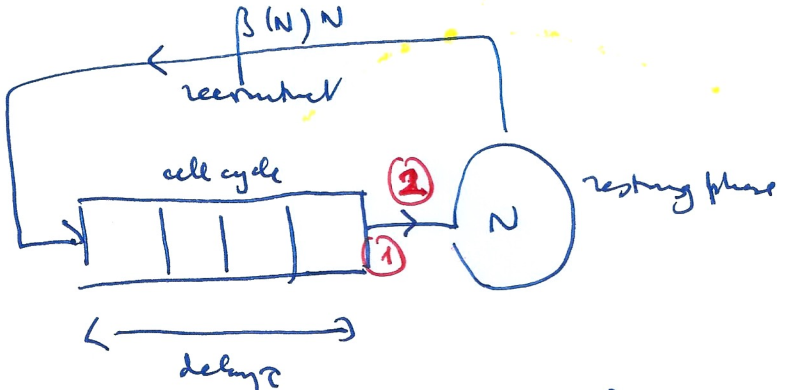
(a) γ apoptosis (cell death) rate

κ loss to maturation stage

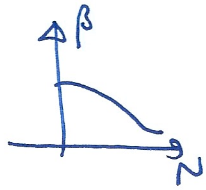
(i) $e^{-\gamma\tau}\beta(N_\tau)N_\tau$ (1) loss of cells from proliferative phase after cell cycle

(ii) $2e^{-\gamma\tau}\beta(N_\tau)N_\tau$ (2) supply to resting phase N after mitosis (factor of 2

(iii) β decreasing to effect control on production of N (high N causes less recruitment to proliferative phase)



(b) $\beta(N) = \beta_0 \operatorname{sech}\left(\frac{N}{\beta_1}\right)$



write $N = \beta_1 n$, $t \sim \tau$

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

$$\Rightarrow \quad \dot{n} = \beta_0\tau\left[n_1 \operatorname{sech} n_1 - n \operatorname{sech} n\right] - \kappa\tau n + \left[2e^{-\gamma\tau}-1\right]\beta_0\tau\, n_1 \operatorname{sech} n_1$$

If we define $g = bn \operatorname{sech} n$ then, if $b = \beta_0\tau$

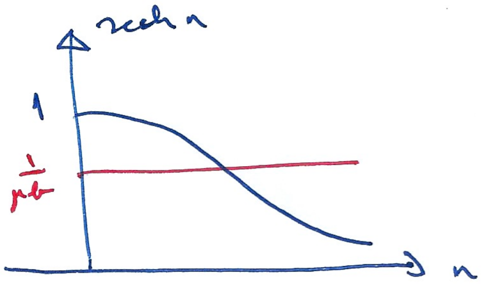
$$\dot{n} = g(n_1) - g(n) + \left[2e^{-\gamma\tau}-1\right]g(n_1) - \kappa\tau n$$

Thus

$$\dot{n} = g(n_1) - g(n) + \varepsilon[\mu g(n_1) - n]$$

$$\varepsilon = \kappa\tau, \quad \mu = \frac{2e^{-\gamma\tau} - 1}{\kappa\tau} \quad b = \beta_0\tau$$

(i) equilibrium



$n = \mu g(n)$

~~$= \mu b\, n\, \text{sech}\, n$~~

$= \mu b n\, \text{sech}\, n$

So $n = 0$ or $\text{sech}\, n = \frac{1}{\mu b}$ if $\mu b > 1$

linearise $n = n^* + m$

$$\Rightarrow \dot{m} = g' m_1 - g' m + \varepsilon[\mu g' m_1 - m]$$

$g' = g'(n^*)$

$m = e^{\lambda t} \Rightarrow \quad \lambda = g' e^{-\lambda} - g' + \varepsilon\mu g' e^{-\lambda} - \varepsilon$

ie $\lambda = -\alpha - \delta e^{-\lambda}$

where $\alpha = \varepsilon + g'$

$\delta = -(1 + \varepsilon\mu) g' > 0$

If $\alpha, \delta > 0$ then $\lambda < 0$ if real.

(ii)

Define $\tau = \varepsilon t$, $n = n(\tau) \Rightarrow n_1 = n(\tau - \varepsilon)$

$\Rightarrow$ Taylor expand $\quad n_1 = n - \varepsilon n' \dots$

$\Rightarrow g(n_1) \simeq g(n) - \varepsilon n' g'(n) \dots$

$$\varepsilon n' \simeq g(n) - \varepsilon n' g'(n) - g(n)$$

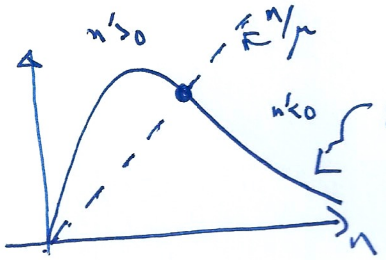
$$+ \varepsilon\left[\mu\{g(n) - \varepsilon n' g'(n)\dots\} - n\right]$$

$$\Rightarrow n' \simeq -n' g'(n) + \mu g(n) - n$$

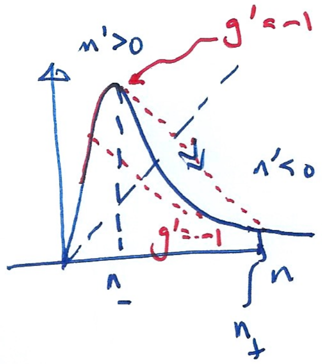
$$\Rightarrow n' \simeq \frac{\mu g(n) - n}{1 + g'(n)}$$

but for $t \sim 1$ $\quad \dot{n} \simeq g(n_1) - g(n)$

[The oscillations are actually of relaxation type, as on the slow time scale



or better



Slow phase finishes at $g' = -1$

$\Rightarrow$ fast phase & note if $n \to n_+$ as $t \to \infty$, $n \to n_-$ as $t \to -\infty$

$$n(t_+) - n(t_-) = \int_{t_-}^{t_+} g(n_1)\,dt - \int_{t_-}^{t_+} g(n)\,dt$$

$$= \int_{t_- - 1}^{t_+ - 1} g(n)\,dt - \int_{t_-}^{t_+} g(n)\,dt = \int_{t_- - 1}^{t_-} g\,dt - \int_{t_+ - 1}^{t_+} g\,dt$$

$\Rightarrow n_+ - n_- \simeq g(n_-) - g(n_+)$ so jump n_- to n_+ 'along' $n + g(n) = \text{constant}$
– red lines above]