C5.12 Math Physiol 2018 q 2

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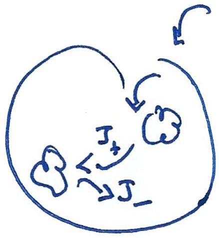


$$\dot{c} = r - kc - [J_+ - J_- - k_s c_s]$$

$$\dot{c}_s = J_+ - J_- - k_s c_s$$

(a) r : production of cytoplasmic Ca^{2+} by stimulation of the IP_3 ~~sensitive~~ store

kc leakage of cytoplasmic Ca^{2+} through cell

kc_s leakage of Ca^{2+} sensitive store to cytoplasm

(b) $$J_- = \frac{V c_s^m}{K_1^m + c_s^m} \cdot \frac{c^p}{K_2^p + c^p}$$

This is the product of two Hill functions (analogous to cooperative enzyme production) : the release ~~depends~~ increases with c_s (as for example $c_s + \text{gate} \rightarrow c$) but is also stimulated by c (CICR) thus

$$c_s + \text{gate} \longrightarrow c \quad :$$

the cytoplasmic Ca^{2+} facilitates the release of the stored Ca^{2+}.

(c) ... 2

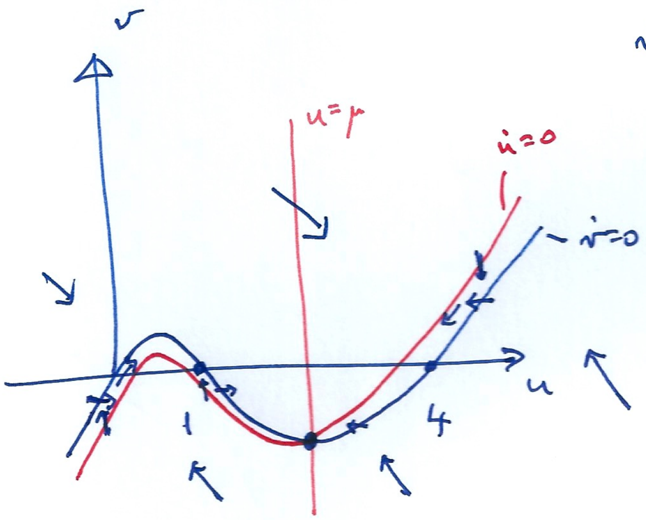
(c)

and $\dot{u} = \mu - u - \frac{5}{\varepsilon} f(u,v)$

$\dot{v} = \frac{1}{\varepsilon} f(u,v)$

$f = u[u^2 - 4u + 5] - v \equiv g(u) - v$

(i)



v nullcline $f = 0$:

$v = u(u-4)(u-1)$

$\dot{u} = 0$ [not sure if the actual nullcline is required – would have depended how the lecturer presented it – I'll do the actual nullcline]

is (with $g(u) = u(u-4)(u-1)$)

$\frac{\varepsilon}{5}(\mu - u) = f = g - v \Rightarrow v = g(u) - \frac{\varepsilon}{5}(\mu - u)$

example above uses $1 < \mu < 4$.

Large v: $\dot{v} < 0$, $\dot{u} > 0$ $\Rightarrow$ other trajectories as shown

Note unique steady state at $u = \mu$, $v = g(\mu)$

[Carrying on formally, linearise at steady state

$$u = \mu + U \qquad v = g(\mu) + V \quad \Rightarrow \text{ linearise } \begin{pmatrix} \dot{U} \\ V \end{pmatrix} \approx M \begin{pmatrix} U \\ V \end{pmatrix}$$

$$M = \begin{pmatrix} -1 - \frac{5}{\varepsilon} f_u & -\frac{5}{\varepsilon} f_v \\ \frac{1}{\varepsilon} f_u & \frac{1}{\varepsilon} f_v \end{pmatrix}$$

So $\det M = -\frac{1}{\varepsilon} f_v$

$\operatorname{tr} M = -1 - \frac{5}{\varepsilon} f_u + \frac{1}{\varepsilon} f_v$

$f = g(u) - v$ so $\det M > 0$ never saddles

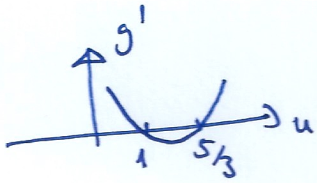
$\operatorname{tr} M = -1 + \frac{1}{\varepsilon}\left[-1 - 5g'\right]$

So ($\varepsilon \ll 1$) steady state is stable if $-1 - 5g' \lesssim 0$

i.e. $g' \gtrsim -\frac{1}{5}$

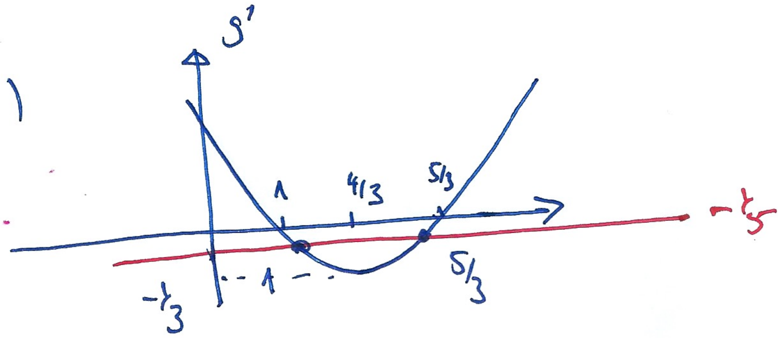
$g' = \left[u^3 - 4u^2 + 5u\right]' = 3u^2 - 8u + 5$

$= (u-1)(3u-5)$



min g' is at $u = \frac{4}{3}$, min $g' = 3 \cdot \frac{16}{9} - \frac{32}{3} + 5 = \frac{15-16}{3} = -\frac{1}{3}$

So ($u = \mu$)



values of u where $g' = -\frac{1}{5}$:

$$3u^2 - 8u + 5 = -\frac{1}{5}$$

are $$3u^2 - 8u + \frac{26}{5} = 0$$

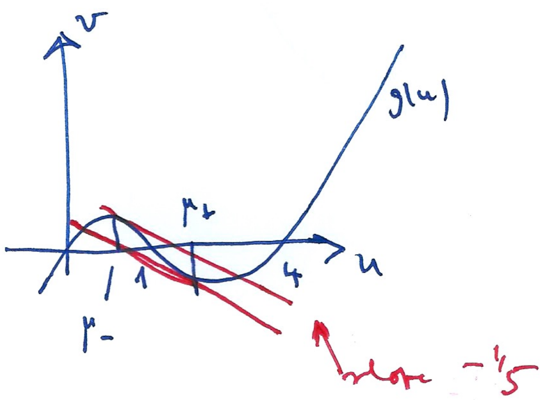
$$u = \frac{1}{6}\left[8 \pm \left\{ 64 - \frac{12.26}{5} \right\}^{1/2} \right]$$

$$= \frac{1}{6}\left[8 \pm \left\{ \frac{320 - 312}{5} \right\}^{1/2} \right]$$

$$= \frac{4}{3} \pm \frac{1}{3}\sqrt{\frac{2}{5}} = \mu_\pm$$

So for $\mu_- \lesssim \mu \lesssim \mu_+$ steady state is unstable.]

But directly (perhaps all that is required)

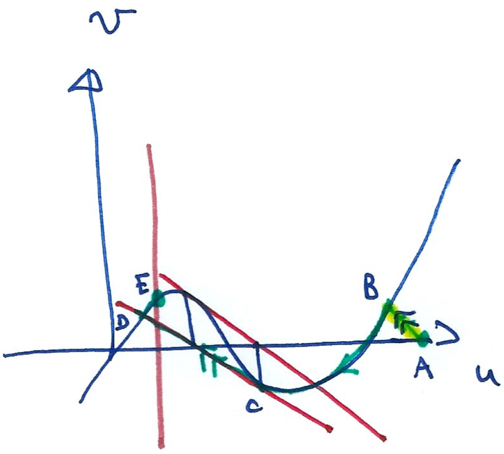


$$\varepsilon \dot{v} = f(u,v) = g(u) - v$$

$$\dot{(u+5v)} = \mu - u$$

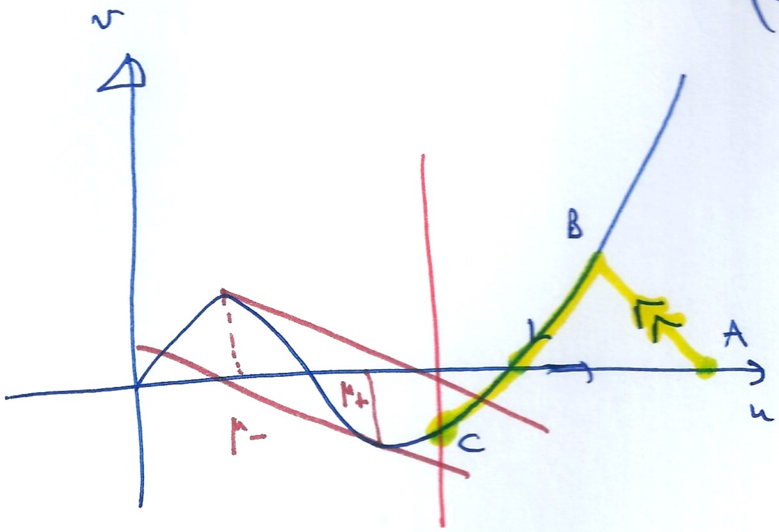
If we define $\mu_\pm$ to be where $g'(u) = -\frac{1}{5}$ (these as above)

then we will get relaxation oscillations for $\mu_- < \mu < \mu_+$:



$\mu < \mu_-$

trajectory follows ABCDE



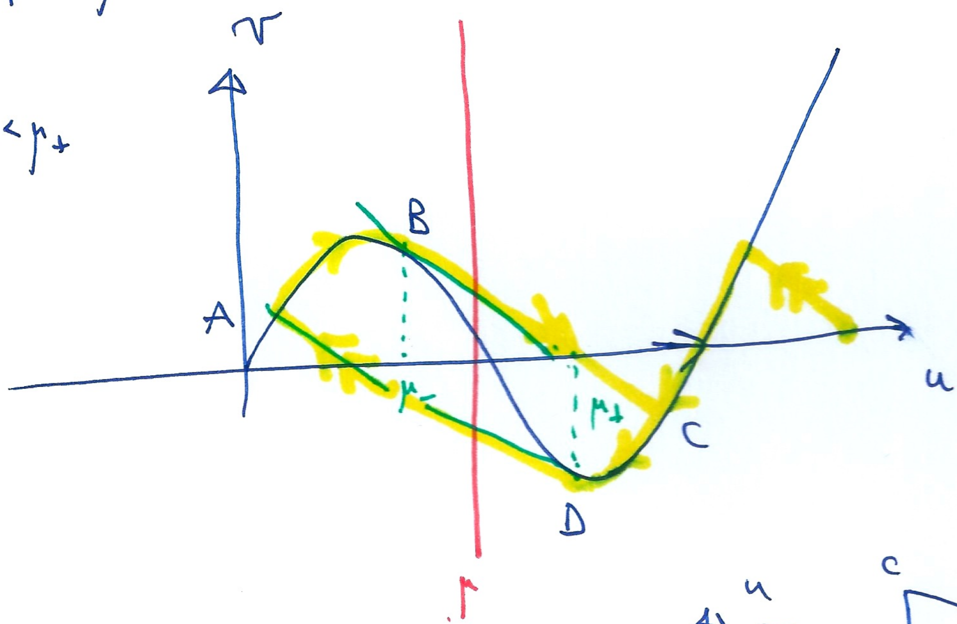
$\mu > \mu_+$

follows ABC

fast slow

(ii) μ_-, μ_+ done above

$\mu_- < \mu < \mu_+$



relaxation oscillation is ABCD