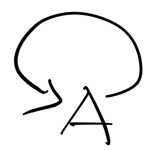
ELL 707 MINOR TEST I 17 marks, 1 hour

1. State in a sentence, what you plan to investigate in the course project.

We plan to investigate approximate quantitative measures for "feedback", "nonlinearity" and "delay" in biomolecular oscillators.

2. Consider the following model of a circuit with positive feedback,



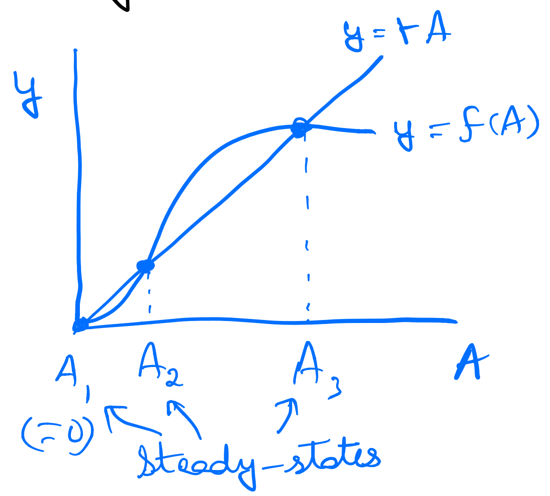
$$\frac{dA}{dt} = f(A) - \gamma A, \quad \text{—— (I)}$$

where A (>0) is the protein concentration, $f(A)$ is a non-decreasing function of A, & $\gamma > 0$ is the degradation constant.

a) For $f(A) = \alpha \cdot \dfrac{A^n}{K^n + A^n}$, where $\alpha (>0)$ is the maximum production rate, $K (>0)$ is the dissociation constant, and n (integer ≥ 2) is the Hill co-efficient, find the number of stable steady-states of (I). (illustrate graphically)

b) What $f(A)$ could be chosen if it is desired to have exactly three distinct stable steady-states and some (≥ 0) unstable steady-states.

a)



$$\frac{df}{dA} = \alpha \frac{nA^{n-1} k^n}{(k^n + A^n)^2} = 0 \text{ at } A = 0$$

$\Rightarrow$ $y = f(A)$ starts below $y = rA$

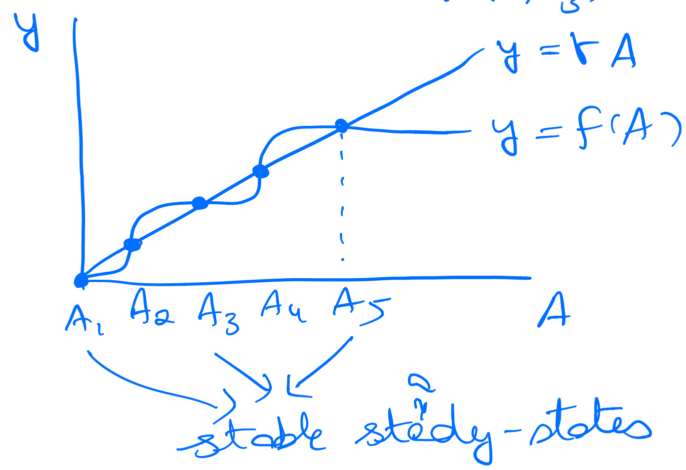
$A_1 < A < A_2 \Rightarrow \frac{dA}{dt} < 0$

$A_2 < A < A_3 \Rightarrow \frac{dA}{dt} > 0$

$A_3 < A \Rightarrow \frac{dA}{dt} < 0$

$\therefore$ 2 stable steady-states (A_1 & A_3)

b)



3. Consider the model $\dot{r} = r(2-r^2)(3-r^2)(5-r^2)$,
$\dot{\theta} = -1.$ — (2)

a) Identify limit cycles and analyse their stability.

b) For (2), the Poincaré-Bendixson Theorem can be used to show that { if — statement

i) R is a closed, bounded subset of X-Y plane,

ii) R does not contain any steady-state (a point where $\dot{x} = \dot{y} = 0$).

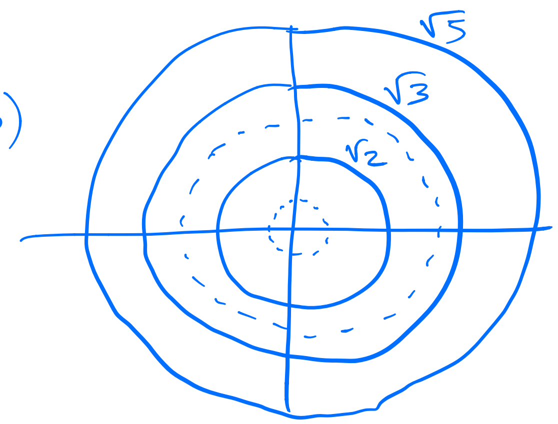
iii) solutions to (2) that are in R at $t = 0$

remain in R for all $t \geq 0$,
then R contains a limit cycle. }

Prove the existence of limit cycle solution(s) for ② by identifying suitable R.

a) Limit cycles, $r = \sqrt{2}$, $r = \sqrt{3}$, $r = \sqrt{5}$

$0 < r < \sqrt{2}$, $\dot{r} > 0$
$\sqrt{2} < r < \sqrt{3}$, $\dot{r} < 0$ } $\Rightarrow r = \sqrt{2}$ is stable
$\Rightarrow r = \sqrt{3}$ is unstable
$\sqrt{3} < r < \sqrt{5}$, $\dot{r} > 0$
$\sqrt{5} < r$, $\dot{r} < 0$ } $\Rightarrow r = \sqrt{5}$ is stable.

b) 

R = region between dashed circles (includes boundary)

i) closed ✓
bounded ✓

✓ ii) $\dot{r} > 0$ in inner circle
$\dot{r} < 0$ in outer circle

$\Rightarrow$ solutions starting in R, stay in R for future time

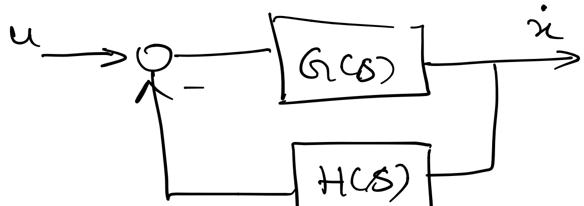
✓ iii) no point in R that is fixed.

$\therefore$ there is a limit cycle in R.

4. The goal of this problem is to investigate the role of delayed negative feedback in generating oscillations.

a) Consider the differential equation

$\ddot{x} + \omega_0^2 x = \underline{u}$ (3) Show that it can be represented in Laplace domain by



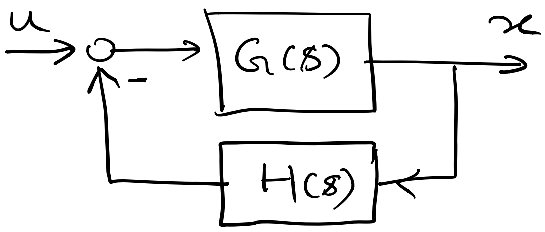
where $G(s) = \frac{1}{s}$ and $H(s) = \frac{\omega_0^2}{s}$.

{Note that the denominator polynomial of $\frac{G(s)}{1+G(s)H(s)}$ has purely imaginary roots, the $\to D(s) = s^2 + \omega_0^2$, $D(s) = 0 \Rightarrow s = \pm j\omega_0$ locations of which correspond to the oscillation frequency of solutions of (3).}

b) Consider the cyclic system of differential equations,

$$\dot{x}_1 = u - Kx_N - x_1, \quad K \in \mathbb{R} \quad (4)$$
$$\dot{x}_i = x_{i-1} - x_i, \quad i = 2, 3, \ldots N$$

i) Show that (4) can be represented as



where $G(s) = \frac{1}{s+1}$.

Find $H(s)$.

(depends on N and K)

ii) Show that the denominator polynomial of $\frac{G(s)}{1+G(s)H(s)}$ is $D(s) = (s+1)^N + K$.

iii) Show that $D(s) = 0$ has no purely imaginary pair of roots $(\pm j\omega, \omega \neq 0)$ if $K = 0$.

iv) Show that $D(s) = 0$ has no purely imaginary pair of roots $(\pm j\omega, \omega \neq 0)$ for $N = 2$ and any $K \in \mathbb{R}$

v) Show that $D(s)=0$ has a pair of purely imaginary roots ($\pm j\omega, \omega\neq 0$) for $N=3$ and some particular K that has to be positive.

a) Take Laplace transform, ($x(0)=0=\dot{x}(0)$)

$$\Rightarrow (s^2+\omega_0^2)\, X(s) = U(s)$$

$$\Rightarrow \quad X(s) = \frac{1}{s^2+\omega_0^2} \cdot U(s)$$

$$= \frac{1}{s} \cdot \frac{\frac{1}{s}}{1+\frac{\omega_0^2}{s}\cdot\frac{1}{s}} \; U(s)$$

$$\Rightarrow \quad sX(s) = \underbrace{\frac{\frac{1}{s}}{1+\frac{\omega_0^2}{s}\cdot\frac{1}{s}}}_{H(s)\;\;\; G(s)} \cdot U(s)$$

(3) solutions are in terms of $\cos\omega_0 t$ and $\sin\omega_0 t$.

b) Take Laplace transform of (4) ($x_i(0)=0=\dot{x}_i(0)$)

$$\Rightarrow \quad sX_1(s) = U(s) - KX_N(s) - X_1(s)$$

$$sX_i(s) = X_{i-1}(s) - X_i(s) \quad i=2,3\ldots N$$

$$\Rightarrow (s+1)\,X_1(s) = U(s) - KX_N(s)$$

$$\Rightarrow \quad X_1(s) = \frac{1}{s+1}\left[U(s) - KX_N(s)\right]$$

& $\quad (s+1)\,X_i(s) = X_{i-1}(s)$

$$\Rightarrow \quad X_i(s) = \frac{X_{i-1}(s)}{s+1}$$

$$\Rightarrow X_N(s) = \frac{1}{s+1}X_{N-1}(s) = \ldots = \frac{1}{(s+1)^{N-1}}X_1(s)$$

$$\Rightarrow \quad H(s) = \frac{K}{(s+1)^{N-1}}$$

ii) $$\frac{G}{1+GH} = \frac{\frac{1}{s+1}}{1+\frac{1}{s+1}\cdot\frac{K}{(s+1)^{N-1}}} = \frac{(s+1)^{N-1}}{(s+1)^N + K}$$

$$\Rightarrow \quad D(s) = (s+1)^N + K .$$

iii) $K=0$, $\quad D(s)=0 \Rightarrow (s+1)^N = 0$

no purely imaginary root.

iv) $N=2$, $\quad D(s)=0$

$$\Rightarrow \quad s^2 + 2s + 1 + K = 0 .$$

Suppose there is purely imaginary root,

$s = j\omega$, $\omega \neq 0$

$$\Rightarrow \quad -\omega^2 + j2\omega + 1 + K = 0$$

$$\Rightarrow \quad \omega = 0 \text{ and } K = -1$$

$\hookrightarrow$ not a pair

v) $N=3$, $\quad D(s)=0$

$$\Rightarrow \quad s^3 + 3s^2 + 3s + 1 + K = 0$$

Suppose there is purely imaginary root,

$s = j\omega$

$$\Rightarrow \quad -j\omega^3 - 3\omega^2 + 3j\omega + 1 + K = 0$$

$$\Rightarrow \quad \omega^3 = 3\omega \text{ \& } K = -1 + 3\omega^2$$

$$\Rightarrow \quad \underset{\text{not a pair}}{\omega = 0}, \quad \underset{\underline{\pm j\sqrt{3}}}{\omega^2 = 3} \Rightarrow \underline{K = 8 > 0}$$