LUNDS UNIVERSITET

Institutionen för
REGLERTEKNIK

Exam FRTF01 - Physiological Models and Computation

January 08 2018, 8-13

Points and grades

All answers must include a clear motivation. The total number of points is 25. The maximum number of points is specified for each subproblem. Preliminary grades:

Betyg 3: 12–16.5 points
4: 17 –21.5 points
5: 22 –25 points

Accepted aid

Lecture slides, any books (without relevant exercises with solutions), including the course textbooks. Standard mathematical tables and Collection of common results and formulae in control. Calculator.

Results

The result of the exam will be posted in LADOK no later than February 6. Information on when the corrected exam papers will be shown, will be given on the course homepage.

1.

a. Given the ion data in Tab. 1, calculate the equilibrium potentials of each of the three ions; Ion_1, Ion_2 and Ion_3, at room temperature, 25°C, by means of the Nernst equation.

Tabell 1: Ion concentrations and valence charge

Ion	**Inner conc. [μM]**	**External conc. [μM]**	**Valence charge**
Ion_1	25	150	+2
Ion_2	130	8.0	+1
Ion_3	6.2	10	-1

Use the following values for the constants, $R = 8.31447$ [J/mol·K] - thermodynamic gas constant, $F = 9.648534 \cdot 10^4$ [C/mol] - Faraday constant.

(1 p)

b. The temperature is lowered. What happens to the equilibrium potential of Ion_1, Ion_2 and Ion_3 (do they increase or decrease)? Motivate your answer.

(1 p)

Solution

a. The Nernst equation for ion [i] is given by

$$E_i = \frac{\mathrm{RT}}{\mathrm{zF}} \ln\left(\frac{C_{out,i}}{C_{in,i}}\right)$$

where z - valence charge, C_{out} the ion concentration outside the cell, C_{in} the ion concentration inside the cell, R - thermodynamic gas constant, F - Faraday constant and T - temperature in Kelvin.

Given $R = 8.31447$ [J/mol·K], $T = 273+25$ [K] and $F = 9.648534 \cdot 10^4$ [C/mol] then $RT/F = 0.0257$ [V] or 25.7 [mV].

Using the Nernst equation with the given values of the inner/external concentrations as well as the valence charge results in $E_1 = 23$, $E_2 = -72$ and $E_3 = -12$ [mV].

b. A decrease in T results in the coefficient RT/F being smaller. Therefore a decrease in T results in a decrease in E_1 and an increase in E_2 and E_3.

2.

a. A patient is administered a drug through infusion into the blood. The current concentration of the drug in the patients blood is C_0 [mg/dl]. The concentration is governed by the kinetics $\dot{C} = -0.8C$ [mg/(dl· h)]. At what time is the concentration of the drug down to 40 % of the initial value? (1 p)

b. The doctors are tired of having to keep administering the drug to keep it close to the desired value C_{opt}. They ask you to decide which constant dose in [mg] to inject the patient with to keep the drug concentration at the level C_{opt} at steady state. The volume of the blood compartment is $V = 50$ [dl]. (2 p)

Solution

a. The solution of $\dot{C} = -0.8C$ is given by $C(t) = C_0 e^{-0.8t}$. Solve $0.4C_0 = C_0 e^{-0.8T}$ for T to get the time.

$$\begin{aligned} 0.4C_0 &= C_0 e^{-0.8T} \\ 0.4 &= e^{-0.8T} \\ \ln(0.4) &= -0.8T \\ T &= \frac{\ln(0.4)}{-0.8} = 1.14\text{hours} \approx 69\text{minutes.} \end{aligned}$$

b. The kinetics of the system is given by

$$\dot{C} = -0.8C + \frac{u}{V}$$

The transfer function of the system is

$$C(s) = \frac{1}{V} \frac{1}{s + 0.8}$$

The static gain is $C(0) = 1/(0.8V)$. And the constant dose that achieves the steady state is given by $u = C_{opt}/C(0)$.

3. Consider the set of differential equations below

$$\begin{aligned} \dot{a} &= -k_{ab}a + k_{ba}b + k_{ca}c \\ \dot{b} &= k_{ab}a - k_{ba}b - k_{bc}b \\ \dot{c} &= k_{bc}b - k_{ca}c \\ y &= c/V_c \end{aligned}$$

where a, b and c are in [mg]. The compartments have distribution volumes V_a, V_b and V_c, respectively. The signal y is a measurement.

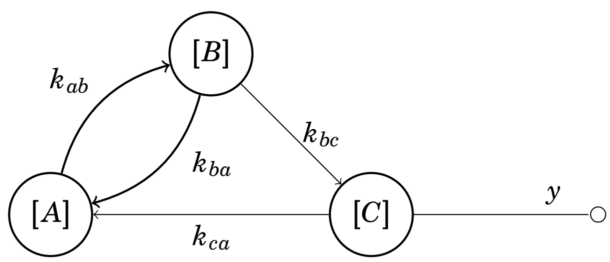
a. Draw a compartment model of the system. (1 p)

b. Write the system on state space form, that is $\dot{x} = Ax$, $y = Cx$. (1 p)

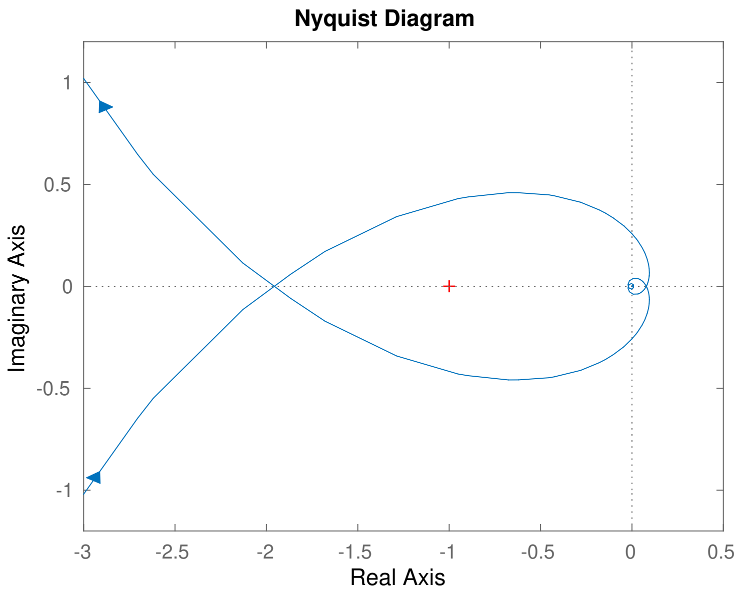
c. What can you say about the sum $a(t) + b(t) + c(t)$ given that $a(0) + b(0) + c(0) = p$, where p is some positive constant. (1 p)

Solution

a.



or use $(a,\ V_a)$, and similarly, in each compartment.



Figur 1: Nyquist plot of the system for problem 4a

b. Let $x = [a\ b\ c]^T$. Then the system can be written as

$$\dot{x} = \begin{bmatrix} -k_{ab} & k_{ba} & k_{ca} \\ k_{ab} & -(k_{ba}+k_{bc}) & 0 \\ 0 & k_{bc} & -k_{ca} \end{bmatrix}$$
$$y = [0 \quad 0 \quad 1/V_c]\, x.$$

c. It is easy to check that $\dot{a} + \dot{b} + \dot{c} = 0$. Thus $a(t) + b(t) + c(t) = q$, where q is some constant. Using the initial conditions we find that $q = p$.

4. Your colleague Doctor Dorian needs help in deciding the property of two inventions that use feedback on a specific physiological system.

a. The first invention utilizes simple output feedback, $u = K(r - y)$ where K is a scalar. Doctor Dorian has managed to find the Nyquist plot of the open-loop system, which can be seen in Fig 1 and tells you that the open-loop is stable. Determine the largest K such that the closed-loop system is stable. (1 p)

b. Draw a block diagram of the closed loop in the previous sub problem. (0.5 p)

c. The second invention is described by

$$\dot{x} = Ax + Bu$$
$$y = Cx$$

With

$$A = \begin{bmatrix} 1 & 0 \\ 2 & 1 \end{bmatrix}, \quad B = \begin{bmatrix} 1 \\ 0 \end{bmatrix}, \quad C = [0 \quad 1]$$

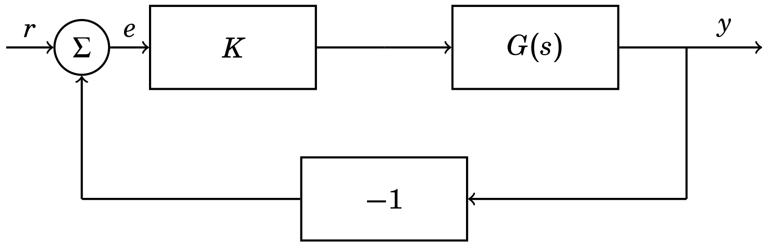
Doctor Dorian suggests you use state feedback, $u = -Lx + l_r r$. Find the transfer function from r to y in terms of the matrices A, B and C. (1 p)

d. Design your controller so that the closed loop has its poles in $-1, -1$. (1.5 p)

Solution

a. From the Nyquist plot it is clear that the amplitude margin is $A_m = 1/2$, and thus the larges K is 1/2.

b.



c. Inserting $u = -Lx + l_r r$ gives $\dot{x} = (A - BL)X + Bl_r r$. The Laplace transform then gives $X(s) = (sI - A + BL)^{-1}Bl_r R(S)$. Thus the transfer function can then be found,

$$Y(s) = \underbrace{C(sI - A + BL)^{-1}Bl_r}_{G(S)} R(S)$$

d. Calculations gives

$$|sI - A + BL| = \det \begin{bmatrix} s - 1 + l_1 & l_2 \\ -2 & s - 1 \end{bmatrix} = s^2 + (l_1 - 2)s + 1 - l_1 + 2l_2$$

This is to be compared with $(s+1)^2 = s^2 + 2s + 1$. Identification of coefficients gives $l_1 = 4$ and $l_2 = 2$.

5. The interaction between predators y, and pray x, can be described by the Lotka-Volterra equations

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \alpha x - \beta xy$$
$$\frac{\mathrm{d}y}{\mathrm{d}t} = \delta xy - \gamma y.$$

a. Find the stationary points (x^0, y^0) of the system. (1 p)

b. Linearize the system around a stationary point with positive (non-zero) x^0 and y^0. (2 p)

c. Determine if the linearized system is stable, marginally stable or unstable for $\alpha, \beta, \gamma, \delta > 0$. (1 p)

Solution

a. $\dot{x} = 0$ for $x = 0$ or $y = \alpha/\beta$ assuming $x \neq 0$. Likewise for $\dot{y}$ we have that $y = 0$ or $x = \gamma/\delta$ assuming $y \neq 0$. Thus the two stationay points that makes $\dot{x} = 0$ and $\dot{y} = 0$ is $(0, 0)$ and $(\gamma/\delta, \alpha/\beta)$.

b. Let

$$f = \begin{bmatrix} \dot{x} \\ \dot{y} \end{bmatrix}.$$

Then

$$\frac{\partial f}{\partial x}(x, y) = \begin{bmatrix} \alpha - \beta y \\ \delta y \end{bmatrix}, \quad \frac{\partial f}{\partial y}(x, y) = \begin{bmatrix} -\beta x \\ \delta x - \gamma \end{bmatrix}.$$

In the point of interest we have

$$\frac{\partial f}{\partial x}(x^0, y^0) = \begin{bmatrix} 0 \\ \delta \frac{\alpha}{\beta} \end{bmatrix}, \quad \frac{\partial f}{\partial y}(x^0, y^0) = \begin{bmatrix} -\beta \frac{\gamma}{\delta} \\ 0 \end{bmatrix}.$$

Let $\Delta x = x - x^0$ and $\Delta y = y - y^0$. Then we have that

$$\begin{bmatrix} \Delta \dot{x} \\ \Delta \dot{y} \end{bmatrix} = \begin{bmatrix} 0 & -\beta \frac{\gamma}{\delta} \\ \delta \frac{\alpha}{\beta} & 0 \end{bmatrix} \begin{bmatrix} \Delta x \\ \Delta y \end{bmatrix}.$$

c. The poles of the systems are given by the solution to $s^2 + \alpha\gamma$. Thus the poles are given by $\pm i\sqrt{\alpha\gamma}$. The poles are on the imaginary axis and the linearized system is marginally stable.

6.

a. Let the transfer function from u to y be given by $G(s) = 2/(s + 3)$. Determine $y(t)$ when $u(t) = \sin(3\omega t)$. (1 p)

b. For the same system, determine $y(t)$ when $u(t) = \theta(t)$ (that is, u is a step). (1 p)

c. For any linear system with zero initial condition, what can you say about the relationship between two outputs $y_1(t)$ and $y_2(t)$ with inputs $u_1(t)$ and $u_2(t)$, respectively, when $2u_1(t) = u_2(t)$. (1 p)

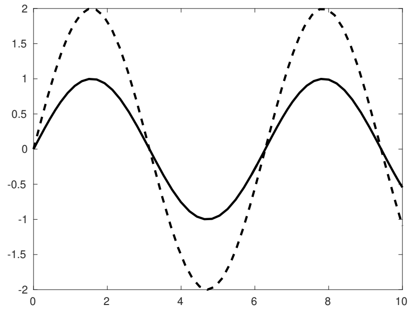
d. In Figure 2 the step responses are plotted for two different step sizes. Which of the two systems can **not** be linear? (1 p)

Solution

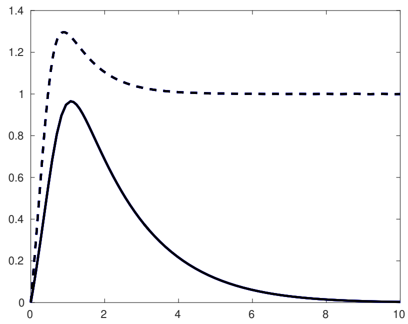
a. Assuming steady state, the output is given by $y(t) = |G(3i)| \sin(3\omega t + \arg(G(3i)))$.

$$|G(3i)| = \frac{2}{\sqrt{9+9}} = \frac{2}{\sqrt{18}} = \frac{\sqrt{2}}{3}$$
$$\arg(G(3i) = -\arctan(1) = -\pi/4$$

It is also possible to use the method in the next subproblem.



(a) System A



(b) System B

Figur 2: Step response with amplitude 1 (solid) and amplitude 2 (dashed).

b. We have that $Y(s) = G(s)U(s) = 2/(s(s+3))$ Using the collection of formulae we find that

$$y(t) = 2/3 \cdot (1 - e^{-3t})$$

c. The output of the first system can be found by

$$y_1(t) = \int_0^t h(t-\tau)u_2(\tau)\ \mathrm{d}\tau,$$

where h is the impulse response of the linear system. Similarly for the second system

$$\begin{aligned} y_2(t) &= \int_0^t h(t-\tau)u_2(\tau)\ \mathrm{d}\tau = \int_0^t h(t-\tau)2u_1(\tau)\ \mathrm{d}\tau \\ &= 2\int_0^t h(t-\tau)u_1(\tau)\ \mathrm{d}\tau = 2y_1(t) \end{aligned}$$

d. System B can not be linear as the responses from two different step sizes can not be related only by a positive scaling factor.

7. Match the step responses in Figure 3 with the transfer functions below:

$$\textbf{i)}\ \frac{1}{s+1} \qquad \textbf{ii)}\frac{0.5}{s+1}$$
$$\textbf{iii)}\ \frac{1}{s^2-0.1s+1} \qquad \textbf{iv)}\ \frac{e^{-s}}{1+s}$$

(Motivation is required for any points, including the last pair!) (2 p)

Solution

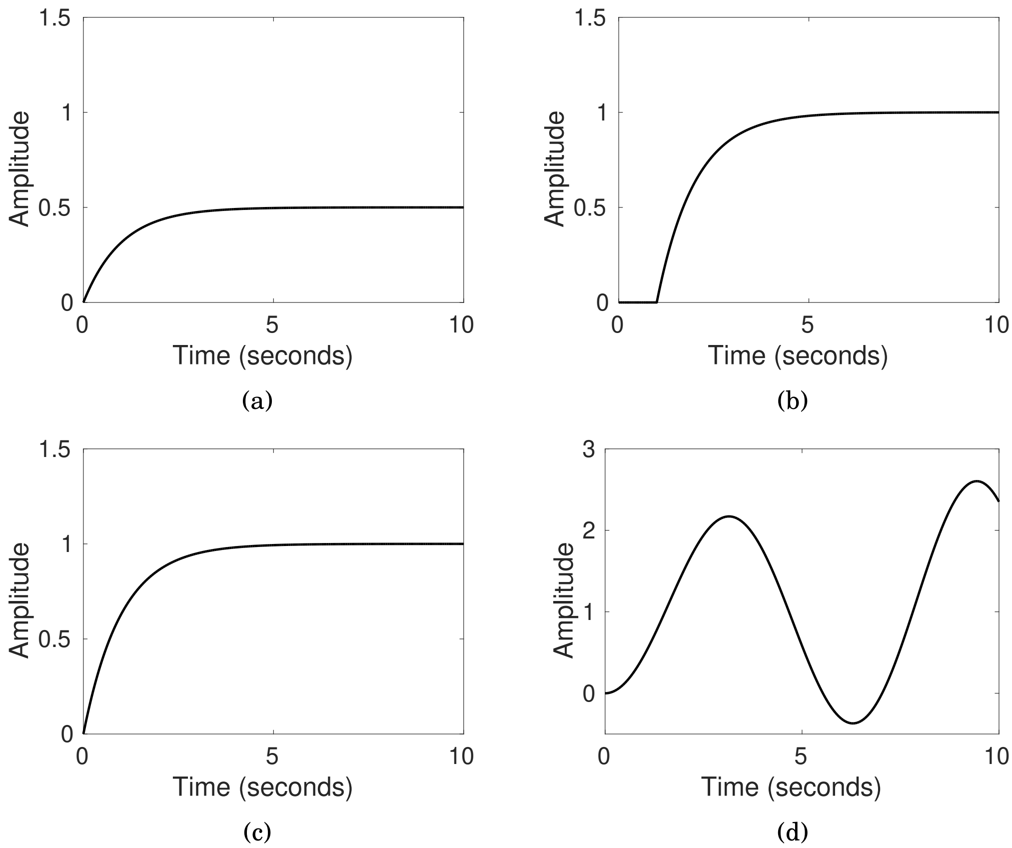
a - ii, b - iv, c- i, d-iii.

The step response in (a) have static gain 0.5.

The step response in (b) have a time delay.

The step response in (c) have static gain 1, but no time delay.

The step response in (d) is unstable (and have complex poles).



Figur 3: Step responses for problem 7.

8. The data in Tab. 3 describes the substrate concentration, $[S]$, and reaction rate, V, of a chemical process. It is an enzymatic reaction following the Michaelis-Menten relationship, i.e,

$$V = \frac{V_{max}[S]}{K_m + [S]}.$$

Use the least-squares method to estimate the parameters V_{max} and K_m.

Tabell 2: Drug data for problem 1

Substrate concentration $[S]$ [units]	Reaction rate V [units/days]
0.5	0.12
1	0.27
2	0.33
4	0.58

(3 p)

Solution

Tabell 3: Drug data for problem 1

Substrate concentration $[S]$ [units]	Reaction rate V [units/days]
0.5	0.12
1	0.27
2	0.33
4	0.58

Rewrite relationship as

$$\frac{1}{V} = \frac{K_m}{V_{max}} \frac{1}{[S]} + \frac{1}{V_{max}}.$$

Now, the parameters K_m/V_{max} and $1/V_{max}$ may be estimated as follows: Let the regressor matrix be

$$\Phi = \begin{pmatrix} 1 & 1/[S]_1 \\ 1 & 1/[S]_1 \\ 1 & 1/[S]_3 \\ 1 & 1/[S]_4 \end{pmatrix} = \begin{pmatrix} 1 & 2 \\ 1 & 1 \\ 1 & 0.5 \\ 1 & 0.25 \end{pmatrix}$$

where $[S]_i$ is the i-th value of $[S]$ in Table 3. Denote

$$y = \begin{pmatrix} 1/V_1 & 1/V_2 & 1/V_3 & 1/V_4 \end{pmatrix}^T = \begin{pmatrix} 8.33 & 3.70 & 3.03 & 1.73 \end{pmatrix}^T$$

where V_i is the i-th value of V is Table 3.
The least-squares solution is then

$$\begin{pmatrix} \frac{1}{\hat{V}_{max}} \\ \frac{\hat{K_m}}{V_{max}} \end{pmatrix} = \left(\Phi^T \Phi\right)^{-1} \Phi^T y = \begin{pmatrix} 0.77 \\ 3.66 \end{pmatrix}$$

which results in $\hat{V}_{max} = 1.30$ and $\hat{K}_m = 4.77$.

Good Luck!