LUNDS UNIVERSITET

Department of
**AUTOMATIC CONTROL**

# Exam FRTF01 - Physiological Models and Computation

**January 11 2017, 14-19**

### 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. Grades:

Grade 3: 12–15.5 points
4: 16–21.5 points
5: 22–25 points

### Accepted aid

Lecture slides, any books (without relevant exercises with solutions), standard mathematical tables and "Formelsamling i reglerteknik". Calculator.

### Results

The result of the exam will be posted in LADOK no later than January 20. Information on when the corrected exam papers will be shown, will be given on the course homepage.

**1.** *Investigate the bacterial growth in a jam pot.* The amount of bacteria at time $t$ is given by $x(t)$ $\mu$g and it changes according to the following differential equation

$$\frac{dx}{dt} = bx - px^2, \quad x(0) = x_0,$$

with initial condition $x(0) > 0$ and parameters $b$, $p > 0$.

**a.** Find the stationary point(s) of the system. (1 p)

**b.** Linearize the system around the stationary point(s), respectively. (1.5 p)

**c.** Determine the stability of the linearized system(s) with regard to the system parameters $b$ and $p$. (1 p)

**d.** Given the original system stated above, assume that $b = 1$ and $p = 0.1$. When there is 11 $\mu$g of bacteria in the jam pot, will the bacterial content be growing or decreasing? Motivate your answer. (1 p)

**e.** Again, assume that $b = 1$ and $p = 0.1$. Draw a plot of the time derivatives given by the original system stated above as well as the linearized system(s) determined in subproblem **b** for $0 \leq x \leq 12$. Do you think any of/the linearized system(s) is a good approximation when $x = 5$? Motivate your answer. (2 p)

*Solution*

**a.** Stationary points are values of $x$ such that $dx/dt = 0$, which is equivalent to $(b - px)x = 0$. Thus, $x = 0$ is a stationary point as well as $x = b/p$.

**b.** Set $f(x) = dx/dt = bx - px^2$. Now, define

$$g(x) = \frac{df}{dx} = b - 2px.$$

Thus, the linearized system around $x = 0$ is given by

$$\Delta\dot{x} = g(0)\Delta x = b\Delta x$$

where $\Delta x = x - 0 = x$. The linearized system around $x = b/p$ is given by

$$\Delta\dot{x} = g(b/p)\Delta x = -b\Delta x$$

where $\Delta x = x - b/p$.

**c.** The linearized system around $x = 0$ is always unstable due to that $b > 0$. On the contrary, however again due to that $b > 0$, the linearized system around $x = b/p$ is always (asymptotically) stable.

**d.** At $x = 11$ the time derivative is negative,

$$\left.\frac{dx}{dt}\right|_{x=11} = 1 \cdot 11 - 0.1 \cdot 11^2 = -1.1.$$

Thus, the bacterial content is decreasing.

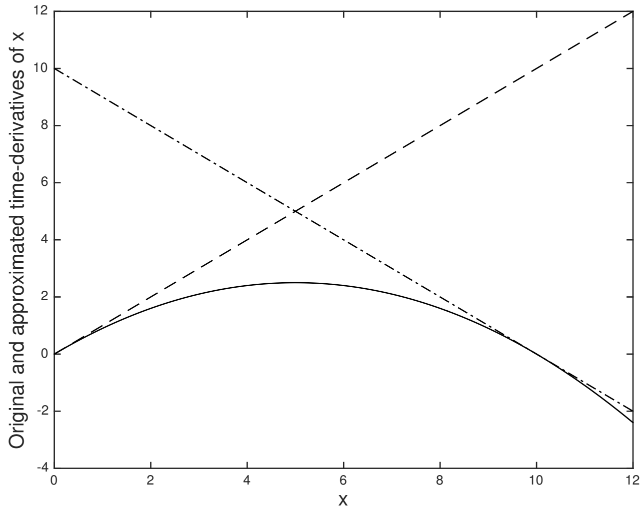


Figure 1: Figure in Problem 1. The solid line gives $dx/dt$ over x. The dashed and dash-dotted lines show the linearized systems $\Delta\dot{x}$ evaluated at the stationary points $x = 0$ and $x = b/p$, respectively.

**e.** The linearized systems has to be considered in the original parameter $x$ instead of $\Delta x$ in order for them to be compared in the same plot as the original system $dx/dt$. Thus, the linearized systems are rewritten as

$$\begin{aligned} &\Delta\dot{x} = b\Delta x,\ \Delta = x - 0 &&\rightarrow \quad \dot{x} = bx, \\ &\Delta\dot{x} = -b\Delta x,\ \Delta = x - b/p &&\rightarrow \quad \dot{x} = -bx + b^2/p, \end{aligned}$$

and with the specified parameters $b = 1$ and $p = 0.1$

$$\begin{aligned} \dot{x} &= x, \\ \dot{x} &= -x + 10. \end{aligned}$$

As can be seen in Figure 1, the two linearized systems are equally as poor approximations of the original systems at $x = 5$. The original system gives

$$\left.\frac{dx}{dt}\right|_{x=5} = 2.5$$

while the two linearized systems both are equal to 5 at $x = 5$.

**2.** *Virus mutations.* The following model describes the dynamics of the concentration of a virus, denoted $x_1$, and the concentration of a mutated strain of this virus, denoted $x_2$, under the influence of a drug $u$:

$$\dot{x} = \begin{pmatrix} 2 & 0 \\ 1 & 3 \end{pmatrix} x + \begin{pmatrix} 1 \\ 0 \end{pmatrix} u,$$

where $x = [\,x_1 \quad x_2\,]^T$.

**a.** Consider $u = 0$. Is the mutated virus strain affecting the growth of the original virus strain? Motivate your answer. (0.5 p)

**b.** Assume that you are able to measure both states $x_1$ and $x_2$. Design a state feedback controller $u = -Lx + r$ such that the poles of the system from $r$ to $y = x_1 + x_2$ are located in -1 and -2. (1.5 p)

**c.** Assume that you can only measure the total amount of virus, that is $y = x_1 + x_2$. Denote the system from $u$ to $y$ by $G_P$. Design a P-controller, denoted $G_R$, that stabilizes the closed-loop system from $r$ to $y$ in Figure 2. (1 p)

*Solution*

**a.** No. It is only the original virus strain that affects the growth of the mutated virus strain. This is clear when writing the differential equations one-by-one with $u = 0$:

$$\begin{aligned} \dot{x}_1 &= 2x_1 \\ \dot{x}_2 &= x_1 + 3x_2. \end{aligned}$$

The change of $x_1$ is only affected by $x_1$ when the control input $u = 0$.

**b.** Consider $L = \begin{pmatrix} l_1 & l_2 \end{pmatrix}$. Then, the closed-loop system is given by

$$\begin{aligned} \dot{x} &= (A - BL)x + Br \\ &= \left( \begin{pmatrix} 2 & 0 \\ 1 & 3 \end{pmatrix} - \begin{pmatrix} 1 \\ 0 \end{pmatrix} \begin{pmatrix} l_1 & l_2 \end{pmatrix} \right) x + \begin{pmatrix} 1 \\ 0 \end{pmatrix} r \\ &= \begin{pmatrix} 2 - l_1 & -l_2 \\ 1 & 3 \end{pmatrix} x + \begin{pmatrix} 1 \\ 0 \end{pmatrix} r. \end{aligned}$$

with $y = \begin{pmatrix} 1 & 1 \end{pmatrix} x$. The characteristic polynomial of the system is given by

$$\begin{aligned} \det\left( sI - \begin{pmatrix} 2 - l_1 & -l_2 \\ 1 & 3 \end{pmatrix} \right) &= \det \begin{pmatrix} s - 2 + l_1 & l_2 \\ -1 & s - 3 \end{pmatrix} \\ &= (s - 2 + l_1)(s - 3) + l_2 = s^2 + (l_1 - 5)s + 6 - 3l_1 + l_2. \end{aligned}$$

Then, $s^2 + (l_1 - 5)s + 6 - 3l_1 + l_2 = (s + 1)(s + 2) = s^2 + 3s + 2$ yields that $l_1 = 8$ and $l_2 = 20$.

**c.** The matrices of the state-space representation are given by

$$A = \begin{pmatrix} 2 & 0 \\ 1 & 3 \end{pmatrix}, \quad B = \begin{pmatrix} 1 \\ 0 \end{pmatrix}, \quad C = \begin{pmatrix} 1 & 1 \end{pmatrix}, \quad D = 0.$$

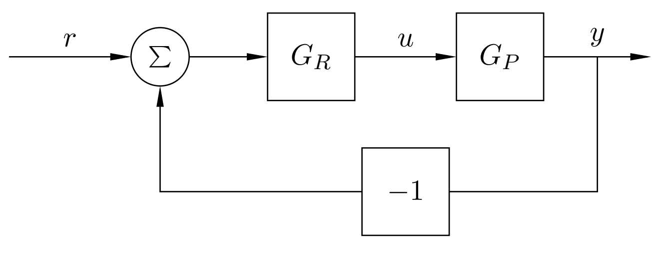


Figure 2: Block-diagram in Problem 2c.

The transfer function of the open-loop system is then given by

$$G_P(s) = C(sI - A)^{-1}B + D = \begin{pmatrix} 1 & 1 \end{pmatrix} \begin{pmatrix} s-2 & 0 \\ -1 & s-3 \end{pmatrix}^{-1} \begin{pmatrix} 1 \\ 0 \end{pmatrix} + 0$$
$$= \begin{pmatrix} 1 & 1 \end{pmatrix} \frac{1}{(s-2)(s-3)} \begin{pmatrix} s-3 & 0 \\ 1 & s-2 \end{pmatrix} \begin{pmatrix} 1 \\ 0 \end{pmatrix} = \frac{1}{s-3}.$$

Given a P-controller, $G_R = K$, the closed-loop system's transfer function is given by

$$G = \frac{G_P G_R}{1 + G_P G_R} = \frac{K}{s-3+K}.$$

In order for $G$ to be stable we have the criterion that $K - 3 > 0$. Thus, any $K > 3$ is a possible choice of a stabilizing P-controller.

**3.** *Linearization.* Consider the following system dynamics

$$\ddot{z} + \sqrt{z}\dot{z}^3 - 2z = u,$$

where $u$ is the input signal and the output signal is given by $y = z^2 + u$.

**a.** Introduce states $x_1 = z$ and $x_2 = \dot{z}$ and find all stationary points $(x_1^0, x_2^0, u^0, y^0)$. (1.5 p)

**b.** Linearize the system around the stationary point corresponding to $u^0 = 4$. (1.5 p)

**c.** Is the linearized system stable? Motivate your answer. (0.5 p)

*Solution*

**a.**

$$\begin{aligned} \dot{x}_1 &= x_2 & (&= f_1(x,u)) \\ \dot{x}_2 &= -\sqrt{x_1}x_2^3 + 2x_1 + u & (&= f_2(x,u)) \\ y &= x_1^2 + u & (&= g(x,u)) \end{aligned} \tag{1}$$

Thus, from the first equation in (1) we get $x_2^0 = 0$. Further, $x_2 = 0$ inserted in the second equation gives

$$0 = 2x_1 + u.$$

The stationary points are $(x_1^0, x_2^0, u^0) = (-t/2, 0, t)$. In stationarity the output signal is given by $y^0 = t^2/4 + t$.

**b.** $u^0 = 4$ gives the stationary point $(x_1^0, x_2^0, u^0, y^0) = (-2, 0, 4, 8)$. The partial derivatives are

$$\begin{aligned} &\frac{\partial f_1}{\partial x_1} = 0, && \frac{\partial f_1}{\partial x_2} = 1, && \frac{\partial f_1}{\partial u} = 0, \\ &\frac{\partial f_2}{\partial x_1} = -\frac{1}{2}\frac{x_2^3}{\sqrt{x_1}} + 2, && \frac{\partial f_2}{\partial x_2} = -3\sqrt{x_1}x_2^2, && \frac{\partial f_2}{\partial u} = 1, \\ &\frac{\partial g}{\partial x_1} = 2x_1, && \frac{\partial g}{\partial x_2} = 0, && \frac{\partial g}{\partial u} = 1. \end{aligned}$$

Introduce new variables

$$\Delta x = x - x^0,$$
$$\Delta u = u - u^0,$$
$$\Delta y = y - y^0.$$

The linearized system is given by

$$\dot{\Delta x} = \begin{bmatrix} 0 & 1 \\ 2 & 0 \end{bmatrix} \Delta x + \begin{bmatrix} 0 \\ 1 \end{bmatrix} \Delta u$$
$$\Delta y = \begin{bmatrix} -4 & 0 \end{bmatrix} \Delta x + \Delta u$$

**c.** The characteristic polynomial of the system is given by

$$\det\left(sI - \begin{pmatrix} 0 & 1 \\ 2 & 0 \end{pmatrix}\right) = \det\begin{pmatrix} s & -1 \\ -2 & s \end{pmatrix} = s^2 - 2.$$

The poles are thus given by $-\sqrt{2}$ and $\sqrt{2}$. Thus the system is unstable.

**4.** *Enzyme kinetics.* Consider the enzymatic reaction

$$E + S \underset{k_r}{\overset{k_f}{\rightleftharpoons}} C \xrightarrow{k_{cat}} E + P$$

where $E$, $S$, $C$ and $P$ are the enzyme, substrate, enzyme-substrate complex and product, respectively. The rate coefficients are $k_f$ (forward reaction), $k_r$ (reverse reaction) and $k_{cat}$ (catalyst reaction).

**a.** Write down the differential equations of the dynamics of $E$, $S$, $C$ and $P$ as governed by mass kinetics. (1 p)

**b.** Assume conservation of enzyme and steady state conditions. The initial amount of enzyme, at which there exist no complex, is given by a positive constant $E_0$. Derive an expression for the production rate on the form

$$\frac{d[P]}{dt} = \frac{V_{max}[S]}{K_m + [S]}$$

where $V_{max}$ and $K_m$ are constants while $[S]$ is the substrate concentration and $[P]$ is the product concentration. (1.5 p)

**c.** In Table 1 you find parameters and initial values for two enzymes; Pepsin and Chymotrypsin. Which enzyme has the largest maximal production rate of the respective product? Motivate your answer. (1.5 p)

*Solution*

**a.**

$$\frac{d[E]}{dt} = (k_r + k_{cat})[C] - k_f[E][S]$$
$$\frac{d[S]}{dt} = k_r[C] - k_f[E][S]$$
$$\frac{d[C]}{dt} = k_f[E][S] - (k_r + k_{cat})[C]$$
$$\frac{d[P]}{dt} = k_{cat}[C]$$

Table 1: Initial values and rate coefficients in Problem 4

| Parameter | Pepsin | Chymotrypsin |
|---|---|---|
| $E_0$ [M] | 0.1 | 0.2 |
| $k_f$ [$M^{-1}s^{-1}$] | $10^4$ | 10 |
| $k_r$ [$s^{-1}$] | 2.5 | 0.01 |
| $k_{cat}$ [$s^{-1}$] | 0.5 | 0.14 |

**b.** Steady state condition of $[C]$:

$$\frac{d[C]}{dt} = k_f[E][S] - (k_r + k_{cat})[C] = 0 \tag{2}$$

Conservation of enzyme: $[E](t) + [C](t) = E_0 \to [E] = E_0 - [C]$ together with (2) gives that

$$k_f(E_0 - [C])[S] - (k_r + k_{cat})[C] = 0 \iff [C] = \frac{k_f E_0[S]}{k_f[S] + k_r + k_{cat}}$$
$$\iff [C] = \frac{E_0[S]}{\frac{k_r+k_{cat}}{k_f} + [S]}.$$

Finally

$$\frac{d[P]}{dt} = k_{cat}[C] = \frac{k_{cat}E_0[S]}{\frac{k_r+k_{cat}}{k_f} + [S]}$$

where $V_{max} = k_{cat}E_0$ and $K_m = \frac{k_r+k_{cat}}{k_f}$.

**c.** The maximal production rate is given when $[S] \to \infty$. Then $d[P]/dt \to V_{max} = k_{cat}E_0$. Thus, the maximal production rate with Pepsin is given by $(V_{max})_{pepsin} = 0.5{\cdot}0.1 = 0.05\ \mathrm{Ms}^{-1}$. The maximal production rate with Chymotrypsin is given by $(V_{max})_{chym.} = 0.14{\cdot}0.2 = 0.028\ \mathrm{Ms}^{-1}$. Thus, Pepsin has the largest maximal production rate.

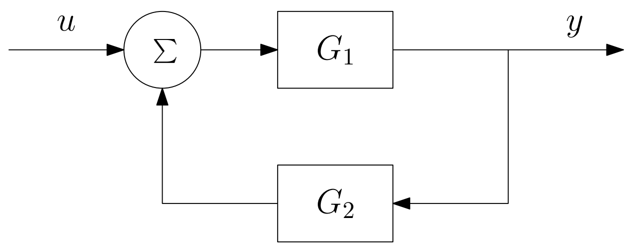


Figure 3: Figure to Problem 5a.

**5.** Two systems, $G_1$ and $G_2$, are interconnected as shown in Figure 3.

**a.** Determine the transfer function from $u$ to $y$ in terms of $G_1$ and $G_2$. (0.5 p)

**b.** Determine the pole(s) of the system when the subsystems are given by

$$G_1(s) = \frac{1}{s+5}, \qquad \text{and} \qquad G_2(s) = 3.$$

Is the system stable? (0.5 p)

**c.** Denote the transfer function from $u$ to $y$, derived in subproblem **a** and **b**, by $G_P$. By introducing a controller $G_R = 4$ in negative feedback according to the block-diagram in Figure 4, is it possible to attenuate disturbances $n$ with frequencies below 2 rad/s with a factor 0.5? Motivate your answer. (1.5 p)

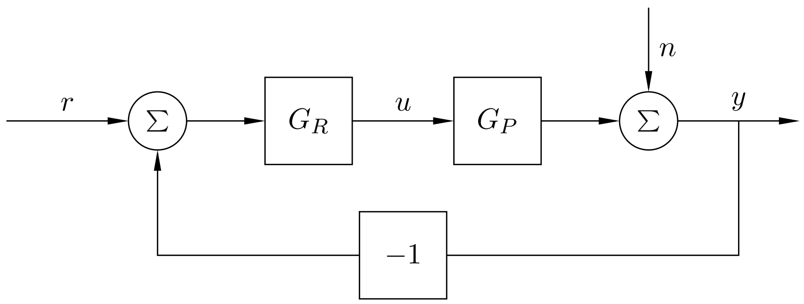


Figure 4: Block-diagram in Problem 5c.

*Solution*

**a.** The transfer function from $u$ to $y$ is given by

$$\frac{Y(s)}{U(s)} = \frac{G_1}{1 - G_1 G_2}.$$

**b.** With the given subsystems, the transfer function becomes

$$\frac{Y(s)}{U(s)} = \frac{1}{s+5-3} = \frac{1}{s+2}.$$

The system has a pole in $-2$. It is thus stable.

**c.** The sensitivity function is given by

$$S = \frac{1}{1 + G_P G_R} = \frac{s+2}{s+6}.$$

Now, $|S(i\omega)| = \sqrt{\frac{\omega^2+4}{\omega^2+36}}$ which is an nondecreasing function in $\omega$. Thus, as $|S(i \cdot 2)| = 0.45 < 0.5$, the controller fulfils the specification.

**6.** *Digestion model.* Consider the following model that describes digestion

$$\begin{aligned} \dot{q}_{\text{sto}} &= -k_1 \cdot q_{\text{sto}} + u \\ \dot{q}_g &= k_1 \cdot q_{\text{sto}} - k_2 \cdot q_g \\ y &= q_g / V_g \end{aligned}$$

where $u$ is the amount of ingested carbohydrates per time unit, $q_{\text{sto}}$ is the amount of glucose in the stomach compartment, $q_g$ is the glucose mass in the gut and $y$ is the measured concentration of glucose in the gut. Model parameters and compartment volumes are described in Table 2.

Table 2: Description of model parameters in Problem 6

| Parameter | Value | Description |
|---|---|---|
| $k_1$ | computed in **b.** | rate of grinding, 1/minutes |
| $k_2$ | $4 \cdot 10^{-3}$ | rate of gastric emptying, 1/minutes |
| $V_{\text{sto}}$ | 0.5 | volume of stomach compartment, l |
| $V_g$ | 1 | volume of gut compartment, l |

**a.** Draw a schematic of the compartment model where you specify the compartments, the rate and volume parameters as given in Table 2, as well as the input and output of the model. (1 p)

**b.** Let $u(t) = 0$. Assume that the initial amount of glucose in the stomach compartment is 70 g. After 30 minutes it is down to 60 g. Determine the time constant $k_1$ and half-life of the glucose metabolism in the stomach. (1.5 p)

**c.** Determine the step response of the system given the parameter values in Table 2 as well as the value for $k_1$ derived in the previous subproblem. In case you did not solve **b** you can use $k_1 = 10^{-3}$. Determine the value of the step response when $t \to \infty$. (1.5 p)

**d.** Figure 5 shows the system responses after eating pizza and salad, respectively, assuming both are consumed with constant rate during 20 minutes. The total glucose content is higher in the pizza than in the salad. Which response (solid line or dashed line) is related to which meal? Motivate your answer. (1.5 p)

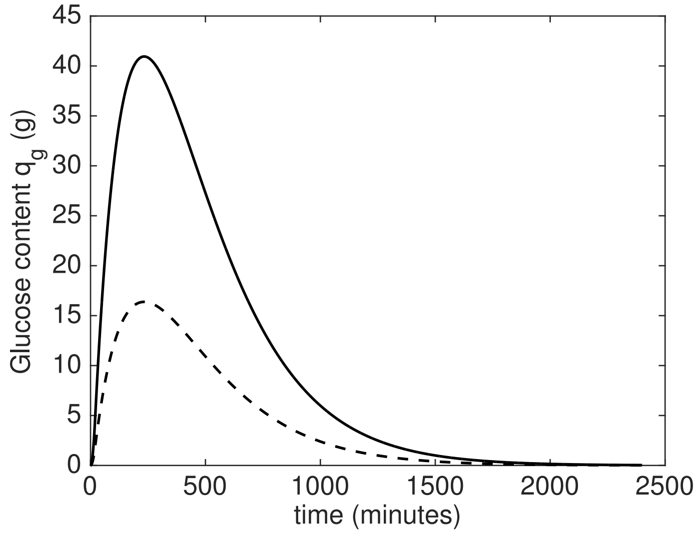


Figure 5: Step responses for Problem 6d.

*Solution*

**a.** A schematic of the compartmental model is given below:

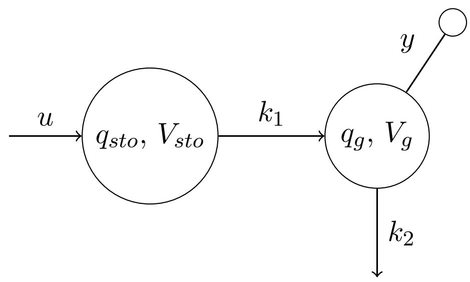


Figure 6: Compartment model.

**b.** With $u(t) = 0$, the differential equation for the stomach compartment becomes

$$\dot{q}_{\text{sto}} = -k_1 \cdot q_{\text{sto}},$$

and the solution is

$$q_{\text{sto}}(t) = C_0 e^{-k_1 t},$$

where $C_0$ is a constant. From the problem text we know that $q_{sto}(0) = 70$ and $q_{sto}(30) = 60$. Thus

$$70 = C_0 e^{-k_1 \cdot 0} = C_0$$

$$60 = C_0 e^{-k_1 \cdot 30} = 70 e^{-k_1 \cdot 25} \rightarrow k_1 = \frac{\ln(7/6)}{30} = 0.0051 \approx 5 \cdot 10^{-3}.$$

The half-life $t_{1/2}$ is then computed as follows

$$\frac{C_0}{2} = C_0 e^{-\frac{\ln(7/6)}{30} \cdot t_{1/2}} \rightarrow \ln(2) = \frac{\ln(7/6)}{30} \cdot t_{1/2}$$
$$\rightarrow t_{1/2} = 134.8967 \text{ minutes } \approx 2 \text{ hours and } 15 \text{ minutes.}$$

**c.** The transfer function of the system from $u$ to $y$ is given by

$$G_{yu}(s) = \frac{Y(s)}{U(s)} = \frac{1}{V_g} \frac{k_1}{(s+k_1)(s+k_2)}.$$

The step response is thus given by

$$y(t) = \mathcal{L}^{-1}\left(\frac{1}{V_g}\frac{k_1}{(s+k_1)(s+k_2)}\frac{1}{s}\right) = \frac{1}{V_g}\frac{1}{k_2}\left(1 + \frac{k_1 e^{-k_2 t} - k_2 e^{-k_1 t}}{k_2 - k_1}\right)$$
$$= \frac{1}{V_g k_2}\left(1 + \frac{k_1 e^{-k_2 t} - k_2 e^{-k_1 t}}{k_2 - k_1}\right) = 250(1 + 4e^{-5\cdot 10^{-3}\cdot t} - 5e^{-4\cdot 10^{-3}\cdot t})$$

where we have used number 24 in the collection of formulae and $k_1 = 5 \cdot 10^{-3}$. Now, $\lim_{t\to\infty} y(t) = 1/V_g k_2 = 250$. This can also be determined by the static gain $G_{yu}(0) = 1/V_g k_2 = 250$ since the system is stable.

**d.** As the total glucose content is higher in the pizza than in the salad, however the pizza and salad are both consumed at constant rate during 20 minutes, it means that both give rise to stepwise constant input functions. However the pizza give rise to an input function with a higher magnitude:

$$u_{\text{pizza}}(t) = \begin{cases} m_1/20 & \text{if } 0 < t < 20 \\ 0 & t \geq 20 \end{cases}$$
$$u_{\text{salad}}(t) = \begin{cases} m_2/20 & \text{if } 0 < t < 20 \\ 0 & t \geq 20 \end{cases}$$

where $0 < m_2 < m_1$ are constants in g. The system's responses given the above input signals are given by

$$y_{\text{pizza}}(t) = \begin{cases} \frac{m_1}{20} y_{\text{step}}(t) & \text{if } 0 < t < 20 \\ \frac{m_1}{20}\left(y_{\text{step}}(t) - y_{\text{step}}(t-20)\right) & t \geq 20 \end{cases}$$
$$y_{\text{salad}}(t) = \begin{cases} \frac{m_2}{20} y_{\text{step}}(t) & \text{if } 0 < t < 20 \\ \frac{m_2}{20}\left(y_{\text{step}}(t) - y_{\text{step}}(t-20)\right) & t \geq 20 \end{cases}$$

where $y_{\text{step}}(t) = 250(1 + 4e^{-5\cdot 10^{-3}\cdot t} - 5e^{-4\cdot 10^{-3}\cdot t})$ is the step response as determined in the previous subproblem. Thus, the responses are identical up to a scaling factor and the pizza should have the largest magnitude as $m_1 > m_2$. Thus, the solid line is given by the pizza.

# Good Luck!