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The quiz is due November 4, 2020 at 11:59pm, over Canvas. It should approximately take 2 hours to complete, but there is no time limit other than the submission deadline. Do not discuss any class-related topics among yourselves before or after you have completed your quiz, and until the submission deadline has passed.

There are 3 problems. Points for each problem are given in [brackets]. There are 100 points total.
1. **[35 pts]** Consider the following biochemical reaction taking place in an organ in the body:

\[ A + B \xrightleftharpoons{k_f}{k_r} C + D \]

where compounds A and B combine to generate compounds C and D at rate \( k_f \), and C and D recombine to regenerate A and B at rate \( k_r \).

(a) **[5 pts]** Show that if compounds B and C are present at much higher concentrations than either A or D, then you may assume that their concentrations are approximately constant, \([B] \approx [B]_0\) and \([C] \approx [C]_0\).

\[
\frac{d}{dt} [A] = \frac{d}{dt} [B] = -\frac{d}{dt} [C] = -\frac{d}{dt} [D] =
- k_f [A][B] + k_r [C][D]
\]

Every mol change in B or C requires a mol change of same magnitude in A and in D, where A and D move in opposite directions. Therefore, and because A and D are always positive, B and C cannot change more than the larger amount of A and D currently present. If B and C are present in much greater amounts, then the relative change in B and C must be very small. Hence we can approximate [B] and [C] to be relatively constant.

\[
[B]_0 - [A]_0 \ll [B] \ll [B]_0 + [D]_0 \implies [B] \approx [B]_0
\]

\[
[C]_0 - [D]_0 \ll [C] \ll [C]_0 + [A]_0 \implies [C] \approx [C]_0
\]
(b) [10 pts] Under those assumptions, and further assuming that both A and D exit the volume $V$ of the organ at a flow rate $Q$, while B and C recirculate in the organ without decay, write the ODEs in the concentrations $[A]$ and $[D]$ that describe both the kinetics and the flow.

\[
\begin{align*}
\frac{d}{dt} [A] &= -\frac{Q}{V} [A] - k_f [A][B]_0 + k_n [C]_0 [D] \\
\frac{d}{dt} [D] &= -\frac{Q}{V} [D] + k_f [A][B]_0 - k_n [C]_0 [D]
\end{align*}
\]

Let: \[\alpha = \frac{Q}{V}\]

\[b = k_f [B]_0\]

\[c = k_n [C]_0 \quad \text{constants}\]

\[
\begin{align*}
\frac{d}{dt} [A] &= -(\alpha + b) [A] + c [D] \\
\frac{d}{dt} [D] &= b [A] - (\alpha + c) [D]
\end{align*}
\]
(c) [5 pts] Find the equilibrium (i.e., the steady-state) concentrations.

\[ \frac{d}{dt} [A] = -(a+b) [A] + c [D] = 0 \]
\[ \frac{1}{vt} [D] = b [A] - (a+c) [D] = 0 \]

\( a \neq 0 \implies [A]_{s.s.} = [D]_{s.s.} = 0 \)

and
\[ [B]_{s.s.} = [B]_0 \]
\[ [C]_{s.s.} = [C]_0 \]
(d) [15 pts] Use Laplace transforms to find the concentration \([A]\) as a function of time, starting from initial conditions \([A](0) = [A]_0\) and \([D](0) = 0\).

\[
\begin{align*}
\mathcal{L}\{[A](s) - [A]_0\} &= -(\alpha + \beta) \cdot [A](s) + C \cdot [D](s) \\
\mathcal{L}\{[D](s) - [D]_0\} &= \beta \cdot [A](s) - (\alpha + C) \cdot [D](s)
\end{align*}
\]

\[
\begin{align*}
(s + \alpha + \beta) \cdot [A](s) &= [A]_0 + C \cdot [D](s) \\
(s + \alpha + C) \cdot [D](s) &= \beta \cdot [A](s)
\end{align*}
\]

\[
(s + \alpha + \beta)(s + \alpha + C) \cdot [A](s) = (s + \alpha + C) \cdot [A]_0 + \beta \cdot [A](s)
\]

\[
[A](s) = \frac{s + \alpha + C}{(s + \alpha + \beta)(s + \alpha + C) - \beta \cdot C} \cdot [A]_0 = \frac{s + \alpha + C}{(s + \alpha)(s + \alpha + \beta + C)} \cdot [A]_0
\]

\[
[A](s) = \frac{1}{\beta + C} \left( \frac{C}{s + \alpha} + \frac{\beta}{s + \alpha + \beta + C} \right) \cdot [A]_0
\]

\[
[A](t) = \frac{1}{\beta + C} \left( C e^{-\alpha t} + \beta e^{-(\alpha + \beta + C) t} \right) \cdot [A]_0
\]

\[
[A](t) = \frac{k_2 [C]_0 + k_f [B]_0 e^{-(k_1 [C]_0 + k_f [B]_0) t}}{k_2 [C]_0 + k_f [B]_0} \cdot e^{-\frac{Q}{V} t} \cdot [A]_0
\]
2. [40 pts] Consider the following set of ODEs describing the dynamics of a biomechanical system with mass $m$ and damping $\gamma$, with force $f(t)$ driving the input, and with position $u(t)$ at the output:

$$\frac{du}{dt} = v(t)$$

$$m \frac{dv}{dt} = -\gamma v(t) + f(t).$$

(a) [5 pts] Find the Laplace transform of position $u(s)$ as a function of the Laplace transform of the force $f(s)$, and initial conditions in position $u(0) = u_0$ and velocity $v(0) = v_0$.

$$S \ U(s) - u_0 = U(s)$$

$$m \left( S U(s) - v_0 \right) = -\gamma \ U(s) + F(s)$$

$$m \left( S (S U(s) - u_0) - v_0 \right) = -\gamma \left( S U(s) - u_0 \right) + F(s)$$

$$\left( m S^2 + \gamma S \right) U(s) = \frac{mu_0 S + mv_0 + \gamma u_0}{S(mS + \gamma)} + \frac{F(s)}{S(mS + \gamma)}$$

$$U(s) = \frac{mu_0 S + mv_0 + \gamma u_0}{S(mS + \gamma)} + \frac{1}{S(mS + \gamma)} F(s)$$

I.C. $2(\delta)$

$H(s)$ $2(c)$
(b) [10 pts] For zero force $f(t) \equiv 0$, and for given initial conditions $u(0) = u_0$ and $v(0) = v_0$, find the position $u(t)$ as a function of time.

$$u(s) = \frac{m u_0}{(ms + \gamma)s} + \frac{m v_0 + \gamma u_0}{(ms + \gamma)s} \quad (f(s) = 0)$$

$$= \frac{u_0}{s + \frac{\gamma}{m}} + \left(\frac{m}{\gamma} v_0 + u_0\right) \left(\frac{1}{s} - \frac{1}{s + \frac{\gamma}{m}}\right)$$

$$= \frac{u_0}{s} + \frac{m}{\gamma} v_0 \left(\frac{1}{s} - \frac{1}{s + \frac{\gamma}{m}}\right)$$

$$u(t) = u_0 + \frac{m}{\gamma} v_0 \left(1 - e^{-\frac{\gamma}{m}t}\right)$$
(c) [5 pts] Find the transfer function \( H(s) = \frac{u(s)}{f(s)} \) of the system, and find the poles and zeros.

\[
H(s) = \frac{u(s)}{f(s)} = \frac{1}{s(\frac{y}{m}s + \delta)}
\]

- **Zeros:** None
- **Poles:**
  \[
  \begin{align*}
  p_1 &= 0 \\
  p_2 &= -\frac{\delta}{m}
  \end{align*}
  \]
(d) [10 pts] Now consider closed-loop feedback, in which the force \( f(t) \) is given by

\[
f(t) = f_{\text{ext}}(t) - K u(t)
\]

where \( f_{\text{ext}}(t) \) is the externally applied force, and \( K \) is the feedback gain. Draw the closed-loop system block diagram, and find the closed-loop transfer function \( F(s) = u(s)/f_{\text{ext}}(s) \).

\[
\begin{align*}
\mathcal{H}(s) f(s) &= \mathcal{H}(s) \left( f_{\text{ext}}(s) - K u(s) \right) \\
F(s) &= \frac{\mathcal{H}(s)}{f_{\text{ext}}(s)} = \frac{\mathcal{H}(s)}{1 + K \mathcal{H}(s)} \\
&= \frac{1}{ms^2 + \delta s + K}
\end{align*}
\]
(e) [10 pts] Find the value of the feedback gain $K$ that minimizes the settling time of the closed-loop system. *Hint:* you may make approximate arguments. Think of settling time in terms of the poles of the system.

\[ \text{Poles: } ms^2 + \delta s + K = 0 \]

\[ p_{1,2} = -\frac{\delta}{2m} \pm \sqrt{\frac{\delta^2 - 4Km}{2m}} \]

Overdamped (discriminant $D > 0$): Two real poles; slow settling and rise time.
Critically damped ($D = 0$): Two identical poles; fast settling and rise time.
Underdamped ($D < 0$): Two complex conjugate poles; faster rise time, but not faster settling.
The critically damped case gives the fastest settling, without ringing.

\[ D = \delta^2 - 4Km = 0 \quad \Rightarrow \quad K = \frac{\delta^2}{4m} \]
3. [25 pts] Linear time invariant biosystems:

   (a) [5 pts] Give two possible explanations of biophysical phenomena that cause non-zero pressure across a vessel.

   1. Resistance in flow due to blood viscosity
   2. Height differences under gravity
   Others (many are possible!):
   3. Velocity nonuniformity due to differences in diameter
   4. Active pumping (forces acting on the vessel walls)
   etc...
(b) [10 pts] What is the time integral of the Delta-Dirac impulse? And what is the time integral of the impulse response of a linear time-invariant system? Explain the connection between the two.

The time integral of the Delta-Dirac impulse is a step function.

\[ u(t) = \int_{-\infty}^{t} \delta(t - \tau) d\tau = \begin{cases} 0 & \text{if } t < 0 \\ 1 & \text{if } t > 0 \end{cases} \]

Alternatively:

\[ \mathcal{L}(\delta(t)) \rightarrow \frac{1}{s} \rightarrow \frac{1}{s} \rightarrow \mathcal{L}(u(t)) \]

The time integral of the impulse response of a LTI system is the step response of that LTI system.
(c) [10 pts] Show that the linear time-invariant system given by the ODE

\[
\frac{du}{dt} = A u(t) + f(t)
\]

with initial condition \( u(0) = u_0 \) is equivalent, for all strictly positive times \( t > 0 \), to a system with the same ODE and zero initial conditions \( u(0) = 0 \) but with modified force \( f(t) + u_0 \delta(t) \), i.e., by absorbing the initial condition as an initial "kick" in the force. \textit{Hint:} consider left and right limits of \( u(t) \) at time \( t = 0 \).

The effect of the "kick" is to step the state variable, from zero to the same level as the initial condition:

\[
\begin{align*}
\uparrow \quad \uparrow \\
u(0^+) &= \ u(0^-) + \int_{0^-}^{0^+} \left( Au(t) + f(t) + u_0 \delta(t) \right) dt \\
&= u_0
\end{align*}
\]

Alternatively:

\[
\begin{align*}
\mathcal{L}\left[s u(s) - 0\right] &= \mathcal{L}\left[Au(s) + (f(s) + u_0 \cdot \delta(t))\right] \\
&\downarrow \quad \mathcal{L}\left[\delta(t)\right] \\
is \text{ equivalent to:} \\
\mathcal{L}\left[s u(s) - u_0\right] &= \mathcal{L}\left[Au(s) + f(s)\right] \\
&\downarrow \\
&\mathcal{L}\text{-c.} \\
&u(0)
\end{align*}
\]