BENG 122A Fall 2023

Quiz 1

Tuesday, October 31, 2023

***Name** (Last, First):* SOLUTIONS

- This quiz is open book, open notes, and online, but web search is prohibited. You may follow electronic links from Canvas or the class web pages, but not any further. **No collaboration or communication in any form is allowed**, except for questions to the instructor and TAs.
- The quiz is due November 1, 2023 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. **[40 pts]** Consider the following biochemical reaction taking place in an organ in the body:

$$\mathrm{A} + \mathrm{B} \underset{k_r}{\overset{k_f}{\rightleftharpoons}} \mathrm{C} + \mathrm{D}$$

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. Compound B enters the volume V of the organ at an input rate $r_B(t)$, and compounds B and D exit the organ at a flow rate Q, while A and C are maintained at constant concentrations $[\mathrm{A}]_0$ and $[\mathrm{C}]_0$ inside the organ.

   (a) [10 pts] Under these assumptions, write the ODEs in the concentrations $[\mathrm{B}](t)$ and $[\mathrm{D}](t)$ that describe both the reaction kinetics in the volume and the flow through the volume. Is the system linear time-invariant? Explain why.

$$\frac{d}{dt}[B] = \frac{r_B}{V} - \frac{Q}{V}[B] - k_f [A]_0 [B] + k_r [C]_0 [D]$$

$$\frac{d}{dt}[D] = - \frac{Q}{V}[D] + k_f [A]_0 [B] - k_r [C]_0 [D]$$

All terms in the ODEs are linear with constant coefficients, so this is a linear time-invariant system.

(b) [5 pts] Find the steady-state (*i.e.*, the equilibrium) concentrations $\overline{[\mathrm{B}]}$ and $\overline{[\mathrm{D}]}$, at zero steady-state input rate $\overline{r_B} = 0$.

$$0 = \frac{\overline{r_B}}{V}^{=0} - \frac{Q}{V}\overline{[B]} - k_f \overline{[A]}_0 \overline{[B]} + k_r \overline{[C]}_0 \overline{[D]}$$

$$0 = - \frac{Q}{V}\overline{[D]} + k_f \overline{[A]}_0 \overline{[B]} - k_r \overline{[C]}_0 \overline{[D]}$$

$$\Rightarrow_{Q \neq 0} \begin{cases} \overline{[A]} = [A]_0 \\ \overline{[B]} = 0 \\ \overline{[C]} = [C]_0 \\ \overline{[D]} = 0 \end{cases}$$

(c) [20 pts] A molar quantity M_B of compound B is released in the volume, all at once, at time zero, *i.e.*, $r_B(t) = M_B\delta(t)$. Use Laplace transforms to find the concentration $[\mathrm{D}](t)$ as a function of time, starting from steady-state initial conditions. Is the dynamics in [D] underdamped, critically damped, or overdamped? Explain.

$$r_B(t) = M_B\,\delta(t) \;\Rightarrow\; r_B(s) = M_B$$

$$[B](0) = \overline{[B]} = 0$$

$$[D](0) = \overline{[D]} = 0$$

Laplace transforms of the ODEs:

$$s[B] = \frac{M_B}{V} - \frac{Q}{V}[B] - k_f[A]_0[B] + k_r[C]_0[D]$$

$$s[D] = -\frac{Q}{V}[D] + k_f[A]_0[B] - k_r[C]_0[D]$$

$$\left(s + \frac{Q}{V} + k_f[A]_0\right)\cdot[B] - k_r[C]_0\cdot[D] = \frac{M_B}{V}$$

$$-k_f[A]_0\cdot[B] + \left(s + \frac{Q}{V} + k_r[C]_0\right)\cdot[D] = 0$$

$$\left(\left(s + \frac{Q}{V} + k_f[A]_0\right)\left(s + \frac{Q}{V} + k_r[C]_0\right) - k_f[A]_0 k_r[C]_0\right)\cdot[D] = k_f[A]_0\frac{M_B}{V}$$

$$[D] = \frac{k_f [A]_0 \frac{M_B}{V}}{\left(s + \frac{Q}{V}\right)^2 + \left(s + \frac{Q}{V}\right)\left(k_f [A]_0 + k_r [C]_0\right) + \cancel{k_f [A]_0 k_r [C]_0} - \cancel{k_f [A]_0 k_r [C]_0}}$$

$$[D](s) = \frac{k_f [A]_0 \frac{M_B}{V}}{\left(s + \frac{Q}{V}\right)\left(s + \frac{Q}{V} + k_f [A]_0 + k_r [C]_0\right)} \quad (*)$$

$$= \frac{k_f [A]_0 \frac{M_B}{V}}{k_f [A]_0 + k_r [C]_0} \cdot \left(\frac{1}{s + \frac{Q}{V}} - \frac{1}{s + \frac{Q}{V} + k_f [A]_0 + k_r [C]_0} \right)$$

Inverse Laplace transform:

$$[D](t) = \frac{k_f [A]_0 \frac{M_B}{V}}{k_f [A]_0 + k_r [C]_0} \cdot \left(e^{-\frac{Q}{V} t} - e^{-\left(\frac{Q}{V} + k_f [A]_0 + k_r [C]_0\right) t} \right)$$

Overdamped second-order dynamics
with two distinct real negative poles:

$$(*) \begin{cases} p_1 = -\frac{Q}{V} \\ p_2 = -\frac{Q}{V} - k_f [A]_0 - k_r [C]_0 \end{cases}$$

(d) [5 pts] Now no longer consider that A and C are maintained at constant concentrations, but instead that they recirculate in the organ without decay, from initial concentrations $[\mathrm{A}](0) = [\mathrm{A}]_0$ and $[\mathrm{C}](0) = [\mathrm{C}]_0$. Is the above approximating assumption that $[\mathrm{A}](t) \approx [\mathrm{A}]_0$ and $[\mathrm{C}](t) \approx [\mathrm{C}]_0$ reasonable under these conditions? Explain (in words) to what extent you expect your answers in (a) through (c) to change accounting for the reaction kinetics in compounds A and C.

(a) With A and C changing, the ODEs are nonlinear.

(b) All of B and D eventually get washed out of the volume, reaching zero steady-state so that the reaction stalls, and A and C settle without decay to non-zero steady-state concentrations.

(c) Some of the initial A converts to C, but less than the released B which only partially converts to D. Therefore the assumption is reasonable as long as the initial A and C are substantially higher in concentration than the released B.

Beyond words:

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

$$\frac{d[B]}{dt} = \frac{r_B}{V} - \frac{Q}{V}[B] + \frac{d[A]}{dt}$$

$$\frac{d[D]}{dt} = -\frac{Q}{V}[D] - \frac{d[A]}{dt}$$

$\overline{r}_B = 0 \Rightarrow \overline{[B]} = \overline{[D]} = 0$ but no constraints on $\overline{[A]}$ & $\overline{[C]}$

$[A](t) \approx [A]_0$, $[C](t) \approx [C]_0$ reasonable when $[A]_0, [C]_0 \gg [B]_0 = \frac{M_B}{V}$

2. **[40 pts]** Consider the following set of ODEs describing the dynamics in the position $u(t)$ and velocity $v(t)$ of a biomechanical system with mass m, stiffness k, and damping γ driven by a force $f(t)$:

$$\begin{aligned} \frac{du}{dt} &= v(t) \\ m\frac{dv}{dt} &= -\gamma\, v(t) - k\, u(t) + f(t)\,. \end{aligned}$$

(a) [10 pts] Find the Laplace transform of output velocity $v(s)$ as a function of the Laplace transform of the input force $f(s)$, and the initial conditions in position $u(0) = u_0$ and velocity $v(0) = v_0$. Find the corresponding transfer function, and the poles and zeros.

$$s\,u(s) - u_0 = v(s)$$

$$m\left(s\,v(s) - v_0\right) = -\gamma\, v(s) - k\, u(s) + f(s)$$

$$\left(ms^2 + \gamma s + k\right) v(s) = -k u_0 + m v_0 s + s f(s)$$

$$v(s) = \frac{-k u_0 + m v_0 s}{ms^2 + \gamma s + k} + \boxed{\frac{s}{ms^2 + \gamma s + k}} \cdot f(s)$$

Transfer function

Poles: $p_{1,2} = -\frac{\gamma}{2m} \pm \frac{\sqrt{\gamma^2 - 4km}}{2m}$

Zero: $z_0 = 0$

(b) [10 pts] Here and further below, consider that the stiffness is negative, $k < 0$. Show that the system is unstable. Could you think of a physical setting of a biosystem with negative stiffness giving rise to unstable dynamics?

$k < 0 \Rightarrow \gamma^2 - 4km > 0$

$\Rightarrow$ Real poles, one greater than zero:

$$-\frac{\gamma}{2m} + \frac{\sqrt{\gamma^2 - 4km}}{2m} > 0 \qquad (\sqrt{\gamma^2 - 4km} > 0)$$

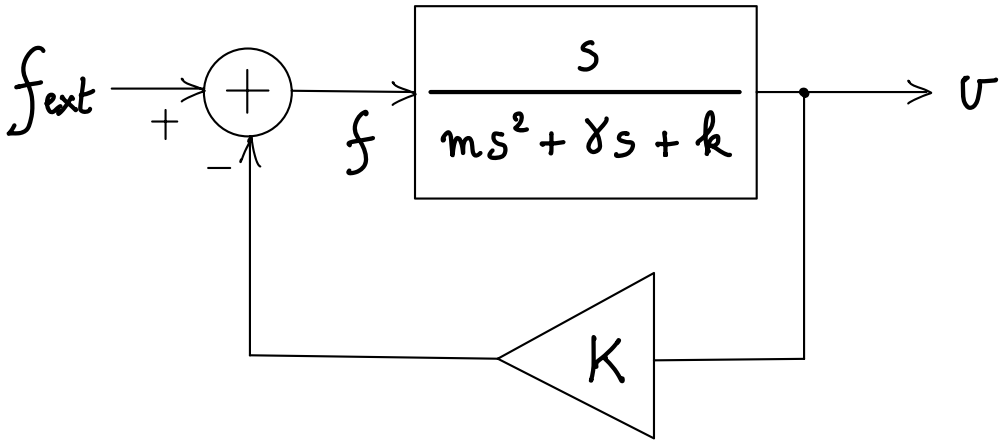
$\Rightarrow$ Unstable

Biophysical example: cartilage beyond its breaking point leading to injury

(c) [10 pts] Now consider closed-loop feedback, in which the force $f(t)$ is given by

$$f(t) = f_{ext}(t) - K\,v(t)$$

where $f_{ext}(t)$ 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 $H_v(s) = v(s)/f_{ext}(s)$. What is the effect of the feedback gain K on the stability of the closed-loop system? Explain.



$$V(s) = \frac{s}{ms^2+\gamma s+k}\,f(s) = \frac{s}{ms^2+\gamma s+k}\left(f_{ext}(s) - K\,V(s)\right)$$

$$\left(ms^2+\gamma s+k\right)V(s) = s\,f_{ext}(s) - Ks\,V(s)$$

$$\left(ms^2+\gamma s+k + Ks\right)V(s) = s\,f_{ext}(s)$$

$$H_v(s) = \frac{V(s)}{f_{ext}(s)} = \frac{s}{ms^2+(\gamma+K)s+k}$$

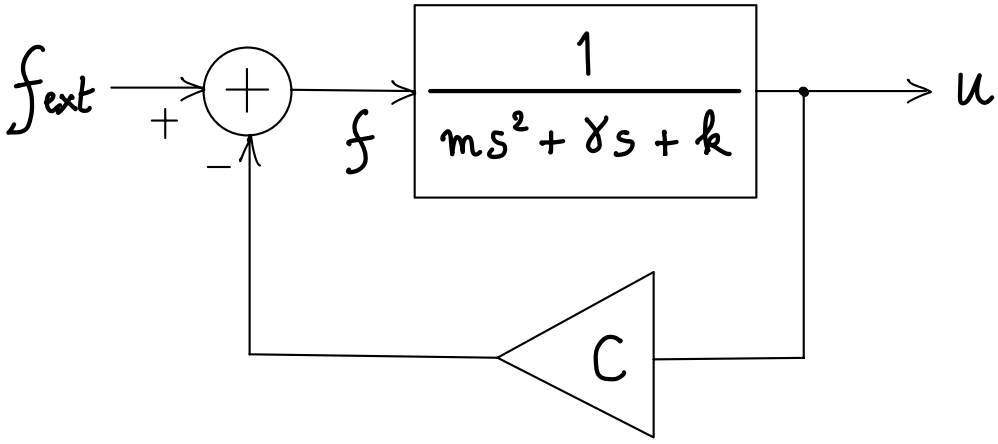
Effective damping

Still unstable: $-\dfrac{\gamma+K}{2m} + \dfrac{\sqrt{(\gamma+K)^2 - 4km}}{2m} > 0$ still! ($\sqrt{\cdots} > 0$)

(d) [10 pts] Again consider closed-loop feedback, but now with position $u(t)$ as the output of the closed-loop system, with a force $f(t)$ given by

$$f(t) = f_{ext}(t) - C\,u(t)$$

where $f_{ext}(t)$ is the externally applied force, and C is the feedback gain. Draw the closed-loop system block diagram, and find the closed-loop transfer function $H_u(s) = u(s)/f_{ext}(s)$. Find the condition on the feedback gain C to ensure stability of the closed-loop system with critical damping.



$$u(s) = \frac{1}{ms^2+\gamma s+k}\, f(s) = \frac{1}{ms^2+\gamma s+k}\left(f_{ext}(s) - C\,u(s)\right)$$

$$\left(ms^2+\gamma s+k\right) u(s) = f_{ext}(s) - C\,u(s)$$

$$\left(ms^2+\gamma s+k + C\right) u(s) = f_{ext}(s)$$

$$H_u(s) = \frac{u(s)}{f_{ext}(s)} = \frac{1}{ms^2+\gamma s+\underbrace{(k+C)}_{\text{Effective stiffness}}}$$

Critically damped for: $\gamma^2 = 4(k+C)m$

$$\Rightarrow C = -k + \frac{\gamma^2}{4m} > 0$$

3. **[20 pts]** Linear time invariant and conservative biosystems:

(a) [5 pts] What is the relationship between the Laplace and Fourier transfer functions of a linear time invariant system? Explain.

They are identical under the substitution $s = j\omega$.

That is because the impulse response is causal, meaning zero for all negative times, so that its Laplace and Fourier transforms are identical for $s = j\omega$.

(b) [5 pts] Do the imaginary components of the poles of a linear time invariant system affect its stability? Explain.

No. The imaginary component gives the rate of oscillation of the carrier of the signal transient, which is bounded to [-1, +1]. Stability is determined by the real component which gives the rate of growth or decay of the envelope.

(c) [5 pts] What determines compliance of an organ? Explain.

Compliance of an organ is determined by its elasticity. As pressure increases, the walls of the organ stretch leading to an increase in organ volume.

(d) [5 pts] Is resistance of blood flow through a vessel inversely proportional to the vessel cross section area? Explain.

Not quite. Because of viscosity, a vessel of twice the cross section area will carry more than twice the flow for the same pressure drop. That's because the twice wider vessel has less surface area for viscous drag than two narrower vessels combined with the same net cross section.