BEGN 122A Fall 2022

Quiz 1

Tuesday, October 25, 2022

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 Thursday October 27, 2022 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:

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

where compound A converts to compound B at a forward reaction rate k_f, and B converts back to A at a reverse reaction rate k_r. Compound A enters the volume V of the organ at an input rate $r_A(t)$, and both compounds A and B exit the volume at a flow rate Q.

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

$$\frac{d[A]}{dt} = \frac{1}{V} r_A(t) - \frac{Q}{V}[A] - k_f[A] + k_r[B]$$

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

Linear time-invariant, because the ODEs are linear in [A] and [B] with constant coefficients.

(b) [5 pts] Show that the steady-state concentrations $\overline{[\mathrm{A}]}$ and $\overline{[\mathrm{B}]}$, at zero steady-state input rate $\overline{r_A} = 0$, are zero.

$$0 = \cancel{\frac{d\overline{[A]}}{dt}} = \cancel{\frac{1}{V}\underbrace{\overline{r_A}}_{=0}} - \frac{Q}{V}\overline{[A]} - k_f\overline{[A]} + k_r\overline{[B]}$$

$$0 = \cancel{\frac{d\overline{[B]}}{dt}} = -\frac{Q}{V}\overline{[B]} - k_r\overline{[B]} + k_f\overline{[A]}$$

$$\Rightarrow \quad \overline{[A]} = \overline{[B]} = 0$$

(unless $Q = 0$ and $k_r = k_f$)

(c) [10 pts] Here and further below, consider that the reverse reaction is much slower than the forward reaction, so that $k_r \approx 0$. We are interested in the dynamics of the concentration of compound B in response to variations in the input rate of compound A. Find the Laplace transfer function $H(s) = [\tilde{\mathrm{B}}](s) \,/\, \tilde{r_A}(s)$, and find the poles. Show that the system is strictly stable at a positive flow rate $Q > 0$, and critically stable at zero flow $Q = 0$.

$$s[\tilde{A}] = \frac{1}{V}\tilde{r}_A(s) - \frac{Q}{V}[\tilde{A}] - k_f[\tilde{A}]$$

$$s[\tilde{B}] = -\frac{Q}{V}[\tilde{B}] + k_f[\tilde{A}]$$

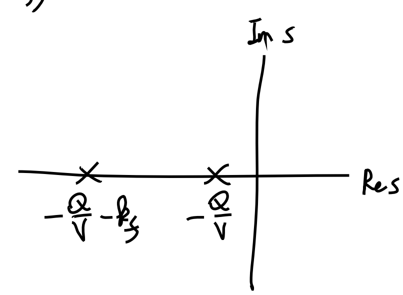
(Laplace transfer functions don't consider initial conditions)

$$\Rightarrow \quad [\tilde{A}](s) = \frac{\frac{1}{V}\tilde{r}_A(s)}{s + \frac{Q}{V} + k_f}$$

$$[\tilde{B}](s) = \frac{k_f[\tilde{A}](s)}{s + \frac{Q}{V}} = \frac{k_f \frac{1}{V}}{\left(s+\frac{Q}{V}\right)\left(s+\frac{Q}{V}+k_f\right)} \cdot \tilde{r}_A(s)$$

$$H(s) = \frac{[\tilde{B}](s)}{\tilde{r}_A(s)} = \frac{\frac{k_f}{V}}{\left(s+\frac{Q}{V}\right)\left(s+\frac{Q}{V}+k_f\right)}$$

Poles: $s = \begin{cases} -\frac{Q}{V} \\ -\frac{Q}{V} - k_f \end{cases}$



Both poles have strictly negative real part when Q > 0. $(k_f \geq 0)$

One pole becomes zero when Q = 0.

(d) [15 pts] Find the concentration [B] as a function of time, starting from zero initial conditions $[\mathrm{A}](0) = [\mathrm{B}](0) = 0$, where a molar quantity M_A of compound A is released in the volume, all at once, at time zero. Show that the concentration decays towards zero as time goes to infinity for a positive flow rate, but settles to a non-zero value at zero flow. What is that concentration? Explain.

$$\overset{(\sim)}{r}_A(t) = M_A\,\delta(t)$$ (released all at once at time zero)

$$\Downarrow$$

$$\tilde{r}_A(s) = M_A$$

$$\Downarrow$$

$$\widetilde{[B]}(s) = H(s)\cdot M_A$$

$$= \frac{\cancel{k_f}}{V}\cdot\frac{1}{\cancel{k_f}}\left(\frac{1}{s+\frac{Q}{V}} - \frac{1}{s+\frac{Q}{V}+k_f}\right)\cdot M_A$$

$$\widetilde{[B]}(t) = \frac{1}{V}\cdot\left(e^{-\frac{Q}{V}t} - e^{-\left(\frac{Q}{V}+k_f\right)t}\right)\cdot M_A$$

$$Q > 0 : \quad \widetilde{[B]}(t) \longrightarrow 0 \quad \text{as} \quad t\to\infty$$

$$Q = 0 : \quad \widetilde{[B]}(t) = \frac{1}{V}\left(1 - e^{-k_f t}\right)\cdot M_A$$

$$\longrightarrow \frac{M_A}{V} \quad \text{as} \quad t\to\infty$$

For a positive flow rate, all A and B eventually exit the volume.

At zero flow, all of the initially released A gets converted to B, preserved and mixed uniformly in the volume 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 and damping γ driven by a force $f(t)$:

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

(a) [10 pts] Find the Laplace transform of output position $u(s)$ 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 transfer function, and the poles and zeros.

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

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

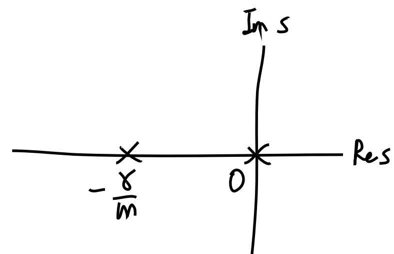
$$v(s) = \frac{m v_0 + f(s)}{ms + \gamma}$$

$$u(s) = \frac{u_0 + v(s)}{s} = \frac{u_0}{s} + \frac{m v_0}{s(ms+\gamma)} + \frac{1}{s(ms+\gamma)}\, f(s)$$

$$H(s) = \left.\frac{u(s)}{f(s)}\right|_{\substack{u_0=0\\ v_0=0}} = \frac{1}{s(ms+\gamma)}$$

Zeros: none

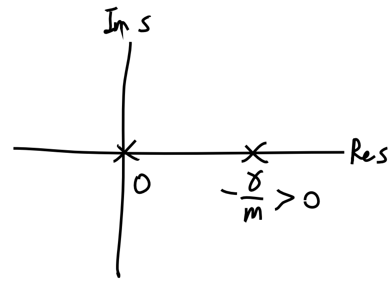
Poles: $s = \begin{cases} 0 \\ -\frac{\gamma}{m} \end{cases}$



$(\gamma > 0)$

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

$\gamma < 0 \Rightarrow$ strictly positive real pole $-\dfrac{\gamma}{m}$: strictly unstable

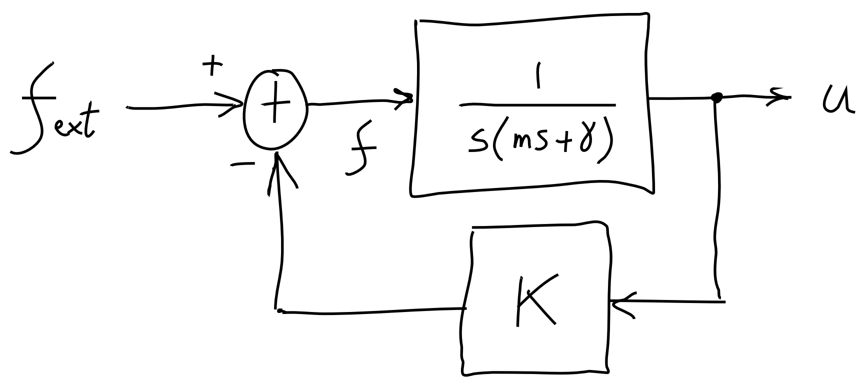


Many examples are possible! For instance: drag force on feet in a slippery bathtub decreases with velocity, leading to a geriatric disaster.

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

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

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



$$H_u(s) = \frac{u(s)}{f_{ext}(s)} = \frac{\frac{1}{s(ms+\gamma)}}{1 + K\frac{1}{s(ms+\gamma)}} = \frac{1}{ms^2 + \gamma s + K}$$

Poles: $s = -\frac{\gamma}{2m} \pm \frac{\sqrt{\gamma^2 - 4Km}}{2m}$

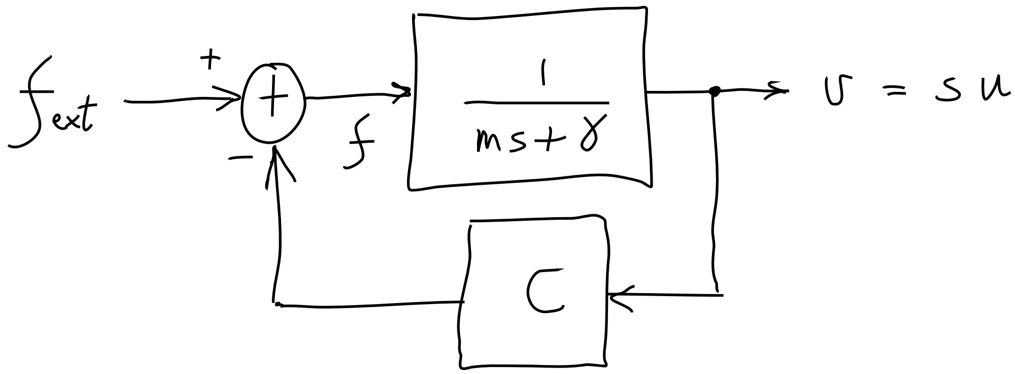
At least one pole has a positive real part

Unstable for any K

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

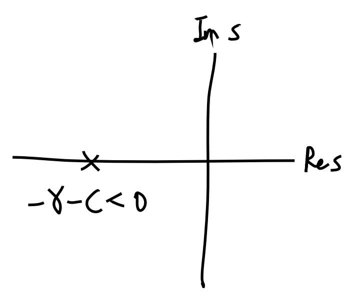
$$f(t) = f_{ext}(t) - C\,v(t)$$

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 $H_v(s) = v(s)/f_{ext}(s)$. Find the condition on the feedback gain C to ensure strict stability of the closed-loop system.



$$H_v(s) = \frac{v(s)}{f_{ext}(s)} = \frac{\frac{1}{ms+\gamma}}{1 + C\frac{1}{ms+\gamma}} = \frac{1}{ms + (\gamma + C)}$$

Strictly stable for $C > -\gamma$



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

(a) [5 pts] Give some examples of aspects of biosystems that are not linear, or that are not time invariant, and the implications of modeling them as linear time invariant systems.

Typical nonlinear aspects: saturation due to physical limits, e.g., maximum displacement or maximum force that a spring can support.

Typical time variant aspects: circadian rhythm modulating body function over the time of the day and night.

LTI models ignore these aspects potentially missing out on some important environmental factors affecting function. However, linearized models around varying operating points can account for them.

(b) [5 pts] Show that $1/s$ represents the Laplace transform of a step function, as well as the Laplace transfer function of an integrator.

Multiplying by 1/s in the Laplace domain corresponds to integration in the time domain. Hence 1/s is the Laplace transfer function of an integrator.

Applied to an impulse, the integrator gives a step function. Multiplying 1/s by 1 (Laplace transform of an impulse) gives 1/s as the Laplace transform of the step function.

(c) [5 pts] How do blood pressure and blood volume vary under dilation of the blood vessels? Explain.

Increasing blood pressure causes dilation of the blood vessels due to vessel wall elasticity, increasing blood volume. These changes in blood volume are proportional to changes in blood pressure as determined by compliance.

(d) [5 pts] Explain why blood velocity in the arterioles deep in the brain is comparable to that in the arteries entering the brain, despite their diameter being over a hundred times smaller.

The arteries branch out to a vasculature network covering the brain with large numbers of arterioles in parallel collectively carrying the blood stream.