Here we again iterate on two of the problems in the previous homework (HW #1 and #2), now studying the stability of system response, and closing the loop with feedback. As before, you may find it helpful to use the available MATLAB Simulink tools.

1. [45 pts] Here we reconsider the linearized form of the Lotka-Volterra model of Problem 1 in HW #1 and #2, with small variations in the populations states $\tilde{u}(t)$ and $\tilde{v}(t)$ driven by small variations in the therapeutic input $\tilde{f}(t)$ around a steady-state operating point $\bar{u}$, $\bar{v}$, and $\bar{f}$:

$$
\frac{d\tilde{u}}{dt} = a\tilde{u} + b\tilde{v} \\
\frac{d\tilde{v}}{dt} = c\tilde{u} + d\tilde{v} + \tilde{f}(t).
$$

(a) [20 pts] Prove generally that this system, for any $a$, $b$, $c$ and $d$, is stable iff (if and only if) $a + d \leq 0$ and $ad \geq bc$. Under what conditions is the system strictly stable, and under what conditions is it critically stable? Stability requires that the system response is bounded for any small-signal perturbation in the input. Strict stability requires that the response to an impulse perturbation approaches zero as time goes to infinity, whereas critical stability allows a bounded but non-zero response as time goes to infinity. Hint: Analyze the poles of the linearized system, and consider their real components which signify the rate of exponential growth or decay in the response magnitude over time.

(b) [25 pts] Now consider the linearized form of the particular Lotka-Volterra model of Problem 1 as given in HW #1 and #2, around any of the four steady-state operating points $(\bar{u}, \bar{v})$ for zero steady-state therapeutic input $\bar{f} = 0$. Compute $a$, $b$, $c$ and $d$ as the coefficients of the Jacobian of the nonlinear Lotka-Volterra model evaluated at each of the four steady-state operating points $(20/17, 1/17)$, $(1, 0)$, $(0, 0)$ and $(0, 3)$, and analyze their stability. In particular, indicate around which of the four steady-state operating points the system is strictly stable, critically stable, and unstable. Plot the output $\tilde{v}(t)$ of the nonlinear system for an impulse perturbation $f(t) = 0.001 \delta(t)$ around the $(1, 0)$ steady-state operating point, i.e., for initial conditions $u(0) = 1$ and $v(0) = 0$, and compare with the output $\tilde{v}(t)$ of the linearized model according to (1). What do you observe, and why?

2. [55 pts] We now return to the model of regulation of glucose metabolism through insulin secretion, as studied in HW #1 (Problem 3) and HW #2 (Problem 2). Specifically, we consider a simple feedback control strategy, where the insulin secretion $I(t)$ is directly proportional to the difference between the actual glucose concentration $G(t)$, and a constant target value $T$ to maintain a healthy metabolic state:

$$
I(t) = K (G(t) - T)
$$

where $K$ is the feedback strength as a control parameter in the closed-loop system. As before, insulin is well-mixed in the blood volume $V$ and decays due to exiting the blood stream at flow rate $Q$:

$$
\frac{dC}{dt} = \alpha I(t) - \frac{1}{\tau} C(t)
$$

1We ignore the fact that $I(t)$ cannot possibly go negative, for now-- we’ll deal with this later!
where $\alpha = 1/V$ and $\tau = V/Q$. We further consider a source of glucose $J(t)$ entering the bloodstream, as input from the digestive system. Unlike insulin, glucose is not excreted by the kidneys so it recirculates in the vascular system without decay:

$$\frac{dG}{dt} = \alpha J(t) - k C(t) G(t)$$

(4)

where the last term, as before, models the kinetics in glycogenesis (conversion of glucose to glycogen) catalyzed by insulin.

(a) [10 pts] Sketch (or print) an equivalent block diagram of the closed-loop system (2)-(4).

(b) [10 pts] Find the steady-state glucose concentration $\bar{G}$ for the closed-loop system in response to a steady-state glucose input $\bar{J}$. Show that, as the feedback strength $K$ approaches infinity, the steady-state glucose concentration approaches the control target $T$.

(c) [20 pts] Analyze the stability of the closed-loop system by linearizing its dynamics for small-signal variations around the steady-state operating point in the glucose input $J(t) \approx \bar{J} + \tilde{J}(t)$, insulin concentration $C(t) \approx \bar{C} + \tilde{C}(t)$, and glucose concentration $G(t) \approx \bar{G} + \tilde{G}(t)$. Specifically, consider the linearized system response $\tilde{G}(t)$ to small perturbations $\tilde{J}(t)$. Is the closed-loop system stable? How does the control parameter $K$ affect the dynamics of the system response?

*Hint:* Show that the nonlinear ODE (4) transforms into the following LTI form:

$$\frac{d\tilde{G}}{dt} = \alpha \tilde{J}(t) - k\bar{C} \tilde{C}(t) - k\bar{C} \tilde{G}(t)$$

(5)

and use it along with the small-signal versions of (2) and (3) to find the closed-loop transfer function $\tilde{G}(s)/\tilde{J}(s)$ and its poles.

(d) [15 pts] Evaluate the response of the closed-loop system (2)-(4) to an initial 50 mmol of glucose in the 5 L blood volume, for a target concentration $T = 5 \text{ mmol/L}$, and with zero initial insulin in the bloodstream. As before, $\alpha = 0.2 \text{ L}^{-1} \text{ min}$, $\tau = 1 \text{ min}$, and $k = 60 \text{ L/min mmol}$. Show the dynamics in the concentrations of insulin $C(t)$ and glucose $G(t)$, for two values of the feedback strength:

i. $K = 0.01 \text{ L/min}$; and

ii. $K = 0.1 \text{ L/min}$.

Explain what you observe.