Guidelines:

- Part I is closed book. Part II is open book, open notes. You will receive Part II after you submit Part I. It is recommended that you spend no more than 30 minutes on Part I.
- Time limit: 3 hours total.
- Show all your work and be as neat as possible.
- 100 points possible.
- Please sign the following pledge:

> *I agree to complete this exam without unauthorized assistance from any person, materials, or device.* _____

Part I (Closed Book) [34 pts]: *Keep answers concise!*

1. [4 pts] Give the general form of a mass balance equation, identifying the major terms involved.

2. [4 pts] Explain the difference between feedback control and feedforward control.

3. [4 pts] Why is a state-space representation of a system useful? Why is a transfer function representation useful? Give one significant and distinct reason for each.

4. [4 pts] Give two examples of how control is achieved in biology at the molecular level.

5. [2 pts] What is a state variable?

6. [3 pts] A linear dynamic system has eigenvalues $\lambda = -2.71, -20.10, -2 \pm i$, and $0.13 \pm 4i$. Is it stable? Why?

7. [2 pts] What is robustness?

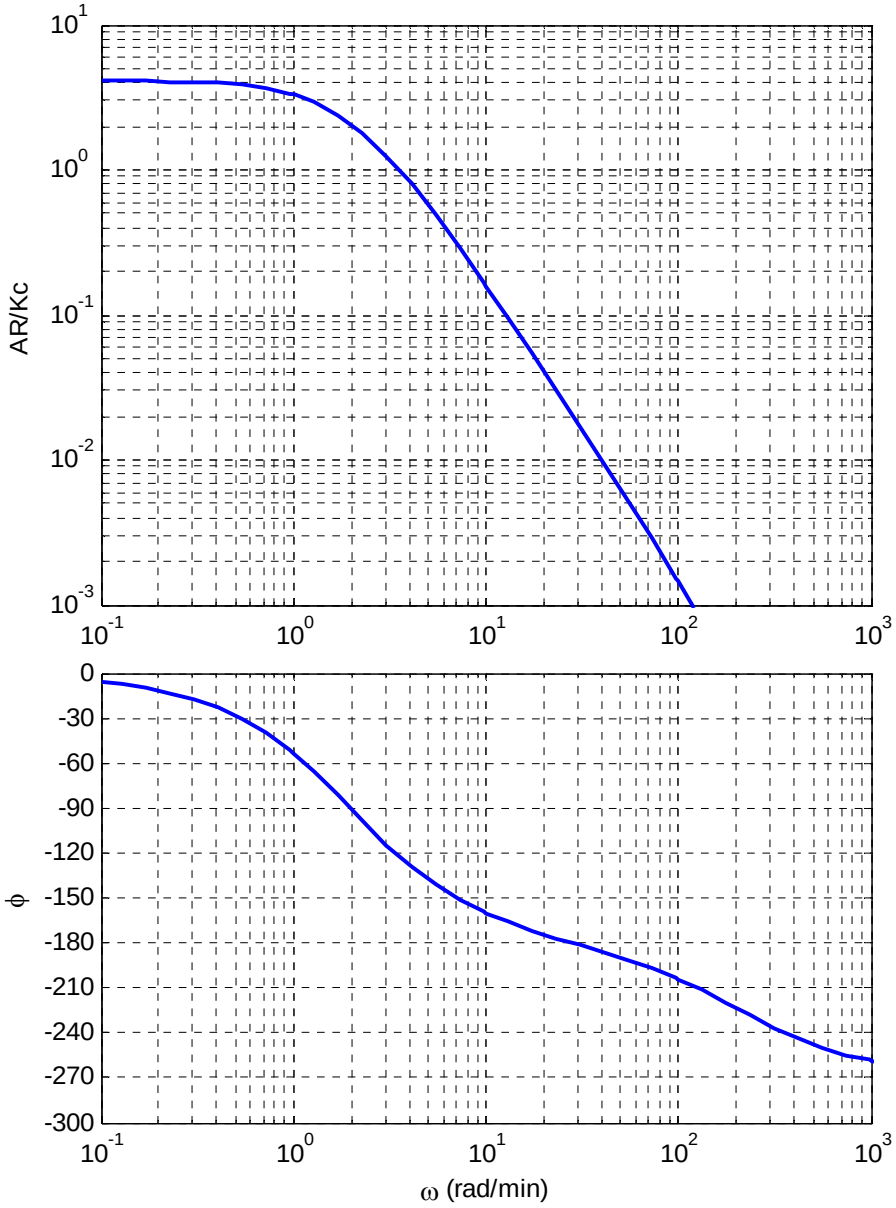
8. [3 pts] Sketch the network motif for autoregulation.

9. [4 pts] Sketch a phase portrait of an attractor (in a two-dimensional system).

10. [4 pts] Give two characteristics of a chaotic system.

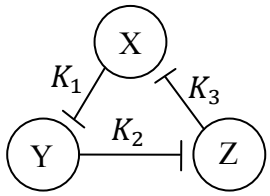
Part II (Open Book) [66 pts]:

1. [20 pts] A standard feedback control process has an open-loop transfer function characterized by the Bode plot below when $K_c = 1$ (P control).



   a. [8 pts] What is the ultimate gain and period of this process?
   b. [6 pts] What controller gain would yield a phase margin of 30º?
   c. [6 pts] For $K_c = 1$, how robust is the process to dead time? That is, how much additional dead time could be present in the process before it becomes unstable, assuming the rest of the parameters and measurements do not have errors.
   d. [Bonus: 5 pts] Sketch the Nyquist plot for this open-loop system.

2. [20 pts] Consider the following engineered motif, the repressilator (Elowitz & Leibler, *Nature* 2000):



   a. [9 pts] Write dynamic equations to describe this system. Use logic assumptions for the transcription repression with binding dissociation constants K_1, $K_2$and K_3 as shown. Define any other parameters you use in your model, and state any assumptions.

   b. [7 pts] If initially $X = X_{SS}$ (the steady-state concentration when X is being expressed and not regulated by any other genes) and $Y = Z = 0$, what are the resulting dynamics? Show your answer as plots of X, Y and Z as a function of time.

   c. [4 pts] What is the function of this motif? I.e., what does it do?

3. [26 pts] A researcher has proposed a simple dynamic model that might simulate the spread of the flu virus. Let S be the fraction of susceptible individuals in the population, and I be the fraction of infected individuals. (The fraction of individuals who have recovered from the disease and are now immune, $R = 1 - I - S$, can be calculated from the other variables, and thus can be omitted in our dynamic model.)

$$\dot{S} = r - rS - bSI$$
$$\dot{I} = bSI - rI - dI - cI$$

In the model above, r represents the birth rate and natural death rate, bSI represents the rate of infection of susceptible people (who then become infected), c represents the rate of healthy recovery and d represents the death rate due to the disease. Let $r = 0.01$, $b = 0.1$, $d = 0.01$ and $c = 0.04$.

a. [4 pts] Sketch the nullclines of the system and indicate the regions where each state variable is increasing or decreasing. Note that S and I must be between 0 and 1.
b. [3 pts] Find all fixed points for this system.
c. [6 pts] Assess the linear stability near the fixed point with the largest value of I.
d. [5 pts] Complete the sketch of the phase portrait of this system.
e. [3 pts] Interpret the meaning of the phase portrait.
f. [3 pts] The H1N1 flu strain is special in that it has a higher rate of infection and a higher mortality rate. How would these two factors affect your model?
g. [2 pts] What elements are missing from the model that could make it more realistic?