1. (slight variation on 3.7.7) We will work on a non-dimensionalized version of the problem from the text. Consider a protein that activates its own transcription in a positive feedback loop, while its promotor has a certain level of basal expression:

$$\dot{p} = \alpha + \frac{\beta p^n}{K^n + p^n} - \delta p.$$

Here α is the basal transcription rate, β is the maximal transcription rate, K is the activation coefficient, and δ is the decay rate of the protein. To ease the analysis, assume that n is large ($n \gg 1$).

(a) Explain the setup for the problem in your own words, including explanations for the following terms: *protein transcription*, *positive feedback*, *promotor*, *basal transcription rate*. Remember to cite your sources (either in your writeup or on the HW Cover Sheet).

Solution:

(b) Show that the system can be put in the dimensionless form

$$\frac{dx}{d\tau} = s - rx + \frac{x^n}{1 + x^n}$$

where $r > 0$ and $s \geq 0$ are dimensionless groups.

Solution:

(c) For $n = 2$ this equation is identical to the model gene activation on HW02. For this problem, though, we assume n is large ($n \gg 1$). Sketch the graph of the nonlinear function $g(x) = x^n/(1 + x^n)$ for $n \gg 1$. What simple shape does it approach as $n \to \infty$?

Solution:

(d) The right side of the equation for x can be written as $g(x) - h(x)$ where $h(x) = rx - s$. Use this decomposition to plot the phase portrait for the system for the following three cases: (i) $\delta K - \alpha > \beta$, so $r - s > 1$, (ii) $\delta K - \alpha = \beta/2$, so $r - s = 1/2$, and (iii) $\delta K - \alpha < 0$ so $r - s < 0$.

Solution:

(e) For now on, assume $\delta K > \beta$, so $r > 1$. Plot the bifurcation diagram for this system showing x^* vs s. Indicate the locations of the bifurcations in sx^*-space. The location of the bifurcations in the diagram will be dependent on r.

Solution:

(f) Discuss how the level of protein behaves if α is very slowly increased from $\alpha = 0$ to $\alpha > \delta K$, so from $s = 0$ so $s > r$, and then very slowly decreased back to $\alpha = 0$ (so $s = 0$). Show that such a pulsed stimulation leads to hysteresis (and include a clear explanation of what is meant by "hysteresis" in this context).

Solution:

2. (5.1.9) Consider the system $\dot{x} = -y, \dot{y} = -x$.
   (a) Sketch the vector field.

   Solution:

   (b) Show that the trajectories of the system are hyperbolas of the form $x^2 - y^2 = C$.

   Solution:

   (c) The origin is a saddle point; find equations for its stable and unstable manifolds.

   Solution:

   (d) ...