In the following exercises I refer to the paper “Network motifs: theory and experimental approaches” by Uri Alon, Nature Rev. Genet. 8:450-461 (http://dx.doi.org/10.1038/nrg2102).

1. (pg 450, “simple regulation”) In the lecture we have derived the dynamics that describes the concentration X in a simple regulation system.
   a. Name an active and a passive (physiological or biochemical) process that cause the concentration of X to decrease when its production stops.
   b. What is the advantage of having the active process in addition to the passive process?
   c. Name three processes that may contribute to the costs (in terms of biosynthetic capacity) of the active process if the steady state concentration of X is to be maintained at the same level as with the passive process only.

2. (page 457, right column) The regulation of Lambda phage life phases, in particular the switching between lysogenic and lytic phases, is given as an example of a process regulated by a developmental toggle switch. The switch was elucidated by the molecular biologists Barbara J. Meyer and Mark Ptashne. Look up the details of this regulation (Wikipedia has a good lemma) and explain how the different components, proteins Cro, cl and cII, form a toggle switch as in figure 7b.
   a. What is the difference between the two main modes of lambda phage life, namely the lysogenic and the lytic life phases, that need to be regulated by the toggle switch?
   b. Which of the proteins “represents” or “maintains” the lysogenic state, and which the lytic state?
   c. How is the lytic phase induced?
   d. To which of the motif components X, Y and Z do the three phage proteins mentioned above correspond? (Start with the paragraphs “Protein function overview” and “Repressor” in the Wikipedia lemma). Draw the diagram with the lambda phage proteins.
   e. What are, biochemically, the positive and negative regulatory processes represented by the arrows in the motif? Name other processes that could have been employed to attain a similar regulation?
   f. What happens to the component corresponding to Z during lysogeny?

3. (Box 1, page 458) Describe in words the dynamics of the composite negative-feedback loop, coupled to a positive feedback loop (upper right) when it generates oscillations. With regard to X and Y, there is a process not explicitly depicted in the figure that is necessary for the occurrence of oscillations: which process? Discuss qualitatively the conditions (parameters) necessary to generate oscillations (or the other way around: how would oscillations be prevented or dampened?)

4. Using the motifs described in the paper, construct hypothetical networks (some of which you may have seen already) that perform the following functions:
   a. Induction of a gene only when an incoming signal persists over a long period of time. What could be the biological function of such a network, compared to “simple regulation” (figure 1a)?
   b. A constant signal inducing an “overshoot” of gene induction, and a subsequent stabilization of induction at a lower level. Mention possible biological functions of such a network
   c. An oscillation between two mutually exclusive (toggled) states, like a cell division cycle.