

# EC5.202: Systems Thinking

## End Semester Examination

Max. Time: 2.0 hrs

Max. Marks: 40

- ✓ 1. A gene product with concentration  $g$  is produced by a chemical  $s$

$$\frac{dg}{dt} = s + k_1 \frac{g^2}{1 + g^2} - k_2 g$$

- ✓ Show that if  $s = 0$  there are two positive steady states if  $k_1 > 2k_2$  and determine their stability based on rate plot. By considering  $s > 0$  show that a critical value  $s_c$  exists such that the steady state switches to a higher value for all  $s > s_c$ . What kind of bifurcation does the system undergo? Draw the bifurcation diagram with respect to  $s$ . [8 marks]

- ✓ 2. Gene  $X$  encodes a repressor that represses gene  $Y$ , which also encodes a repressor. Both  $X$  and  $Y$  negatively regulate their own promoters.

✓ a. Draw the circuit diagram.

- ✓ b. At time  $t = 0$ ,  $X$  begins to be produced at rate  $\beta$ , starting from an initial concentration of  $X = 0$ . What are the dynamics of  $X$  and  $Y$ ? What are the response times of  $X$  and  $Y$ ? Assume logic input functions, with repression thresholds  $K_{XX}$ ,  $K_{XY}$  for the action of  $X$  on its own promoter and on the  $Y$  promoter, and  $K_{YY}$  for the action of  $Y$  on its own promoter.

- ✓ c. At time  $t = 0$ , production of  $X$  stops after a long period of production, and  $X$  concentration decays from its initial steady-state level. What are the dynamics of  $X$  and  $Y$ ? What are the response times of  $X$  and  $Y$ ? [5 marks]

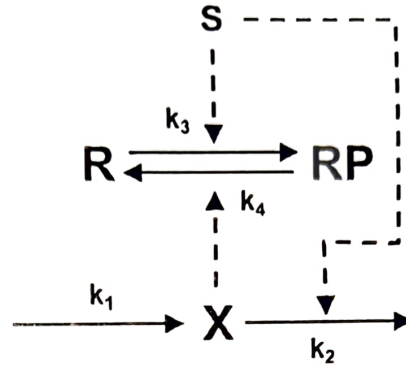
- ✓ 3. A multi-input FFL is made of two coherent FFLs with inputs  $X1$  and  $X2$ , SUM logic at  $Y$  and ( $X1$  OR  $X2$ ) AND  $Y$  logic at the output  $Z$ . Assume all parameters are equal to one. Draw the circuit. Write equations using logic input functions.

- a. Show that a simultaneous brief stimulation of  $X1$  and  $X2$  can lead to an output, even if each input stimulated alone would not.
- b. Show that (a) can work even if the brief input pulses are timed with a small delay. [5 marks]

4. Consider an incoherent FFL in which production of  $Z$  is  $\beta_1$  if  $Y^* < K$ . Production goes down to  $\beta_2$  when  $Y^* \geq K$ . What is the speedup compared to simple regulation with production rate  $\beta_2$  (derive it)? Assume equal degradation rate for the two circuits. [5 marks]

5. Show that the given circuit can perform fold detection. How is it related to adaptation? [5 marks]

6. How the steady state concentration of  $R_p$  changes with respect to signal  $S$ ? Comment about the response curve. [3 marks]



7. How nervous system respond to different intensity of stimuli (excitatory and inhibitory)? Draw and explain. [3 marks]
8. What are different motifs of neuronal network? Briefly explain their role. [3 marks]
9. During development from an egg to an embryo, cells need to make irreversible decisions to express the genes appropriate to their designated tissue types and repress other genes. One common mechanism is positive transcriptional feedback between two genes. There are two types of positive feedback made of two transcription factors. The first type is of two positive interactions  $X \rightarrow Y$  and  $Y \rightarrow X$ . The second type has two negative interactions  $X \rightarrow Y$  and  $Y \rightarrow X$ . What are the stable steady states in each type of feedback? Which type of feedback would be useful in situations where genes regulated by both  $X$  and  $Y$  belong to the same tissue? Which would be useful when genes regulated by  $X$  belong to different tissues than the genes regulated by  $Y$ ? [3 marks]