T-61.5110 Modeling biological networks

Exam, May 17, 2010

You are NOT allowed to use calculators or any other additional equipments/material in the exam. Please write your answers in English. Please write carefully so that I can read your writing.

1. Consider the prokaryotic auto-regulation model in Figure 1, which is taken from the course book: g=gene, r=transcript, P=protein, $P2$=protein dimer complex (formed of two proteins P), $RNAP$=RNA polymerase, p=binding/operator site of $RNAP$, q=binding/operator site of P2; RNAP can transcribe the gene g unless $P2$ blocks the transcription. Construct the corresponding coupled chemical reactions (i.e., reaction network model). Also formulate the model as a Petri net $(P, T, Pre, Post, M)$ using the so-called matrix formalism. (6 points)

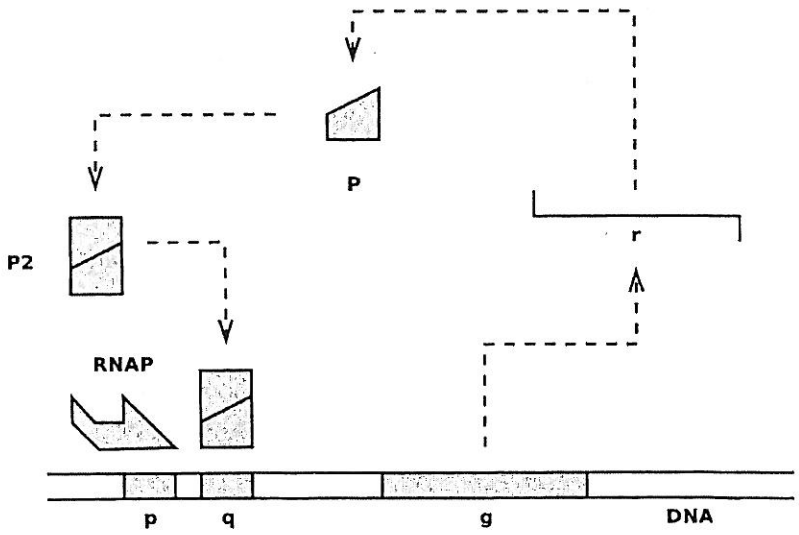

Figure 1: A simplified prokaryotic auto-regulation model.

2. Consider the following (Michaelis-Menten) ODE system

$$\begin{aligned} d[S]/dt &= k_2[SE] - k_1[S][E] \\ d[E]/dt &= (k_2 + k_3)[SE] - k_1[S][E] \\ d[SE]/dt &= k_1[S][E] - (k_2 + k_3)[SE] \\ d[P]/dt &= k_3[SE] \end{aligned}$$

Use conservation laws via the p-invariance to reduce the dimension of the system. Also explain why dimensionality reduction for ODEs is useful in general. (6 points)

3. Explain how the maximum likelihood principle and the steepest descent (i.e., gradient descent) optimization method can be applied to estimate parameters of ordinary differential equation (ODE) models, given a parametric ODE model and time-series measurements (without missing values). (6 points)

4. Explain the Gillespie algorithm for simulating coupled chemical reactions. (You can assume general rate constants $c_1, \ldots, c_v$ and hazard functions $h_1(\mathbf{x}, c_1), \ldots, h_v(\mathbf{x}, c_v)$ for all reactions.) In addition to the Gillespie simulation algorithm itself, briefly explain the connection between Gillespie algorithm and the theory of continuous-time Markov processes. (6 points)

5. Modeling approaches can be categorized into deterministic (e.g. ODEs) and stochastic (e.g. coupled chemical reactions) modeling methods. Briefly discuss benefits and drawbacks of deterministic and stochastic approaches in the context of simulation and modeling of biomolecular systems. (6 points)