CS-E5880 Modeling biological networks

Exam, February 15, 2018

Lecturer: Harri Lähdesmäki

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. Maximum number of points: 30 (will be scaled to 60 for final grading).

1. Describe the following models/algorithms.
   a) Describe the Bernoulli random network model. (2 points)
   b) Briefly explain the greedy hill-climbing algorithm for selecting an optimal network structure given experimental data. You can assume e.g. the static or dynamic Bayesian network modeling framework (or any other biological network model), and you can use any meaningful score for network structures (e.g. the posterior probability/marginal likelihood or cross-validated predictive performance) in your answer. (4 points)

2. a) Explain the Euler method for numerical integration (i.e., simulation) of ODE models from a given initial state. (3 points)
   b) Consider mass-action stochastic kinetics and a second-order reaction R_i : $X_k + X_k \rightarrow X_l$. Explain how the reaction hazard $h_i(\mathbf{x}, c_i)$ for the ith reaction R_i is computed. In addition, explain how the reaction hazard is computed for a third-order reaction R_j : $X_k + X_l + X_m \rightarrow X_n$. (3 points)

3. a) Explain the Gillespie algorithm for simulating coupled chemical reactions. You can assume general stochastic 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. (4 points)
   b) For a chemical reaction network model with a stoichiometric matrix S, explain the reachability of a state M^* from an initial state M. (2 points)

4. Approaches to model biological networks can be categorized into qualitative models (e.g. Boolean networks, discrete-valued Bayesian networks, undirected graphical networks) and quantitative models (e.g. ODEs and coupled chemical reaction networks). Discuss the benefits and drawbacks of qualitative and quantitative network models. Discuss the following items:
   - Accuracy of models, i.e., how realistic a network model is
   - Computational complexity/difficulty to simulate and analyze a model
   - Computational aspects and difficulty of inferring a network model from data, including network structure selection and parameter estimation
   - What kind of measurement data is needed for network structure selection and parameter estimation
   - Applicability in practical work

   Use Boolean networks *or* Bayesian networks *or* Gaussian Markov random fields as an example of qualitative approaches, and use ODEs *or* coupled chemical reaction networks as an example of quantitative approaches. (6 points)

5. Consider the standard 'lock-and-key' model of enzyme activity shown in Figure 1. Describe how one can derive the ODE-based model of Michaelis-Menten biochemical kinetics from the elementary reactions shown in Figure 1. You do not need to provide the full derivation with all the details but describe the assumptions/approximations/properties that are used to derive the Michaelis-Menten biochemical kinetics rate law. Specify also the actual Michaelis-Menten rate law. (6 points)

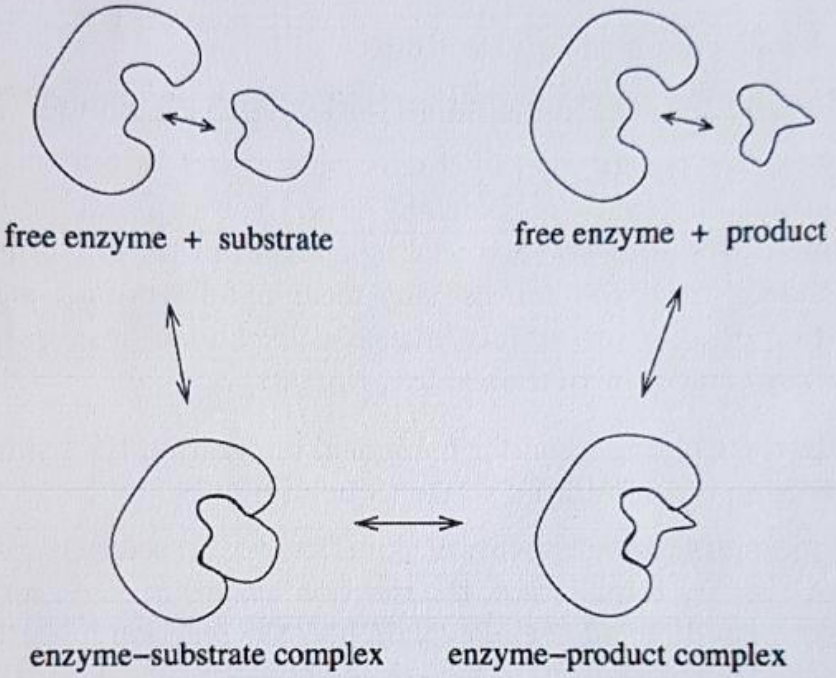

Figure 1: (a) A diagram representing the standard 'lock-and-key' model of enzyme activity (taken from Ingalls (2013)).