Dugga 1, TBMT19, 2014-01-31

Each question gives 3 points. 7 points are required to pass. You have approx. 45 min.

1) Consider the following model, in reaction form

(R1) x1 => x2 v1 = k1*x1

(R2) x2 => v2 = Vmax*x2/(Km + x2)

(x1(0),x2(0)) = (2,3); k1 = 1, yhat = ky*x2, ky = 1, Vmax = 2,Km = 1

a) What are the states?
b) What are the parameters?
c) What can be measured?

ANSWER:

a) x1, x2 b) k1, Vmax, Km, ky, x1(0), x2(0) c) x2 times a scaling parameter

(note that the sloppy version of formulating was used here, i.e. x1 = #x1)

2) Consider the following set of reactions:

(R1) A => B

(R2) B=>

(R3) A =>

a) What are the corresponding differential equations? Assume mass action kinetics for R1 and R2, and Michaelis-Menten kinetics for R3. Don't forget to specify the initial conditions. Specify some values for any parameters you might introduce.
b) Expand the model to say that you can measure something that is proportional to the rate of the second reaction, R2.

ANSWER:

a) x1 = [A], x2 = [B], v1 = k1*x1, v2 = k2*x2, v3 = Vmax*x1/(Km + x1)

d/dt(x1) = -v1 – v3

d/dt(x2) = v1 – v2

Vmax = Km = 3, k1 = k2 = 8.76, x1(0) = 1, x2(0) = 88

b) Add the following equation: yhat = v2*ky where ky = 8

3) Cost functions

a) What is the input and output of a cost function?

b) What are the residuals, and how do they relate to the cost function?

c) What is the difference between a local and a global optimization algorithm?

ANSWER:

a) Input: parameters, Output: cost, i.e. a measure of the agreement with data

b) The residuals are the differences between measured data (y) and corresponding simulated data for a specific parameters (yhat(p)). In the cost function, all the residuals are squared, normalized with the variance of the measurement noise, and finally summed together.

c) A local optimization algorithm stops at local minima, but a global optimization algorithm finds, or at least attempts to find, the global minimum.