Dugga 2, 2013

3 questions, with 3 points each. 7 points needed to pass

1 Model formulation

Consider the following model:

d/dt(A) = u – k1*A – k2

d/dt(B) = k1*A

A(0) = 0.5, B(0) = 1. k1 = 2, k2 = 3.

yhat(t,p) = k*B

a) Which are the reactions?

ANSWER

=>A (u)

A=> B (k1)
A=> nothing (k2)

Common mistakes: to miss u.

b) What are the new equations if the k1-reaction is changed into a Michaelis-Menten expression?

ANSWER

d/dt(A) = u – Vmax*A/(Km+A) – k2

d/dt(B) = Vmax*A/(Km + A)

Vmax = Km = 2, k1 disappears

Common mistake: to forget values for Vmax and Km (these are also equations, although not differential equations)

c) How could you describe the yhat-equation in words; what does it mean?

That you can measure B times a scaling constant k

2. Optimization and statistical tests

a) What is the input and output of an optimization algorithm?

ANSWER:

Input: startguess of parameters, cost

Output: optimized parameters (potentially many, if one uses a modified optimization algorithm)

b) What is the null-hypothesis of a chi-square test? What do you conclude if it is rejected?

ANSWER: That the residuals are small (of the size of the noise, which is assumed to be normally distributed). If H0 is rejected, the residuals must be big, and the model is rejected.

c) What do you conclude if you do not reject a likelihood ratio test?

ANSWER: Nothing (or that the models are not significantly different)

3. Closing the loop

a) What is the problem with predictions in systems biology? Why does this problem typically not appear in physics?

ANSWER: The problem is that you cannot determine the parameters once and for all, and often not even uniquely at any given instant. Therefore the predictions will be uncertain, and many predictions will even be arbitrarily uncertain. In physics the parameters are often natural constants, which can be looked up in physics handbook.

b) You have a well-determined prediction in a model, concerning the concentration of a state B, at a certain time point, t=15. How could that be a reason to measure B experimentally at that time point?

ANSWER: This core prediction can be used to test the model, and see if it can be rejected

c) You have another prediction, of C, at time point t=20. This prediction, however, is very uncertain, more than that of many other states. How could that uncertainty be a reason to measure C at this time point?

ANSWER: Such a measurement would determine the parameters (and thus other predictions) in the model better.