Dugga 2, 2012-01-30

Each question gives 3p. 7p are needed to pass. For all sub-questions, there is a one-sentence answer that gives full points, but you can use longer answers if you want. 25 minutes. Good luck!

Gunnar

1) Consider the following two reactions

R1) A + B => C
R2) C => B

a) Assume that both reactions are irreversible, and that R1 follows mass action and R2 Michaelis-Menten kinetics. What are then the ordinary differential equations?

b) Add initial conditions, parameter values, and a measurement equation, where you assume that we can measure the concentration of B plus an unknown constant. You can make up values for unknown constants when/if you need them.

c) Consider the equations below. What are the corresponding reactions (i.e. the interaction graph)?

d/dt(x1) = -k1*x1 + k2
d/dt(x2) = k1*x1 - Vmax*x2/(Km + x2)
yhat(t,p) = ky*x2

2) Statistical tests:

a) What is your conclusion if a chi-square test is rejected?

b) What is your conclusion if a likelihood ratio test is *not* rejected?

c) Give one reason why you might sometimes have the following scenario: a model is rejected by a whiteness test but not by a chi-square test. If you want, do a drawing of what the residuals might look like.

3. Predictions

a) Explain a potential problem with trusting predictions from a biological model obtained using a single parameter set.

b) What is the difference between a “beach statement” and a core prediction?

c) Say that your model-based analysis has given you one or several predictions that lead you to claim that doing a particular new experiment would give you new knowledge regarding the analysed model(s). Give an example of what such a prediction could be, and what would be the corresponding new knowledge. Remember to specify if it is a unique prediction or not.

FACIT

1 a)
d/dt(A) = -k1*A*B
d/dt(B) = -k1*A*B + k2*C/(km+C)
d/dt(C) = k1*A*B - k2*C/(km+C)

b)
A(0) = 100
B(0) = 100
C(0) = 0

Yhat(t,p) = ky + B

k1 = 2, k2 = 1, km = 0.5, ky = 2

c)
R1: X1 => X2
R2: => X1 (X1 increases with constant rate)
R3: X2 => (X2 decreases according to Michaelis Menten kinetics)

2 a)
The model cannot fit to data, because of too large residuals, and can be rejected with the given significance.

b)
The null hypothesis cannot be rejected (i.e. we conclude nothing).

c)
If the residuals are small but correlated (for instance always positive)

3 a)
Since one typically does not know the parameter values, these predictions really only says “It may be this way, but also in some other way”, which is a weak although not entirely useless statement

b)
A beach statement is a weak statement made from a single parameter set saying “it may (or may not) be this way”, while a core predictions is a shared property among all acceptable parameters. In other words, a core prediction must be true or the model should be rejected.

c)

Overall answer can fall into three categories (each of them would give full points)
i) Because you have a unique prediction (i.e. a core prediction) that you want to measure experimentally to *test the model*
ii) Because you have two different models giving two different/non-overlapping unique

predictions; then you do the corresponding experiment to *distinguish between the models*
iii) Because you have a very non-unique but prediction (a beach-statement) regarding an important part of the model; then you want to do the corresponding experiment to *better determine the model* (i.e. not to test the model)

Finally, you can also give a specific example. Here is one, loosely copied from one of the students:

If you have a model that uniquely predicts that a pistol always hit spot-on-target (within 1 cm). Then testing the ability of the pistol to hit the target is a good experiment to do. If you do a few shots, and always hit at least 1 meter away, the model should most likely be rejected (according to both common sense, and according to a chi-square test)