My Dugga-id is:

Dugga 2, TBMT19, 2014-02-05

3 questions, with 3 points each. 7 points needed to pass. You can answer in Swedish and write on both sides of the paper. Don't forget to write name and personal number on all papers you hand in. If you want to know your results from the public results list: remember your Dugga-id above.

1 Model formulation

Consider the following model:

d/dt([A]) = u1 – Vmax*[A]/(Km+[A]) – k2*[A]

d/dt([B]) = k2*[A] – u2

[A](0) = 0.5, [B](0) = 1. Vmax = 2, Km = 2.5, k2 = 3.

yhat(t,p) = ky*[B]/(Km_y + [B]) ky=4, Km_y = 5

a) Which are the reactions? (or alternatively: What is the interaction graph?)
b) What are the new equations if the k2-reaction is changed into a Michaelis-Menten expression?
c) How could you describe the yhat-equation in words; what does it mean?

ANSWER:

a) => A => B=> Ø , and A=> Ø,

b) Km2 = 4 and

d/dt([A]) = u1 – Vmax*[A]/(Km+[A]) – k2*[A]/(Km2 + [A])

d/dt([B]) = k2*[A]/(Km2 + [A]) – u2

c) You can measure B in a way where the measurement device is saturated: different high values of [B] cannot be distinguished, since they all display the measured value ky = 4

2. Statistical tests

a) Name at least one benefit of testing a model with respect to independent validation data.

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

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

ANSWER:

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a) One benefit is that you can check for over-fitting, and another is that you then are less dependent on statistical tests: you can see if the model has problems or not.

b) The null-hypothesis is that the residuals are small (comparable to the measurement noise). If it is rejected, you conclude that the residuals are larger than the measurement noise, and that the model cannot describe the data, and should be rejected – something is missing in the model.

c) Nothing

3. Closing the loop

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

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?

c) You have another prediction, of the reaction rate v2, at time point t=20. This prediction, however, is very uncertain, more than that of many other predictions. How could that uncertainty be a reason to measure this rate at this time point?

ANSWER:

a) The problem with predictions in biology is that you seldom know all the values of all the parameters. In fact, you can seldom determine them uniquely from the data. In physics, these parameters have been determined once and for all.

b) The reason is probably that you want to test the prediction, i.e. see if the model is reliable, and can describe independent validation data.

c) Measuring a very uncertain prediction will determine the parameters in the model more than if you measure a prediction that is more determined. So, you would then measure v2(t=20) because you want to determine the model better.