

Omdugga 2014-02-19

All questions give 3 points. Do 1-3 for Omdugga 1, 3-5 for Omdugga 2, 1-5 for both. 7/9 to pass one, 12/15 to pass both. You can write in Swedish and on both sides of the page. Personal-number and Dugga-id on all pages.

NOTE: the yellow expression has been changed compared to the original Omdugga, to make for a more fun/meaningful question.

1. Consider the following little model:

$$d/dt(x1) = u - k1*x1*x2 - k2*x1$$

$$d/dt(x2) = k2*x1 - k3*x2$$

$$k1 = 1, k2 = 2, k3 = 3, x1(0) = 2, x2(0) = 3, \hat{y}(t,p) = k_y*x1*k2, k_y = 4$$

a) What are the states? b) What are the parameters? c) What can be measured? (to get full point: describe what can be measured in words)

ANSWER:

a) x_1 and x_2 , b) $k_1, k_2, k_3, x_1(0), x_2(0), k_y$ c) you can measure the rate of the k_2 -reaction times an unknown scaling parameter

2. a) What is the input and output of a cost function?
b) How does Euler's forward method for simulation work?
c) What are the residuals in question 1, if the experimental data are $y(0) = 6$?

ANSWER:

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

b) Start in the initial conditions, calculate the derivatives, step in the direction of the derivative. Calculate new derivatives, and repeat until you reached your end time.

$$c) r = y - \hat{y} = 6 - 4*2*2 = 6-16 = -10$$

3. Consider again the model in question 1

a) What are the reactions? Or, alternatively, what is the interaction graph?
b) What changes if the k_2 -reaction now allows for a saturation of the rate?

ANSWER:

a) $\Rightarrow x_1 \Rightarrow x_2 \Rightarrow \emptyset$ and $x_1 \Rightarrow \emptyset$ (note that sloppy notation is used, i.e. $x_1 = [x_1]$)

b) The equations become:

$$d/dt(x1) = u - k1*x1*x2 - k2*x1/(K_m + x1)$$

$$d/dt(x_2) = k_2 \cdot x_1 / (K_m + x_1) - k_3 \cdot x_2$$

and K_m needs a value.

4. Optimization and tests

- a) What is the difference between the input to a model and the input to an optimization algorithm?
- b) What is the null hypothesis of a chi-square test?
- c) What happens if you do not reject a whiteness test?

ANSWER:

a) A model input is often called u , and it is something that can be controlled and measured. The model input is that which we assume is being *done* to the system.

Optimization algorithm input: a start guess for the parameters and the cost function.

b) that the residuals are small, i.e. comparable to the measurement noise

c) you do not conclude anything

5. Closing the loop

- a) A core prediction has been tested experimentally, and the experiment shows that a value outside the predicted interval has been obtained. What can we then conclude? How would that be different if the prediction was not known to be a core prediction?
- b) You have two models that are acceptable given the current data. How can you use predictions to design an experiment that *ensures* that a new experiment will be able to distinguish between the models?
- c) Is it better to have a well-determined or an undetermined prediction when trying to convince a biologist to collect experimental measurements of that prediction? Motivate your answer.

ANSWER:

a) If the measurement is outside a core prediction, the model can be rejected. For a simulation, not known to be a core prediction, nothing can be said: other parameter values may still be able to describe the new data.

b) Find core predictions that are different between the two models and that can be done experimentally – there is your experiment

c) Formally, both well-determined and undetermined predictions may be used as arguments for doing an experiment. Well-determined predictions leads to experiments that tests the model. Undetermined predictions are useful because measuring them will provide much knowledge about the uncertainties in the parameter space (the new data are guaranteed to reduce the space of acceptable parameters). In summary, the question of which is the more convincing argument therefore ultimately depends on the situation and on the personality of the biologist.