Omdugga 2015-02-18

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. Personal-number, name and Dugga-id on all pages.

1. Consider the following little model:

   d/dt([A]) = u – k1*[A] –k2*[A]*[B]

   d/dt([B]) = +k1*[A] – k3

   k1 = 1, k2 = 2, k3 = 3, [A](0) = 2, [B](0) = 3, yhat(t,p) = ky*[A], ky = 4

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

ANSWER: a) [A] and [B], b) k1, k2, k3, [A](0), [B](0), ky, c) [A] times a scaling constant ky

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 y(0) = 3 ?

ANSWER: a) input: parameters, output: cost, i.e. agreement with data

b) take a step in the direction of the gradient (the flow), recalculate the gradient, take a new step, etc

c) r = y – yhat = [t = 0] = 3 – 4*2 = -5

3. Consider again the model in question 1
   a) What are the reactions?
   b) What changes if you assume that the k1-reaction has a saturation?

a) => A => B => 0 and A=>0 (B catalyzes this last reaction)

b)

d/dt([A]) = u – k1*[A]/(Km + [A]) –k2*[A]*[B]

d/dt([B]) = +k1*[A]/(Km + [A]) – k3

Km = 8

Optimization and tests

a) What is the input and output of a global optimization algorithm?
b) What is the null hypothesis of a likelihood ratio test?
c) What happens if you do not reject a chi-square test?

ANSWER: a) input: start guess, output: the best global optimum that has been found

b) That the models are equally good

c) You can not say anything, the model is kept for now

4. Closing the loop
   a) A core prediction is tested experimentally, and the experiment shows that a value outside the predicted interval was 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) What is the point of independent validation data? Why is it beneficial?

ANSWER:

a) We can then reject the model structure (the biological hypothesis implemented in these equations). Otherwise, we would not have been able to say anything more than that the particular parameter(s) plotted could be rejected

b) This is ensured if you find an experimental design where the predictions of the two models are different and further away from each other than the uncertainty in the measurement data. I.e. you need predictions with uncertainty, also called core predictions

c) Independent validation data is beneficial for a wide variety of reasons, for instance because they allow you to see that the model can predict something in a new scenario/situation, for which it hasn't previously seen any data. It is also beneficial because you can simplify the statistical tests (e.g. the degrees of freedom in the chi-square test can then be calculated based on the number of data points only). Finally, cross-validation is good to test for overfitting. (any one of these 3 reasons would give full points in an exam)