Dugga B 2023

TBMT37 / TBMT19

Please, write your Dugga-ID on all pages and your answers in Swedish or English. You need at least 2 points per assignment <u>or</u> 12 points in total to pass. Good luck! /Elin

1 Model formulation and model parts

Consider the following model:

$$\frac{d[A]}{dt} = -v1 + v2 + v4 \qquad v1 = k1 \cdot [A] \cdot u \qquad [A](0) = 5 \qquad k1 = 4$$

$$\frac{d[B]}{dt} = v1 - v2 - v3 \qquad v2 = k2 \cdot [B] \qquad [B](0) = 2 \qquad k2 = 2$$

$$v3 = k3 \cdot [B] \qquad [C](0) = 3 \qquad k3 = 1$$

$$\frac{d[C]}{dt} = v3 - v4 \qquad v4 = k4 \cdot [C] \qquad k4 = 2$$

$$\hat{y} = ky \cdot [C] \qquad ky = 0.5$$

$$u = 1$$

(a) Draw the corresponding interaction graph / reactions. (1 point)

(b) Update the relevant reaction rates by including a saturation with respect to [A]. (1 point)

(c) What is characterising model states? (1 point)

2 Model simulation

Explain the Euler forward method and use this method to compute [C] in the model above at $\Delta t = 0.1$. (3 point)

3 Parameter estimation

(a) Explain in detail different methods to evaluate the agreement between model simulations and data. (2 points)

(b) What are the input(s) and output(s) to an optimization algorithm? (1 point)

4 Statistical tests

(a) Formulate the null hypothesis for a likelihood ratio test. (1 point)

(b) What do you conclude when you reject the null hypothesis in a chi2-test? (1 point)

(c) Give an example of a situation where you would use a Whiteness test. (1 point)

5 Predictions and experimental design

What is a core prediction? Give an example of a core prediction and discuss which conclusions you can draw using this core prediction. You can for example make a drawing in your answer. (3 points)

Answers: Dugga B 2023

1

(a) $A \rightarrow B$
$B \rightarrow A$
$B \rightarrow C$
$C \rightarrow A$

(b) $v1 = \frac{Vmax \cdot [A] \cdot u}{Km + [A]}$

(c) Model states are changing with time

2

In the Forward Euler method we take small time steps in the direction of the flow/gradient. $[C](0.1) = [C](0) + [\dot{C}](0)\Delta t = [C](0) + (k3 \cdot [B](0) - k4 \cdot [C](0))\Delta t = 3 + (1 \cdot 2 - 2 \cdot 3) \cdot 0.1 = 2.6$

3

(a) To evaluate the agreement between model simulations and data, we use both visual inspection, where we simply look at the data and model simulation in the same graph, and a cost function that could look like this:
$v(p) = \sum \frac{(y(t) - \hat{y}(t,p))^2}{SEM(t)^2}$
where the sum is over all measured time points. The input to a cost function is the values of the parameters, p, and the output to a costfunction is the agreement between model simulations and data, $v(p)$. The cost function uses the residuals, $y(t) - \hat{y}(t,p)$, i.e. the difference between data $y(t)$ and model simulation $\hat{y}(t,p)$, and the data uncertainty (SEM, standard error of the mean) as weight. Terms are squared so that they always contribute positively to the cost.

(b) The input is a startguess of the parameter values, and the output is the best found parameter values.

4

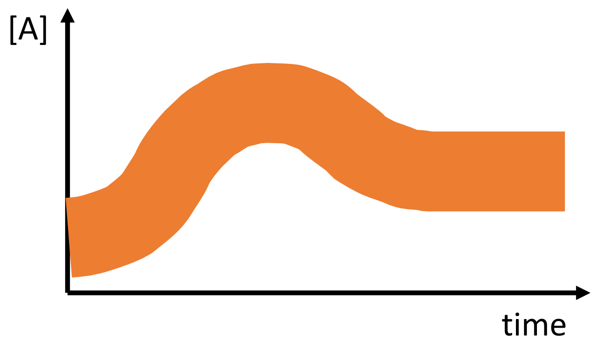
(a) H0: The models are equally good at explaining the experimental data.

(b) You conclude that the residuals are too large and you reject the model.

(c) When I have a model that is not rejected by a chi2 test, but I suspect that the residuals are correlated due to e.g. some systematic error.

5

A core prediction is a well defined prediction of a model property that can be tested experimentally. A core prediction is created by collecting an approximation of all parameters that are in agreement with training data. Here is an example of a core prediction:



I suggest to measure the concentration of A at some different time points (for example at time=0, in the peak, and in the steady state) to see if the model can predict the new data. These measurements will always provide new knowledge. When we get the data, we either reject the model or strengthen our trust in the model since we know the uncertainty for this specific prediction.