

1 Regarding construction of a model

You need to understand the basic properties regarding the following symbols/components in a model

- states (sv:tillstånd), x
- parameters, p
- input signals (sv: insignaler), u
- output signals (sv: utsignaler), $\hat{y}(t, p)$
- initial conditions (sv: initialvärden) $x(0)$

You also need to be able to pin-point the above symbols/entities in all three versions of model formulations: interaction graphs, reactions lists, and state-space descriptions, where the latter is given by the following three equations

$$\dot{x} = f(x, p, u) \quad (1)$$

$$x(0) = x_0 \quad (2)$$

$$\hat{y}(t, p) = g(x, p, u) \quad (3)$$

You generally also need to be able to go between these three ways of formulating a model, and to be able to exchange entities so that they correspond to different assumptions. For instance, how to (a) make a rate expression saturated (sv: att göra ett hastighetsuttryck mättat), (b) assume that a rate depends on some else or something more (c) assume that you can measure something more/differently

You also need to know how to formulate a rate expression using mass-action kinetics and using Michaelis-Menten kinetics, and to know that the latter has a saturation, and that it kicks in when the saturated substrates approaches the Michaelis-Menten constant K_M , so that the rate never exceeds V_{\max} . You do need to know the basic assumptions underlying an ODE, but you do not need to know how to formulate models encompassing different volumes.

2 Regarding formulation and optimization of the cost function

- You need to know the basic idea for simulating a model: step in the direction of the flow, but do not take too long steps
- You need to know the basic function of a cost function: (a) to give an automatic measure for the agreement between the model and the data, and (b) that it takes the parameters as inputs and returns the cost as output. The cost is calculated by summing the normalized and squared (or normed) residuals weighted by the measurement uncertainty (the cost function might also contain other terms).

- You need to know that the optimization algorithm takes a cost function and a starting guess as input (along with some other optimization settings), and returns an optimized parameter value \hat{p} as output.
- You need to know that local optimization methods only search downwards in the cost function landscape, but that global optimization methods may "escape" from local minima.

3 Regarding statistical tests

You need to know

- the basic idea behind a chi-square test: to test the size of the residuals, and see if they are unrealistically large
- the basic idea behind a correlation test (e.g. the whiteness test): to find out whether the residuals are unrealistically correlated
- some of the benefits of using validation data: e.g., that you know the degrees of freedom in a chi-square test, and that you can detect overfitting (explain overfitting)
- the basic idea behind a likelihood ratio-test: to compare two models
- what happens if a chi-square or correlation or model-comparison test leads to a rejection

4 Regarding core predictions and experimental validation

You need to know

- why it is problematic to simply look at simulations from a single parameter point: because they are usually not uniquely determined, and thus only "beach statements"
- what a beach statement is: a statement of the quality "it might be like this, or it might be in some other way"
- what a core prediction is: a statement of the quality "if the model is true, the following prediction must hold"
- how to obtain core predictions in practice: by finding shared properties among all acceptable parameters
- what might be reasons to perform an experiment, based on a core-prediction analysis: e.g. (a) because you want to validate a model (b) because you want to distinguish between two models (c) because you want to get more information in a poorly determined part of the model