

# Feedback

Q1: Can the conservation laws change the model from the “real” reactions or is it designed to be “close enough”?

A1: The conservation law is based on the ideal (unrealistic) assumption of a closed system. A living cell is an example for an open system, that is, energy AND matter are transferred in and out of the cell. This is necessary to drive the reactions within the cell. However, closed systems are often those used in chemical/biochemical experiments (obtaining quantitative data from a single, living cell is a big challenge). In this case, assuming conservation of concentrations is absolutely valid.

Btw: The use concentrations is already a simplification as the underlying (physical) nature of a cell is discrete – not continuous!

Q2: What is Michaelis-Menten Kinetics used for?

A2: The Michaelis-Menten kinetics is the simplest enzyme kinetic reaction. Many (thousands!) enzymatic reactions occur in cells. For instance, phosphorylation is such a reactions (a kinase catalyses the phosphorylation of a substrate – phosphorylation is an important regulatory mechanism). Michaelis-Menten Kinetics is a quantitative model of enzyme kinetics.

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Q3: What is the benefit of using the quasi-equilibrium assumption?

A3: Using the quasi-steady state assumption is a powerful approach to simplify the mathematical description. A cell is far from equilibrium (unless it is dead). However, in chemical/biochemical experiments (where we often have a closed system) the quasi-equilibrium/quasi-steady-state assumption is a reasonably good approximation provided that the reactions leading to reactive intermediates are faster than others in the overall reaction mechanism.

Q4: Does system biology seek to understand interactions at higher levels of abstraction than at the molecular level?

A4: Although systems biology is lacking a general definition, research in this area is in general based on the underlying cell chemistry. However, the level of “detailedness” can still be different and depends on the focus of research. Some researchers therefore distinguish between molecular, cellular and developmental systems biology. Cell SB includes also modelling of spatial phenomena (diffusion). Developmental SB focuses on the development of organisms from single cells which (necessarily) includes intercellular signalling.

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Q5: Why  $K' = 2E_2 / E_1S$ ?

A5: There was a mistake on the corresponding slide! It must be  $dE_1/dt = -k_2E_1S + 2k_{-2}E_2$ . Then, assuming a steady state ( $dE_1/dt=0$ ) we get  $k_2E_1S = 2k_{-2}E_2$  and hence  $K' = k_2/k_{-2} = 2E_2/E_1S$ .

Q6: Why are there differences in the number of (synonymous) codons that lead to a specific amino acid? E.g. only one codon translates to M. Is it a coincidence that M is also the start amino acid of all synthesised proteins?

A6: Since there are 64 ( $= 4 \times 4 \times 4$ ) possible codons, but only 20 amino acids, there are necessarily many cases in which several codons correspond to the same amino acid. Only two – methionine (M) and tryptophan (T) – have a single codon. According to Lodish et al., GUG is used as the initiator codon in a few bacterial mRNAs, and CUG is occasionally used as an initiator codon for methionine in eukaryotes. But, indeed, synthesis of all polypeptide chains in prokaryotic and eukaryotic cells begins with the amino acid methionine.

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Q7: Did I walk into a Yr12 chemistry refresher course?

A7: It was actually too undemanding for a Yr12 chemistry course. But if you enjoyed it, then you are certainly the right person to do systems biology! More seriously, complex systems are embedded into the real world – the world of phenomena we are interested in, in this case the biochemical world of cells. Since modelling always includes the identification of the system's components and a (formal) description of their relationships, modelling of genetic regulatory systems and pathways as reaction networks requires a biochemical background. In this sense, understand the first lecture as an introduction into the system's "real world" (or what we consider of it to be real).

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Further remarks (attempts to answer questions revealing misunderstandings):

- Transcription/translation:  
Transcription: process generating mRNA from DNA.  
Translation: production of proteins from mRNA.

Both are important processes in reaction networks. However, the relationship between a cell's reaction network and its physiology cannot be reduced to the translational and post-translational reactions. Important regulatory processes occur on the transcriptional level!

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- Enzymes:

Enzymes promote a chemical change in the molecules, called substrates, they bind to, accelerating (catalysing) the reaction that the substrate can undergo. The catalysed reaction rate (the reaction velocity) can be up to  $10^{14}$  times the rate of the uncatalysed reaction! Most of the chemical reactions in a cell are enzymatic. Enzymes often have multiple binding sites, that is, these molecules are able to bind two or more substrates – with the bounded substrates affecting the binding of the next substrate and the rate of the catalysed reaction. The substrate binding region is part of the enzyme's active site.

