What I always wanted to know about kinetic modelling, but …

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Abstract

Nature uses the same processes over and over again, in creative fashion for every new environment. Kinetic modelling is the modelling the processes occurring in nature, NOT applying some fancy mathematical function, but the laws of nature and rules of discipline. The majority of processes in our food are chemical reactions. Chemical kinetics are most appropriate to describe these processes. Process parameters are rather fundamental and specific for that reaction and can be transferred to the same process in different conditions. Creatively design an appropriate reaction mechanism and their differential equations. Try out different mechanisms if necessary (nature is very creative), but NEVER change the resulting mathematics.

Keywords: modelling, kinetics, enzyme activity & amp, denaturation, steady state, resusability

PROLOGUE

Possibilities of developing models based chemical kinetics are highlighted by roaming through the realm of enzymes. Rules, problems and dos and don'ts are indicated during the development of models for different aspects of enzymes. Enzymes are everywhere in living materials. Everyone active in horticulture or agriculture will have to deal with them, understand their importance in different situations. Sometimes dominant, sometimes just there, sometimes negligible. Not only their action upon substrates but also the behaviour of enzymes themselves (stability, denaturation) will be modelled as examples of kinetic modelling.

WHAT ARE KINETICS?

Kinetic modelling is based on the rules and laws of chemical kinetics. The majority of processes occurring in fruit and vegetables are of a chemical nature, with a few contributions of physical processes, e.g., effect temperature (Arrhenius) and mass transport (Fick). And even this last one can be approximated with a reaction mechanism. To make the situation a little bit easier, only a few reaction mechanisms do occur in nature: first order, second order, and occasionally zero order, all three with a distinct difference between substrate and product. All reaction pathways are composed of these three mechanisms in a cascade of reactions. Sometimes the dynamics are important, sometimes the steady state. So, nature is very lazy, using the same processes over and over again, but in endless different combinations and in endless different levels. Modelling nature should not be very difficult, but extremely complex.

WHY MODELLING AT ALL?

Some benefits can be gained by developing models based on processes/mechanisms occurring in nature. They enhance our knowledge on what is going on and how the interactions may be. They represent the modern version of understanding the problem and interpreting of the results. The ultimate goal of modelling (in my view) is to be able to describe and predict the behaviour of any produce grown in any region, during any season, at any climate, weather or storage condition. For that purpose we need models that can be reused in similar conditions with parameter values that can be transferred from one experiment to another. For the time being, this is far out of reach. And looking at the efforts in specialized

literature, it will take still quite some time. Progress is not fast but nevertheless steady.

HOW TO MODEL

Just for clarity and completeness, a quick way to deduce the differential equations form a reaction mechanism. This is the core of mathematical aspects of chemical kinetics.

$$n_a \cdot A + n_b \cdot B \xrightarrow{k} n_c \cdot C + n_d \cdot D \tag{1}$$

For the reagents (A and B) the differential equations is

$$\frac{1}{n_a} \cdot \frac{\partial A}{\partial t} = \frac{1}{n_b} \cdot \frac{\partial B}{\partial t} = -k \cdot A^{n_a} \cdot B^{n_b} \tag{2}$$

For the reaction products (C and D) the differential equations is

$$\frac{1}{n_c} \cdot \frac{\partial C}{\partial t} = \frac{1}{n_d} \cdot \frac{\partial D}{\partial t} = +k \cdot A^{n_a} \cdot B^{n_b} \tag{3}$$

The total sum of n on one side of the reaction mechanism can for all plausible situations never be greater than 2. The total differential for a compound in a multi reaction mechanism is the sum of all differentials of that compound in all of the reactions.

$$\frac{\delta A}{\delta t} = \sum_{n=1}^{N_{react}} \frac{\delta A_n}{\delta t} \tag{4}$$

One of the basic rules/laws of nature is that any reaction repeated in the exactly same conditions will yield exactly the same results. That also applies to chemical reactions. One can learn some practical rules already from this very fundamental statement. When the model developed reflects reality completely or to some degree, the rate constants in that model should be real constants and the same in all possible combinations of concentration/amount of reagents. Temperature strongly affects kinetics. But since temperature for itself can't change concentrations, temperature affects only (and most of the time exclusively) the rate constant.

The simplest relation between T and rate constant is the Arrhenius equation (Equation 5). Eyring is theoretically better/stronger and valid in a larger temperature range, but more difficult to apply and understand. Within the temperature range encountered in pre- and post-harvest horticulture Arrhenius is perfectly applicable.

$$k = k_{ref} \cdot e^{\frac{Ea}{R}\left(\frac{1}{T_{ref}} - \frac{1}{T}\right)} \tag{5}$$

So, if our model delivers rate constants at different temperatures, that do NOT obey Arrhenius' law, the harsh conclusion has to be drawn: our model, our mechanism is either incorrect, or an important part of the system (another process or actor) is neglected.

LET'S START WITH A SIMPLE EXAMPLE

Let's consider the simplest mechanism to start with: an exponential decay, frequently encountered in softening in a large number of fruits: a simple first order reaction:

$$S \xrightarrow{k} P \tag{6}$$

So no matter what the concentration of substrate S is, at the same temperature product P is produced with exactly the same rate constant k. So, when the rate constant in our model delivers different values for different conditions, the logical conclusion is that our model is either incorrect, or an important part of the system (another process or actor) is neglected. We come to that later.

Using the rules of chemical kinetics, reaction mechanisms (Equation 6) can be converted into a set of differential equations.

$$\frac{\delta S}{\delta t} = -k \cdot S \quad , \quad \frac{\delta P}{\delta t} = k \cdot S \tag{7}$$

At constant conditions (mainly T), this set of differential equations (Equation 7) can be solved (using mathematical packages like Maple, Mathematica, Matlab, etc.) into an analytical solution. Using the mass conservation laws, associated with the mechanism, is now and again necessary to reach a practical solution. The analytical solution can be used in data analysis by nonlinear regression procedures. Al statistical packages nowadays contain procedures to estimate parameters in nonlinear systems.

For the simple first order mechanism, the analytical solution is:

$$S = S_0 \cdot \mathrm{e}^{-k \cdot t} \quad , \quad P = S_0 \cdot \left(1 - \mathrm{e}^{-k \cdot t}\right) + P_0 \tag{8}$$

which is the well-known exponential behaviour.

INTERMEZZO 1: NOTATION

Modelling is expressing processes occurring in our product in mathematical terms. So we rely (we really should) strongly on the rules of mathematics. They try (always) to be very exact. So, a compound that changes with time, has a differential with respect to time and should be noted as such. So mathematics requires a notation like S(t) instead of simply S. But then S also depend on temperature (through the rate constant k) and should therefore be noted as S(t,T). When more external variables come into play (RH, P, water activity, pH, etc.) this kind of notation gets very clumsy, hiding the most important information in a model, e.g., its structure. Every time one points to variables, the whole series of reference has to be repeated. Stating once which variable depends on which factor should be preferred.

ALREADY SOMEWHAT MORE COMPLEX

However, real life is never that simple. Usually the substrate does not decrease toward zero but to a finite end value Smin.

One could adapt mathematically the equations (Equation 7 or 8) directly, but that is never a good idea. In more complex mathematical formulations, one is bound to make at least one error. Creative imagination is really asked for in modelling real life processes, but only (preferably) at the level of mechanisms. As long as it is plausible and can be defended, any proposed mechanism is better than a purely empirical relation.

So, let us reflect what this statement means in term of mechanism.

When some of the substrate does not change, even at infinite time, part of the substrate does not react. So we have a part that is active (S_a) and a part that is not (S_{min}).

So, only S_a is changing with S_{min} constant. Taking that into the mechanism:

$$\begin{aligned} &S_a \xrightarrow{k} P \\ &\text{with } S_{\text{min}} = \text{constant and } S_a = S - S\text{min} \end{aligned} \tag{9}$$

delivers the same differential equations as in Equation 7 in Sa, Substituting S_a=S-S_{min} and again integrating the differential equation yields the “final” analytical solution:

$$S = \left(S_0 - S_{\min}\right) \cdot \mathrm{e}^{-k \cdot t} + S_{\min} \;,\; P = \left(S_0 - S_{\min}\right) \cdot \left(1 - \mathrm{e}^{-k \cdot t}\right) + P_0 \qquad (10)$$

Some examples on behaviour of S and P are shown in Figure 1.

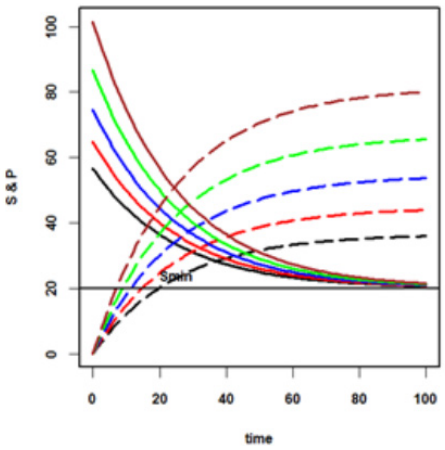

Figure 1. Simulated example for five different instances of a first order mechanism, in decay S (full lines) as in production P (dashed lines) (Equation 8).

INTERMEZZO 2: STATE OF COMPOUNDS

Kinetic modelling relies on chemical kinetics. That is the science of reactions in ideal gas conditions. It is assumed that solutions are close enough to ideal gasses to allow the rules to be applied. A vast majority of reactions in our fruit and vegetable does occur in solutions (inside cells, intercellular moister, etc.). But quite a number of reactions can't be considered to run in solutions (cell wall decay, membrane decay). We should be aware of difficult extensions when developing kinetic models on compounds in a solid state. Applying in these conditions may deliver incorrect solutions, but it does provide anyway (very) fruitful and successful intermediates.

INCLUDING ENZYME ACTIVITY AND DENATURATION

Let's move to a somewhat more difficult system. In (almost) all these chemical reactions in our food, enzymes are involved in one way or another. Enzymes are organic compounds that have the power/capability to catalyse a specific reaction. So for every reaction there is a specific enzyme. A catalyst makes a reaction possible and enhances its speed of conversion. Without being consumed by the reaction. In mechanism terms this can be represented by Equation 11.

$$S + En \xrightarrow{k} P + En \qquad (11)$$

with En the molar concentration of an enzyme.

In differential equations this becomes:

$$\frac{\delta S}{\delta t} = -k \cdot S \cdot En \;,\; \frac{\delta P}{\delta t} = k \cdot S \cdot En \;,\; \frac{\delta En}{\delta t} = 0 \qquad (12)$$

Solving this set of differential equations, and allowing for a distinct final value S_{min} (see above), provides an equation quite similar as Equation 10.

$$S = \left(S_0 - S_{\min}\right) \cdot \mathrm{e}^{-k \cdot En_0 \cdot t} + S_{\min} \qquad (13)$$

In Figure 2 the same examples are show as in Figure 1, but now including the enzyme effects. The only difference is the presence of the enzyme level in the exponent. And that enzyme level poses a major problem. Molar enzyme concentrations of enzymes are almost impossible to assess. What is being assessed is the enzyme activity as the substrate conversion per time unit. When that is filled in in Equation 12, enzyme activity turns out to be:

$$Act_{En} = k \cdot E_n = k\,En_0 \cdot e^{-k_d t} \tag{14}$$

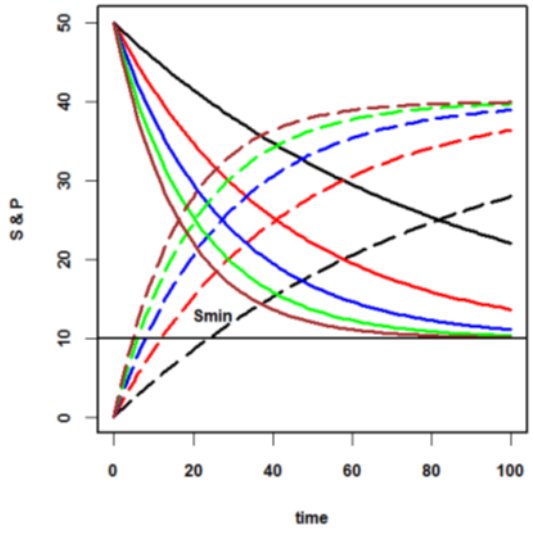

Figure 2. Simulated example for five different instances of a first order mechanism catalysed by an enzyme, in decay S (full lines) as in production P (dashed lines) (Equation 13).

So, the activity of an enzyme is the (molar) concentration En multiplied by its own rate constant. That means that the activity of an enzyme (as usually defined) depends on the temperature (through the rate constant k) at which it is put to work. At ambient temperatures, no big deal, as long as one keeps realizing this. But at higher temperatures, enzymes start to degrade and lose their catalysing capacity.

So, the mechanism becomes:

$$\begin{aligned} S + En &\xrightarrow{k} P + En \\ En &\xrightarrow{k_d} \text{inactive enzyme} \end{aligned} \tag{15}$$

Upon integration, the set of differential equations (not shown) delivers a full scale model for S, P and En.

$$S = S_0 \cdot e^{\left(\frac{-k \cdot En_0 \cdot \left(1+e^{-k_d \cdot t}\right)}{k_d}\right)},\ P = S_0 \cdot \left(1 - e^{\left(\frac{-k \cdot En_0 \cdot \left(1+e^{-k_d \cdot t}\right)}{k_d}\right)}\right) + P_0,\ En = En_0 \cdot e^{-k_d \cdot t} \tag{16}$$

The exponent in the equation for S and P ($\left(1+e^{-k_d \cdot t}\right)/k_d$) turns out to be a very generic structure for destruction/production. The effect of temperature on rate constant and the denaturation of the enzyme is split up in Figure 3. In Figure 4 an example is shown for the enzyme activity as a function of time and temperature. Clearly, the maximal activity of enzymes depends on the time it is allowed to work. Early in the process, the whole of the enzyme is active, later in the process, the enzyme denatures gradually. The effect of denaturing

behaviour can be observed when plants grown (try to) at high temperatures (above 35°C) and during pasteurisation (75°C) of fruit, vegetables, milk and meat.

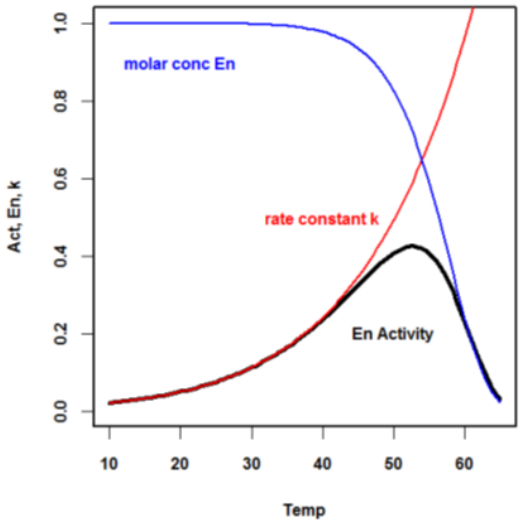

Figure 3. Enzyme activity split up in Temperature effect (rate constant) and molar concentration (En) (Equation 14).

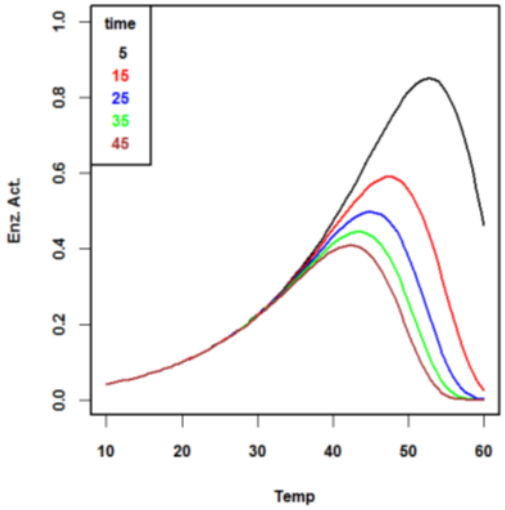

Figure 4. Simulated example for enzyme activity as a function of time and temperature (Equation 14).

INTERMEZZO 3: CONCENTRATION

Dealing with chemical reactions and chemical kinetics, to have the stoechiometry in order all concentrations are expressed as molar concentration. This is for kinetic modelling in horticulture and agriculture rarely done. Only in rather complex mechanisms this could be mandatory. Since all instances of a compound appear (always?) in combination with rate constants, the conversion factor of "normal" concentrations (like g L^{-1}) to molar concentrations are automatically included in the estimated value of the rate constant. Disadvantage is than that the value of the rate constant may/will be different in different experiments.

One more point needs to be mentioned: in chemical kinetics concentrations are usually

indicated by brackets. [S] means then the concentration of compound S. This is for itself a very useful distinction between compound and its concentration. Just like the mathematical notation, however, this kind of notation is becoming very rapidly very annoying. Again defining once that S means the concentration of compound "S" should be sufficient.

ENZYME TURNOVER

In living systems, enzymes are continuously renewed. This turnover is hence a balance between production and removal. The steady state between these two processes determines for a major part the observed activity of an enzyme. The simplest representation is:

$$\xrightarrow{k_f} En \xrightarrow{k_d} \tag{17}$$

where enzyme En is generated out of some always present component (e.g. photo assimilates) and decays into non active forms.

When not in steady state the activity changes according (integrating the set of differential equations):

$$En = \frac{k_f}{k_d} - \frac{\left(k_f - k_d \cdot En_0\right)}{k_d} \cdot e^{-k_d \cdot t} \tag{18}$$

otherwise the steady state is just the ratio of both reaction rate constants: $En = k_f/k_d$. The behaviour is shown in Figure 5.

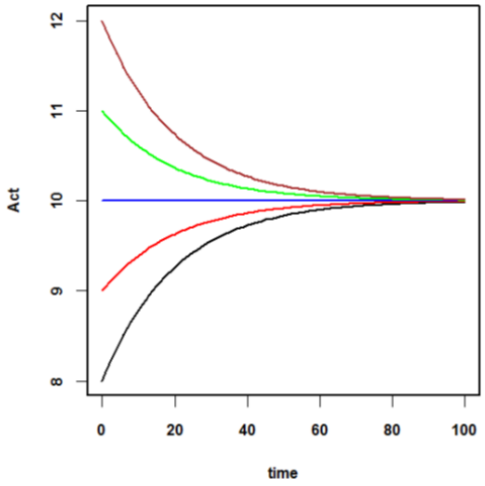

Figure 5. Enzyme turnover at different starting levels, all going to the steady state value (Equation 20).

Since both rate constants (kf and kd) depend on temperature, most probably the steady state value also depends on temperature.

INTERMEZZO 4: STEADY STATE

The definition of steady state is very simple and very clear: the variable does not change in time. Mathematically: the differential with respect to time is zero. That can only be the case when that state variable appears in two reactions, one decreasing in level, the other increasing in level. That is easy to check in the set of differential equations. The problem, however, is when is it allowed in model development to assume a study state on one or more state variables. In other words, how do we check in the available data whether a steady state approach is appropriate? Theoretical considerations may provide a clue, but no golden rule

available! One has to try out every time again whether it works properly.

ISOENZYMES

Very frequently (almost always) isoenzymes are present that have the same or a very similar action upon a substrate. These isoenzymes may have the same properties, very similar ones or sometimes completely different. That means that the temperature dependence may be quite different.

A plausible mechanism is shown in Equation 19.

$$\begin{aligned} S + En_1 &\xrightarrow{ks_1} P + En_1 \\ S + En_2 &\xrightarrow{ks_2} P + En_2 \end{aligned} \tag{19}$$

The analytical solution is quite similar as for the single enzyme working on a substrate (Equation 13), but now with the activity of both enzymes in the exponent:

$$S = \left(S_0 - S_{\min}\right) \cdot \mathrm{e}^{-\left(ks1 \cdot En_{1,0} + ks_2 \cdot En_{2,0}\right) \cdot t} + S_{\min} \tag{20}$$

It looks tempting to express the combined activities of both isoenzymes into one parameter (total activity). That is however not commendable, since both versions can/will have a different sensitivity to temperature and change with temperature not entirely according to the Arrhenius equation.

Two different enzymes producing the same product out of the same substrate is not very likely. Much more plausible the two different enzymes produce a different product. So, the mechanism is adapted:

$$\begin{aligned} S + En_1 &\xrightarrow{ks_1} P_1 + En_1 \\ S + En_2 &\xrightarrow{ks_2} P_2 + En_2 \end{aligned} \tag{21}$$

The differential equations (not shown) are to too different. The analytical solutions are very different. The properties of one enzyme affect the effect of the other.

$$\begin{aligned} P_1 &= P_{10} + \frac{S_0 \cdot \left(1\text{-}\mathrm{e}^{-\left(ks_1 \cdot En_{1,0} + ks_2 \cdot En_{2,0}\right) \cdot t}\right) \cdot ks_1 \cdot \mathrm{En}_{10}}{ks_1 \cdot En_{1,0} + ks_2 \cdot En_{2,0}} \\ P_2 &= P_{20} + \frac{S_0 \cdot \left(1\text{-}\mathrm{e}^{-\left(ks_1 \cdot En_{1,0} + ks_2 \cdot En_{2,0}\right) \cdot t}\right) \cdot ks_2 \cdot \mathrm{En}_{20}}{ks_1 \cdot En_{1,0} + ks_2 \cdot En_{2,0}} \end{aligned} \tag{22}$$

In Figure 6 an example is shown for a system of two enzymes working on the same substrate but producing a different product. The faster the first enzyme works, the less the effect of the second one. This examples shows that it is essential to start afresh from a new mechanism every time, and not rely on previously developed mathematical equations.

INTERMEZZO 5: GENES & MODELLING

Information coming from the area of genetics is highly interesting. Evidence on the very complex action of genes expressed during development is strong and convincing. Genes that govern or control some developmental processes constantly are discovered. However, the actions of genes are for the major part considered on a qualitative level, while kinetic modelling considers processes on a quantitative level. That genes affect developmental processes is evident, but how exactly they affect the mechanisms of our models is still unclear.

For kinetic modellers, some mechanistic details how these genes induce the production of proteins is of prime importance. How does this production of proteins take place? What secondary compounds are needed? Energy (ATP), sugars (photo assimilates), other enzymes? Are these proteins themselves enzymes that affect the next reaction in a cascade. What is desperately needed to advance both fields, modelling as well as genetics, is a fruitful, logical and fundamental viewpoint how to connect both interesting and innovative techniques in biology, horticulture and agriculture.

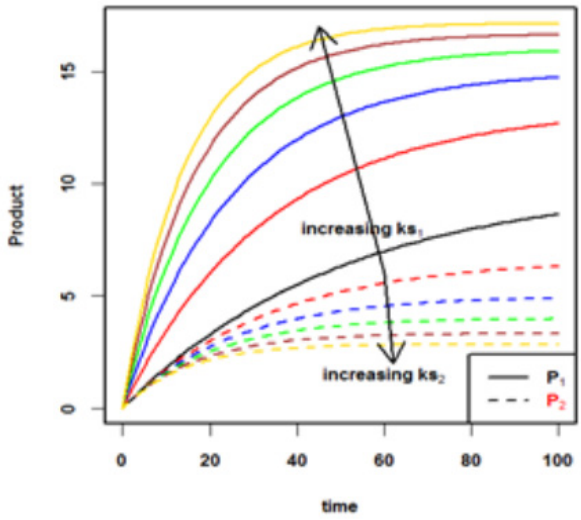

Figure 6. The effect of rate constant of the first enzyme of the effect of the second enzyme, bit working on the same substrate but producing a different product.

ENZYME ACTION IN STEADY STATE

The models developed in previous section constitute highly simplified versions of what is (presumably) going on with enzymatic catalysis. Enzymes do not directly catalyse the conversion reaction, but over an intermediate step, first forming an active complex in an equilibrium reaction. The active complex formed is then broken down:

$$S + En \underset{k_b}{\overset{k_f}{\Leftrightarrow}} AC$$
$$AC \xrightarrow{k_p} P + En \qquad (23)$$

Assuming a steady state on the active complex (AC), i.e., the concentration of AC does not change during the reaction, the differential equations become:

$$\frac{\delta S}{\delta t} = -\frac{k_p \cdot k_f \cdot S \cdot (AC_0 + En_0)}{k_p + k_b + k_f \cdot S} \qquad \frac{\delta P}{\delta t} = \frac{k_p \cdot k_f \cdot S \cdot (AC_0 + En_0)}{k_p + k_b + k_f \cdot S} \qquad (24)$$

This set of differential equations cannot be solved into an analytical solution. It is too complex. Simulations (and data analysis) has to make use of numeric integration. One example is shown in Figure 7. The linear part of the curve, when the concentration of substrate S is abundantly present, relative to the concentration of the enzyme, is usually use to determine the activity of that enzyme (see previous section). This is the so-called Michaelis-Menten kinetics. Very powerful. So powerful that modellers tend to use Equation 24 for every enzyme catalysed reaction. And that may often be wrong. Michaelis-Menten kinetic is a way to deduce

the set of differential equations. This set should be developed for each and every system anew. When one (or more) additional compound is active in the mechanism the results are/may be completely different.

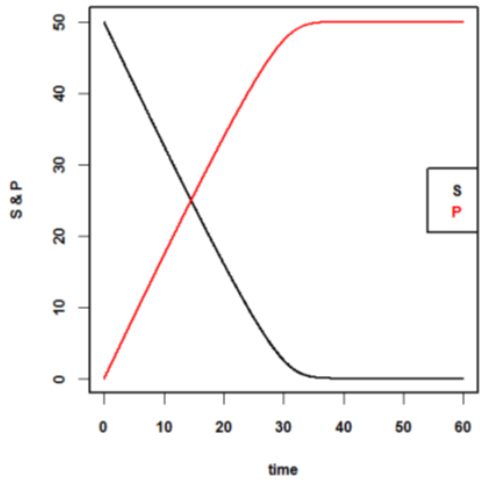

Figure 7. Simulated example for enzyme activity as a function of time by numerical integration (Equation 24) according to Michaelis-Menten kinetics.

INTERMEZZO 6: COMBINING AND TRANSFORMATION

We all like to have some structure and simplicity in our world. It is therefore tempting to combine parameters or variables wherever possible. To make it simpler. Even Ockham (13th -14th century) stated Ockham's razor: in explaining a thing no more assumptions should be made than are necessary. This is translated into make things as simple as possible. But Einstein added to that: but not simpler. Both statements really cover the whole situation. Combining variables into one symbol (activity) or transforming variables (pH, pK) can be very useful, as long as one keeps realizing the nature of the underlying variables (see section on denaturation). Statisticians use Ockham's razor to minimise the number of parameters in a model. Kinetic modellers should use mechanisms as simple as possible, and then stick to the rules of chemical kinetics and mathematics all the way. Until it hurts. And it keeps hurting even after 30 years of developing models.

ENZYME ACTIVITY AND pH

pH has a marked effect on the activity of (some) enzymes. For day to day application, the notion pH is a very useful and easy concept. For modelling purposes pH is really not suited at all. It is merely a man-made convention to make the range of change more common. In other words, the variable pH does not exist in real world, but it is a short way of indicating the concentrations of H^+ and OH^-. And in kinetic modelling, one has to work with concentrations, not the logarithm of these.

The effect of acid H^+ ions or basic OH^- ions on the activity of an enzyme is probably caused by a change in stereo configuration at or in the neighbourhood of the active sites. As in almost all protonation reactions, these reactions will occur very fast. The different configurations are instantaneously in steady state. The protonated and hydroxylated enzymes are assumed to be completely inactive or at least less active. This can be represented by the following mechanisms:

$$\begin{aligned} En + H^+ &\overset{K_{EH}}{\leftrightarrow} EnH^+ \\ En + OH^- &\overset{K_{EOH}}{\leftrightarrow} EnOH^- \end{aligned} \qquad (25)$$

where K_{EH} and K_{EOH} are the equilibrium constants of the reactions ($k_{backward}/k_{forward}$).

The water dissociation is defined as usual as:

$$K_w = H^+ \cdot OH^- \cong 10^{-14} \quad and \quad OH^- = \frac{K_w}{H^+} \tag{26}$$

The amount of EnH^+ and $EnOH^-$ can now be expressed in terms of actual amount of active enzyme and pH by:

$$EnOH^- = \frac{K_w \cdot En}{K_{EOH} \cdot H^+} \quad , \quad EnH^+ = \frac{En \cdot H^+}{K_{EH}} \tag{27}$$

The total amount of enzyme in any configuration has to remain constant:

$$En_{tot} = EnH^+ + EnOH^- + En \tag{28}$$

Combining Equations 25 and 26, and solving for En, an expression is obtained for the active enzyme at any H^+ concentration (or pH):

$$En = \frac{En_{tot}}{1 + \frac{H^+}{K_{EH}} + \frac{K_w}{K_{EOH}} \cdot \frac{1}{H^+}} \tag{29}$$

Again this model for the amount of available active enzyme configuration can be converted into an apparent activity (Act) as for the temperature model (Equation 14). This results in:

$$Act = \frac{k \cdot En_{tot}}{1 + \frac{H^+}{K_{EH}} + \frac{K_w}{K_{EOH}} \cdot \frac{1}{H^+}} \tag{30}$$

Again, in this equation k and En_{tot} only appear in combination with each other. It is therefore impossible to estimate both variables at the same time. Both parameters are therefore combined in a new parameter called Act_{tot}. Combining with Equation 14 for the temperature denaturation, results in the final equation:

$$Act = \frac{Act_{tot} \cdot e^{-kd \cdot t}}{1 + \frac{H^+}{K_{EH}} + \frac{K_w}{K_{EOH}} \cdot \frac{1}{H^+}} \tag{31}$$

The behaviour of this already complex model is elucidated in Figure 8. It describes the activity of an enzyme over the complete range of pH, i.e., a molar concentration ranging over a factor of 1E14 (8 left and centre). The optimal pH for a specific enzyme can be obtained by solving the differential of Equation 30 with respect ot H^+, putting it equal to zero and solve it for H^+. Expressing the results in pX notation (like pH: -log10[x]), one obtains:

$$pH_{opt} = \frac{pK_w + pK_{EH} + pK_{EOH}}{2} \tag{32}$$

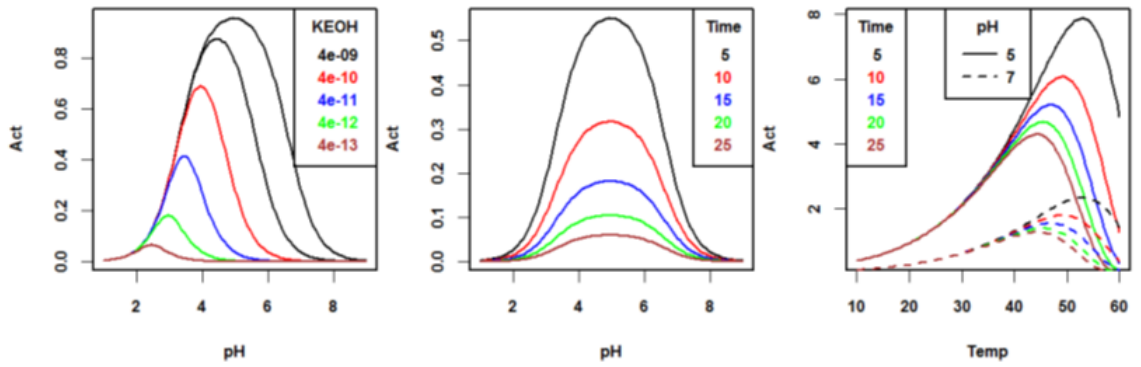

Figure 8. Simulated examples for effect of dissociation constant (left), pH (centre) and temperature (right) on the activity of an arbitrary (denaturing) enzyme (Equation 29).

INTERMEZZO 7: REUSABILITY AND TRANSFERABILITY

Developing process oriented models, especially kinetic models, almost automatically provides the benefit of a modular structure. Not in the usual meaning (reusing formulations), but by reusing processes and deducing the formulation anew for a new situation/condition. What is/should be (strictly) reusable however are estimated kinetic parameter (rate constants) values for the same fundamental process in another condition (different values of state variables). Unlike empirical models, only based on gathered data, kinetic models ascertain transferability of parameters over experimental setups. As long as the occurring processes are the same, data from different experiments/growing regions/harvest seasons (etc.) can be combined and analysed together. Even in completely different experimental setups, and with different measuring techniques. Hugely increasing the reliability of the analyses if all assumptions are correct. If not, the results of the analysis will clearly indicate that with a very low level of explained part.

EPILOGUE

The above explained models only concern enzymes, their behaviour and their action. And there are many more issues, not only in enzymology, needing some attention. That leaves out quite a large number of interesting problems and approaches.

Especially some rules on when to apply steady state and when to apply active complexes would be worthwhile. How can we see in measured data when to look for these? How can we see whether a model is too simple or can further be simplified? How can we see what constitutes an appropriate mechanism for this process in this data set? All these questions have to be answered on the spot, virtually without any guidance. But exactly that fact makes kinetic modelling so powerful: we can and have to include all our knowledge and experience gathered over the years on the product and the processes under consideration. A central question at the start of every model development should therefore always be: what do we know about the process in this product under these conditions and circumstances? This we call “problem decomposition”, a technique widely used/known in ICT.

Another crucial point taken from this overview on kinetic modelling is: do not use previously deduced equations, but deduce the mathematics always anew. Just to avoid structural errors you will later on regret very deeply!!

What is needed above all, a huge creativity in designing mechanisms.

And enjoy doing so!

References

These references comprise an anthology of (mostly self-written) papers, all related to action and properties of enzymes. The more generic ones are grouped upfront, followed by dedicated ones.

Generic papers

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