Comparison of approximate kinetics for unireactant enzymes: Michaelis-Menten against the equivalent server

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Abstract. Mathematical models are widely used to create complex biochemical models. Model reduction in order to limit the complexity of a system is an important topic in the analysis of the model. A way to lower the complexity is to identify simple and recurrent sets of reactions and to substitute them with one or more reactions in such a way that the important properties are preserved but the analysis is easier.
In this paper we consider the typical recurrent reaction scheme $E + S \rightleftharpoons ES \longrightarrow E + P$ which describes the mechanism that an enzyme, E, binds a substrate, S, and the resulting substrate-bound enzyme, ES, gives rise to the generation of the product, P. If the initial quantities and the reaction rates are known, the temporal behaviour of all the quantities involved in the above reactions can be described exactly by a set of differential equations. It is often the case however that, as not all necessary information is available, only approximate analysis can be carried out. The most well-known approximate approach for the enzyme mechanism is provided by the kinetics of Michaelis-Menten. We propose, based on the concept of the flow-equivalent server which is used in Petri nets to model reduction, an alternative approximate kinetics for the analysis of enzymatic reactions. We evaluate the goodness of the proposed approximation with respect to both the exact analysis and the approximate kinetics of Michaelis and Menten. We show that the proposed new approximate kinetics can be used and gives satisfactory approximation not only in the standard deterministic setting but also in the case when the behaviour is modeled by a stochastic process.

1 Introduction

Mathematical models are widely used to describe biological pathways because, as it is phrased in [1], they "offer great advantages for integrating and evaluating information, generating prediction and focusing experimental directions". In the last few years, high-throughput techniques have increased steadily, leading to

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the production of a huge volume of data used to derive the complex texture behind the biological/biochemical mechanisms, and creating in this way the structure needed for mathematical modelling. Indeed, many models based on the combination and the integration of various elements in order to investigate their relationships and behaviour have been devised which become more complex with the growth of available data. The complexity is reflected in the number of dynamic state variables and parameters, as well as in the form of the kinetic rate expressions.

Such complexity leads to difficulties both from the point of view of defining the model as the parametrisation becomes unfeasible and for what concerns the analysis of the model. It is often the case hence that in order to have a model which is feasilble for the analysis simplifications must be performed.

In this paper we focus our attention on the simplified, approximate treatment of a set of reactions that very often appears as building blocks of complex models. We consider the reactions

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} ES \xrightarrow{k_2} E + P \tag{1}$$

describing that the enzyme, E, attaches reversibly to the substrate, S, forming the substrate-bound enzyme ES which gives rise then to the product P releasing the enzyme. This and similar enzymatic reactions are widely studied in biology. The most common approximate approach to deal with them is provided by the Michaelis-Menten (MM) kinetics (called also Michaelis-Menten-Henri kinetics) which, based on quasi-steady-state assumptions, connects the speed of producing P directly to the concentration of E and P, omitting the explicit modeling of ES.

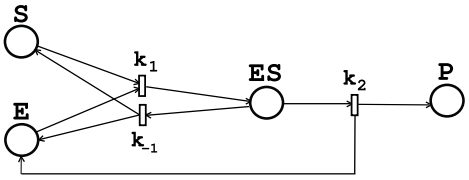

Fig. 1. Petri net representation of the reactions given in (1)

System of enzymatic reactions can be described by Petri nets [2] (Figure 1 shows the Petri net corresponding to the reactions given in (1)) and then analysed by methods developed for this formalism. We propose for the reactions in (1) an alternative to the approximate Michaelis-Menten kinetics. This new approximate kinetics is based on a concept widely used in the analysis of Petri nets and models described by other formalisms like queueing networks and process algebras. This concept is called the flow equivalent server [3]. The application of this concept, similarly to the Michaelis-Menten kinetics, leads to a simplified set

of reactions in which the intermediate complex ES is not modeled explicitly. The difference is, however, that, since the application of the flow equivalent server (FES) is based on assumptions that are different and less strict than those used by the Michaelis-Menten kinetics, the resulting approximation is more robust.

The concept of flow equivalent server has already been used in [4] where a complex signal transduction model was considered. In that paper we have shown that this concept can be applied not only to the small set of reactions given in (1) but also to bigger submodels. This leads to a simplified model which has less parameters and whose analysis is not as heavy as that of the complete one. For the model presented in [4] it was shown that the quantitative temporal behaviour of the simplified model coincides satisfactorily with that of the complete model and that important qualitative properties are maintained as well. In this paper our goal is to study in detail the goodness of the FES based approximation for the reactions in (1) and to compare it to the widely-used approximate kinetics of Michaelis, Menten and Henri.

The paper is organised as follows. Section 2 provides the necessary background, Section 3 describes the concept of the flow equivalent server and Section 4 presents the results of the comparison between the approximation approaches. We conclude with a discussion and an outlook on future works in Section 5.

2 Background

In 1901 Henri [5] proposed a partly reversible reaction scheme to describe the enzymatic process. According to this scheme the enzyme E and the substrate S form, through a reversible reaction, the enzyme-substrate complex ES. This complex can then give rise to the product P through an irreversible reaction during which the enzyme is freed and can bind again to other molecules of the substrate. This scheme is summarised in (1) where k_1 is the rate of the binding of E and S, k_{-1} is the rate of the unbinding of ES into E and S and k_2 is the rate at which ES decays to the product P freeing the enzyme E.

There are two typical approaches to associate a quantitative temporal behaviour to the reactions in (1). The first results in a deterministic representation while the other in a stochastic one. In the following we give a brief idea of both approaches. For a detailed description see, for example, [6, 7].

The deterministic approach describes the temporal behaviour of a reaction with a set of ordinary differential equations (ODE). For the reactions in (1) we have

$$\begin{aligned}
\frac{d[E]}{dt} &= -k_1[E][S] + (k_{-1} + k_2)[ES] \qquad (2)\\
\frac{d[S]}{dt} &= -k_1[E][S] + k_{-1}[ES]\\
\frac{d[ES]}{dt} &= k_1[E][S] - (k_{-1} + k_2)[ES]\\
\frac{d[P]}{dt} &= k_2[ES]
\end{aligned}$$

where $[X]$ is the concentration of molecule X at time t. These equations state that the rate at which the concentration of a given molecule changes equals the difference between the rate at which it is formed and the rate at which it is utilised. The four equations can be solved numerically to yield the concentration of E, S, ES and P at any time t if both the initial concentration levels ($[S]_0$, $[E]_0$, $[ES]_0$, $[P]_0$) and the reaction rates (k_1, k_{-1}, k_2) are known. In the deterministic approach the concentrations of the molecules are described by continuous quantities.

In the stochastic approach a continuous time Markov chain (CTMC) is used to describe the process. Each state of the chain is described by a vector of integers in which the entries give the quantities of the molecules, which, accordingly, assume discrete values. These discrete values are resulting either directly from molecule count or from discretization of continuous values. Reactions are modeled by transitions between the states. For example, from state $|x_1, x_2, x_3, x_4|$ where x_1, x_2, x_3 and x_4 are the quantities of the molecules E, S, ES and P, respectively, there is a transition to state $|x_1 - 1, x_2 - 1, x_3 + 1, x_4|$ with rate $k_1 x_1 x_2$ which corresponds to the binding of one molecule E with one molecule S to form one molecule of ES. It is easy to see that even for small models the corresponding CTMC can have a huge state space whose transition rate structure is non-homogeneous. Exact analytical treatment of these chains is often unfeasible and in most cases simulation is the only method that can be used for their analysis.

2.1 Michaelis-Menten approximate kinetics

Under some assumptions, the temporal, quantitative dynamics of the mechanism described by the reactions in (1) can be summarised as follows. Initially we have a certain amount of substrate, denoted by $[S]_0$, and enzyme, denoted by $[E]_0$, and no complex ES ($[ES]_0 = 0$). Assuming that k_2 is significantly smaller than k_1 and k_{-1}, a brief transient period occurs during which the amount of the complex ES quickly increases up to a "plateau" level where it remains stable for a long period of time. As the ratio of $[S]_0/[E]_0$ increases, the time needed to reach the condition $d[ES]/dt \approx 0$ decreases and the period during which $d[ES]/dt \approx 0$ increases. In this period we have approximately

$$\frac{d[ES]}{dt} = k_1[E][S] - [ES](k_{-1} + k_2) = 0$$

from which, considering that the total amount of enzyme is conserved, i.e. $[E] + [ES] = [E]_0$, the quantity of ES can be expressed as

$$[ES] = \frac{[E]_0[S]}{\frac{k_{-1}+k_2}{k_1} + [S]} = \frac{[E]_0[S]}{k_M + [S]} \tag{3}$$

where the term $k_M = \frac{k_{-1}+k_2}{k_1}$ is called the Michaelis-Menten constant. Applying (3), the speed of the production of P can be approximated by

$$v_{MM} = \frac{k_2[E]_0[S]}{[S] + k_M} \tag{4}$$

Accordingly, after the "plateau" level of ES is reached, the kinetic parameters k_1, k_{-1} and k_2 together with $[S]$ and the initial total quantity of the enzyme, $[E]_0$, determine the overall rate of the production of P.

Applying the approximate kinetics of Michaelis and Menten, the differential equations describing the reactions become

$$\begin{aligned} \frac{d[E]}{dt} &= 0 \\ \frac{d[S]}{dt} &= -\frac{k_2[E][S]}{[S]+k_M} \\ \frac{d[P]}{dt} &= \frac{k_2[E][S]}{[S]+k_M} \end{aligned} \tag{5}$$

3 Approximate kinetics by flow equivalent server

In this section we derive an alternative approximate kinetics for the analysis of enzymatic reactions, based on the concept of the flow equivalent server. This technique was originally proposed in the context of the steady-state solution of queueing networks [3, 8, 9] and can be adapted to our purposes with a proper interpretation of the assumptions on which it is based. The idea behind this concept is to consider the reactions given in (1) as a fragment of a large biological system in which substrate S is produced by an "up-stream" portion of the system and product P is used "down-stream" within the same system. The goal of the flow equivalent method is to consider the flow of moles that move from the substrate to the product, in the presence of an enzyme that catalyse this phenomenon, and to evaluate its intensity in order to define the overall speed of a "composite" reaction that captures this situation in an abstract manner.

Figure 2 depicts the Petri net corresponding to the reactions of (1) organised in order to make explicit the relationship between the substrate S and the product P, via the enzyme E, enclosing in a dashed box the elements of the system whose dynamics we want to mimic with the composite transition. This

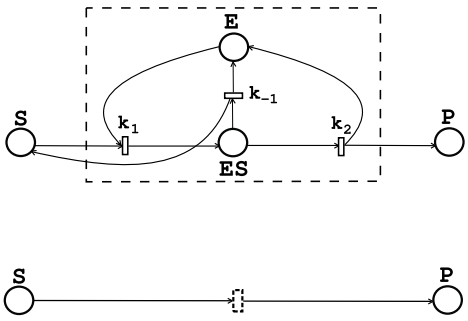

Fig. 2. Petri net of the reactions in (1) organised for computation of the flow equivalent-transition (above) and its approximation (below)

picture makes evident the fact that the speed of the composite transition must depend not only on the speeds of the transitions included in the box but also on the quantities present in the box, namely, the total amount of enzyme. Assuming to know the kinetic constants of the reactions inside the box and the quantity of the enzyme, the speed of the composite transition also depends on the amount $[S]$ that participates in the reactions and that may change during the evolution of the whole system. Following this point of view, it is possible to conceive a characterisation of the speed of the composite transition that is conditioned on the quantity of S. The flow equivalent approach accounts for this observation by computing the intensity of the flow of moles that reaches place P assuming that the total amount of S remains constant. Technically, this is obtained by short-circuiting the output and input places of the sub-net (introducing an immediate transition [10] that connects place P with place S) and by computing the throughput along the short-circuit which will be conditioned on the initial amount of S and that will thus be computed for all the possible values of S. In general, this amounts to the construction of a table that looks like that depicted in Figure 3, where S_1, S_2, ..., S_n represent different values of the amount of substrate S for which the speeds of the composite reaction $v_{FES}(S_1)$, $v_{FES}(S_2)$, ..., $v_{FES}(S_n)$ are computed, given that k_1, k_{-1}, k_2, and $\#E$ are assumed to be the values of the kinetics constant of the reactions in the box and of the amount of enzyme E.

In practice, this corresponds to the construction and to the (steady state) solution of the continuous time Markov chain (CTMC) that corresponds to the sub-model in isolation. Providing the speed of the composite transition in the tabular form highlighted by Figure 3 is convenient for cases where the domain of the function is "small", but may be impractical in many common situations. Despite the computational complexity of the approach, we must notice that the equilibrium assumption of the flow equivalent method is used only to obtain an approximate characterisation of the throughput for different sets of initial conditions and does not mean that the equivalent speed can only be used for steady state analysis.

The concept of flow equivalent server described above is used traditionally in a stochastic setting. However, it can be applied in a deterministic setting as well using arguments that are summarized by the following points. The complexity of the approach in the stochastic setting becomes prohibitive when the amount of the substrate S becomes very large. On the other hand, this is the case in

Given $k_1, k_{-1}, k_2,$ and $\#E$	
S_1	$v_{FES}(S_1)$
S_2	$v_{FES}(S_2)$
$\cdots$	$\cdots$
S_n	$v_{FES}(S_n)$

Fig. 3. Flow Equivalent Server characterisation

which the stochastic (or at least the average) behaviour of the model is conveniently captured by a set of ODE, i.e., by a deterministic model. Moreover, in the case of our model, the equilibrium solution of the set of differential equations corresponding to the short-circuited model is simple enough to obtain an analytic expression for the speed of the composite transition as it is described in the following.

We assume that the initial condition is $[E]_0 = M_1$, $[S]_0 = M_2$, $[ES]_0 = 0$, and $[P]_0 = 0$. We will denote the steady state measures of the compounds by $[E], [S], [ES]$ and $[P]$. In the short-circuited version of the reactions given in (1), moles transformed in P are immediately moved back to S and consequently its steady state measure is zero (i.e., $[P] = 0$). The steady state measures of the other compounds can be determined by considering

– the fact that in steady state the rate of change of the quantities of the different compounds is zero, i.e., we have

$$\begin{aligned} \frac{d[E](t)}{dt} &= 0 = -k_1[E][S] + k_{-1}[ES] + k_2[ES] \\ \frac{d[S](t)}{dt} &= 0 = -k_1[E][S] + k_{-1}[ES] + k_2[ES] \\ \frac{d[ES](t)}{dt} &= 0 = +k_1[E][S] - k_{-1}[ES] - k_2[ES] \end{aligned} \tag{6}$$

which are three dependent equations;

– and the following equations expressing conservation of mass

$$[E] + [ES] = M_1, \quad [S] + [ES] = M_2 \tag{7}$$

In (6) and (7) we have three independent equations for three unknowns. There are two solutions but only one of them guarantees positivity of the unknowns. The speed of producing P is given by the steady state quantity of ES multiplied by k_2. This speed is

$$v_{FES} = \frac{k_2\left([E] + [S] + k_M - \sqrt{([E] - [S])^2 + 2k_M([E] + [S]) + k_M^2}\right)}{2} \tag{8}$$

Accordingly, the set of ordinary differential equations describing the reactions given in (1) becomes

$$\begin{aligned} \frac{d[E]}{dt} &= 0 \\ \frac{d[S]}{dt} &= -\frac{k_2\left([E] + [S] + k_M - \sqrt{([E] - [S])^2 + 2k_M([E] + [S]) + k_M^2}\right)}{2} \\ \frac{d[P]}{dt} &= \frac{k_2\left([E] + [S] + k_M - \sqrt{([E] - [S])^2 + 2k_M([E] + [S]) + k_M^2}\right)}{2} \end{aligned} \tag{9}$$

which explicitly reflects the assumption of the conservation of E and the observation that substrate S is transformed into product P.

4 Numerical illustration

In this section, we first compare in Section 4.1 the MM and FES approximate kinetics from the point of view of the speed they assign to the production of P as function of the reaction rates (k_1, k_{-1}, k_2) and the concentration of the enzyme and the substrate $([E], [S])$. Subsequently, in Sections 4.2 and 4.3 we compare the quantitative behaviour of the approximations to that of the full model in the deterministic and in the stochastic setting, respectively.

It is easy to check that as the quantity of the substrate tends to infinity the two approximate kinetics lead to the the same speed of production. In both cases for the maximum speed of production we have

$$v_{\max} = \lim_{[S]\to\infty} v_{MM} = \lim_{[S]\to\infty} v_{FES} = k_2[E] \tag{10}$$

Another situation in which the two approximate kinetics show perfect correspondence is when the quantity of the enzyme is very low. This can be shown formally by observing that

$$\lim_{[E]\to 0} \frac{v_{MM}}{v_{FES}} = 1 \tag{11}$$

4.1 Production speeds

A typical way of illustrating the approximate Michaelis-Menten kinetics is to plot the production speed against the quantity of the substrate. Figure 4 gives such illustrations comparing the speeds given by the two approximate kinetics. Reaction rate k_2 is either 0.1, 1 or 10 and reaction rates k_1 and k_{-1} are varied in order to cover different situations for what concerns the ratio k_1/k_{-1}. Two different values of $[E]$ are considered. The limit behaviours expressed by (10) and (11) can be easily verified in the figures. On the left sides of the figure it can be observed that for small values of $[E]$ the two approximations are almost identical for all considered values of the reaction rates, thus in agreement with the trend conveyed by (11). It can also be seen that for larger values of $[E]$ the two approximations are rather different and the difference is somewhat increasing as k_2 increases, and becomes more significant for higher values of k_1/k_{-1}. In all cases the curves become closer to each other when the amount of $[S]$ increases.

4.2 Deterministic setting

In this section we compare the different kinetics in the deterministic setting. Once the initial quantities and the reaction rates are defined, the systems of differential equations given in (2),(5) and (9) can be numerically integrated and this provides the temporal behaviour of the involved quantities, used as references for the comparisons.

For the first experiments we choose such parameters with which the two approximate kinetics result in different speeds of production. Based on Figure 4 this is achieved whenever the quantity of the enzyme is comparable to the quantity

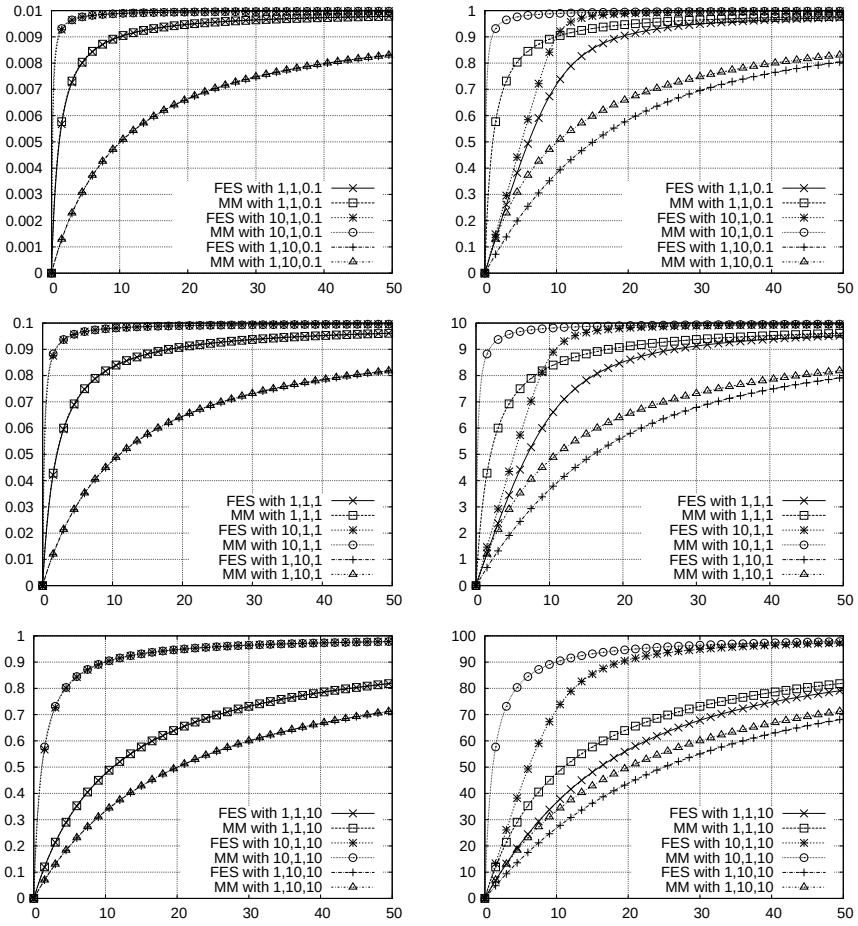

Fig. 4. Production speed as function of substrate quantity with $[E] = 0.1$ for the figures on the left side and with $[E] = 10$ on the right side; reaction rates are given in the legend in order k_1, k_{-1} and k_2

of the substrate. Accordingly, we set $[E]_0 = [S]_0 = 10$. For the full model $[ES]_0$ needs to be set too, and we choose $[ES]_0 = 0$. This choice does not help the approximations. They assume that the total enzyme concentration $[E]_0 + [ES]_0$ is immediately distributed between $[E]$ and $[ES]$, thus making possible an immediate (consistent) production of P. On the contrary, in the full model the production of $[ES]$ takes time and thus the speed of the production of P must start from 0, growing to a high value only later. Figures 5 and 6 depict the quantity of the product and the speed of its production as functions of time for two different sets of reaction rates. In both figures the kinetics based on flow equivalence provides precise approximation of the production of P. The Michaelis-Menten

kinetics instead fails to follow the full model, but this is not surprising as the derivation of this kinetics assumes small amount of enzymes. It can also be seen that high values of k_1/k_{-1} (Figure 6) lead to worst approximation in case of Michaelis-Menten kinetics. On the right hand side of the figures one can observe that for the full model the speed of producing P is 0 at the beginning and then it increases fast to the speed foreseen by the FES approximation.

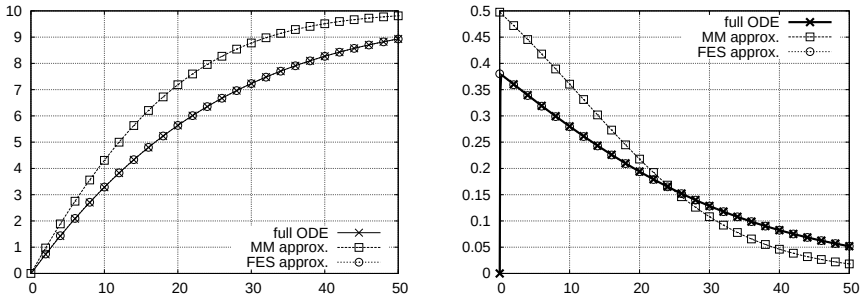

Fig. 5. Quantity of product (left) and speed of production (right) as function of time with $k_1 = 1$, $k_{-1} = 10$, $k_2 = 0.1$, $[E] = 10$ and initial quantity of substrate equals 10

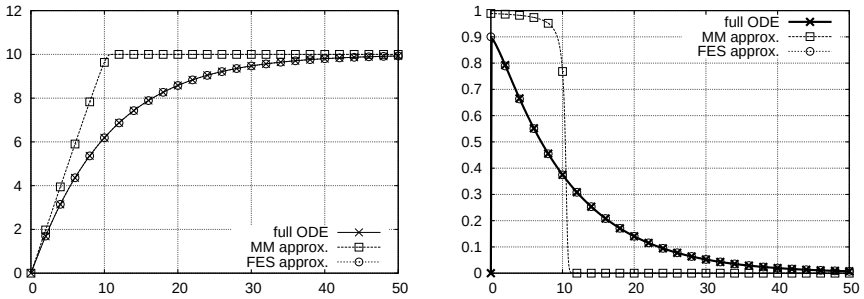

Fig. 6. Quantity of product (left) and speed of production (right) as function of time with $k_1 = 10$, $k_{-1} = 1$, $k_2 = 0.1$, $[E] = 10$ and initial quantity of substrate equals 10

A second set of experiments is illustrated in Figures 7 and 8. We choose sets of parameters with which the speed of production of the MM and FES approximations are similar. In these cases both approximations are close to the reference behaviour. Still, it can be seen that for high values of k_1/k_{-1} (Figure 8) the approximation provided by the Michaelis-Menten kinetics is slightly less precise.

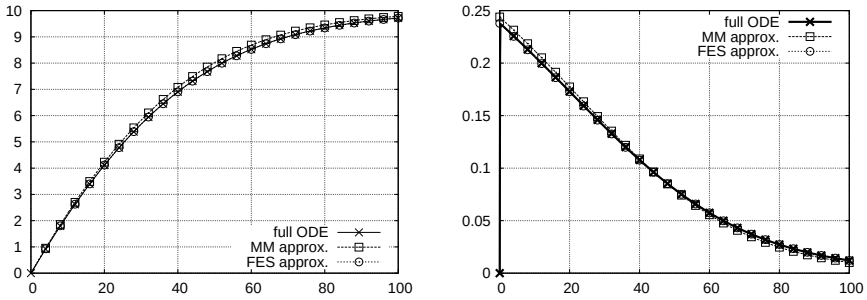

Fig. 7. Quantity of product (left) and speed of production (right) as function of time with $k_1 = 1$, $k_{-1} = 10$, $k_2 = 0.5$, $[E] = 1$ and initial quantity of substrate equals 10

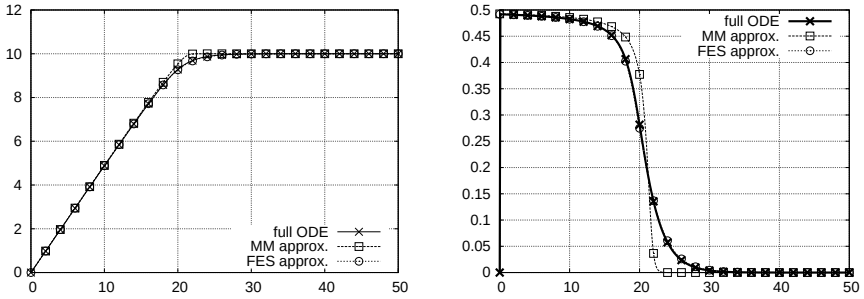

Fig. 8. Quantity of product (left) and speed of production (right) as function of time with $k_1 = 10$, $k_{-1} = 1$, $k_2 = 0.5$, $[E] = 1$ and initial quantity of substrate equals 10

In the following we turn our attention to the cases in which both the approximations are less reliable. In Figure 9 we plotted the case $k_1 = 0.1$, $k_{-1} = 0.1$, $k_2 = 0.1$, $[E] = 1$, $[S]_0 = 1$ and $[ES]_0 = 0$. As mentioned earlier, with $[ES]_0 = 0$ the initial production speed in the original model is 0 while it is immediately high in the approximate kinetics. With low values of k_1 and k_{-1}, the time taken by the system to reach the quasi-steady-state situation assumed by the approximate kinetics is quite long. For this reason there is a longer initial period in which P is produced by the approximations at a "wrong" speed. Furthermore, decreasing k_1 and k_{-1} would lead to a longer period in which the approximate kinetics are not precise (see Figure 9).

Another way of "disturbing" the approximations is to dynamically change the quantity of the substrate in the system. In the original model, because of the intermediate step yielding ES, the speed of producing P changes only after some delay. On the contrary, the approximations react immediately. The harsher the change in the quantity of the substrate the larger is the difference between the original model and the approximations. This phenomenon is reflected in the

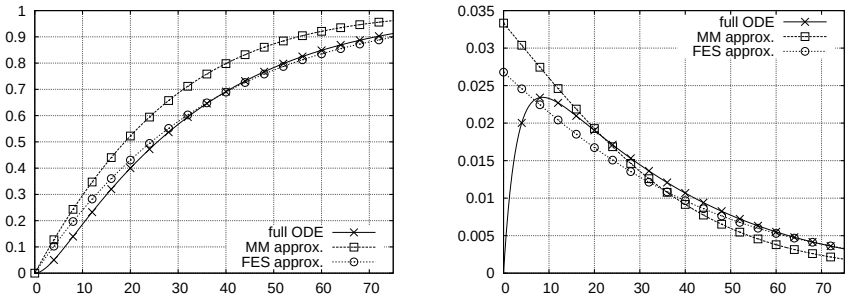

Fig. 9. Quantity of product (left) and speed of production (right) as function of time with $k_1 = 0.1$, $k_{-1} = 0.1$, $k_2 = 0.1$, $[E] = 1$ and initial quantity of substrate equals 1

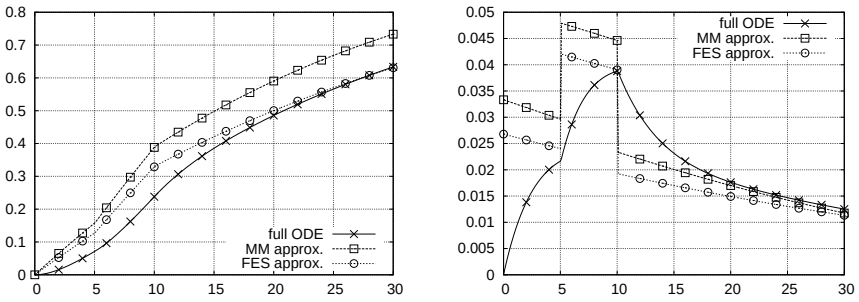

Fig. 10. Quantity of product (left) and speed of production (right) as function of time with $k_1 = 0.1$, $k_{-1} = 0.1$, $k_2 = 0.1$, $[E] = 1$, initial quantity of substrate equals 1 and adding substrate to the system according to (12)

model by adding the following term to the differential equation that describes the quantity of the substrate:

$$10(U(t-5) - U(t-5.1)) - 10(U(t-10) - U(t-10.1)) \tag{12}$$

where U denotes the unit-step function. The effect of (12) is to add 1 unit of substrate to the system in the time interval $[5, 5.1]$ and to take away 1 unit of substrate from it in the time interval $[10, 10.1]$. The resulting behaviour is depicted in Figure 10. The approximations change the speed of producing P right after the change in the quantity of the substrate while the original model reacts to the changes in a gradual manner. Naturally, if the quantity of the substrate undergoes several harsh changes then the MM and the FES kinetics can result in bad approximation of the full model.

4.3 Stochastic setting

In the following we compare the different kinetics in the stochastic setting, by analysing the corresponding CTMCs. In particular, we determine by means of

simulation the average and the variance of the quantity of the product as function of time. The simulations were carried out in Dizzy [11].

The reaction rates for the first set of experiments are $k_1 = k_{-1} = k_2 = 1$. As in the previous section, this choice allows to test a situation where the speed of the two approximations are different. For the same reason, we choose the same initial quantity for the enzyme and the substrate $[E]_0 = [S]_0 = 1$. In the stochastic setting the discretization step, denoted by δ, has to be chosen as well. This choice has a strong impact because as the granularity with which the concentrations are modeled is increased, the behaviour of the CTMC tends to the deterministic behaviour of the corresponding ODE. Figures 11 and 12 depict the average and the variance of the quantity of the product with $\delta = 0.01$ and $\delta = 0.001$, respectively. In both figures the approximate kinetics based on flow equivalence gives good approximation of the original average behaviour while the Michaelis-Menten approximation results in too fast production of P. On the right side on the figures one can observe that also the variance is approximated better by the FES approximation.

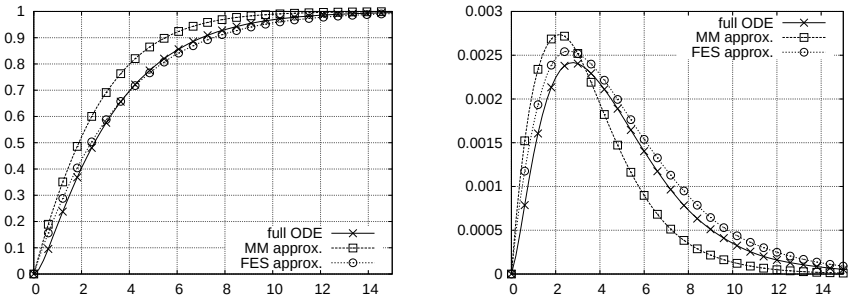

Fig. 11. The average (left) and the variance (right) of the quantity of the product as function of time with $k_1 = 1$, $k_{-1} = 1$, $k_2 = 1$, $[E]_0 = [S]_0 = 1$ and $\delta = 0.01$

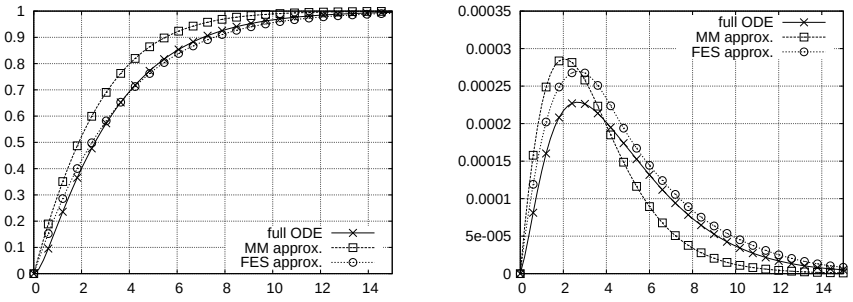

Fig. 12. The average (left) and the variance (right) of the quantity of the product as function of time with $k_1 = 1$, $k_{-1} = 1$, $k_2 = 1$, $[E]_0 = [S]_0 = 1$ and $\delta = 0.001$

For the second set of experiments we set $k_1 = 10$ and $k_{-1} = k_2 = 1$ and as initial states we choose again $[E]_0 = [S]_0 = 1$. In this case too, as it was shown in Figure 4, the speeds of production of P as predicted by the MM and FES approximations are quite different. Figures 13 and 14 depict the resulting behaviour for two different values of δ. As in case of the deterministic setting, the Michaelis-Menten approximation suffers from the increased k_1/k_{-1} ratio and becomes less precise than before. The FES based approach still results in good approximation for both the average and the variance of the production.

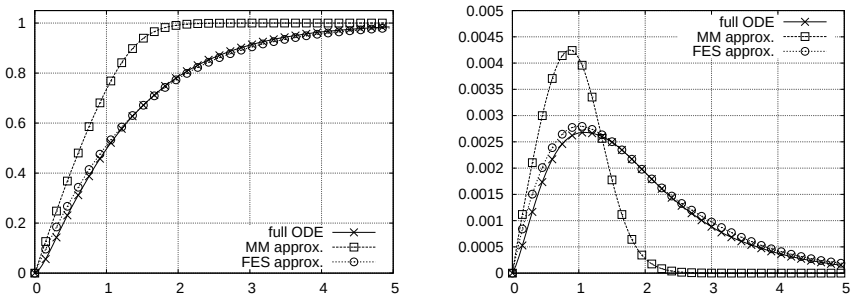

Fig. 13. The average (left) and the variance (right) of the quantity of the product as function of time with $k_1 = 10$, $k_{-1} = 1$, $k_2 = 1$, $[E]_0 = [S]_0 = 1$ and $\delta = 0.01$

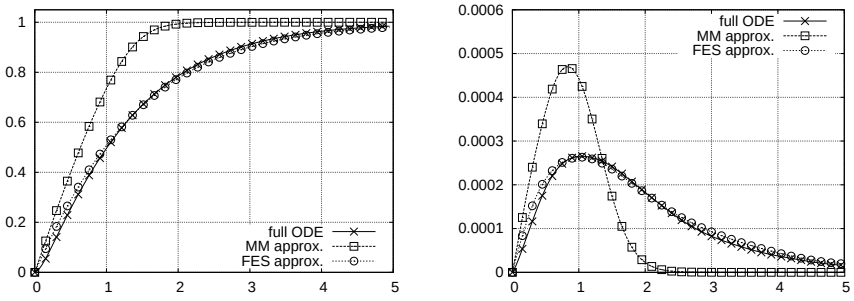

Fig. 14. The average (left) and the variance (right) of the quantity of the product as function of time with $k_1 = 10$, $k_{-1} = 1$, $k_2 = 1$, $[E]_0 = [S]_0 = 1$ and $\delta = 0.001$

5 Conclusion

In this paper we have considered the approximate treatment of the basic enzymatic reactions $E+S \rightleftharpoons ES \longrightarrow E+P$. In particular, an approximate kinetics, based on the concept of flow equivalent server, has been proposed for its analysis. This FES approximate kinetics has been compared to both the exact model and to the most common approximate treatment, namely, the Michaelis-Menten kinetics. We have shown that the FES kinetics is more robust than the one of Michaelis-Menten.

The FES approximation for the basic enzymatic reactions is computationally convenient due to the fact that it has been possible to find an analytic expression for the speed of the composite reaction in this case. While it is very unlikely for this to be true in the case of more complex kinetics, the method is very general and we will study it further within this context to see if it is possible to find other functional expressions for the speed of the composite reaction. One direction of research will be computing the flow equivalent characterization of the kinetics for a number of specific parameter sets and then of constructing the functional representations via interpolation.

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