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Simulation of Complex Chemical Kinetics

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Kinetic what-if simulations can be important for both the optimisation of an industrial process as well as the design of future experiments in the evolving process of a detailed kinetic analysis on laboratory scale. From our viewpoint as coordination chemists we present SIMKIN, a tool for an easy intuitive and fast simulation of chemical kinetics. As one of the key features, an intelligent model parser translates conventional chemical equations consisting of virtually any reaction steps including feedbacks into the rate law. The corresponding differential equations are then solved by standard routines for numerical integration, and the concentration profiles of the involved species plotted versus the reaction time. By means of selected kinetic examples of increasing complexity taken from coordination chemistry we demonstrate the capabilities and versatility of the program. A MATLAB® version with a complete graphical user interface can be requested from the authors free of charge.

Keywords: Kinetic modelling, kinetic simulator, rate law

INTRODUCTION

The knowledge of the mechanism and its kinetics is crucial for the understanding of any chemical process. The keystone for a reaction mechanism is its rate law. It describes the relation between the velocity of a reaction and the concentration of chemical species. The dynamics of the elementary reactions can mathematically be expressed by a set of coupled differential equations that needs to be integrated simultaneously in order to derive the species concentrations for the course of the entire reaction [1]. For example, the first order reaction $A \xrightarrow{k} B$ is specified by the set of differential equations $[\dot{A}] = \partial[A]_t/\partial t = -[\dot{B}] = -\partial[B]_t/\partial t = -k \cdot [A]_t$ with the explicit solutions $[A]_t = [A]_0 \cdot e^{-kt}$ and, if $[B]_0$=0 M, $[B]_t = [A]_0 \cdot (1 - e^{-kt})$, describing an exponential decay of reactant A over the time t and a concomitant growth of B. As a consequence, for any given initial concentration $[A]_0$ and rate constant k, the concentration profiles $[A]_t$ and $[B]_t$, i.e. the kinetic behaviour of the species A and B, can be predicted and simulated. The capability to predict the course of reactions is an intrinsic property of kinetic models and is for example important for the optimisation of industrial processes [2]. On a laboratory scale, the ability to perform reliable *what-if* simulations can be an invaluable tool to design further experiments in the evolving process of a detailed kinetic analysis.

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Unfortunately, only very basic rate laws have explicit mathematical solutions, i.e. solutions that can be written in algebraic form [3]. Typical examples are reaction mechanisms which include only first order steps [4] as well as very few, simple second order reactions [5]. For all other cases there is no analytical solution of the corresponding system of ordinary differential equations (*odes*). These have to be solved numerically [6]. The development of increasingly sophisticated ordinary differential equation solvers (*ode*-solvers) went hand-in-hand with the advancement of computer technology [7]. Today, even very complex systems of *odes* such as that describing the oscillating Belousov-Zhabotinsky (BZ) reaction [8] can be integrated in seconds on a standard personal computer. Nevertheless, due to the inherent non-linear character of kinetics, relatively simple looking reaction mechanisms can already be quite challenging and such simulations help to enhance their kinetic understanding. For example, the variation of the initial concentrations of the reactants on a theoretical basis can lead to very unexpected or surprising outcomes, which, in turn, suggest an expansion of the experiments.

Several computer programs have been reported that can compute the concentration profiles for a given chemical reaction model by means of *ode*-solvers. Since the determination of concentration profiles is an integral part for the numerical analysis of experimental data, e.g. fitting of spectrophotometric absorbance measurements to a kinetic model [9], the simulation routines are usually embedded into relatively complex [10-13] or commercial software packages [14,15].

From our viewpoint as coordination chemists and kineticists, it was our motivation to develop a versatile tool for an easy, intuitive simulation of chemical kinetics with a model that can be setup by conventional chemical equations, and thus is useful in both research and education. In the next section, we briefly introduce some of the basic principles that have been applied to develop the kinetic simulator SIMKIN. Our emphasis is, however, on the presentation of selected kinetic examples with increasing complexity in order to address a broad kinetic community, in particular in coordination chemistry.

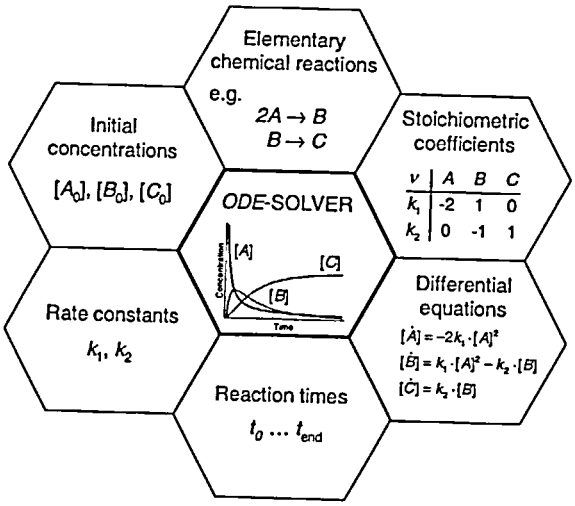

FIGURE 1
The conceptual basis of SIMKIN on the example reaction $2A \rightarrow B$, $B \rightarrow C$.

THE BASIC PRINCIPLES OF SIMKIN

It is not our intention to go deeply into numerical mathematics in order to explain how to numerically integrate ordinary differential equations. For this task, many routines have already been published [7,16] and, more importantly, are implemented in MATLAB® [17], the software environment we have used for the development of the simulator. We will, however, give an outline comprising the essential steps to determine the kinetic concentration profiles, starting from a given set of initial conditions and a user defined reaction mechanism with its rate constants. To attain a minimum grade of abstractness we have chosen to walk through an example mechanism rather than producing complicated generalized formulae.

Consider, for example, the dimerisation of a compound A followed by a first order decomposition of the intermediately formed dimer B to give another species C. The mechanism comprises two irreversible elementary steps, a second order dimerisation $2A \rightarrow B$, and a first order decomposition $B \rightarrow C$, with the rate constants k_1 and k_2, respectively. This relatively simple mechanism has no explicit, algebraic solution for its corresponding set of differential equations and

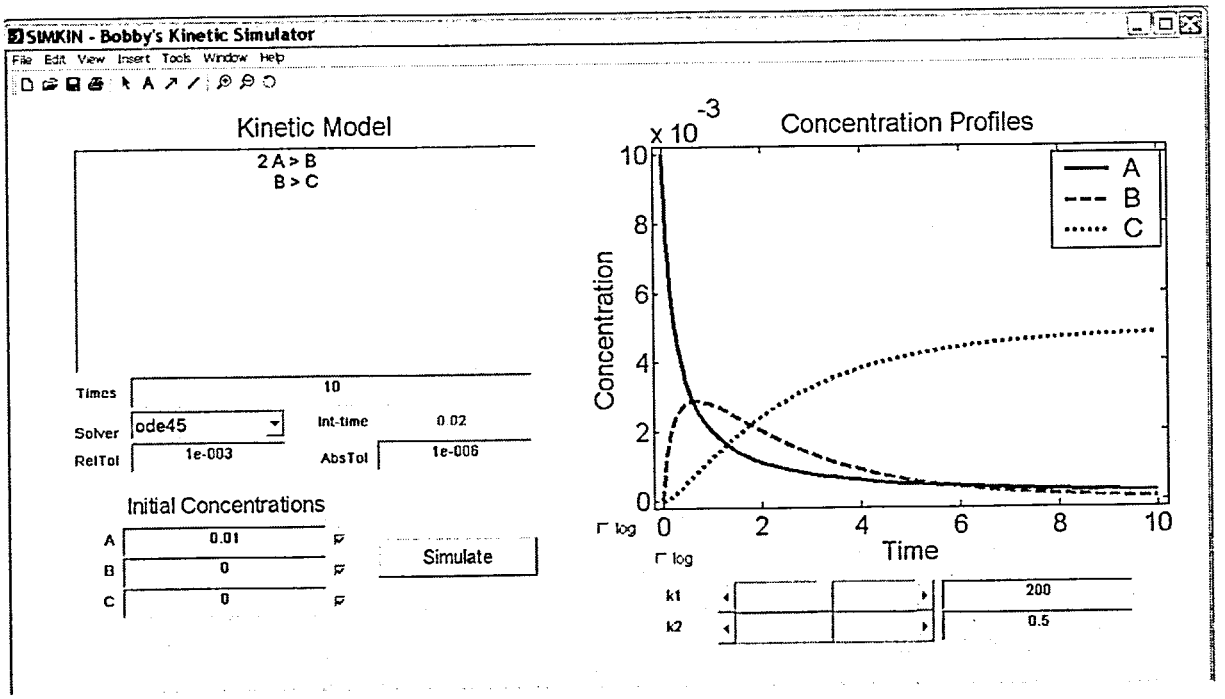

FIGURE 2
Screenshot of SIMKIN for the example mechanism $2A \rightarrow B, B \rightarrow C$.

an *ode*-solver is mandatory [5]. Figure 1 shows the information that has to be passed to the solver in order to determine the concentration profiles for species *A*, *B* and *C*. We have developed an intelligent model translator that extracts species names and corresponding stoichiometric coefficients ν from a reaction mechanism written in form of conventional chemical equations. From this and the rate constants k_1 and k_2, the differential equations are automatically set up and solved for the specific initial concentrations $[A]_0$, $[B]_0$, $[C]_0$ at a time span $t_0 \ldots t_{end}$.

In Figure 2, a screenshot of SIMKIN demonstrates the kinetics of this mechanism for the initial concentrations $[A]_0 = 0.01$ M, $[B]_0 = [C]_0 = 0$ M and the rate constants $k_1 = 200\ M^{-1}s^{-1}$, $k_2 = 0.5\ s^{-1}$ up to the reaction time $t_{end} = 10$ s. A relative and an absolute tolerance (default: RelTol = $1 \cdot 10^{-3}$, AbsTol = $1 \cdot 10^{-6}$) define the accuracy of the calculation of concentrations and thus the precision of the simulation. All relevant conditions and options are readily available on the graphical user interface and can be changed at any time. The simulation takes about 0.02 s (Int-time) on a Pentium 4, 2GHz system. We used MATLAB®'s *Runge-Kutta* type solver (*'ode45'*) [16], which is fast and adequate for many chemical mechanisms. Modern solvers have a variable step size control, i.e. they automatically determine the intervals for integration within the desired time span (here: 10s). As we will demonstrate later, reactions that involve very fast and slow stages and/or species at relatively high and low concentrations often require more sophisticated solvers.

KINETIC EXAMPLES

Reversible Oxygenation of Biomimetic Copper(I) Complexes

Various tri- and tetradentate ligand-copper(I)-systems are able to reversibly bind dioxygen via a copper(II) superoxo intermediate and/or a peroxo bridged adduct and mimic the behaviour of their biological analogues such as hemocyanin or

(a)

Kinetic Model

```
CuL + O2 > LCuO2
  LCuO2 > CuL + O2
CuL + LCuO2 > LCuO2CuL
  LCuO2CuL > CuL + LCuO2
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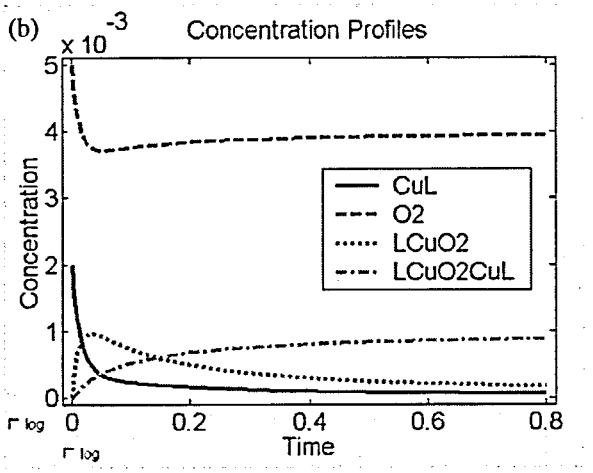

FIGURE 3
Reversible oxygenation of $[Cu^{(I)}(tmpa)]^+$. (a) The kinetic model as typed into the editor, (b) the calculated concentration profiles. (Both are sections from an actual screenshot).

tyrosinase [18]. In order to elucidate kinetics and thermodynamics of these biomimetic oxygenation reactions Zuberbühler and co-workers have completed extensive stopped-flow investigations on various copper(I)-ligand systems ($Cu^{(I)}L$) during the past decade [18,19] and mechanism (1) is generally accepted.

$$LCu^{(I)} + O_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} LCu^{(II)}O_2$$
$$LCu^{(I)} + O_2Cu^{(II)}L \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} LCu^{(II)}O_2Cu^{(II)}L \qquad (1)$$

Charges have been omitted for clarity. Generally, the superoxo intermediates $LCu^{(II)}O_2$ are very short-lived and their first kinetic observation during the investigation of the $[Cu^{(I)}(tmpa)]^+$ system (L = tmpa = tris(2-pyridylmethyl)amine) was a milestone in copper(I) dioxygen chemistry [20]. We have performed simulations applying mechanism (1) at the initial concentrations ($[Cu^{(I)}(tmpa)]^+_0 = 2 \cdot 10^{-3}$ M and $[O_2]_0 = 5 \cdot 10^{-3}$ M using the latest kinetic results ($k_1 = 1.18 \cdot 10^4$ $M^{-1}s^{-1}$, $k_{-1} = 15.9$ s^{-1}, $k_2 = 1.34 \cdot 10^4$ $M^{-1}s^{-1}$, $k_{-2} = 2 \cdot 10^{-5}$ s^{-1}, at T=-90°C) [21] for the oxygenation of this complex system in propionitrile.

Apart from its bioinorganic importance we have chosen this reaction as an example for two reasons: a) to demonstrate the capability of SIMKIN in modelling reversible reactions, and b) to draw the attention to a kinetically surprising aspect which is not easy to predict without simulation. The definition of reversible reactions within the model editor is straight-forward. They simply have to be written as two separate forward reactions using the symbol '>' as the arrow (compare Figure 3a with mechanism (1)). It is note-worthy that the only other reserved symbol for model building is '+', and all others can be used for a flexible species naming, i.e. names of various length including numbers or symbols. The result of this simulation reveals an astonishing behaviour in the concentration profile of O_2 (see Figure 3b). After an initial fast decrease due to its consumption in the formation of the $[(tmpa)Cu^{(II)}O_2]^+$ superoxo adduct it is then slightly increasing together with the formation of the dinuclear $[(tmpa)Cu^{(II)}O_2Cu^{(II)}(tmpa)]^{2+}$ complex. The reason for this unexpected, 'overshooting' behaviour lies in the moderate excess of O_2 combined with the relatively fast formation of the superoxo intermediate in the first equilibrium. The second part of the reaction then becomes much slower due to a reduced availability of $[Cu^{(I)}(tmpa)]^+$, whose consumption, however, leads to a re-equilibration of the first equilibrium reaction and a release of O_2.

Kinetics of the Oxidation of the Aqueous Copper(I)-acetonitrile System with $[(NH_2)_5Co^{(III)}X]^{2+}$

Recently [22], Jordan and co-workers have published an elegant indirect kinetic method to determine the stability constants for the complexation of copper(I) with acetonitrile (an) in water. According to their findings, in acidic solutions the rate for the

oxidation of aqueous copper(I) with $[(NH_2)_5Co^{(III)}X]^{2+}$ ($X=N_3^-,Br^-$) depends on the acetonitrile concentration, which in turn determines the concentration of the different $Cu^{(I)}(an)_n$ species.

$$[(NH_3)_5Co^{(III)}X]^{2+} + Cu^{(I)}(an)_n + 5H^+ \xrightarrow{CH_3CN/H_2O} Co^{(II)} + Cu^{(II)} + 5NH_4^+ + X^- + n\text{-}an \quad (2)$$

They analysed spectrophotometric measurements of the observed rate as a function of the acetonitrile concentration (in excess) and derived stability and rate constants supporting the following mechanism for $X=N_3^-$.

$$\begin{aligned}
&Cu^{(I)} + an \rightleftharpoons Cu^{(I)}(an) && \log K_1 = 2.63\\
&Cu^{(I)}(an) + an \rightleftharpoons Cu^{(I)}(an)_2 && \log K_2 = 1.39\\
&Cu^{(I)}(an)_2 + an \rightleftharpoons Cu^{(I)}(an)_3 && \log K_3 = 0.27\\
&Co^{(III)} + Cu^{(I)} \xrightarrow{k_{Cu} = 1420\ M^{-1}s^{-1}} Co^{(II)} + Cu^{(II)}\\
&Co^{(III)} + Cu^{(I)}(an) \xrightarrow{k_{CuL} = 2.9\ M^{-1}s^{-1}} Co^{(II)} + Cu^{(II)} + an\\
&Co^{(III)} + Cu^{(I)}(an)_2 \xrightarrow{k_{CuL_2} = 0.5\ M^{-1}s^{-1}} Co^{(II)} + Cu^{(II)} + 2an
\end{aligned} \quad (3)$$

Cobalt(III) ligands and charges have been omitted for brevity. The $Cu^{(I)}(an)_n$ equilibrium species react with different rate constants k_{CuL_n} of decreasing magnitude with increasing coordination number n. They were not able to derive a stability constant for $Cu^{(I)}(an)_4$ since the species is not significantly formed under the chosen conditions.

We have selected this particular mechanism to demonstrate how SIMKIN can easily handle equilibria that are much faster than the observed kinetics. Protonation equilibria coupled with complex formation kinetics in aqueous solutions comprise other typical cases, the mechanisms, however, tend to be more complicated due to additional complexation equilibria [23]. In order to make an equilibrium 'fast'—compared to the observed kinetics—the corresponding forward (k_+) and backward (k_-) rate constants have to be defined high enough to provide an instant redistribution of the equilibrium species at every reaction time of the simulation, while maintaining the ratio k_+/k_- according to the equilibrium constant K. For the numerical solution of differential equations that combine very fast and slow steps and/or species of relatively high and low concentration so-called 'stiff' solvers with an advanced step-size control are often mandatory [6,7].

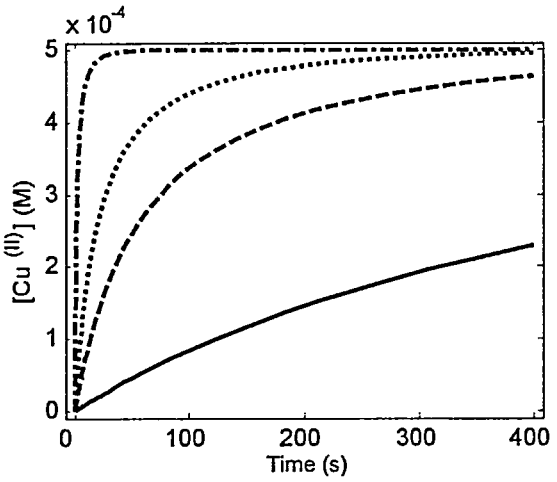

FIGURE 4
Formation of copper(II) during the oxidation of $5\cdot10^{-4}$ M copper(I) with $5.84\cdot10^{-4}$ M $[(NH_2)_5Co^{(III)}N_3]^{2+}$ in $1.81\cdot10^{-1}$ M (—), $4.89\cdot10^{-2}$ M (- - -), $2.37\cdot10^{-2}$ M (···) and $8\cdot10^{-4}$ M (-·-) aqueous acetonitrile.

In SIMKIN we use MATLAB®'s '*ode23s*' [16], a modified Rosenbrock method which has proven to give fast reliable results.

Using the stability constants $\log K_{1\text{-}3}$ determined for mechanism (3) [22] the ratios of forward and backward rate constants k_+/k_- have been set according to $K_1=k_1/k_{-1}=4.2658\cdot10^{10}/10^8\ M^{-1}$, $K_2=k_2/k_{-2}=2.4547\cdot10^9/10^8\ M^{-1}$ and $K_3=k_3/k_{-3}=1.8621\cdot10^8/10^8\ M^{-1}$, respectively. Figure 4 shows the oxidation kinetics employing the concentration profile of copper(II) as a function of the acetonitrile concentration as the result from different simulations applying mechanism (3). It clearly reveals the increase of the reaction rate with decreasing acetonitrile concentration. Except for the lowest acetonitrile concentration all initial concentrations for the simulations (see Figure 4) were taken from the supporting material.

As a prerequisite for his mathematical type of kinetic analysis, in each kinetic run Jordan had to maintain a constant acetonitrile concentration (large excess). The reasons for that are comparable to those that lead to the requirement of buffers when protonation equilibria couple to the observed kinetics [23-25]. It is important to note that SIMKIN has no such limitation since an overall shift of the equilibrium is covered by the numerical solution of

the differential equations corresponding to mechanism (3). Accordingly, in Figure 4 the kinetics for a hypothetical low-excess acetonitrile concentration is also shown (legend - . -).

Since the calculation of concentration profiles is generally an integral part of non-linear regression programs for the kinetic analysis of experimental data [9] an appropriate implementation of the method described above can lead to benefits, such as eliminating the necessity to maintain constant concentrations of a reactant [26].

The Belousov-Zhabotinsky Reaction

Theoreticians have long considered oscillating chemical reactions to be impossible since they appeared to contradict the second law of thermodynamics [27,28]. This prejudice only changed when Zhabotinsky found irrefutable experimental evidence [29] of Belousov's oscillations [30] and also the theoretical barrier was broken by Prigogine [31,32]. In our last example we demonstrate that SIMKIN even handles exotic chemical reactions such as the oscillating *Belousov-Zhabotinsky* (BZ) system.

The BZ reaction involves the oxidation of an organic species such as malonic acid (MA) by an acidified aqueous bromate solution in the presence of a metal ion catalyst such as the $Ce^{(III)}/Ce^{(IV)}$ and the $[Fe^{(II)}(phen)]^{2+}/[Fe^{(III)}(phen)]^{3+}$ (ferroin/ferriin) couple [8]. At excess MA concentration the stoichiometry of the net reaction is

$$2BrO_3^- + 3MA + 2H^+ \xrightarrow{catalyst} 2BrMA + 3CO_2 + 4H_2O \qquad (4)$$

A short induction period is typically followed by an oscillatory phase visible by an alternating colour of the aqueous solution due to the different oxidation states of the metal catalyst. Typically, several hundred oscillations with a periodicity of approximately a minute gradually die out within a couple of hours and the system slowly drifts towards its equilibrium state (see Figure 5).

In order to understand the BZ system Field, Körös and Noyes developed the so-called *FKN* mechanism (for details see [8,33]). From this, Field and Noyes later derived the *Oregonator* model (5) [34], an especially convenient kinetic model to match individual experimental observations and predict experimental conditions under which oscillations might arise.

$$\begin{aligned} BrO_3^- + Br^- &\xrightarrow{k_1} HBrO_2 + HOBr \\ BrO_3^- + HBrO_2 &\xrightarrow{k_2} 2HBrO_2 + 2M_{ox} \\ HBrO_2 + Br^- &\xrightarrow{k_3} 2HOBr \\ 2HBrO_2 &\xrightarrow{k_4} BrO_3^- + HOBr \\ MA + M_{ox} &\xrightarrow{k_5} \tfrac{1}{2} f Br^- \end{aligned} \qquad (5)$$

M_{ox} represents the metal ion catalyst in its oxidised form. It is important to note that this model is based on an experimentally determined empirical rate law and does clearly not comprise elementary processes. The five reactions in model (5) provide the means to kinetically describe the four essential stages of the BZ reaction:

- formation of $HBrO_2$
- autocatalytic formation of $HBrO_2$
- consumption of $HBrO_2$
- oxidation of malonic acid (MA)

The stoichiometric coefficient f represents an 'adjustable' parameter, typically between 0.5 and 2.4 [8,35]. In our simulations we set $f=1$ and used the rate constants k_1=1.28 $M^{-1}s^{-1}$, k_2=33.6 $M^{-1}s^{-1}$, k_3=2.4·10^6 $M^{-1}s^{-1}$, k_4=3·10^3 $M^{-1}s^{-1}$, k_5=1 $M^{-1}s^{-1}$ (for $[H]^+$=0.8 M) at the initial concentrations $[BrO_3^-]_0$=0.063 M, $[Ce^{(IV)}]_0$=0.002 M (=$[M_{ox}]_0$) and $[MA]_0$=0.275 M, as given in an experimental recipe for the BZ reaction [8]. As before, a '*stiff*' solver (*ode23s*) [16] is mandatory in order to correctly solve the differential equations. Typical computation times are between 0.4 and 7s depending on the overall simulation time at reasonable relative and absolute tolerances (RelTol=10^{-3}, AbsTol=10^{-7}).

The simulation results shown in Figure 5 reveal the fast oscillating behaviour of the metal catalyst as well as the concomitant stepwise and overall slow oxidation of malonic acid. During each oscillation period of approximately 60 s, the oxidation of MA proceeds by one step when $Ce^{(IV)}$ is available and comes essentially to an halt when $[Ce^{(IV)}]$ gets too low. The gradual decrease in the amplitude with

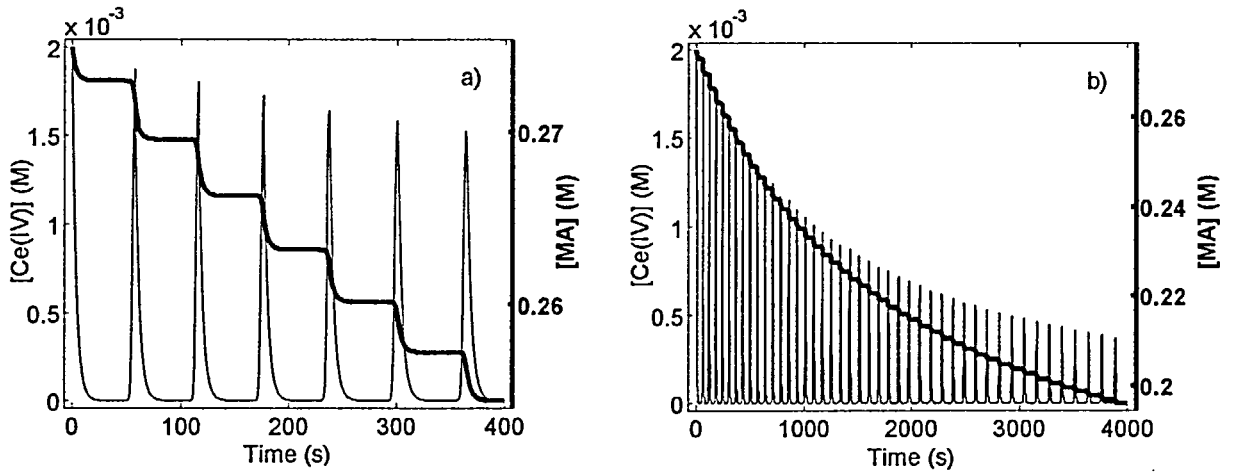

FIGURE 5.
The Belousov-Zhabotinsky reaction as represented by the Oregonator model. Simulated concentration profiles for the metal catalyst $Ce^{(IV)}$ (thin lines and ordinates) and malonic acid (MA, thick lines and ordinates) (a) at the start of the oscillations and (b) towards the thermodynamic equilibrium.

progress of the reaction goes together with the slow convergence towards the equilibrium state for the oxidation of MA.

CONCLUSIONS

Kinetic simulations can provide significant insights into reaction mechanisms. In this contribution we have developed SIMKIN and demonstrated its application to a number of inorganic reaction mechanisms. The discussed examples cover simple irreversible reactions through to complex reversible or feedback reactions such as in autocatalysis.

Chemical equations of variable reaction order are entered by the user in the conventional format and an intelligent parser converts them into the corresponding differential equations. A simple graphical user interface allows the definition of the initial concentrations, rate constants, reaction time and the algorithm for numerical integration. A plot of the concentration profiles displays the results of the simulation. All results can be saved and are readily available in the MATLAB® environment. All these features provide an intuitive and flexible way to quickly simulate virtually any reaction mechanism on a standard personal computer, typically within seconds.

In order to increase the range of applications future extensions to SIMKIN could allow for a change in temperature and ionic strength during the course of the reaction as well as handling the flow-in and flow-out of reactants and products.

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