Requirements are formulated for a reaction kinetics package to be useful for an as wide as possible circle of users and illustrated with examples using ReactionKinetics, a Mathematica based package.

Keywords: kinetics, mathematical modelling, dynamic simulation, computational chemistry, graphs of reactions, stochastic models

1. Introduction

In Part I of our paper we formulate the requirements for a reaction kinetics package to be useful for an as wide as possible circle of users. We try to answer the question: What should an ideal package know?

In Part II [Nagy et al., 2011] we enumerate the major problems arising when writing and using such a package.

Throughout we try to illustrate everything with the present version of the package and the kinetic examples are mainly taken so as to join to the lectures presented at the workshop MaCKiE 2011 (http://www.mackie2011.uni-hd.de/). In many cases the examples will not show all the fine details necessary to be given when really using our program: a detailed program documentation will be given later. Furthermore, trivial examples are chosen in some cases to transparently illustrate the functioning of the package.

Also, there is no place to explain the theoretical background, we refer to the literature, and also to our future, more detailed work.

2. History

In the late sixties, early seventies of the last century, at the time when the computer became accessible for an ordinary scientist, kineticists immediately started to write codes for at least three different problems: for parsing large sets of reaction steps, solving induced kinetic differential equations and simulating the stochastic model of chemical reactions, see an early review: Garfinkel et al. [1970].

Nowadays a few existing widely used program with multiple capabilities are e.g.

CHEMKIN www.sandia.gov/chemkin/index.html

XPPAUT www.math.pitt.edu/~bard/xpp/xpp.html

KINALC garfield.chem.elte.hu/Combustion/kinalc.htm
but there exists an almost infinite number of them (which we are going to review later; see also Tomlin et al. [1997]) with much less capabilities.

3. Coverage

Our major governing principle is that the program should continuously include recent methods developed in most areas of reaction kinetics modeling. A conference like MaCKiE 2011 is an excellent occasion, a great help to learn newer methods.

We show a few examples from the recent literature.

3.1. Testing detailed balance

3.1.1. Preliminaries and definition

The long story starts possibly with Wegscheider [1901/2], but the first explicit formulation (without any formula) of the principle of detailed balance has been given by Fowler and Milne [1925]: in real thermodynamic equilibrium all the subprocesses (whatever they mean) should be in dynamic equilibrium separately in such a way that they do not stop but they proceed with the same velocity in both directions.

One can say that this principle means that time is reversible at equilibrium, that is why the expression microscopic reversibility is usually used as a synonym.

The modern formulation of the principle accepted by IUPAC Gold et al. [1997] essentially means the same: “The principle of microscopic reversibility at equilibrium states that, in a system at equilibrium, any molecular process and the reverse of that process occur, on the average, at the same rate.”

Neither the above document nor the present authors assert that the principle should hold without any further assumptions; for us it is an important hypothesis the fulfilment of which should be checked individually in different models.

Now let us consider a reaction consisting only of reversible steps:

\[
\sum_{m=1}^{M} \alpha(m, p) X(m) \rightleftharpoons \sum_{m=1}^{M} \beta(m, p) X(m), \quad (p = 1, 2, \ldots, P) \tag{1}
\]

where we have \( P \) pairs of reaction steps, \( \alpha, \beta \) are the matrices with molecularities as elements, their difference is the stoichiometric matrix, and \( k_p \quad (p = -P, \ldots, -1, 1, 2, \ldots, P) \) are the reaction rate coefficients. Now, the induced kinetic differential equation of the above reaction is as follows:

\[
\frac{\dot{c}(t)}{t} = \sum_{p=1}^{P} (\beta(-, p) - \alpha(-, p)) \left( k_p [c(t)^\alpha(p)] - k_{-p} [c(t)^\beta(p)] \right) \tag{2}
\]

where \( c(t) \in \mathbb{R}^M \) describes the concentrations of the species at time \( t \).

\textbf{Definition 1} Assume that \( c^* \in (\mathbb{R}^+)^M \) and it makes the righthand side of (2) to be equal to zero, furthermore the condition

\[
k_p (c^*)^\alpha(p) = k_{-p} (c^*)^\beta(p) \tag{3}
\]

is fulfilled for every \( p = 1, 2, \ldots, P \). Then we say that reaction (1) is detailed balanced at the stationary point \( c^* \). If the reaction is detailed balanced at all of its positive stationary points, then it is detailed balanced.

3.1.2. Methods to test detailed balance

The most naïve way to check conditions (3) is the direct one: having found one (or all of) the positive stationary points substitute it (them) into (3) and see if it holds or not. Or, it may be enough to solve equations (3) for positive \( c^* \)’s to get all the candidates in which reaction (1) is detailed balanced. However a nonlinear system of equations is required to be solved, which makes the problem difficult.

Fortunately, there is a more elegant way to look at the problem, namely Feinberg [1989] has proved that the following two conditions are necessary and sufficient for the reaction (1) to be detailed balanced.

\textbf{Condition 1} (circuit conditions) Suppose that we have chosen an arbitrary spanning forest for the Feinberg–Horn–Jackson graph of reaction (1). It is possible to find a set of \( P - N + L \) independent circuits, where \( N \) denotes the number of vertices (complexes):

\[
N := |[\alpha(\cdot, r); r = 1, 2, \ldots, R] \cup [\beta(\cdot, r); r = 1, 2, \ldots, R]|,
\]
whereas $L$ is the number of connected components (linkage classes) of the Feinberg–Horn–Jackson graph (in which all the complexes are written down exactly once and they are connected with reaction arrows). For each of these circuits we write an equation which asserts that the product of the reaction rate coefficients in the clockwise direction and counterclockwise direction is equal. Thus we have $P - N + L$ equations for the reaction rate coefficients.

Before formulating Condition 2 we need another important definition.

**Definition 2** The deficiency is the number of complexes $N$ minus the number $L$ of connected components of the Feinberg–Horn–Jackson graph and the number $S$ of independent reaction steps (or, the rank of the stoichiometric matrix).

**Condition 2** (spanning forest conditions) Assume that reaction (1) shows deficiency $\delta$. Furthermore, assume that the edges of an arbitrarily selected the spanning forest $F$ has been given an orientation. Then there exists $\delta$ independent non-trivial solutions to the vector equation

$$\sum_{(i,j) \in F} (B(j,i) - A(i,j)) a(i,j) = 0$$

for the $a(i,j)$ numbers. With these solutions one can construct the spanning forest conditions which are

$$\prod_{(i,j) \in F} \alpha(a(i,j)) = \prod_{(i,j) \in F} \beta(a(i,j))$$

where $\alpha(i,j)$'s are the corresponding reaction rate coefficients (associated to the edge $(i,j)$).

### 3.1.3. Applications

Here we present only one example. Take the model of Wegscheider, i.e. GetProblem["Wegscheider"] to obtain

"A" ↔ "B", 2 "A" ↔ "A" + "B".

Now

DetailedBalanced["Wegscheider", $k_1$, $k_2$, $k_2$, $k_2$]

results in

$$\{k_1 \cdot k_2 = k_2 \cdot k_1\}$$

providing the condition for the reaction to be detailed balanced.

There are several applications for e.g. in chirality, models of ion channels, combustion theory in progress.

### 3.2. Absolute concentration robustness

One might look for sufficient conditions to ensure the independence of a stationary concentration coordinate from outer conditions: does it only depend on reaction rate coefficients and on no initial concentrations? [Shinar and Feinberg, 2010].

#### 3.2.1. Motivation

A simple example follows. Let us consider the reaction

$$r_1 := (A + B \xrightarrow{k_1} 2B, B \xrightarrow{k_2} A),$$

where $A$ may be interpreted as the inactive form of a protein and $B$ as its active form, e.g. trypsinogen and trypsin respectively. (Let us remark in passing that this model is an irreversible version of the Wegscheider model above.) The induced kinetic differential equation of this reaction is given by

$$\begin{align*}
a'(t) &= -k_1 a(t)b(t) + k_2 b(t) \\
b'(t) &= k_1 a(t)b(t) - k_2 b(t).
\end{align*}$$

Calculation of the stationary points (under the condition that $a(0) = a_0, b(0) = b_0$) proceeds quite naturally:

StationaryPoints[$r_1, \{k_1, k_2\}, \{a_0, b_0\},$
Conditions -> \{a_0 + b_0 > k_2/k_1\},
Positivity -> True]

The stationary concentration $a^*$ of $A$, being $\frac{k_2}{k_1}$, is always positive (together with $b^* = a_0 + b_0 - \frac{k_1}{k_2}$, at least if $a_0 + b_0 > \frac{k_2}{k_1}$), and does not depend on total mass: the reaction shows absolute concentration robustness with respect to $A$.

However, in the reaction $A \xrightarrow{k_1} B$ neither $A$, nor $B$ has this property, both coordinates of the stationary concentration vector do depend on $a_0 + b_0$ (as one can easily find it without any program): $a^* = k_1 \frac{a_0 + b_0}{k_1 + k_2},$ $b^* = k_2 \frac{a_0 + b_0}{k_1 + k_2}.$
stationary concentrations both numerically and absolutely robust:

\[ \text{Figure 1: The Feinberg–Horn–Jackson graph of the reaction } r1 \text{ obtained by ShowFHJGraph[r1,Style[#,Red,14]&/@{k1, k2}, VertexLabeling->True,DirectedEdges->True]}. \]

The question is what kind of general conditions can be given to assure absolute concentration robustness. An easy to check set of conditions has been formulated by Shinar and Feinberg 2010.

### 3.2.2. Conditions

**Theorem 1** Suppose that a reaction endowed with mass action kinetics has a positive stationary point, and its deficiency is one. Then, if there exist two complexes lying in nonterminal strong components of the Feinberg–Horn–Jackson graph which only differ in a single species, then the reaction shows absolute concentration robustness with respect to this species.

The notions in the theorem are widely used and can be found in the paper cited above. In the case of the simple example above: ReactionsData[r1]["deficiency"] gives \( \delta = 4 - 2 - 1 = 1 \).

We have shown earlier that there exists a positive stationary point.

To see that there exist two nonterminal complexes only differing in a single species we draw the Feinberg–Horn–Jackson graph of the reaction, and gladly observe that \((A + B) - A = B.\) (To make it clear, complex \(A + 2B\) and \(B\) differs in both \(A\) and \(B\).)

The last condition is also checked by our program, it would be really hard to test this property in a large reaction set by hand.

Here is how to learn which species of the given reaction are absolutely robust: AbsoluteRobustness[r1] gives \([A]\).

Let us remark that the program is also capable to calculate the stationary concentrations both numerically and symbolically in more complicated cases. Nevertheless one should be cautious.

**Remark 1** The theoretical and computational problem lies in showing that a positive stationary point exists. Why? Because if the initial value problem to describe a reaction is \(c' = f \circ c, c(0) = c_0\) then the chemically meaningful stationary point \(c^*\)

1. should obey \(f(c^*) = 0\),
2. should be nonnegative,
3. should be on the level sets of the linear first integrals, and
4. should be on the level sets of the nonlinear first integrals.

The situation is that one cannot in general find (global) nonlinear first integrals.

Let us consider reaction \(r1\) in detail. The solutions to \(f(c^*) = 0\) in this case are \(a' \geq 0\) and \(b' \geq 0\), respectively. They are on the level curves of the linear first integral \(\psi(p,q) = p + q\) if and only if \(0 \leq a_0 + b_0 - \frac{c}{k_1}\) No nonlinear global first integral independent from \(\psi\) exists.

Let us return to detailed balancing. Certainly, the conditions were not found to treat the trivial examples above. Their role will be clearer if we cite another—this time more complicated—example from the paper.

Let us consider a model where ATP is the cofactor in the osmoregulation system of Escherichia coli: EnvZ-OmpR.

\[
\begin{aligned}
r5 &= \{X \leftrightarrow XT \rightarrow X_p, X_p + Y \leftrightarrow X_p Y \rightarrow X + Y_p, \\
&\quad XT + Y_p \leftrightarrow XTY_p \leftrightarrow XT + Y\};
\end{aligned}
\]

The existence of a positive stationary point can be proved either numerically, or symbolically using StationaryPoints[r5, Positivity -> True] and—waiting for a very long time.

The result given by ReactionsData[r5]["deficiency"] is \(\delta = n = 1 - s = 9 - 3 - 5 = 1\).

To see that there exist two nonterminal complexes only differing in a single species we draw the Feinberg–Horn–Jackson graph of the reaction (Figure 3.2.2) and find that \((X + Y_p) - \)
Figure 2: The Feinberg–Horn–Jackson graph of reaction r5 obtained by ShowJHGraph[r5,VertexLabeling->True,DirectedEdges->True] with proper complex colourings (purple ones are the terminal complexes).

\[ \text{XT} = \text{YP}, \text{therefore the reaction is absolutely robust with respect to Y_p, the phosphorylated form of the response-regulator, a species of crucial importance in the reaction.} \]

3.2.3. The conditions are only sufficient but not necessary

The fact that the conditions are only sufficient but not necessary can also be seen on the examples given by [Shinar and Feinberg, 2010], see also the Supplementary material. Here we give another example, the one shown by Professor Ross in his lecture (see also [Ross, 2008, p. 2136]):

\[ \text{j}_r = \begin{align*}
0 &\rightarrow X_1 \leftrightarrow X_2 \leftrightarrow X_3 \leftrightarrow X_4 \leftrightarrow X_5 \leftrightarrow X_6 \leftrightarrow X_7 \leftrightarrow X_8 \rightarrow 0
\end{align*} \tag{4} \]

The result given by ReactionsData[jr]["deficiency"] is \( \delta = n - l - s = 9 - 1 - 8 = 0 \), (no wonder, \( \text{j}_r \) is a compartmental system), the theorem cannot be applied, although all the stationary concentrations are only dependent on the reaction rate coefficients. Expression

\[
\text{StationaryPoint}[	ext{jr},
\{k_0,k_1,k_{-1},k_2,k_{-2},k_3,k_{-3},k_4,k_{-4},
k_5,k_{-5},k_6,k_{-6},k_7,k_{-7},k_8\},
\{c_1[0],c_2[0],c_3[0],c_4[0],c_5[0],c_6[0],c_7[0],c_8[0]\}]
\]
gives the result symbolically, what we do not reproduce here verbatim, because of the length of the formulae. Here is an equivalent symbolic form:

\[
c_i = \frac{k_0 \sum_{j=1}^{9-i} \prod_{l=10-j}^{8} k_l \left( \prod_{l=1}^{8-j} k_l \right)} {\prod_{l=i}^{8} k_l} \quad (i = 1, 2, \ldots, 8)
\]

the proof and generalization of which is left to the reader.

Once here, we can also qualitatively reproduce Fig. 3 of the paper by [Ross, 2008]. Let us use the following set of reaction rate coefficients:

\[
\text{rrc} = \{0.1,2,0.1,8,5,3,0.4,1,1,6,0.5,4,2,10,1,1\} \tag{5}
\]

and let the initial concentrations be the same as the stationary concentrations except that we add 100 to the initial value of the initial concentration of \( X_1 \). Then the return of the perturbed concentrations —which was calculated by

\[
\text{Concentrations}[	ext{jr}, \text{rrc}, \text{ini}+100\text{UnitVector}[8,1],
\{0,4\}]
\]

— to the (asymptotically stable) original stationary state is as seen on our Fig. 3.2.3.

More examples and many further interesting details can be found in the mentioned Science paper.

3.3. Improved methods of stochastic simulation

As in Part II of our paper [Nagy et al., 2011] we have exposed we have built in all the relevant direct and approximate methods
Figure 4: Stochastic Lotka–Volterra model with reaction rate coefficients $k_1 = 1$, $k_2 = 1/1000$, $k_3 = 1$ and initial conditions $x_0 = 600$, $y_0 = 400$, using tau-leaping methods and compiled functions, where 2.157 CPU time units were elapsed.

as well as explicit and implicit ones into our program package. For a long while several fancy improvements are known and are involved, here we intend to mention only two ways.

The first one is more theoretical and relies on numerical techniques which have already been applied successfully when solving ordinary differential equations. We mentioned a few of them in Nagy et al. [2011] but further ideas can and will improve the approximation methods of stochastic simulation of chemical reactions.

The other way is based on recent developments and programming tricks. The latest versions of Mathematica enable us to use compiled functions in a more efficient and delicate way which are e.g. thousands of times more effective in function evaluation compared to the "usual" evaluations (see the function Compile). Another direction of recent developments concerns parallel computing (see the functions Parallelize, ParallelMap, etc.), and the use of GPUs (see the functions CUDALink and OpenCLLink, etc.).

Here stands an example: the Lotka–Volterra model is

$$ X \xrightarrow{k_1} 2X, \quad X + Y \xrightarrow{k_2} 2Y, \quad Y \xrightarrow{k_3} 0, $$

and see Figure 4 for the simulation results.

3.4. Methods of reaction generation and decomposition

A fundamental problem of stoichiometry is the decomposition of overall reactions into elementary steps. The definition of “elementary” (or “simple”) reactions varies; we call here a step elementary if it is of order at most two. Ideally, a reaction kinetics package should not only provide the user with the list of possible decompositions (or at least a large number of decompositions, as their number may be huge, or even infinite), but it should also assist the user in the identification of elementary steps themselves, or even in the generation of possible intermediate species that may take part in an elementary step. Clearly, the complete automation of this three-step process is a formidable task, as a large amount of domain specific expertise and data must be incorporated into each step. A more reasonable goal is to provide the user with a generous list of solutions, all of which adhere to the basic conservation laws (e.g., all elementary steps must conserve the number of atoms of each element and total charge) and other combinatorial constraints imposed by the problem; and leave all further processing to the user. At this abstract level the generation of elementary steps with given reactants and the generation of decompositions of a given overall reaction are essentially equivalent, as we shall see immediately.

Suppose that the species are made of $D$ different elements, and assign a $(D + 1)$-dimensional vector $a_m$ to species $X(m)$ where the first $D$ components are the quantities of each constituent, and the last component is electric charge. A similar vector can be assigned analogously to every complex as well.

Now, a reaction

$$ \sum_{m=1}^{M} \alpha_m X(m) \rightarrow \sum_{m=1}^{M} \beta_m X(m) $$

obeys the laws of atomic and charge balance if and only if the vectors $a_m$ describing the atomic structure of the species satisfy the linear system of equations

$$ \sum_{m=1}^{M} \alpha_m a_m = \sum_{m=1}^{M} \beta_m a_m. $$

All combinatorially feasible elementary reactions can be generated by expressing each possible reactant complex (correspond-
Let \( \sum_{m=1}^{M} \alpha_m a_m \) be a vector satisfying \( 1 \leq \sum_{m} \alpha_m \leq 2 \), and let \( a_m \) be a vector with nonnegative integer coefficients. Hence, we are looking for the nonnegative integer solutions \( x \) of a system of linear equations
\[
A x = b,
\]
where \( A \) is the atomic matrix, with columns \( a_1 \) through \( a_M \) (\( M \) denotes the number of species) and \( b \) is a vector corresponding to the reactants. With \( M \) species, the elementary reactions are obtained by solving \( 2M + \binom{M}{2} \) such systems.

Similarly, if \( M \) is the number of species, an \( M \)-dimensional vector is associated to every reaction involving these species. The \( m \)-th component of the vector shows the change in the quantity of species \( X_m \) in the reaction; if a species is only a reactant, its component is negative; if it is only a product, the coefficient is positive; if it occurs on both sides, the coefficient might be either positive or negative, or even zero. The matrix \( \gamma \) with column vectors corresponding to the elementary reactions is the stoichiometric matrix of the mechanism. A combination of elementary steps with coefficients \( x \) is a decomposition of the overall reaction if and only if
\[
\gamma x = w,
\]
where \( w \) is the vector associated with the overall reaction. Again, we are primarily interested in nonnegative integer solutions \( x \), though nonnegative rational solutions also can be interpreted as decompositions of the overall reaction.

While the complexity of this problem is very high (indeed, deciding whether there exists even a single solution is NP-hard), research in these fields have yielded several relatively practical algorithms and heuristics for its solution. Further cross-fertilization between fields in this problem is essential, but one must also keep in mind that different applications produce problem instances with strikingly different characteristics, which in turn call for different methods. Indeed, in our investigations in [Kovács et al., 2004] and [Papp and Vizvár, 2006], we have found that entirely different algorithms are the most effective in elementary step generation and in the generation of the decompositions. In particular, note the following obvious differences:

- in elementary step generation multiple relatively small systems need to be solved, all of which share the coefficient matrix, whereas in decomposition a single large-scale system is solved;
- in elementary step generation all but one row consist of nonnegative numbers only, in decomposition every row and column may contain entries of different sign;
- in elementary step generation the number of solutions is always finite, in decomposition it is often infinite.

Elaborating on the last point, if a sequence of steps forms a cycle in which no species are generated or consumed, it can be added to any decomposition an arbitrary number of times. A straightforward application of Dickson's lemma [Dickson, 1913] show is that the converse is also true:

**Lemma 1** The number of decompositions is finite if and only if the elementary reactions cannot form a cycle. Furthermore, the number of decompositions that do not contain a cycle is always finite.

The lemma motivates two further problems related to decompositions: first, one needs to be able to decide whether the elementary reactions can form cycles or not, which amounts to the solution of a linear programming problem. Second, if cycles do exist, the goal changes from generating all decompositions to generating all *minimal* (that is, cycle-free) decompositions, and all *minimal cycles* (that is, cycles that cannot be expressed as a sum of two cycles). The latter is equivalent to the problem of generating all minimal \( P \)-invariants of a Petri net [Martínez and Silva, 1982].

Another approach to handle the explosion in the number of solutions is to restrict the attention to the simplest decompositions and cycles, those that consist of a small number of steps. Returning to our discussion of basic requirements for a general purpose reaction kinetics package, it has become clear to us that our package must implement a number of methods for the problems of reaction generation and decomposition, along with
an algorithm selection heuristic to choose the one most suited for the problem at hand.

Currently three algorithms are implemented for the solution of these problems, including one of our own developed with very large-scale problems in mind. Additionally, we provide two preprocessing methods to identify the steps that must take part in every decomposition, and the ones that cannot take part in any. (This greatly reduces the computation time for some of the algorithms.) We also provide a heuristic that generates a typically large number of decompositions much faster than the rigorous algorithms, but without any guarantee that it finds all minimal decompositions.

3.4.1. Example

We conclude this section with an example for elementary step generation. The oxalate–persulphate–silver oscillator [Clarke, 1992] involves 16 species, shown in Table 1; these can form $2 \cdot 16 + \binom{16}{2} = 152$ complexes that may be the reactants of an elementary step. The species consist of five atomic constituents, and have charge, hence they can be represented by a $6 \times 16$ atomic matrix, generated by the AtomMatrix command of our package. From this matrix the ElementaryReactions command generates all elementary steps involving them. In this tiny example each algorithm currently implemented proved to be rather efficient; the number of combinatorially possible elementary steps is 89.

In Part II of our paper we shall revisit this problem, and provide a detailed example of obtaining a decomposition for a complex overall reaction.

### Table 1: Species of the oxalate–persulphate–silver oscillator

| Species       |
|---------------|
| Ag⁺          |
| Ag²⁺         |
| H⁺           |
| SO₄²⁻        |
| SO₂⁻         |
| C₂O₄²⁻       |
| Ag(C₂O₄)     |
| OH⁻          |
| H₂O          |
| CO₂⁻         |
| O₂            |
| HO₂          |
| H₂O₂         |
| O₂CO₂⁻       |
| CO₂          |

4. Applications

Although there are big differences in the different fields of chemical kinetics, e.g. the role of thermodynamic data is more important in combustion, much less important in inorganic chemistry, still we hope the package will be used for more and more realistic applications in many fields. Here we only mention a few of our previous applications with the ancestors of the present package.

- Reactions on a surface, reactions in plasma: Sipos et al. [1974].
- Enzyme kinetics: Tóth [2002].
- Signal transduction: Tóth and Rospars [2005].
- Ion channels: Nagy et al. [2009].

5. Formats

A useful program should be compatible with usual formats such as CHEMKIN, PrIme, SBML etc. What we can do at the moment is that we can read in data of different formats but not in an automatic way. The main method to transform data in different forms is to use pattern matching, including if necessary or useful such tools as RegularExpression. Suppose we have the file hydrox.dat from the website [http://www.math.bme.hu/~nagyal] describing a model of hydrogen oxidation. Then, we can import and transform it like this:

```plaintext
Import["hydrox.dat"] /. {x__, "SPECIES", Shortest[y__], "END", z__} :> y
```

The problem is obviously similar to, or may be considered to be part of parsing.

6. Speed and Accuracy

It is important to be able to handle a reaction during a reasonable time interval even if it consists of a large number of reaction steps and species. Similarly, the accuracy should also be enough for comparisons with measurements.
Let us mention a few more specific problems where the number of species and of reaction steps can be really high—beyond the well known areas of atmospheric chemistry, metabolism and combustion. One might wish to treat reaction chromatography in such a way that one divides a column into thousands of plates, assumes the same reaction on each of the plates and also assumes (linear) diffusion between the plates. This is the problem mentioned by Prof. Trapp in his lecture at the conference. Let us also mention here the less known paper by Shapiro and Horn [1979a,b] which gives a qualitative treatment of such systems using the tools of Chemical Reaction Network Theory.

Or, one might describe the transformation taking place among thousands of polymers with different molecular weight, as mentioned in the poster by P. van Steenberge et al. Another problem might be the treatment of molecules sitting at different energy levels of which one might have several millions. A possible first step to treat such a system might be to measure the time needed to solve the induced kinetic differential equation of a model as a function of size as follows.

lendvay[n_] := Table[X_i ↔ X_i+1, {i, 1, n - 1}]

Concentrations[lendvay[1000], Array[N[#] &, 1998], Array[0.1 N[#] &, 1000], {0, 1}] // Timing

It turned out that such a model can be solved in 30 seconds using Mathematica without our package, without Parallelize and without using GPU and similar tools, i.e. one can say, only applying Low Performance Computing. This is quite a promising start in this direction.

7. Language: Mathematica, what else?

We do not want to enter into an infinitely long discussion about the advantages and disadvantages of mathematical program packages, we are only making a few remarks, which are possibly acceptable by the majority of our readers.

Mathematica is capable of symbolic and numeric calculations, creating graphics (in fact, even whole presentations and publications) within the same framework. In numerical computations it is not worse than any other program [Weisstein, Inc.]. It uses as many cores/processors as you have in parallel, it implements OpenCL and CUDA to use GPUs, you can ask it to calculate the C form of a compiled function if you need, etc.) Using a symbolic-numeric mathematical programming language such as Mathematica is extremely helpful in creating very transparent programs; code that can even be read as "pseudo-code" for those readers who are most reluctant to get acquainted with the software.

In a meticulous analysis of the consecutive reaction Yablonsky et al. [2010] have found a symbolically expressed necessary and sufficient condition for the three concentration time curves to have a single point of intersection (see also [Tóth and Simon, page 341]). As a final application of our package we show how to solve this (and also similar, symbolically untractable problems) numerically.

8. Outlook

Having collected so much requirements with illustrations in the second part we are going to turn to the problems and diffi-
culties when writing and using a program package pretending to solve so many problems of reaction kinetics.

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