

## Simulation of the Oregonator model by using Deterministic ARMS

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### Abstract

We propose a deterministic method for simulating chemical reactions, Deterministic Abstract Rewriting System on Multisets (DARMS), which is based on the concept of *Mass Action Law*. The feasibility and utility of DARMS are demonstrated by applying it to the Oregonator, which is well-known model of the Belousov Zhabotinskii (BZ) reaction.

### 1 Abstract Rewriting System on Multisets, ARMS

ARMS was proposed in 1996 [6] as an abstract model of chemical reactions, *Artificial Chemistry* (AC), in the context of the Artificial Life (AL). We rigidly proved that an ARMS can be regarded as a Chemical Master Equation (CME) and, through continuous approximation, the deterministic Reaction Rate Equation (RRE), which is denoted by a set of ordinal differential equations can be obtained from an ARMS [7].

Basically, an ARMS is a construct  $\Gamma = (A, w, R)$ , where  $A$  is an alphabet,  $w$  is a multiset present in the initial configuration of the system, and  $R$  is the set of multiset rewriting rules.

Let  $A$  be an *alphabet* (a finite set of abstract symbols). A *multiset* over  $A$  is a mapping  $M : A \mapsto \mathbf{N}$ , where  $\mathbf{N}$  is the set of natural numbers;  $0, 1, 2, \dots$ . For each  $a_i \in A$ ,  $M(a_i)$  is the *multiplicity* of  $a_i$  in  $M$ , we also denote  $M(a_i)$  as  $[a_i]$ .

We denote by  $A^\#$  the set of all multisets over  $A$ , with the empty multiset,  $\emptyset$ , defined by  $\emptyset(a) = 0$  for all  $a \in A$ .

A multiset  $M : A \mapsto \mathbf{N}$ , for  $A = \{a_1, \dots, a_n\}$  is represented by the state vector  $w = (M(a_1), M(a_2), \dots, M(a_n))$ ,  $w$ . The union of two multisets  $M_1, M_2 : A \mapsto \mathbf{N}$  is the addition of vectors  $w_1$  and  $w_2$  that represent the multisets  $M_1, M_2$ , respectively. If  $M_1(a) \leq M_2(a)$  for all  $a \in A$ , then we say

that multiset  $M_1$  is included in multiset  $M_2$  and we write  $M_1 \subseteq M_2$ .

A *reaction rule*  $r$  over  $A$  can be defined as a couple of multisets,  $(s, u)$ , with  $s, u \in A^\#$ . A set of reaction rules is expressed as  $R$ . A rule  $r = (s, u)$  is also represented as  $r = s \rightarrow u$ . Given a multiset  $w \subseteq s$ , the application of a rule  $r = s \rightarrow u$  to the multiset  $w$  produces a multiset  $w'$  such that  $w' = w - s + u$ . Note that  $s$  and  $u$  can also be zero vector (empty).

The *reaction vector*,  $\vec{r}_j$  denotes the change of the number of  $a_i$  molecules produced by one reaction of rule  $r_j$ .

#### 1.1 ARMS with chemical kinetics

We modify the ARMS for modeling chemical kinetics and this enables us to use experimentally obtained reaction rates directly, similar to the derivation of the Gillespie's “-leap method” [4].

In order to handle experimental data, we employ multisets with real multiplicities; such a multiset  $X : A \mapsto \mathbf{R}$  for  $A = \{a_1, \dots, a_n\}$  is represented by the state vector  $\mathbf{x} = (X(a_1), X(a_2), \dots, X(a_n))$ .  $X(a_i)$  denotes the molar concentration of specie  $a_i$ .

Let us assume that there are  $N \geq 1$  molecular species  $\{a_1, \dots, a_n\}, a_i \in A$  that interact through reaction rules  $R = \{r_1, \dots, r_m\}$ . As the time evolution of  $\mathbf{x}$  unfolds from a certain initial state, let us suppose the state transition of the system to be recorded by marking on a time axis the successive instants  $t_1, t_2, \dots$  as  $X(t_j)$  ( $j = 1, 2, \dots$ ). We specify the dynamical state of  $\mathbf{x}(t) \equiv (X(a_1(t)), X(a_2(t)), \dots, X(a_N(t)))$ , where  $X(a_i(t))$  is the molar concentration of  $a_i$  specie at time  $t$ ,  $t \in \mathbf{R}$ .

#### Chemical kinetics

We assume that all chemical reactions take place in a well-stirred reactor; this assumption is required due to the strong dependence of the reaction rate on the concentration of the reagent species. We define the

function  $f_j$ , called the *propensity function* for  $r_j \in R$  by

$$f_j(x) = c_j h_j, \quad (1)$$

where  $c_j$  denotes the average probability that a particular combination of  $r_j$  reactant molecules will react in the next infinitesimal time interval  $dt$  and  $h_j$  is the number of possible combinations of the species of  $r_j$  in  $dt$ .

$f_j \mathbf{x}(t) dt$  means that the probability that reaction  $r_j$  will occur in the next infinitesimal time interval  $[t, t + dt]$ , ( $j = 1, \dots, m$ ).

The time evolution of  $\mathbf{x}(t)$  is a jump Markov process on the  $N$ -dimensional non-negative lattice. In this case, an ARMS has a *macroscopically infinitesimal time scale*,  $\Delta$ , where reaction rules can be applied several times simultaneously, yet since the stoichiometrical change of the state during  $\Delta$  is small enough, none of the propensity functions change appreciably.

The parameter  $\Delta$  corresponds to (small time interval) in the Gillespie's method [4] and it satisfies the *Leap Condition* given below; an amount  $\Delta$  that spans a *very large* number of applying every reaction rules still satisfies the Leap Condition.

*Leap Condition:* We require  $\Delta$  to be small enough that the change in the state during  $[t, t + \Delta]$  will be so small that no propensity function will suffer an appreciable (i.e., macroscopically noninfinitesimal) change in its value.

We also assume that the number of applications of each reaction rule in  $\Delta$  obeys

$$\langle P(f_j(\mathbf{x}), \Delta) \rangle = f_j(\mathbf{x})\Delta \gg 1 (\forall j = 1, \dots, m), \quad (2)$$

where  $P(f_j(\mathbf{x}), \Delta)$  is the *Poisson* random variables is the number of reactions that occur in  $\Delta$ .

Here, let us consider the probability function  $Q$ , defined by  $Q(z_1, \dots, z_k | \Delta, \mathbf{x}, t)$ , which means the probability, given  $\mathbf{X}(t) = \mathbf{x}$ , that in the time interval  $[t, t + \Delta]$  exactly  $z_j$  times of rule applications or  $r_j$  will occur, for each  $j = 1, \dots, m$ .  $Q$  is evidently the joint probability density function of the  $M$  integer random variables,  $Z_j(\Delta, \mathbf{x}, t)$  means the number of times, given  $\mathbf{X}(t) = \mathbf{x}$ , that reaction rule  $r_j$  will apply in the time interval  $[t, t + \Delta]$  ( $j = 1, \dots, m$ ).

If the equation (2) is satisfied, the *Poisson* random numbers will be practically indistinguishable from *normal* random numbers, which are uncorrelated statistically independent normal random variables with mean 0 and variance 1.

Then the jump Markov process can be approximated by the *continuous* Markov process defined

by the standard form of *chemical Langevin equation* (CLE).

$$\begin{aligned} \lambda_i &= \sum_{j=1}^m z_{j \ i} = \sum_{j=1}^m f_{j \ ji} = \sum_{j=1}^m [f_j(\mathbf{x})\Delta + (f_j(\mathbf{x})\Delta)^{\frac{1}{2}}n_j]_{ji} \\ &= \sum_{j=1}^m z_{j \ i} f_j(\mathbf{x})\Delta + \sum_{j=1}^m z_{j \ i} f_j^{\frac{1}{2}}(\mathbf{x}) n_j \Delta^{\frac{1}{2}}, \end{aligned} \quad (3)$$

where  $n_j$  is temporally uncorrelated statistically independent normal random variables. Since  $Z_j(\Delta, \mathbf{x}, t) = P(f_j(\mathbf{x}, \Delta))$ , it is equal to  $f_j(\mathbf{x})\Delta$ , by the equation (2).

In case  $f_j(\mathbf{x})\Delta \rightarrow \infty$ , (2) implies that in the part  $f_j(\mathbf{x})\Delta + (f_j(\mathbf{x}\Delta))^{\frac{1}{2}}n_j$  of the equation (3) the second term becomes negligibly small compared to the first term and  $\lambda_i$  in the limit ( $f_j(\mathbf{x})\Delta \rightarrow \infty$ ), because

$$\begin{aligned} \lambda_i &= \sum_{j=1}^m z_{j \ i} f_j(\mathbf{x})\Delta = \sum_{j=1}^m [f_j(\mathbf{x})\Delta]_{ji} \\ &= \sum_{j=1}^m z_{j \ i} f_j(\mathbf{x})\Delta. \end{aligned} \quad (4)$$

This is the Euler formula (piecewise linear approximation) for numerically solving the RRE. It shows how to derive the continuous and deterministic RRE of traditional chemical kinetics from the stochastic method. Since  $z_{j \ i} f_j(\mathbf{x})$  represents the stoichiometric change in the next infinitesimal time, it can be regarded as the reaction rate of  $r_j$ ,  $v_j$ , and we obtain:

$$\lambda_i = \sum_{j=1}^m z_{j \ i} f_j(\mathbf{x})\Delta \equiv \sum_{j=1}^m v_j(\mathbf{x})\Delta. \quad (5)$$

In the Gillespie leap method, the number of applications of each rule within  $\Delta$  is randomly generated according to the *Poisson* or *Normal* distribution and  $\lambda_i$  is calculated.

In the ARMS,  $\lambda_i$  is calculated by using the reaction rate given by the equation (5). As in the numerically solving an ordinary differential equation of the form  $dX/dt = f(X)$  by the Euler method, a leap down the stepwise time axis by  $\Delta$  according to  $X(t + \Delta) = X(t) + f(X(t))\Delta$  will produce errors whenever the function  $f$  changes during that  $\Delta$  increment.

It is well-known that the second-order Runge-Kutta procedure can reduce these errors; use the simple Euler method to estimate the “midpoint” value of  $X$  during  $\Delta$ , and then calculate the actual increment in  $X$  by evaluating the slope function  $f$  at that estimated midpoint. The midpoint value can be obtained from the

expected state change  $\lambda$  as  $\mathbf{x} + \frac{\lambda}{2}$ . In the Gillespie's leap method, this procedure is used and it shows that this procedure can reduce numerical errors [4].

## 1.2 Algorithm of DARMS

In Deterministic Abstract Rewriting System on multisets (DARMS) [8], reaction rules are applied in maximally parallel and deterministic way. Hence, the DARMS accommodates P Systems, while it has background in theoretical chemistry.

*Step 0*(Initialization). The time  $t$  is set to 0 and the set of vectors  $V = (\delta_1, \delta_2, \dots, \delta_N)$  ( $j = 1, 2, \dots, m$ ), expressing the stoichiometric change of each species, are initialized. Then all inputs of the system are assigned to their respective variables,

- $X(a_1), X(a_2), \dots, X(a_N)$  are set to the initial quantities of species;
- $k_1, \dots, k_m$  to set  $m$  rate constants corresponding to the  $m$  reactions;
- $t_{stop}$  to the ending instant of simulation;
- set the value of  $\Delta$ ;

*Step 1*(Calculation of state change vector  $\Lambda_t$ ). According to reaction rules, stoichiometric change of each specie  $\lambda_i$  is calculated as well as the state change vector;  $\Lambda_t = (\lambda_1, \lambda_2, \dots, \lambda_N)$  is calculated, where  $\lambda_i = \sum_{j=1}^m j i v_j \mathbf{x}(t) \Delta$ .

*Step 2*(System update and branching). The quantity of each species and  $t$  is updated, by using  $\Lambda_t$  and  $\Delta$ :

$$\begin{aligned} \mathbf{x}(t) &= \mathbf{x}(t - \Delta) + \Lambda_{t-\Delta}, \\ t &:= t + \Delta. \end{aligned}$$

If  $t \geq t_{stop}$  or if there are no reactions left in the reactor, the simulation is stopped and the results are sent to the output stream. Otherwise, the simulation returns to *Step 1*.

## 2 The Oregonator

The Belousov-Zhabotinskii (BZ) reaction displays a remarkable repertoire of exotic behavior, including periodic and chaotic temporal oscillations, multiple stable stationary states, temporally and spatially periodic expanding target patterns, rotating multi-armed spiral waves.

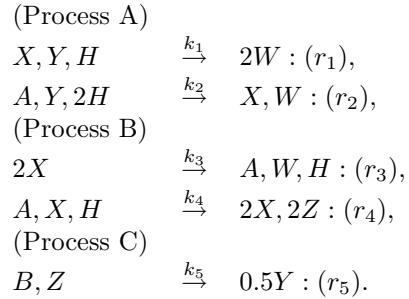


Table 1: Oregonator

The chemical kinetic description of BZ reaction was put forward by Field, Körös (FKN) [2]. FKN can be considered as the best understanding of the process by recognizing that there are two different over-all processes that can occur in the system.

The FKN mechanism can be described as three concurrent (and at times competing) processes:

- Process A: The three steps reduction of bromate to bromine.
- Process B: The introduction of hypobromous acid to compete as a reducing agent for bromate.
- Process C: The reduction of the catalyst formed from Processes A and B.

The Oregonator scheme is outlined in Table 1:

As for reaction constants, a combination of Tyson's "Lo" and Field-Försterling values (TFF parameter) are used [5]:  $k_1 : 10^6 M^{-2} S^{-1}$ ,  $k_2 : 2M^{-3} S^{-1}$ ,  $k_3 : 2 \times 10^3 M^{-1} S^{-1}$ ,  $k_4 : 10M^{-2} S^{-1}$ ,  $k_5 : B \times 2 \times 10^{-2} S^{-1}$ , where  $M$  stands for one molar, and  $S$  stands for a second.

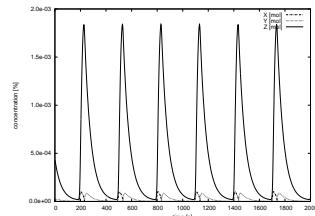


Figure 1: DARMS,  $\Delta = 0.0001$ : Population dynamics of  $X, Y, Z$ , where the vertical axis illustrates the molar concentration of chemicals (mole) and the horizontal axis illustrates the time, where each stepwise is  $\Delta$ . It shows a typical pattern of oscillations

## 2.1 Simulation of the Oregonator

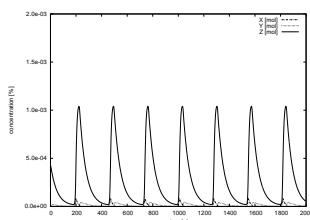


Figure 2: DARMS,  $\Delta = 0.1$ : Population dynamics of  $X, Y, Z$ , where the vertical axis illustrates the molar concentration of chemicals (mole) and the horizontal axis illustrates the time, where each stepwise is  $\Delta$ . The amplitudes of oscillations are smaller than the case when  $\Delta$  is smaller than 0.1.

In the Oregonator [3], chemicals  $A$  and  $B$  are resources and assumed that they are continuously supplied or largely existing in comparison with other chemicals.  $W$  is the final product of these reactions and typical oscillations among  $X$ ,  $Y$  and  $Z$  emerge. Reactions of generating  $X$  ( $Hb_rO_2$ ) are triggers of oscillations and these reactions increase the concentration of  $Z$  ( $C_e^{4+}$ ) and then high concentration of  $Z$  leads to reactions generating  $Y$  ( $B_r$ ); since this reaction required  $Z$ , the concentration of  $Z$  is decreased.

We simulate the Oregonator by using the DARMS with the TFF parameter. We examine each case when  $\Delta = 0.0001, 0.001, 0.01, 0.1, 1.0$ . When the values of  $\Delta$  are between 0.0001 and 0.01, the stoichiometric change of species show typical oscillations (Figure 1); these typical oscillations can also be seen through numerical simulation of the reaction rate equation that are expressed by a set of differential equations. At  $\Delta = 0.1$ , the amplitude of oscillation becomes small, while the patterns of oscillations were kept the same (Figure 2).

At  $\Delta = 1.0$ , the pattern of oscillations become different from the typical one, where the amplitude of oscillation of  $X$  and  $Z$  become small, and the amplitude of  $Y$  declines to nearly zero (Figure 3). The reason is that the value of  $\Delta$  becomes large: since the calculation of the DARMS requires piecewise linear approximation, as the  $\Delta$  becomes larger, the quality of approximation decreases.

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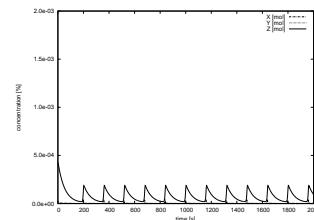


Figure 3: DARMS,  $\Delta = 1.0$ : Population dynamics of  $X, Y, Z$ , where the vertical axis illustrates the molar concentration of chemicals (mole) and the horizontal axis illustrates the time, where each stepwise is  $\Delta$ . The pattern of oscillation is different from the typical one.

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