Dynamics of the Chemical Master Equation, a strip of chains of equations in d-dimensional space.

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We investigate the multi-chain version of the Chemical Master Equation, when there are transitions between different states inside the long chains, as well as transitions between (a few) different chains. In the discrete version, such a model can describe the connected diffusion processes with jumps between different types. We apply the Hamilton-Jacobi equation to solve some aspects of the model. We derive exact (in the limit of infinite number of particles) results for the dynamic of the maximum of the distribution and the variance of distribution.

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I. INTRODUCTION

The Chemical Master Equation (CME) \textsuperscript{[1],[2],[3],[4]} is the main tool to investigate chemical reactions with few molecules. This statistical physics model describes also the branching-annihilation processes and (in strip version, considered in the current article) the discrete version of the connected diffusion.

For reactions with few molecules the number of molecules fluctuate, and we can describe the reaction process through the probabilities of having a given number of molecules. While working with D types of molecules, we work with the probabilities of having given integer number of molecules \(P(X_1,...X_D, t)\), thus the variables are located at the nodes of a D-dimensional lattice, where integer \(X_i\) describe the number of molecules of the \(i\)-th type. One solves a linear system of differential equations for \(P(X_1,...X_D, t)\) to define the probability of having the given numbers of molecules at time \(t\). The CME is a linear equation, like the Shroedinger equation for the wave function. We assume that the system does not interact with the environment, and during the measurement we observe just some collection of integers for the different types of molecules, defined by probabilities \(P(X_1,...X_D)\).

While the numerical solution of CME is possible using the Gilepsee algorithm, the analytical investigation of CME is very important. The problem was solved exactly in the infinite system size (the maximal number of particles) limit for \(D=1\) using quantum mechanics or mapping to the Hamilton-Jacobi equation (HJE) \textsuperscript{[5],[6],[7],[8],[9]}. In \textsuperscript{[10]} an implicit expression was obtained for the dynamics of the population distribution variance, following the HJE method of \textsuperscript{[11],[12],[13]}. To obtain an exact complete solution of CME in dimensions \(D \geq 2\) is a very hard problem and only a few solutions are known, see \textsuperscript{[14]}.

Sometimes the CME is organized as a strip of systems of equations \textsuperscript{[15],[16]}. In \textsuperscript{[1]} strips of one dimensional chains of equations (the variables are located on 1-D axes and the time derivative of some variable depends on its neighbors) are considered as a model of coupled diffusion processes: a situation in 2 dimensional space, when there is a diffusion in one dimension, and jump process in the other dimension (continuous diffusion later is replaced by discrete jumps). \textsuperscript{[16]} considers a strip of three chains of equation, each of chains defined in 2-dimensional space, identifying the model with genetic switch phenomenon. Again we have a diffusion, completed by jump process.

In the current article we formulate the following general problem: we investigate the CME, organized as a strip of \(d\) chains of equations, each defined in D-dimensional space with a maximal number of a given type of molecule \(N\), where \(d \ll N\).

We will also give differential equations, defining the solution of the moments of distributions of the model for the general \(d,D\) case. Two mathematical methods have been applied to solve the CME in the limit of large number of molecules: diffusion approximation and the HJE. The HJE method allows to apply the methods of Hamilton mechanics \textsuperscript{[18]}, the Hamilton equation for the characteristics \textsuperscript{[19],[20]}. For the recent introduction to the method see \textsuperscript{[21]}. In this article we consider the situation when the HJE method is valid while describing the solution of the CME.

Let us first review known results of the CME. In the simplest case \((D=1,d=1)\) and one step processes \((K=1)\), we have a system of equations, see Fig. 1 for illustration,

\[
\frac{dP(X,t)}{Nd t} = R_1(X-1)P(X-1,t) + R_{-1}(X+1)P(X+1,t) + R_0(X)P(X,t)
\]

\[
R_0(X) = -(R_1(X) + R_{-1}(X)),
\]

FIG. 1: The CME for the case \(d = 1, D = 1, K = 1\). Possible states of the system (indicated as boxes with the number of molecules inside) are located on the 1-d space \((D = 1)\). There are transitions only between neighbors \((K = 1)\). There is only one chain \((d = 1)\). The back transition rates is \(R_{-1}\) and the forward transition rate is \(R_1\), see Eq. (1).

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where \( 0 \leq X \leq N \), and \( N \) is the maximal possible number of molecules, a large number. \( R_1(X) \) is the forward 1-step transition rate, and \( R_{-1}(X) \) is the back 1-step transition rate.

A similar equations has been formulated for the virus evolution problems. In case of virus evolution models \([22],[23]\), there is inhomogeneous term (fitness function) on the right hand side of equation, and \( P(X) \) describe the density of different types of viruses.

While in virus evolution models one can consider a mixed state at the start, in case of the CME, by Eq.(1), there is a definite value \( n \) for \( X \) at the start. Therefore

\[
P(X,0) = \delta_{X,n} \tag{2}
\]

If during an elementary reaction event there is a consumption or birth of several molecules with maximal consumption (birth) number \( K \), then our system of equations is modified:

\[
\frac{dP(X,t)}{Nd t} = \sum_{-K \leq m \leq K} R_m(X - m)P(X - m,t) \tag{3}
\]

Here \( R_{\pm m}(X), m \neq 0 \) are the rates of \( m \)-step transitions, therefore are nonnegative numbers, while \( R_0(X) = -\sum_{-K \leq m \leq K} R_m(X) \) a generalization of the expression by Eq.(1) ensures a probability conservation condition, see Fig. 2 for an illustration. The probability rate in the CME are defined via reaction rates in case of infinite number of molecules, see \([3]\). Different rates \( R \) in our equations describe different elementary reaction events. In the literature, models with \( K \leq 3 \) has been considered. The derivative \( dP(X)/dt \) depends on \( P(X') \) for the neighbors and that’s why we name our system of equations as a "chain" of equations.

Consider the case of D-dimensional space,

\[
\frac{dP(\vec{X},t)}{N dt} = \sum_{l=1}^{D} \sum_{n_l=-K}^{K} R_{n_l}(\vec{X} - \vec{n})P(\vec{X} - \vec{n},t) \tag{4}
\]

Here \( \vec{X} \) is a D-dimensional vector, where \( D \) is the number of different type of molecules participating in the reaction, and for \( \vec{n} \neq 0 \) the nonnegative number \( R_{\vec{n}} \) describe the probabilities of the jump with the change of the number of the \( l \)-th type via \( n_l, 1 \leq l \leq D \), and negative number \( R_{\vec{n}} \) ensures the probability conservation. As an illustration consider the case \( D = 4 \). The process, when the molecules of types 1, 2, 3 collide giving a birth of 3 molecules of type 4 is described via a coefficient \( R_{-1,-1,-1,3}(x_1 + 1, x_2 + 1, x_3 + 1, x_4 - 3) \). If these three molecules just catalyze the birth of one molecule of type 4 the process is described via coefficient \( R_{0,0,0,1}(x_1, x_2, x_3, x_4 - 1) \).

If there are \( n \) reactants, then the coefficient in the CME \( R \) is connected with the coefficient in the chemical kinetic equation \( \dot{R} \) with the scaling \( R = \dot{R}/N^n \), see \([4]\).

The Hamilton-Jacobi equation (HJE) is a powerful method to investigate the CME at large values of \( N \). For illustration consider Eq.(1). For the case \( N \gg 1 \) we assume an ansatz

\[
P(X,t) = \exp[Nu(x,t)], \quad x = \frac{X}{N}. \tag{5}
\]

The ansatz by Eq.(5) is similar to the WKB approximation in quantum mechanics \([9]\). Eq.(5) gives with \( 1/N \) accuracy:

\[
-H(x,p) = r_-(x)e^{-p} + r_+(x)e^p - (r_+(x) + r_-(x))
\]

and one obtains \([6]\):

\[
\frac{\partial u(x,t)}{\partial t} + H(x,u') = 0
\]

where we denote \( r_-(x) = R_{-1}(Nx) \), \( r_+(x) = R_{+}(Nx) \). Equation (7) is a partial differential equation of a special form, the Hamilton-Jacobi equation. According to the standard handbook of classical mechanics \([13]\), it can be solved using the solution of Hamilton’s equation for \( x(t), p(t) \), where \( x(t) \) describes the characteristic curves of HJE \([21],[19],[13]\). The \( N \) in the dominator of the left hand side of Eqs.(3),(4) is written arbitrary. We are choosing a proper scaling \( N^n \) with some integer \( n \), to get a smooth, \( N \) independent functions \( u(x) \) near the maximum of the distribution, \( x = y(t) \).

We can return to the case \( N \to \infty \). We consider the more general case \( N^n, n > 1 \), then rescaling \( t \to t/N^{n-1} \) return to the case of article. The HJE approach allows to define the whole distribution \( P(X) \) or \( u(x) \). In the following sections we will derive the HJE version of the CME for more involved situations than Eq.(3). In this work we are mainly interested in the dynamics of the maximum of distribution (the point \( x \) where \( u'(x,t) = 0 \)) and in the variance of the distribution \( P(X,t) \), given by \( u''(x,t) \) at the point of maximum. For our purposes there is no need to apply a powerful method of characteristics. We will use directly the HJE. We are interested in the solution \( u(x,t) \) near the maximum of the distribution, \( x = y(t) \) in our notation. We can derive exact relations by expanding in the HJE the solution in degrees of \( (x - y(t)) \). Such a method has been applied in \([10]\), where we derived the Van Kampen’s large system size expansion method from HJE.

In Section II-A we derive HJE for the \( d > 1, D = 1 \) case. While we derive the HJE to describe the full distribution, it is more informative to calculate the motion of the maximum and the variance. We derive corresponding ODEs in Sections...
II-B and II-C. In Section II-D we considered an example of
$D = 1, d = 2$. In Section III-A we consider the strip of D
dimensional equations. In the Appendix we present the equa-
tions to define the dynamics of the third moment of distribu-
tion, investigation of evolution insertion-deletion model [29].
In section III-B we give the finite size corrections to the bulk
solution, following to [11], [8], [9].

II. THE STRIP OF ONE DIMENSIONAL CHAINS

A. Derivation of HJE

Here we consider the CME, when the probability depends
on two integer coordinates, $l$ and $X$, thus we work with
$P_l(X, t)$. There is a probability conservation condition
\[ \sum_{1 \leq i \leq l} \sum_{0 \leq X \leq N} P_l(X, t) = 1 \tag{8} \]
In Eq.(8) the maximal number of molecules is constrained by
$N$, a reasonable constraint in case of chemical reaction in a
finite volume, and $d \ll N$.

In principle only one boundary condition at $X = 0$ can be
present or some large parameter $N$. In both cases HJE method
can be applied.

We consider a large $N$ limit:
\[ N \to \infty. \tag{9} \]
There is a system of equations
\[ \frac{dP_l(X, t)}{N dt} = \sum_{1 \leq n \leq d} \sum_{-K \leq m \leq K} R_{lnm}(X - m)P_n(X - m, t), \tag{10} \]
There are transitions along the states of one chain (maxi-
mal jump is K-step), described by nonnegative coefficients
$R_{lnm}, m \neq 0$ and there are jumps between different chains,
described by nonnegative $R_{lnm}$ with $l \neq n$. There are nega-
tive $R_{l00}$, and there is an equation
\[ \sum_{1 \leq l \leq d} \sum_{-K \leq m \leq K} R_{lnm}(X) = 0 \tag{11} \]
to support the probability conservation condition.

The system is slightly modified near the borders $X = 0$
and $X = N$. In principle, we can use a one-sided boundary
condition, but for our case of solution, described by the HJE,
the boundary conditions are irrelevant.

Let as assume that at the limit $N \to \infty$ (condition a.), the
rates are described via smooth functions
\[ R_{lnm}(X) = r_{lnm}(x), \quad x = \frac{X}{N} \tag{12} \]
We consider the models under the condition
\[ \det\{A_{ln}\} = 0, \quad A_{ln} = \sum_{-K \leq m \leq K} r_{lnm}(x) \tag{13} \]
Eq. (13) is a consequence of probability conservation condi-
tion during the transitions between different chains at the
position $X$, see model by Eq.(31) as an example.

Let us consider the following ansatz:
\[ P_l(X) = v_l \exp[Nu(x, t)], \quad x = \frac{X}{N}. \tag{14} \]
We assume that the maximum of different components
$P_l(X)$ are near the same $X$. Thus, if the maximum is at
the points $X_1$ and $X_2$, then
\[ \frac{|X_1 - X_2|}{N} \ll 1. \tag{15} \]
The smoothness of functions $r_{lnm}$ in Eq.(12) is crucial for the
ansatz Eq.(14). In [13] we considered an example, when the
exponential ansatz $\exp[Nu(x)]$ is invalid for non-smooth
functions of transition rates.

We put also the condition b:
\[ d \ll N. \tag{16} \]
Then we have the following system of equation:
\[ v_l \frac{\partial u}{\partial t} = \sum_{1 \leq n \leq d} \sum_{-K \leq m \leq K} r_{lnm}(x)v_n e^{-mu'}. \tag{17} \]
We dropped the terms $dv_l/dt$, assuming $d \ll N$, where $N$ is
the system size or some large parameter.

As the system of equations for $v_l$ should be consistent, we
have the condition:
\[ \det[M_{ln}(x, u')] - q\delta_{ln}(x) = 0, \quad M_{ln}(x, u') = \sum_{-K \leq m \leq K} r_{lnm}(x)e^{-mu'}, \quad q = \frac{\partial u}{\partial t}. \tag{18} \]
We assumed that $M_{ln}(x, u')$ is a (smooth) analytical func-
tion of $x$, and all the terms of $M$ have the same, zero
degree of $N$ (the case of the same, non-zero degree of $N$
could be investigated after re-scaling of time). In this case we can
consider $N \to \infty$ limit in a proper way. We denote $x = X/N$.
Eq.(13) gives
\[ \det[M_{ln}(x, 0)] = 0 \tag{19} \]
Eq. (18) is our main equation. It has a high degree of $q = \frac{\partial u}{\partial t}$
and, therefore, it defines a standard HJE with the first degree
of $q$ as in Eq.(7) and corresponding Hamiltonian implicitly.
To construct the full solution $u(x, t)$ we have to find such an
explicit Hamiltonian. Fortunately, there is no need for an ex-
plicit Hamiltonian to investigate the properties of the solution
near the maximum of distribution. Expanding the left hand
side of Eq.(18) in the degrees of $q$, we re-write Eq.(18) as
\[ \sum_{l=0}^d (-q)^l H_l = 0 \tag{20} \]
Eq. (19) gives:

\[ H_0(x, p)|_{p=0} = 0 \]
\[ p \equiv \frac{\partial u}{\partial x} \]  
(21)

In investigating the CME we are first interested in the maximum of the distribution, then in the variance.

**B. The dynamics of the maximum of distribution**

Let us first consider the dynamics of the maximum. While calculating the dynamics of the maximum, it is enough to consider 0-th and first terms in Eq. (20).

We assume the ansatz

\[ u = -\frac{V(t)}{2} (x - y(t))^2. \]  
(22)

Let us differentiate Eq. (20) with respect to x, and consider the point \( x = y(t) \). The higher terms of \( q^i \) disappear, as \( q \sim (x - y(t)) \). We obtain:

\[ -V \frac{\partial H_0(x, p)}{\partial p}|_{p=0} = q_x H_1 = 0. \]  
(23)

Using \( H_0 = det[M_{ln}] \),
\[ H_1 = -\frac{d}{dx} \partial M_{ln}(x, u') - q_b \]  
we obtain

\[ \frac{dy(t)}{dt} = -\frac{H_0', p(y, 0)}{H_1(y, 0)} = b(y). \]  
(24)

Eq. (24) defines the dynamics of concentration in case of the infinite number of molecules. It is the first step in the investigation of the CME.

**C. The dynamics of the variance**

To investigate the dynamics of the variance, we should consider the \( q^2 \) term in Eq. (20). We will consider the solution near \( x = y(t) \). Dropping the higher terms in \( (x - y(t)) \), we obtain:

\[ \frac{d^2}{dx^2} (q^2 H_2 - q H_1 + H_0)|_{p=0} = 0. \]  
(25)

Using \( \frac{dH(x, p)}{dx} = H' + H' p' \), we calculate

\[ \frac{d^2 H(x, p)}{dx^2} = H''_{xx} + 2 H''_{xp} p' + H''_{pp} (p')^2. \]  
(26)

Putting Eq. (26) into Eq. (25), we obtain

\[ \frac{d^2}{dx^2} [q^2 H_2 - q H_1 + H_0] = 2(q_x)^2 H_2 - q_x^2 H_1 - 2 q_x [H'_{xx} + H'_{xp} p'] \]
\[ + H''_{xx} + 2 H''_{xp} p' + H''_{pp} (p')^2 = 0. \]  
(27)

Using the ansatz (22), we derive from Eq. (27)

\[ \hat{V} H_1 + V^2 [2 b^2 H_2 + 2 b H_1' + H''_{pp}] + \]
\[ + V [-2 b H_1' - 2 H''_{0xp}] + H''_{0xx} = 0. \]  
(28)

We use the notation \( b(y) \) from Eq. (18). Using that \( H''_{0xx} = 0, -b H_1 - H''_{0xp} = 0 \), we obtain

\[ \hat{V} H_1 + V^2 [2 b^2 H_2 + 2 b H_1' + H''_{0pp}] + \]
\[ + V [-2 b H_1' - 2 H''_{0xp}] = 0. \]  
(29)

Using \( dy/dt = b(y) \), and denoting \( Q = 1/V \), we finally have

\[ \frac{dQ}{dy} = A(y) + QB(y) \]
\[ B(y) = \frac{[2 b^2 H_2 + 2 b H_1' + H''_{0pp}]}{-b(y) H_1(y, 0)} \]
\[ A(y) = \frac{2 b^2 H_2 + 2 b H_1' + H''_{0pp}}{-b(y) H_1(y, 0)}. \]  
(30)

Eq. (30) defines the dynamics of the variance \( <(x - y(t))^2> = Q/N \).

**D. The case of two 1-D chains, the genetic switch model**

Consider the case \[^1\]:

\[ \frac{dP_{1,n}}{dt} = k N [P_{1,n-1} - P_{1,n}] + \rho [(n + 1) P_{1,n+1} - n P_{1,n}] \]
\[ - n h P_{1,n} + N f P_{2,n} \]
\[ \frac{dP_{2,n}}{dt} = k N [P_{2,n-1} - P_{2,n}] + \rho [(n + 1) P_{2,n+1} - n P_{2,n}] \]
\[ + n h P_{1,n} - N f P_{2,n}. \]  
(31)

Thus, there are back (\( \rho n \)) and forward (\( KN \)) transition rates in the 1-d chains, as well as \( n h \) and \( N f \) transition rates between different chains. Fig. 3 illustrates our CME.
The system is modified at the boundaries:
\[ \frac{dP_{1,0}}{dt} = -kNP_{1,0} + \rho P_{1,1} + N f P_{2,0} \]
\[ \frac{dP_{2,0}}{dt} = -kNP_{2,0} + \rho P_{2,1} - f P_{2,0} \]
\[ \frac{dP_{1,N}}{dt} = kNP_{1,N-1} - \rho N P_{1,N} - Nh P_{1,N} + f N P_{2,N} \]
\[ \frac{dP_{2,N}}{dt} = kNP_{2,N-1} - \rho N P_{2,N} + N h P_{1,N} - f N P_{2,N} \]
(32)

Eq.(18) gives
\[ M_{11} = k(e^{-u'} - 1) + \rho x(e^{u'} - 1) - xh \]
\[ M_{12} = f \]
\[ M_{22} = k(e^{-u'} - 1) + \rho x(e^{u'} - 1) - f \]
\[ M_{21} = xh. \] (33)

Thus we define the function \( b(y) \) for the dynamic of the maximum:
\[ \frac{dy}{dt} = b(y) \equiv k - \rho y \] (34)

and functions \( A, B \) to define the dynamic of the variance:
\[ A(y) = \frac{k + \rho y}{k - \rho y} \]
\[ B(y) = -\frac{2\rho}{k - \rho y}. \] (35)

Our analytical results are in excellent agreement with numerical solutions of the original system (31) (see Fig. (4,5)).

Let us derive the time dependence of the ratio \( \frac{v_2}{v_1} \) at the maximum of distribution. From Eq.(18) we have for our case:
\[ v_1 M_{11}|_{x=y(t)} + v_2 M_{12}|_{x=y(t)} = 0 \] (36)

Using Eq. (33) we get:
\[ \frac{v_2}{v_1}|_{x=y(t)} = \frac{y(t)h}{f} \] (37)

The comparison of the numerics with our analytical results is given in Fig. 6. While \( y(t) \) and \( Q(t) \) follow to theoretical results immediately, after period of time \( T \ll N \), the \( v_2/v_1 \) follows to our theoretical result after period of time \( T \ll N \). We derived \( y(t), Q(t) \) using the expressions of \( P_1(X) + P_2(x) \), thats why \( y(t), Q(t) \) follow the theoretical dynamics rather faster than \( v_2/v_1 \). As \( y(t), Q(t) \) do not depend on the ratio \( v_2(0)/v_1(0) \) of initial values of probabilities at the maximum point, we don’t give these values in the Figures 4,5.

III. STRIP OF D-DIMENSIONAL SYSTEMS OF EQUATIONS

A. The bulk solution of the model

Consider the following system of equations
\[ \frac{dP(X)}{N dt} = \sum_{1 \leq n \leq d} \sum_{\vec{m}} R_{l} (\vec{X} - \vec{m}) P_{n} (\vec{X} - \vec{m}, t). \] (38)

Here the sum via \( \vec{n} \) is over the vector space of the stoichiometry vectors of all of reactions. Now there are transitions in the same D-dimensional space with the rate \( R_{l} \) and transitions between different D-dimensional spaces with the rates \( R_{l} \), \( l \neq n \). The negative \( R_{l} \) are chosen to ensure the probability conservation condition.
\[ \sum_{1 \leq l \leq m} \sum_{\vec{m}} R_{l} (\vec{X} - \vec{m}) = 0 \] (39)

where at the limit \( N \to \infty \)
\[ R_{l} (\vec{X} - \vec{m}) = \frac{r_{l} (\vec{X}) + \frac{r_{l} (\vec{X})}{N} + O(\frac{1}{N^2})} {N^2} \] (40)
Differentiating the equation $H_0 - q H_1 + H_2 q^2$ with respect to $x_i$, $x_j$, we obtain for the correlation functions:

$$
H_1 \frac{dV_{ij}(t)}{dt} + 2 H_2 \sum_l V_{il} b_l \sum_n V_{jn} b_n + \sum_l V_{il} b_l \sum_n H'_l v_n + \sum_l V_{il} b_l \sum_n H'_l v_n - \sum_l V_{il} b_l H'_{l x_j} - \sum_l V_{il} b_l H'_{l x_i} - \sum_l H''_{l x_i x_j} V_{il} = 0.
$$

(47)

This is a complete system of equations.

B. The finite $N$ corrections

Let us assume that the finite size corrections are $u_1/N$ for $u$ and $h_1/N$ for $v_1$. Thus, we have:

$$
P_l(\bar{x}, t) = (v_1 + h_1/N) \exp[Nu(\bar{x}, t) + u_1(\bar{x}, t)]
$$

(48)

The Hamilton-Jacobi equation for the correction terms will be:

$$
\frac{v_1}{t} \frac{\partial u_1}{\partial t} + h_1 \frac{\partial u_1}{\partial t} = \sum_{1 \leq n \leq d} \sum_{n, \bar{m}} Q_{ln} v_n + \sum_{n, \bar{m}} r_{ln \bar{m}}(\bar{x}) h_n e^{-\sum_k m_k w'_k}.
$$

$$
Q_{ln} = \sum_{\bar{m}} (r_{ln \bar{m}}(\bar{x}) + r_{ln \bar{m}}(\bar{x}) * G).
$$

$$
\frac{1}{2} \sum_{i, k=1}^D \left( \frac{\partial^2 u_1}{\partial x_i \partial x_k} \right) m_i m_k - \sum_k m_k \frac{\partial u_1}{\partial x_k}.
$$

(49)

From the consistency of $v_1$ system we get the following equation for $u'_1$:

$$
det[Q_{ln} - \frac{\partial u_1}{\partial t} \delta_{ln}] = 0
$$

(50)

Having the solution for $u'_1$, we define the correction terms $h_n$.

C. When we need in several $H_i$?

In [28] has been investigated the $D = 2, d = 2$ model in our classification.

$$
\frac{dP_{mn}}{dt} = (A - f(n)) P_{mn} + g(n) Q_{mn},
$$

$$
\frac{dQ_{mn}}{dt} = f(n) P_{mn} + (A + a(E^{-1} - 1) - g(n)) Q_{mn}.
$$

(51)
where $E_j^n f(n) = f(n + j)$ and $A = (E_n^1 - 1)n + \gamma(E_n^1 - 1)n + \gamma bm(E_n^{-1} - 1)$.

The authors applied HJE approach to investigate the steady state, using same Hamiltonian, proportional to $H_0$ in our notification. Their Hamiltonian gives exact equation for the steady state, while for the dynamic it is only an approximation, and to get correct dynamics in \cite{[54]} has been done some rescaling.

Our approach provides the exact dynamics in this case, using $H_1$ for the dynamics of the maximum, and $H_2$ for the dynamics of the variance.

For $H_1(p = 0)$ we obtain an expression:

$$H_1(p = 0, n/N) = f(n) + g(n)$$

(52)

It is a nontrivial function of $n/N$, therefore $H_0$ alone is not enough to give a correct dynamics of the maximum.

IV. CONCLUSION

In the present article we solved the Chemical Master Equation for the case of a strip of 1 dimensional chains of equations. Such a master equation appears in the problem of connected diffusion in discrete time: diffusion in space direction plus random jumping between discrete set of states. We found a solution for the general case of the model when the width of the strip is smaller than the length, and calculated the dynamics of the maximum and the variance in the large size limit. We applied our method to get the solution for the problem of a gene switch model. The numerics confirmers that the dynamics of the maximum and the variance follows to our analytical results after very short period of time.

We also investigated the case of a strip of equation chains, each one defined in D-dimensional space, and gave a system of ODEs to define the motion of the maximum point and the dynamics of the variance. In the appendix we give the ODE systems for the investigation of the insertion-deletion-substitution problem in evolution.

We considered the situation when Hamilton Jacobi equation is valid, assuming that the maximum of distribution for different chains are at the same point. This was the case in the example considered in section II-D, satisfying two conditions: a) where the rates $r(x)$ are smooth functions and b) $d \ll N$. In \cite{[54]} a $D = 2$ model has been considered where condition b) is broken. As a result, the solution of the system of equations could not be described via the HJE ansatz of a smooth function $u(x_1, x_2)$. To investigate the validity of our main assumption Eq.(14), one needs to undertake further work with more thorough mathematics. Because nowadays the HJE is becoming popular in solving the CME, as well as for the solution of the diffusion process in case of weak noise, this issue (the validity of the HJE ansatz) is becoming more important. Another related fundamental open problem is the limit of the application of diffusion approximation in master equations of evolution research \cite{[54]}. While the diffusion approach is a rather pure approximation in case of the inhomogeneous master equation \cite{[54][11][13]}, it is a very closely related technique to solve the HJE for homogenous master equations (as considered in the current article), see also \cite{[54]}. Clarifying the limits of the powerful HJE method could help to clarify the limits of the diffusion method as well.

Besides the HJE (WKB in literature) method, quantum mechanical approach and the moment closing method have been applied to investigate CME. The advantage of the method: it allows a series expansion in higher degrees of $1/N$, a uniform convergence of our approximation, which looks like a moment closing approach. Sometimes a quantum mechanical approach is as effective as the HJE one, but HJE has wider area of applications.

Let us briefly discuss some related works. In \cite{[54]} has been solved the related model, using the generating function method, and has been derived several impressive results in the large number of particles limit. This exact method is heavier than HJE approach, used in current work, and has narrow area of application. In \cite{[54]} the gene expression has been investigated using spectral method. Perhaps the method is good for the numerics.

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where we eventually get the following differential equation for $T(y)$:

$$
\frac{dT}{dy} bH_1 = - T \left[ 6Vb^2 - 3bH'_{1x} + 6VbH'_{1p} - 3H''_{0xp} + 3VH''_{0pp} \right] - 3\frac{dV}{dy} b(H'_{1x} - VH'_{1p} - 2Vb) + 3Vb(2VH''_{1pp} - 2VH''_{0pp}) + 3VH'''_{0xp} - 3V^2H'''_{0pp} + V^3H''_{0ppp}
$$

where $V = 1/Q, b = dy(t)/dt$.

### Appendix B: High dimensional case

#### 1. The dynamics in D-dimensional space

For the model given by Eq.(4) we get the HJE for the function $u(\vec{x},\vec{p})$ with following Hamiltonian:

$$
\frac{\partial u}{\partial t} + H(\vec{x},\vec{p}) = 0,
$$

$$
-H(\vec{x},\vec{p}) = \sum_{\vec{n}} \left[ R_{\vec{n}}(N\vec{x} - \vec{n}) e^{-\vec{a}\vec{p}} - R_{\vec{n}}(N\vec{x}) \right].
$$

Let us consider an ansatz

$$
u(\vec{x}) = -\frac{1}{2} \sum_{i,j} V_{ij} (x_i - y_i(t))(x_j - y_j(t)).$$

Substituting into the above equation, and differentiating by $x_i$, we get:

$$
\sum_{i,j} V_{ij} \frac{dy_j}{dt} = \sum_{i,j} V_{ij} ' H'_{pi}.
$$

The last system of equation is consistent at:

$$
\frac{dy_j}{dt} = H'_{pi}.
$$

As a result, we have the following system for the $V_{ij}$

$$
\frac{dV_{ij}}{dt} = \sum_{lm} \frac{\partial^2 H}{\partial p_l \partial p_m} V_{li} V_{mj} - \sum_{i} \frac{\partial^2 H}{\partial p_i \partial x_j} V_{ij} - \sum_{l} \frac{\partial^2 H}{\partial x_l \partial x_j} V_{il}.
$$

#### 2. The dynamics for the evolution model with insertions and deletions

Consider the following model, describing the insertions and deletions, $P(N, L)$ is the density of the states having genome length $N$ and $L$ of + spins, $a$ is the mutation rate, $b$ is the deletion rate, $c$ is the rate to insert + or - spins:

$$
\frac{dp(N, L)}{dt} = \frac{p(N, L)}{N_0} \left( N_0 - N \frac{(a + b) - c}{N_0} \right) + a \left( \frac{L}{N_0} p(N, L - 1) + p(N, L + 1) \frac{N - L}{N_0} \right) \frac{N + 1}{N_0} + b \left[ p(N + 1, L + 1) + p(N + 1, L) \right] \frac{N + 1}{N_0} + c \left[ p(N - 1, L - 1) \frac{L}{N_0} + p(N - 1, L) \frac{N - L}{N_0} \right].
$$
We should re-write the equation for \( P(N, L) = p(N, L) \binom{N}{L} \).

\[
\frac{dP(N, L)}{dt} = 
\begin{align*}
& \frac{N}{N_0} - (a + b) \frac{N}{N_0} - c \frac{N + 1}{N_0} \\
+ a \left( \frac{N - L + 1}{N_0} \right) P(N, L - 1) + \frac{L + 1}{N_0} P(N, L + 1) \\
+ b \left( \frac{L + 1}{N_0} P(N + 1, L + 1) + \frac{N - L + 1}{N_0} P(N + 1, L) \right) \\
+ \frac{c}{2} \left( \frac{N}{N_0} P(N - 1, L - 1) + \frac{N}{N_0} P(N - 1, L) \right).
\end{align*}
\]

(B.7)

We have HJE

\[
-H(x_1, x_2, p_1, p_2) = N_0 - (a + b + c)x_1 + \\
a[x_1 - x_2]e^{-x_2 + x_2e^{p_2}} + b(x_2e^{p_1} + x_1 - x_2)e^{p_1} + \\
\frac{c}{2}[x_2e^{-p_1 - x_1} + x_1e^{-p_1}].
\]

(B.8)

We are again interested to find the dynamics of the maximum and the variance. Let us introduce the following ansatz:

\[
u(x_1, x_2, t) = -\frac{1}{2} V_{11}(x_1 - y_1(t))^2 - \\
\frac{1}{2} V_{22}(x_2 - y_2(t))^2 - V_{12}(x_1 - y_1(t))(x_2 - y_2(t)).
\]

(B.9)

For the maximum dynamics we get:

\[
\frac{dy_1}{dt} = (c - b)y_1 \\
\frac{dy_2}{dt} = a(y_1 - 2y_2) - by_2 + \frac{c}{2} y_1.
\]

(B.10)

The solutions of the latter equation is:

\[
y_1(t) = y_{10}e^{(c-b)t}, \\
y_2(t) = y_{20}e^{-(2a+b)t} + \frac{y_{10}}{2} e^{(c-b)t} - e^{-(2a+b)t}.
\]

(B.11)

Thus, we get the following expression:

\[
\frac{y_2(t)}{y_1(t)} = \frac{y_{20}}{y_{10}} e^{-(2a+c)t} + \frac{1}{2} [1 - e^{-(2a+c)t}]
\]

\[
limit_{t \to \infty} \frac{y_2(t)}{y_1(t)} = \frac{1}{2}.
\]

(B.12)

For the variances we eventually get the following system of equations:

\[
-\frac{dV_{11}}{dt} = a[2V_{12} + y_1 V_{12}^2] \\
+ b[y_2(V_{11} + V_{12})^2 - 2V_{11} + (y_1 - y_2) V_{11}^2] + \frac{c}{2} [4V_{11} + 2V_{12} + y_1(V_{11} + V_{12})^2 + y_1 V_{12}^2].
\]

(B.13)

\[
-\frac{dV_{12}}{dt} = a[V_{22} - 2V_{12} + y_1 V_{12} V_{22}] \\
+ b(-2V_{12} + y_2(V_{12} + V_{22})(V_{12} + V_{11}) + (y_1 - y_2) V_{11} V_{12}] \\
+ \frac{c}{2} [2V_{12} + V_{22} + y_1(V_{12} + V_{22})(V_{12} + V_{11}) + y_1 V_{11} V_{12}].
\]

(B.14)

\[
-\frac{dV_{22}}{dt} = a[-4V_{22} + y_1 V_{22}^2] \\
+ b[-2V_{22} + y_2(V_{12} + V_{22})^2 + (y_1 - y_2) V_{12}^2] + \frac{c}{2} [y_1(V_{12} + V_{22})^2 + y_1 V_{12}^2].
\]

(B.15)