

REGULARITY AND APPROXIMABILITY OF THE SOLUTIONS TO THE CHEMICAL MASTER EQUATION *

LUDWIG GAUCKLER AND HARRY YSERENTANT¹

Abstract. The chemical master equation is a fundamental equation in chemical kinetics. It is an adequate substitute for the classical reaction-rate equations whenever stochastic effects become relevant. In the present paper we give a simple argument showing that the solutions of a large class of chemical master equations, including all those in which elementary reactions between two and more molecules do not generate a larger number of molecules than existed before, are bounded in weighted ℓ_1 -spaces. As an illustration for the implications of this kind of regularity we analyze the effect of truncating the state space. This leads to an error analysis of the finite state projection of the chemical master equation, an approximation that underlies many numerical methods.

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1. INTRODUCTION

The chemical master equation is a fundamental equation in chemical kinetics. It is an adequate substitute for the classical reaction-rate equations in the case of small population numbers when stochastic effects become relevant, a situation that often arises in biological systems. See the recent reviews [6, 11, 12] and the classical papers [4, 5] for an introduction. There is an ongoing effort to tackle the chemical master equation numerically, the major challenge being its high dimensionality: for a system of d interacting species the chemical master equation is a differential equation with state space \mathbb{N}_0^d , \mathbb{N}_0 the set of nonnegative integers. Various numerical methods have been proposed, for instance Galerkin methods [1, 19], spectral methods [3], sparse grid methods [7, 9], wavelet methods [15, 22], tensor methods [2, 8, 14, 16], and hybrid methods [9, 10, 13, 18]. In the papers on numerical methods known to us no attention is paid to the regularity (or the decay) of the solutions to the chemical master equation, although this is inherently related to approximability and particularly relevant in high dimensions. In the present work we give a simple argument showing high regularity in weighted ℓ_1 -spaces for a large class of chemical master equations, including all those in which elementary reactions between two and more molecules do not generate more molecules than were initially present. Almost all examples considered in the aforementioned papers are of this kind. As an illustration for the implications of high regularity we analyze the effect of truncating the state space. This leads to an error analysis for the finite state projections of the chemical master equation, approximations that underlay more or less explicitly most numerical methods.

Keywords and phrases: chemical master equation, regularity, finite state projections

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¹ Institut für Mathematik, Technische Universität Berlin, Straße des 17. Juni 136, 10623 Berlin, Germany
e-mail: gauckler@math.tu-berlin.de, yserentant@math.tu-berlin.de

The chemical master equation can be regarded as a differential-difference equation, a differential equation in time and a difference equation in the rest of the variables, or in other words a possibly infinite system

$$\frac{d}{dt} p(\Omega; t, x) = \sum_{r=1}^R \left(a_r(t, x - \nu_r) p(\Omega; t, x - \nu_r) - a_r(t, x) p(\Omega; t, x) \right), \quad x \in \Omega, \quad (1.1)$$

of ordinary differential equations. The solution components are labeled by vectors $x \in \mathbb{Z}^d$ and take the value

$$p(\Omega; t, x) = 0, \quad x \notin \Omega, \quad (1.2)$$

for all x outside a given subset Ω of \mathbb{Z}^d . The ν_r are given elements in \mathbb{Z}^d and the coefficient functions

$$a_r : \mathbb{R}_{\geq 0} \times \mathbb{Z}^d \rightarrow \mathbb{R}_{\geq 0} : (t, x) \rightarrow a_r(t, x) \quad (1.3)$$

are assumed to be nonnegative and continuous in the variable t for each single x . We denote their sum by

$$a(t, x) = \sum_{r=1}^R a_r(t, x). \quad (1.4)$$

In chemical kinetics, Ω is a subset of \mathbb{N}_0^d or in the limit case the set \mathbb{N}_0^d itself. The value $p(\Omega; t, x)$ represents then the probability that there are x_i copies of the molecule S_i at time t . Consider an elementary reaction



in which m_1 molecules of species 1, m_2 molecules of species 2, \dots react to n_1 molecules of species 1, n_2 molecules of species 2 and so on. The corresponding vector ν_r , the stoichiometric vector of the reaction, is composed of the differences $n_i - m_i$. The coefficient function $a_r(t, x)$, that is denoted as propensity function of the reaction, is in chemical kinetics a constant or time-dependent multiple of the polynomial

$$a_r(t, x) \sim \prod_{i=1}^d \binom{x_i}{m_i} \quad (1.6)$$

of order $m_1 + \dots + m_d$ in the components of x as long as $x_i \geq m_i$ for all i and takes the value 0 otherwise. That is, it is proportional to the number of possibilities to select the reacting molecules from the given ones. The here omitted factor of proportionality measures the reactivity of the substances.

If the set Ω is finite, (1.1) is a linear system of ordinary differential equations of usual kind for the solution components $p(\Omega; t, x)$, $x \in \Omega$. Existence and uniqueness of its solution for given initial values $p(\Omega; 0, x)$, $x \in \Omega$, is guaranteed by standard results from the theory of ordinary differential equations. The situation is different for infinite sets Ω , and in particular for the limit case

$$\Omega = \mathbb{N}_0^d \quad (1.7)$$

in which one is primarily interested. The aim of this note is to study the minimal nonnegative solutions of the chemical master equation (1.1) on arbitrary subsets Ω of \mathbb{Z}^d for nonnegative, summable initial values.

The existence of such solutions can be shown by an elegant, comparatively elementary argument by Reuter and Ledermann [20]. Martcheva *et al.* [17] use semigroup techniques to study a related class of infinite systems of ordinary differential equation in ℓ_1 -like sequence spaces. The present paper is strongly influenced by the work of Reuter and Ledermann and utilizes the techniques developed there. Our aim is to show that the solutions

constructed following Reuter and Ledermann grow at most like

$$\sum_{x \in \Omega} \gamma(t, x) p(\Omega; t, x) \leq c(t) \sum_{x \in \Omega} \gamma(0, x) p(\Omega; 0, x), \quad (1.8)$$

where $\gamma : \mathbb{R}_{\geq 0} \times \mathbb{Z}^d \rightarrow \mathbb{R}_{\geq 0}$ is a weight function that is differentiable in t and satisfies an estimate

$$\dot{\gamma}(t, x) + \sum_{r=1}^R a_r(t, x) (\gamma(t, x + \nu_r) - \gamma(t, x)) \leq \kappa(t) \gamma(t, x) \quad (1.9)$$

for all x in the domains Ω under consideration, where $\kappa : \mathbb{R}_{\geq 0} \rightarrow \mathbb{R}_{\geq 0}$ is a given continuous function and

$$c(t) = \exp \left(\int_0^t \kappa(s) ds \right). \quad (1.10)$$

We will restrict ourselves in the discussion of this condition to subsets Ω of \mathbb{N}_0^d . The trivial example of a weight function satisfying an estimate (1.9) is $\gamma(t, x) = 1$. In this case, $\kappa = 0$ and (1.8) transfers to the estimate

$$\sum_{x \in \Omega} p(\Omega; t, x) \leq \sum_{x \in \Omega} p(\Omega; 0, x). \quad (1.11)$$

The other extreme is exponentially growing weight functions like

$$\gamma(t, x) = \exp(\vartheta \langle x \rangle), \quad \langle x \rangle = \sum_{i=1}^d x_i, \quad (1.12)$$

with $\vartheta > 0$ a given parameter. An estimate (1.9) then holds if the coefficient functions $a_r(t, x)$ are bounded for those r for which $\langle \nu_r \rangle > 0$; the behavior of the other coefficient functions is of no significance in this context.

In view of applications to chemical kinetics, we are primarily interested in polynomial weight functions. The key observation is that the differences $\gamma(t, x + \nu_r) - \gamma(t, x)$ are then polynomials of a one times lower degree. We will consider in this paper in particular the polynomial-like weight functions

$$\gamma(t, x) = \max(1, \langle x \rangle)^m, \quad (1.13)$$

where the exponent m can be an arbitrary real number greater than zero. The crucial estimate (1.9) is then satisfied if the coefficient functions $a_r(t, x)$ grow at most linearly in x , or more precisely in the sum of the components of x , for all reactions r for which $\langle \nu_r \rangle > 0$, that is, if for these r

$$a_r(t, x) \leq \alpha(t) \langle x \rangle \quad (1.14)$$

for all $x \neq 0$ in Ω respectively \mathbb{N}_0^d with some continuous function α . In chemical kinetics, this condition excludes elementary reactions (1.5) between two or more molecules that generate a larger number of molecules than existed before, that is, for which $m_1 + \dots + m_d$ is two or greater and $n_1 + \dots + n_d$ greater than $m_1 + \dots + m_d$. This assumption is satisfied in virtually all examples considered in the cited papers on numerical methods. To name just a few, we mention the genetic toggle switches considered in [1, 2, 14, 15, 22], the models describing the spread of an infectious disease considered in [15, 22] and the models for bacteriophages considered in [2, 14].

2. THE CHEMICAL MASTER EQUATION ON FINITE STATE SPACES

We begin studying the case of finite subsets Ω of \mathbb{N}_0^d or more generally of \mathbb{Z}^d . As mentioned, the existence and uniqueness of the solutions of the chemical master equation (1.1), (1.2) for given initial values is then

guaranteed by standard results from the theory of ordinary differential equations and does not pose a problem. For the rest of this section, we will fix the state space Ω and will denote the solutions by

$$p(t, x) = p(\Omega; t, x). \quad (2.1)$$

Our first observation is the well-known fact that the solutions remain nonnegative for nonnegative initial values.

Lemma 2.1. *If the set Ω is finite and $p(0, x) \geq 0$ for all $x \in \Omega$, the solution $p(t, x) = p(\Omega; t, x)$ of the chemical master equation (1.1), (1.2) remains nonnegative for all $t \geq 0$.*

Proof. Let $T > 0$ be arbitrarily given and assume that $a(t, x) \leq \mu$ holds for the sum (1.4) of the coefficient functions for $0 \leq t \leq T$ and $x \in \Omega$. The functions $q(t, x) = e^{\mu t} p(t, x)$ satisfy then the differential equations

$$\frac{d}{dt} q(t, x) = \mu q(t, x) + \sum_{r=1}^R \left(a_r(t, x - \nu_r) q(t, x - \nu_r) - a_r(t, x) q(t, x) \right), \quad x \in \Omega,$$

which are, in obvious vector notation, equivalent to a system

$$q(t) = q(0) + \int_0^t (\mu I + A(s)) q(s) ds, \quad 0 \leq t \leq T,$$

of integral equations that can be solved by Picard-iteration. Since the integral operator on the right hand side maps, by the choice of the constant μ , componentwise nonnegative functions to componentwise nonnegative functions, the solution of this integral equation is componentwise nonnegative for $0 \leq t \leq T$. Thus

$$p(t, x) \geq 0, \quad x \in \Omega,$$

for $0 \leq t \leq T$, and, since $T > 0$ was arbitrary, for all $t \geq 0$. \square

We come now to our central estimate (1.8), here first for solutions on finite state spaces Ω .

Lemma 2.2. *If the set Ω is finite and $p(0, x) \geq 0$ for all $x \in \Omega$, the then nonnegative solution $p(t, x) = p(\Omega; t, x)$ of the chemical master equation (1.1), (1.2) satisfies the a priori estimate*

$$\sum_{x \in \Omega} \gamma(t, x) p(t, x) \leq c(t) \sum_{x \in \Omega} \gamma(0, x) p(0, x), \quad (2.2)$$

where $\gamma(t, x)$ is a weight function satisfying the estimate (1.9) and $c(t)$ the function given by (1.10).

Proof. We restrict ourselves first to the case that the weight function γ does not depend on t . Since the sum is finite, we can differentiate the left hand side of (2.2) and obtain from (1.1)

$$\frac{d}{dt} \sum_{x \in \Omega} \gamma(x) p(t, x) = \sum_{r=1}^R \sum_{x \in \Omega} \left(a_r(t, x - \nu_r) \gamma(x) p(t, x - \nu_r) - a_r(t, x) \gamma(x + \nu_r) p(t, x) \right) + \Delta(t),$$

where we have used the abbreviation

$$\Delta(t) = \sum_{r=1}^R \sum_{x \in \Omega} a_r(t, x) (\gamma(x + \nu_r) - \gamma(x)) p(t, x).$$

Because of the nonnegativity of all terms and since $p(t, x) = 0$ for all x outside Ω ,

$$\sum_{x \in \Omega} a_r(t, x - \nu_r) \gamma(x) p(t, x - \nu_r) \leq \sum_{x \in \Omega} a_r(t, x) \gamma(x + \nu_r) p(t, x);$$

the sum on the left hand side is simply a sum of function values at points in a subset of Ω . The double sum on the right hand side of the equation above attains therefore always values less equal zero, which leads to

$$\frac{d}{dt} \sum_{x \in \Omega} \gamma(x) p(t, x) \leq \sum_{r=1}^R \sum_{x \in \Omega} a_r(t, x) (\gamma(x + \nu_r) - \gamma(x)) p(t, x)$$

and, as $p(t, x)$ is nonnegative, by assumption (1.9) finally to the estimate

$$\frac{d}{dt} \sum_{x \in \Omega} \gamma(x) p(t, x) \leq \kappa(t) \sum_{x \in \Omega} \gamma(x) p(t, x).$$

To proceed, we introduce the abbreviation

$$S(t) = \sum_{x \in \Omega} \gamma(x) p(t, x)$$

for the quantity to be estimated. Since, as just shown,

$$\frac{d}{dt} \frac{S(t)}{c(t)S(0)} = \frac{S'(t) - \kappa(t)S(t)}{c(t)S(0)} \leq 0$$

and $c(0) = 1$, the proposition $S(t) \leq c(t)S(0)$ follows. If γ depends on t , the additional term

$$\sum_{x \in \Omega} \dot{\gamma}(t, x) p(t, x)$$

arises, that is covered by assumption (1.9), too. \square

The lemma applies in particular to the weight function $\gamma = 1$, for which $\kappa = 0$, and leads to the basic estimate

$$\sum_{x \in \Omega} p(t, x) \leq \sum_{x \in \Omega} p(0, x) \tag{2.3}$$

for the nonnegative solutions of the chemical master equation already mentioned in the introduction.

The question arises whether an exponential growth as in (2.2) can actually be observed. The answer is no, not for finite state spaces and time-independent weight functions. The reason is obvious. As follows from (2.3),

$$\sum_{x \in \Omega} \gamma(x) p(t, x) \leq \left(\max_{x \in \Omega} \gamma(x) \right) \sum_{x \in \Omega} p(0, x). \tag{2.4}$$

That means that the left hand side of this inequality remains bounded for all times $t \geq 0$. The point is, however, that we need bounds that are independent of Ω and still hold when Ω approaches an infinite domain like \mathbb{N}_0^d .

3. THE MONOTONICITY PRINCIPLE

Our aim is to extend the results of Sect. 2 from finite to infinite state spaces Ω , and in particular to the state space $\Omega = \mathbb{N}_0^d$. Following Reuter and Ledermann [20], we start from the following monotonicity principle.

Lemma 3.1. *Let $\Omega_1 \subseteq \Omega_2$ be two finite subsets of \mathbb{Z}^d and let $p(\Omega_1; t, x)$ and $p(\Omega_2; t, x)$ be nonnegative solutions of the chemical master equation (1.1), (1.2) on the state spaces Ω_1 respectively Ω_2 . Then*

$$p(\Omega_1; t, x) \leq p(\Omega_2; t, x) \tag{3.1}$$

for all $x \in \mathbb{Z}^d$ and all $t \geq 0$, provided this holds at the initial time $t = 0$.

Proof. The proof is based on the same idea as that of Lemma 2.1. Let $T > 0$ be arbitrarily given and let μ be the corresponding upper bound introduced there for the sum of the coefficient functions. Let

$$e(t, x) = e^{\mu t} \chi(x) \{p(\Omega_2; t, x) - p(\Omega_1; t, x)\},$$

with χ the characteristic function of the set Ω_1 . Moreover, let

$$\sigma(t, x) = e^{\mu t} \sum_{r=1}^R (1 - \chi(x - \nu_r)) a_r(t, x - \nu_r) p(\Omega_2; t, x - \nu_r).$$

For all elements x in the smaller of the two sets Ω_1 and Ω_2 then

$$\frac{d}{dt} e(t, x) = \mu e(t, x) + \sum_{r=1}^R \left(a_r(t, x - \nu_r) e(t, x - \nu_r) - a_r(t, x) e(t, x) \right) + \sigma(t, x).$$

One deduces from that as in the proof of Lemma 2.1 that the functions $t \rightarrow e(t, x)$, $x \in \Omega$, considered as the unique solution of the above system of differential equations with given right hand side $\sigma(t, x) \geq 0$ and given initial values $e(0, x) \geq 0$, are nonnegative for $0 \leq t \leq T$. As $T > 0$ was arbitrary and $p(\Omega_1; t, x)$ vanishes outside the smaller of the two sets Ω_1 and Ω_2 , this proves the inequality (3.1). \square

4. EXISTENCE AND REGULARITY OF MINIMAL SOLUTIONS

With help of the technique of Reuter and Ledermann [20], we are now in the position to treat the case of the initial value problem (1.1), (1.2) on arbitrary subsets Ω of \mathbb{Z}^d and in particular on the set $\Omega = \mathbb{N}_0^d$. We start from a summable set of nonnegative initial values $p(0, x)$, $x \in \Omega$, and first introduce the finite state projections

$$p(\Omega'; t, x), \quad \Omega' \text{ a finite subset of } \Omega, \quad (4.1)$$

the solutions of the chemical master equation (1.1), (1.2) on the sets Ω' for the initial values

$$p(\Omega'; 0, x) = p(0, x), \quad x \in \Omega'. \quad (4.2)$$

Theorem 4.1. *Let $\Omega_1 \subseteq \Omega_2 \subseteq \dots$ be a sequence of finite subsets of \mathbb{Z}^d that exhaust Ω . The finite state projections $p(\Omega_n; t, x)$, $n = 1, 2, 3, \dots$, converge then monotonely from below to a solution $p(t, x) = p(\Omega; t, x)$ of the chemical master equation on the set Ω that satisfies the estimate*

$$\sum_{x \in \Omega} p(t, x) \leq \sum_{x \in \Omega} p(0, x). \quad (4.3)$$

Proof. The solutions $p(\Omega_n; t, x)$ are by Lemma 2.1 nonnegative and satisfy by (2.3) the estimate

$$\sum_{x \in \Omega} p(\Omega_n; t, x) \leq \sum_{x \in \Omega} p(0, x).$$

They converge therefore by Lemma 3.1 for given x monotonely to a measurable limit function $t \rightarrow p(t, x)$. The sum of these limit functions is bounded by the sum of the initial values $p(0, x)$. Because of (1.1)

$$p(\Omega_n; t, x) = p(0, x) + \int_0^t \sum_{r=1}^R \left(a_r(s, x - \nu_r) p(\Omega_n; s, x - \nu_r) - a_r(s, x) p(\Omega_n; s, x) \right) ds$$

holds for $x \in \Omega_m$ and $n \geq m$. The dominated convergence theorem leads therefore to

$$p(t, x) = p(0, x) + \int_0^t \sum_{r=1}^R \left(a_r(s, x - \nu_r) p(s, x - \nu_r) - a_r(s, x) p(s, x) \right) ds,$$

first for the elements $x \in \Omega_m$. As the Ω_m exhaust Ω , these integral equations are fulfilled for all $x \in \Omega$. As the limit functions $t \rightarrow p(t, x)$ and the coefficient functions as well are locally bounded in t , the integrands are locally bounded and the limit functions therefore continuous. As the coefficient functions are continuous in t , the integrands are continuous in the integration variable and the limit functions $t \rightarrow p(t, x)$ thus, by the fundamental theorem of calculus, continuously differentiable and satisfy the differential equations (1.1) for all $x \in \Omega$. \square

The solutions from Theorem 4.1 are characterized by an extremal property and are therefore in some sense unique. Let Ω' be an arbitrary finite subset of the set Ω under consideration. Since the Ω_n exhaust Ω , Ω' is a subset of Ω_n for all sufficiently large indices n . By the monotonicity principle from Lemma 3.1 for these n

$$p(\Omega'; t, x) \leq p(\Omega_n; t, x) \leq p(\Omega; t, x). \quad (4.4)$$

Since $p(\Omega_n; t, x)$ tends on the other hand to the value $p(\Omega; t, x)$ of the constructed solution as n goes to infinity, this observation shows that this solution is the least upper bound of the finite state projections.

Theorem 4.2. *For summable nonnegative initial values $p(\Omega; 0, x)$, the least upper bound*

$$p(\Omega; t, x) = \sup p(\Omega'; t, x) \quad (4.5)$$

of the finite state projections $p(\Omega'; t, x)$ solves the initial value problem (1.1), (1.2) on the set Ω under consideration and satisfies the estimate (4.3).

If the set Ω is finite, the least upper bound (4.5) of the finite state projections $p(\Omega'; t, x)$ is the finite state projection $p(\Omega; t, x)$, that is, as to be expected again the unique solution of the then finite system (1.1), (1.2).

We will restrict ourselves in the sequel to the minimal solutions from Theorem 4.2. It is then easy to see that the *a priori* estimate from Lemma 2.2 transfers to the present case of possibly infinite sets Ω and in particular to the set $\Omega = \mathbb{N}_0^d$, provided the right hand side of (2.2) is finite for the given initial values:

Theorem 4.3. *The solution $p(t, x)$ of the chemical master equation from Theorem 4.2 satisfies the estimate*

$$\sum_{x \in \Omega} \gamma(t, x) p(t, x) \leq c(t) \sum_{x \in \Omega} \gamma(0, x) p(0, x), \quad (4.6)$$

where $\gamma(t, x)$ is a weight function satisfying the estimate (1.9) and $c(t)$ the function given by (1.10).

Proof. Lemma 2.2 and the choice of the initial values yield

$$\sum_{x \in \Omega'} \gamma(t, x) p(\Omega_n; t, x) \leq c(t) \sum_{x \in \Omega} \gamma(0, x) p(0, x)$$

for every sequence of finite sets Ω_n that exhaust Ω and every given finite subset Ω' of Ω . As n goes to infinity,

$$\sum_{x \in \Omega'} \gamma(t, x) p(t, x) \leq c(t) \sum_{x \in \Omega} \gamma(0, x) p(0, x)$$

follows, and from that, if one lets tend Ω' to Ω , finally the proposition. \square

For summable, not necessarily nonnegative initial values $p(0, x)$, one can compose from the given minimal solutions p_- and p_+ for the nonnegative initial values

$$p_-(0, x) = \max(0, -p(0, x)), \quad p_+(0, x) = \max(0, p(0, x)). \quad (4.7)$$

a solution of the chemical master equation on the set Ω under consideration, namely

$$p(t, x) = p_+(t, x) - p_-(t, x). \quad (4.8)$$

For finite state spaces Ω , the so defined solution is, of course, again the unique solution of the finite system (1.1), (1.2) of ordinary differential equations for the given initial values.

Theorem 4.4. *Under the same assumptions as in Theorem 4.3, the estimate*

$$\sum_{x \in \Omega} \gamma(t, x) |p(t, x)| \leq c(t) \sum_{x \in \Omega} \gamma(0, x) |p(0, x)|, \quad (4.9)$$

holds for solution (4.8), independent of the sign of the initial values.

Proof. The solutions p_- and p_+ are nonnegative and can be estimated with help of Theorem 4.3. Because

$$p_-(0, x) + p_+(0, x) = |p(0, x)|$$

the proposition thus follows applying the triangle inequality to the left hand side of (4.9). \square

Theorem 4.4 means in particular that

$$\sum_{x \in \Omega} |p(t, x)| \leq \sum_{x \in \Omega} |p(0, x)|, \quad (4.10)$$

that is, that the chemical master equation is ℓ_1 -contractive.

In view of applications in chemical kinetics, we are mainly interested in polynomial-like weight functions, in particular in the weight function (1.13), and may assume that Ω is a subset of the d -fold cartesian product \mathbb{N}_0^d of the set of the nonnegative integers. The crucial condition (1.9) is in this case satisfied if the coefficient functions $a_r(t, x)$ for which $\langle \nu_r \rangle > 0$ grow at most linearly in x in the sense of (1.14). Reactions between two or more molecules that generate more molecules than existed before are then excluded. The weighted ℓ_1 -norms

$$\sum_{x \in \Omega} \langle x \rangle^m |p(t, x)| \quad (4.11)$$

remain then uniformly bounded on finite time intervals for arbitrary exponents $m > 0$, corresponding initial values provided. This can be seen as a kind of regularity property. Consider the Fourier transforms

$$\widehat{p}(t, \omega) = \sum_{x \in \Omega} p(t, x) e^{i\omega \cdot x} \quad (4.12)$$

of the solutions. As with summable initial values the estimate (4.10) holds, this Fourier series converges uniformly for all times $t \geq 0$ and defines a continuous function of $\omega \in \mathbb{R}^d$. If the weighted ℓ_1 -norm (4.11) remains finite, also the partial derivatives of order less than or equal m of its partial sums converge uniformly. The Fourier transforms (4.12) of the solutions are therefore, under the given growth condition on the coefficient functions and for corresponding initial values, infinitely differentiable functions of ω . Observations of this kind are helpful in the construction of numerical methods and partly explain their success.

Again the question arises whether the estimate from Theorem 4.3 is sharp and whether the norms (4.11) can actually grow exponentially in time. This time the answer is a clear yes, as the example of the equation

$$\partial_t p(t, x) = x p(t, x - 1) - (x + 1) p(t, x), \quad x = 0, 1, 2, \dots, \quad (4.13)$$

with initial values $p(0, x) = \delta_{x,0}$ shows. The solution of this initial value problem is unique and given by

$$p(t, x) = e^{-t} (1 - e^{-t})^x. \quad (4.14)$$

To calculate its norms (4.11), or in the language of probability theory the moments of these geometric distributions, we first observe that for all real numbers q of absolute value less than one and all natural numbers m

$$\sum_{k=0}^{\infty} k^m q^k = \frac{q}{1-q} \sum_{k=0}^{\infty} ((k+1)^m - k^m) q^k = \frac{q}{1-q} \sum_{r=0}^{m-1} \binom{m}{r} \sum_{k=0}^{\infty} k^r q^k$$

holds. These sums can therefore be calculated recursively. This leads to the representation

$$\sum_{k=0}^{\infty} k^m q^k = \frac{1}{(1-q)^{m+1}} P_m(q),$$

with here not nearer specified polynomials $P_m(q)$ of degree m . The moments of the distribution (4.14) are thus

$$\sum_{x=0}^{\infty} x^m p(t, x) = P_m(1 - e^{-t}) e^{mt}. \quad (4.15)$$

They grow exponentially in time, asymptotically like $\sim e^{mt}$. This is essentially the growth that is predicted by Theorem 4.3 and Theorem 4.4. Let $\gamma(x) = \max(1, x^m)$ be the weight function (1.13). Then

$$\lim_{x \rightarrow \infty} \frac{(x+1)(\gamma(x+1) - \gamma(x))}{\gamma(x)} = m, \quad (4.16)$$

which establishes a direct connection between the here observed growth rate and our central assumption (1.9) respectively the function (1.10) from Theorem 4.3 and Theorem 4.4. It is interesting to compare (4.15) with the corresponding quantities for the finite state projections of the given equation on the set of nonnegative integers less than or equal n , the partial sums of the infinite series (4.15). These partial sums remain not only bounded, as stated by (2.4), but even tend exponentially to zero as t goes to infinity. This effect does not depend on the choice of the initial values, as one recognizes rewriting the corresponding finite system of differential equations in matrix form. The eigenvalues of its coefficient matrix are $\lambda_k = -k$, $k = 1, \dots, n+1$.

Another question is whether growth conditions on the coefficient functions of the given or similar kind are really necessary to have this sort of regularity of the chemical master equation. The example of the equation

$$\partial_t p(t, x) = x^2 p(t, x - 1) - (x + 1)^2 p(t, x) \quad (4.17)$$

on the one-dimensional set $x = 0, 1, 2, \dots$ of integers with initial values $p(0, 0) = 1$ and $p(0, x) = 0$ for $x \geq 1$ shows that one can in general not expect that the norms (4.11) remain bounded for all times if this holds at the initial time. The solutions of this initial value problem can, starting from the solution $p(t, 0) = e^{-t}$ of

$$\partial_t p(t, 0) = -p(t, 0), \quad (4.18)$$

be calculated recursively via the variations of constants formula

$$p(t, x) = x^2 \int_0^t e^{-(x+1)^2(t-s)} p(s, x-1) ds, \quad (4.19)$$

by means of which one obtains by induction on x the lower estimate

$$p(t, x) \geq \frac{2}{(x+1)(x+2)} \left(e^{-t} - \frac{4x}{x+3} e^{-4t} \right) \quad (4.20)$$

for the solution. For $t \geq \ln(8)/3$ therefore

$$p(t, x) \geq \frac{e^{-t}}{(x+1)(x+2)}. \quad (4.21)$$

This means that the quantities $x p(t, x)$, $x = 1, 2, \dots$, can, for these t , not sum up to a finite value.

5. THE MINIMAL SOLUTIONS AS PROBABILITY DENSITIES

The value $p(t, x)$ represents in chemical kinetics the probability that there are x_i copies of the molecule i at time t , that is, the solution should behave like a probability density. That means that the sum

$$\sum_{x \in \Omega} p(t, x) \quad (5.1)$$

should be constant in time and take the value 1 for all t . This can indeed be shown for the minimal solutions on the full set $\Omega = \mathbb{N}_0^d$ under a condition on the coefficient functions that is satisfied in chemical kinetics. The main technical problem is that the infinite sum (5.1) cannot simply be differentiated with respect to t .

Lemma 5.1. *Assume that $a_r(t, x)$ takes the value zero at all x for which $x + \nu_r$ possesses at least one negative component. For every minimal solution $p(t, x)$ for nonnegative initial values on the full set $\Omega = \mathbb{N}_0^d$ then*

$$\sum_{x \in \Omega} p(t, x) = \sum_{x \in \Omega} p(0, x) \quad (5.2)$$

holds for all times $t \geq 0$, on condition that the sums

$$\sum_{x \in \Omega} a_r(t, x) p(t, x) \quad (5.3)$$

remain uniformly bounded on finite time intervals.

Proof. Let χ be the characteristic function of an arbitrary finite subset of $\Omega = \mathbb{N}_0^d$. By (1.1) then

$$\frac{d}{dt} \sum_{x \in \mathbb{Z}^d} \chi(x) p(t, x) = \sum_{r=1}^R \left(\sum_{x \in \mathbb{Z}^d} \chi(x) a_r(t, x - \nu_r) p(t, x - \nu_r) - \sum_{x \in \mathbb{Z}^d} \chi(x) a_r(t, x) p(t, x) \right).$$

Shifting the first of the two inner sums, this yields

$$\frac{d}{dt} \sum_{x \in \mathbb{Z}^d} \chi(x) p(t, x) = \sum_{r=1}^R \sum_{x \in \mathbb{Z}^d} (\chi(x + \nu_r) - \chi(x)) a_r(t, x) p(t, x).$$

The key observation is that one can restrict the inner sum on the right hand side to those points x for which both x itself and $x + \nu_r$ are contained in \mathbb{N}_0^d . The reason is that $p(t, x)$ vanishes for all x outside \mathbb{N}_0^d and $a_r(t, x)$ by assumption for all x for which $x + \nu_r$ is not contained in \mathbb{N}_0^d . Integrating this equation,

$$\sum_{x \in \mathbb{Z}^d} \chi(x) p(t, x) - \sum_{x \in \mathbb{Z}^d} \chi(x) p(0, x) = \sum_{r=1}^R \int_0^t \sum_{x \in \mathbb{Z}^d} \delta_r(x) a_r(s, x) p(s, x) ds$$

follows, where $\delta_r(x) = \chi(x + \nu_r) - \chi(x)$ if both x and $x + \nu_r$ are contained in \mathbb{N}_0^d and $\delta_r(x) = 0$ otherwise. We insert for χ now the functions χ_n with values $\chi_n(x) = 1$ for the $x \in \mathbb{N}_0^d$ with $\langle x \rangle < n$ and $\chi_n(x) = 0$ for all other x . The assigned functions $\delta_{r,n}$ take then a value $\delta_{r,n}(x) \neq 0$, if and only if x and $x + \nu_r$ in \mathbb{N}_0^d and

$$n \leq \langle x \rangle < n - \langle \nu_r \rangle \text{ if } \langle \nu_r \rangle < 0, \quad n - \langle \nu_r \rangle \leq \langle x \rangle < n \text{ if } \langle \nu_r \rangle > 0.$$

Under the given assumption on the sums (5.3), the left hand side of the inequality

$$\left| \sum_{x \in \mathbb{Z}^d} \delta_{r,n}(x) a_r(t, x) p(t, x) \right| \leq \sum_{x \in \mathbb{Z}^d} a_r(t, x) p(t, x)$$

tends therefore to zero as n goes to infinity and the dominated convergence theorem yields

$$\lim_{n \rightarrow \infty} \sum_{r=1}^R \int_0^t \sum_{x \in \mathbb{Z}^d} \delta_{r,n}(x) a_r(s, x) p(s, x) ds = 0.$$

Since the left hand side of the equation above tends at the same time to the difference of the values (5.2), this proves the proposition and shows that the values $p(t, x)$ sum up at all times t to the same value. \square

If one excludes reactions between two or more molecules that generate more molecules than existed before, the assumption that the sums (5.3) remain uniformly bounded on finite time intervals is no longer needed.

Theorem 5.2. *Assume that the coefficient functions $a_r(t, x)$ are polynomially bounded in x , that they grow at most linearly in x in the sense of (1.14) for all indices r for which $\langle \nu_r \rangle > 0$, and that $a_r(t, x) = 0$ for all x for which $x + \nu_r$ possesses at least one negative component. For the given solutions on $\Omega = \mathbb{N}_0^d$ then*

$$\sum_{x \in \Omega} p(t, x) = \sum_{x \in \Omega} p(0, x) \tag{5.4}$$

holds for all times $t \geq 0$, summable initial values provided.

Proof. We assume first that the initial values $p(0, x)$ are nonnegative and vanish for all x except for finitely many. We know from the discussion in the previous section that under the given assumptions the sums (5.3) then remain finite and bounded on finite time intervals. As just shown, this proves (5.4) under the given restriction to the initial values. The general case is treated decomposing the solution correspondingly. \square

A related result has been proved in [21] on the basis of semigroup techniques.

6. ERROR ESTIMATES FOR THE FINITE STATE PROJECTIONS

By construction of the given minimal solution $p(t, x)$ for nonnegative initial values on the full set \mathbb{N}_0^d ,

$$0 \leq p(\Omega; t, x) \leq p(t, x) \tag{6.1}$$

holds for all finite state projections $p(\Omega; t, x)$, Ω a finite subset of \mathbb{N}_0^d . The finite state projections $p(\Omega; t, x)$ converge monotonely to $p(t, x)$ when Ω increases and approaches \mathbb{N}_0^d . To estimate the speed of convergence, information on the behavior of $p(t, x)$ for large x as provided by Theorem 4.3 is needed. Our starting point is

Lemma 6.1. *Let $p(t, x)$ be the given minimal nonnegative solution of the chemical master equation (1.1), (1.2) on the set \mathbb{N}_0^d and let $p(\Omega; t, x)$ be the approximation of $p(t, x)$ that takes the same initial values as $p(t, x)$ on the finite subset Ω of \mathbb{N}_0^d , that vanishes outside Ω , and that solves the equation (1.1) for all $x \in \Omega$. Then*

$$\sum_{x \in \mathbb{N}_0^d} (p(t, x) - p(\Omega; t, x)) \leq \sum_{x \notin \Omega} p(t, x) + \int_0^t \sum_{r=1}^R \sum_{x \in \Omega(r)} a_r(s, x) p(\Omega; s, x) ds, \quad (6.2)$$

where $\Omega(r)$ denotes the set of all $x \in \Omega$ for which $x + \nu_r$ is located outside Ω but still in \mathbb{N}_0^d .

Proof. Let Ω' be an arbitrary finite subset of \mathbb{N}_0^d that covers Ω and consider the nonnegative difference

$$e(t, x) = p(\Omega'; t, x) - p(\Omega; t, x)$$

of the corresponding finite state projections. Its ℓ_1 -norm satisfies the differential equation

$$\frac{d}{dt} \sum_{x \in \Omega'} e(t, x) = \sum_{r=1}^R \sum_{x \in \Omega'} \left(a_r(t, x - \nu_r) e(t, x - \nu_r) - a_r(t, x) e(t, x) \right) + \tau(t),$$

where the remainder is given by the expression

$$\tau(t) = \sum_{r=1}^R \sum_{x \in \Omega' \setminus \Omega} a_r(t, x - \nu_r) p(\Omega; t, x - \nu_r).$$

As all terms are nonnegative, one gets an upper bound for $\tau(t)$ replacing the inner sum by the sum over all x outside Ω but still in \mathbb{N}_0^d . Since $p(\Omega; t, x) = 0$ outside Ω , the remainder can therefore be estimated as

$$\tau(t) \leq \sum_{r=1}^R \sum_{x \in \Omega(r)} a_r(t, x) p(\Omega; t, x).$$

Since $e(t, x)$ is nonnegative and vanishes outside the finite set Ω' ,

$$\sum_{x \in \Omega'} a_r(t, x - \nu_r) e(t, x - \nu_r) \leq \sum_{x \in \Omega'} a_r(t, x) e(t, x).$$

From the differential equation above and the estimate for the remainder one obtains therefore the estimate

$$\frac{d}{dt} \sum_{x \in \Omega'} e(t, x) \leq \sum_{r=1}^R \sum_{x \in \Omega(r)} a_r(t, x) p(\Omega; t, x)$$

for the derivative. Integration yields

$$\sum_{x \in \mathbb{N}_0^d} (p(\Omega'; t, x) - p(\Omega; t, x)) \leq \sum_{x \notin \Omega} p(\Omega'; 0, x) + \int_0^t \sum_{r=1}^R \sum_{x \in \Omega(r)} a_r(s, x) p(\Omega; s, x) ds$$

and with that, taking the supremum over all Ω' under consideration, finally the proposition. \square

We return now to chemical kinetics and our standard case of the polynomial-like weight functions (1.13). We restrict ourselves as before again to the case that for all reactions r for which $\langle \nu_r \rangle > 0$ the coefficient functions $a_r(t, x)$ grow at most linearly in $\langle x \rangle$, that is, satisfy an estimate (1.14), and exclude with that again reactions between two and more molecules that generate a larger number of molecules than existed before. Let

$$\Omega_n = \{x \in \mathbb{N}_0^d \mid \langle x \rangle < n\}. \quad (6.3)$$

The sets $\Omega_n(r)$ from Lemma 6.1 are in this case empty for all reactions r for which $\langle \nu_r \rangle \leq 0$. If $\langle \nu_r \rangle > 0$,

$$\Omega_n(r) = \{x \in \mathbb{N}_0^d \mid x + \nu_r \in \mathbb{N}_0^d, n - \langle \nu_r \rangle \leq \langle x \rangle < n\}. \quad (6.4)$$

If the weighted ℓ_1 -norm (4.11) is bounded at time $t = 0$ and remains therefore bounded on all finite time intervals, the ℓ_1 -norm of the error thus tends by Lemma 6.1 like

$$\mathcal{O}(n^{-m+1}) \quad (6.5)$$

to zero as n goes to infinity. The constants will in general strongly increase with m and the length of the time interval under consideration but are basically independent of the dimension d of the state space, that is, in chemical kinetics of the number of species involved. The curse of dimensionality is hidden in the choice of the state spaces (6.3). We conclude that, corresponding initial values provided,

$$\lim_{n \rightarrow \infty} n^m \sum_{x \in \mathbb{N}_0^d} (p(t, x) - p(\Omega_n; t, x)) = 0 \quad (6.6)$$

uniformly on every finite time interval for all $m > 0$. This means that the finite state projections $p(\Omega_n; t, x)$ converge in the ℓ_1 -norm super-algebraically to the solution, faster than any power of $1/n$ tends to zero.

The finite state projections of a solution of a chemical master equation do in general not remain probability densities when time proceeds. It is therefore common practice to modify the equation slightly near the boundary of the given finite domain Ω , replacing the coefficient functions $a_r(t, x)$ by their truncated variants

$$a_r(\Omega; t, x) = \begin{cases} a_r(t, x), & \text{if } x + \nu_r \in \Omega, \\ 0, & \text{otherwise.} \end{cases} \quad (6.7)$$

The solutions $\tilde{p}(\Omega; t, x)$ of the so modified equations (1.1), (1.2) have then again the property that

$$\sum_{x \in \Omega} \tilde{p}(\Omega; t, x) = \sum_{x \in \Omega} \tilde{p}(\Omega; 0, x). \quad (6.8)$$

The proof transfers almost verbatim from that of Lemma 5.1, simply replacing the full set \mathbb{N}_0^d by the given finite set Ω . The only difference is that one can, as Ω is itself a finite set, directly insert the characteristic function χ of Ω there, which makes the detour via a limit process as in the proof of Lemma 5.1 unnecessary. The question is which impact this modification has on the discretization error.

Lemma 6.2. *If $\tilde{p}(\Omega; 0, x) = p(\Omega; 0, x)$ for all x in the finite set Ω , for all times $t \geq 0$*

$$p(\Omega; t, x) \leq \tilde{p}(\Omega; t, x). \quad (6.9)$$

Proof. Let μ be an upper bound for the sum (1.4) of the coefficient functions and set

$$e(t, x) = e^{\mu t} \{\tilde{p}(\Omega; t, x) - p(\Omega; t, x)\}.$$

Because of $a_r(\Omega; t, x - \nu_r) = a_r(t, x - \nu_r)$ for the points $x \in \Omega$, for all $x \in \Omega$ then

$$\frac{d}{dt} e(t, x) = \mu e(t, x) + \sum_{r=1}^R \left(a_r(\Omega; t, x - \nu_r) e(t, x - \nu_r) - a_r(\Omega; t, x) e(t, x) \right) + \tau(t, x),$$

where the remainder is given by the expression

$$\tau(t, x) = e^{\mu t} \sum_{r=1}^R (a_r(t, x) - a_r(\Omega; t, x)) p(\Omega; t, x)$$

and thus nonnegative. The proposition follows from that by arguments as in the proof of Lemma 2.1. \square

The ℓ_1 -distance of the original finite state projection and its modification can be estimated as follows.

Lemma 6.3. *Assume that $a_r(t, x) = 0$ if $x + \nu_r \notin \mathbb{N}_0^d$ and let $\Omega(r)$ as in Lemma 6.1 consist of the $x \in \Omega$ for which $x + \nu_r$ is located outside Ω but still in \mathbb{N}_0^d . If $\tilde{p}(\Omega; 0, x) = p(\Omega; 0, x)$ for all $x \in \Omega$, for all times $t \geq 0$ then*

$$\sum_{x \in \Omega} (\tilde{p}(\Omega; t, x) - p(\Omega; t, x)) \leq \int_0^t \sum_{r=1}^R \sum_{x \in \Omega(r)} a_r(s, x) p(\Omega; s, x) ds. \quad (6.10)$$

Proof. We start again from the by Lemma 6.2 nonnegative difference

$$e(t, x) = \tilde{p}(\Omega; t, x) - p(\Omega; t, x)$$

of the modified and the original finite state projection. As in the proof of the previous lemma for all $x \in \Omega$ then

$$\frac{d}{dt} e(t, x) = \sum_{r=1}^R \left(a_r(\Omega; t, x - \nu_r) e(t, x - \nu_r) - a_r(\Omega; t, x) e(t, x) \right) + \delta(t, x) p(\Omega; t, x),$$

where we have used the abbreviation

$$\delta(t, x) = \sum_{r=1}^R (a_r(t, x) - a_r(\Omega; t, x))$$

here. Since $e(t, x)$ is nonnegative and vanishes outside the finite set Ω ,

$$\sum_{x \in \Omega} a_r(\Omega; t, x - \nu_r) e(t, x - \nu_r) \leq \sum_{x \in \Omega} a_r(\Omega; t, x) e(t, x).$$

From the differential equation above one obtains therefore the estimate

$$\frac{d}{dt} \sum_{x \in \Omega} e(t, x) \leq \sum_{x \in \Omega} \delta(t, x) p(\Omega; t, x)$$

for the derivative of the norm. As $e(0, x) = 0$, integration yields

$$\sum_{x \in \Omega} (\tilde{p}(\Omega; t, x) - p(\Omega; t, x)) \leq \int_0^t \sum_{r=1}^R \sum_{x \in \Omega} (a_r(s, x) - a_r(\Omega; s, x)) p(\Omega; s, x) ds. \quad (6.11)$$

Using that the difference $a_r(s, x) - a_r(\Omega; s, x)$ takes the value $a_r(s, x)$ for the elements $x \in \Omega(r)$ and vanishes everywhere else in Ω , the proposition follows. \square

That is, the additional error introduced by the truncation of the coefficient functions can, under an assumption that was already needed to prove the results from Sect. 5 and without that the modification (6.7) does not make sense, be estimated by the same terms as the original error. The convergence behavior is thus not affected by the change of the coefficient functions. Corresponding initial values provided, the modified finite state projections still converge in the ℓ_1 -norm super-algebraically to the solution.

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