Towards Automatic Global Error Control: Computable Weak Error Expansion for the Tau-Leap Method

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Abstract. This work develops novel error expansions with computable leading order terms for the global weak error in the tau-leap discretization of pure jump processes arising in kinetic Monte Carlo models. Accurate computable a posteriori error approximations are the basis for adaptive algorithms; a fundamental tool for numerical simulation of both deterministic and stochastic dynamical systems. These pure jump processes are simulated either by the tau-leap method, or by exact simulation, also referred to as dynamic Monte Carlo, the Gillespie algorithm or the Stochastic simulation algorithm. Two types of estimates are presented: an a priori estimate for the relative error that gives a comparison between the work for the two methods depending on the propensity regime, and an a posteriori estimate with computable leading order term.

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1. Introduction

In this work we derive a global weak error expansion with computable leading order term for the tau-leap method. The tau-leap method was originally proposed by Gillespie in [10], for approximating homogeneous and well stirred stochastically reacting chemical systems. In such systems different species undergo reactions at

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random times to form new species or to decay. Each reaction can be modeled by a *propensity function*, directly related to the number of particles, indicating the probability of a reaction to happen per unit of time. The notion *well stirred* here means that the number of reactive particle collisions are low compared to the total number of collisions. Depending on the number of particles in the system and the time to next reaction the reaction process can be modeled differently:

For all possible regimes, a homogeneous well stirred system in thermal equilibrium can be modeled by the *chemical master equation* (CME). This ordinary differential equation describes the time evolution of the probability of each particle configuration, *cf.* [9]. Since the dimension of the solution space is of the order of all the possible configurations, the CME is in practice impossible to solve. On the other hand, the system can still be simulated *exactly* using the *Stochastic simulation algorithm* (SSA), also introduced by Gillespie in [11]. The SSA numerically simulates the Markov process described by the CME by using dynamic Monte Carlo sampling, also referred to as *kinetic Monte Carlo*. Although the SSA generates exact path realizations for the Markov process it is only tractable for low propensities. Indeed, since each reaction is simulated exactly by sampling the next reaction to happen and the time to this reaction, the total computational work becomes roughly inversely proportional to the total propensity. The tau-leap method, on the other hand, approximates the SSA by evolving the chemical system with fixed time steps, keeping the propensity fixed in each time step, and can be seen as a forward Euler method for a stochastic differential equation driven by Poisson random measures, *cf.* [17]. In the limit, as the time steps go to zero, the tau-leap solution converges to the SSA, see [24].

As the number of particles in the system grows the SSA is sometimes approximated by the *chemical Langevin diffusion equation*. Further, if both the number of particles and the total volume of the system goes to infinity at the same speed, *i.e.* the randomness of the system becomes negligible, then the concentration of each species over time can be modeled by a deterministic system of ordinary differential equations, the *reaction rate equations* (RREs). Because of different time scales in the reactions, RREs are often are *stiff*, indicating the need for stable tau-leap methods and adaptive time-stepping. Implicit stable tau-leap methods that deal with stiff cases have been proposed by [4, 23]. Several authors have discussed the importance of leap selection procedures to increase efficiency [6, 12] and to avoid negative populations [1, 5, 7, 26].

Representing the number of particles for the species in the system by the stochastic vector \( X(t) \), the goal in this work is to approximate the real valued quantity, \( \mathbb{E}[g(X(T))] \), for some given function \( g \) and initial configuration \( X(0) \). We here derive an *a posteriori* estimate for the global weak error \( \mathbb{E}[g(X(T)) - g(\bar{X}(T))] \) between exact (SSA) solution \( X \) and the tau-leap solution \( \bar{X} \), based on an exact global error representation, *cf.* Lemma 4.1. The error representation uses the value function defined by the Kolmogorov backward equation (2.1). Also, an *a priori* estimate for the relative global weak error that is independent of the number of particles is derived. Both the a priori and a posteriori error estimates are based on a continuous extension and point wise bounds of the discretely defined value function and its derivatives. In [16], similar \( L\)-infinity bounds, exponentially dependent on the propensity function, were derived. This work improves those estimates showing that the value function and its derivatives only grows polynomially with the
population. This result is based on weighted estimates and a stochastic representation of the weighted derivatives in terms of pure jump processes with modified propensities.

Adaptive time stepping algorithms based on computable a posteriori error estimates are fundamental tools for numerical simulation of both deterministic and stochastic dynamical systems. In our case, the leading order term of the error expansion is approximated by a discrete dual weighted propensity residual, similar to [18, 19] for deterministic differential equations, and [20, 21, 22, 25] for stochastic differential equations of diffusion and jump-diffusion type. To the best of the authors’ knowledge there are still no results on optimal adaptive time stepping algorithms based on a posteriori error estimates for the global weak error in the tau-leap method.

The outline of this work is as follows: first, Section 2 presents the mathematical setting together with the main assumptions and the relation with the Kolmogorov backward equation upon which our results are based. Next, Section 3 introduces the tau-leap method and a numerical scheme for avoiding negative populations (following [1]), here called the Poisson bridge tau-leap method. Section 4 presents the main results, namely an a priori bound on the relative error of the tau-leap method (Theorem 4.4), and a computable a posteriori error approximation using a discrete dual (Theorem 4.15). Also, from the a priori bound in Theorem 4.4 a work comparison between the tau-leap method and SSA is made. Finally, Section 5 provides a numerical verification of our a posteriori error estimate in Theorem 4.15.

2. Problem

We consider a well stirred system of $d$ chemical species, which interact through $M$ chemical reaction channels. The system is assumed to be confined to a constant volume $\Omega$ and to be in thermal, but not necessarily chemical, equilibrium at some constant temperature. With $X_i(t)$ denoting the number of molecules of species $i$ in the system at time $t$, we want to study the evolution of the state vector $X_t = (X_1(t), \ldots, X_d(t))$, given that the system was initially in some state $X_{t_0} = x_0$. It is here assumed that $X_t, x_0 \in \mathbb{Z}_+^d$ where $\mathbb{Z}_+$ denotes the set of non-negative integers. The goal of the computation is the approximation of the quantity

$$E[g(X_T)],$$

where $g : \mathbb{R}^d \to \mathbb{R}$ is a given function.

Each of the $j = 1, \ldots, M$ reactions is characterized by the change

$$x \to x + \nu_j$$

where $\nu_j \in \mathbb{Z}^d$ is a stoichiometric vector that indicates the change in the state vector $x \in \mathbb{Z}_+^d$, produced by a single firing of the reaction $j$. Now that we have defined what happens when each reaction takes place, we also need to indicate how often each of those reactions may occur in time. This information is carried by the propensity functions, $a_j : \mathbb{Z}_+^d \to \mathbb{R}, j = 1, \ldots, M$, which tell the probability of the reaction $j$ happening during the infinitesimal interval $(t, t+dt)$ i.e.

$$P\left( j \text{ fires during } (t, t+dt) \mid X_t = x \right) = a_j(x)dt, \quad j = 1, \ldots, M.$$
Usually the functions $a_j$ are just polynomials, see Remark 2.2. The compensator of our reaction process is state dependent, and the Kolmogorov backward equation for this pure jump process and a smooth observable $g : \mathbb{R}^d \to \mathbb{R}$ is

$$
\partial_t u + \sum_{j=1}^{M} a_j(x) \left( u(x + \nu_j, t) - u(x, t) \right) = 0, \quad \text{in } \mathbb{Z}_+^d \times [0, T),
$$

with the corresponding value function

$$
u(x, t) := \mathbb{E}[g(X_T) \mid X_t = x].$$

Here, natural boundary conditions restrict the species to the set $\mathbb{Z}_+^d$, see Remark 2.3.

Let $Z := \{\nu_1, \ldots, \nu_M\}$. It is interesting to see that the previous equation can be rewritten in the following way

$$
\partial_t u + a_0(x) \int_Z \left( u(x + z, t) - u(x, t) \right) q(x, dz) = 0, \quad \text{in } \mathbb{Z}_+^d \times [0, T),
$$

$$
u(\cdot, T) = g, \quad \text{on } \mathbb{Z}_+^d \times \{T\},
$$

$$
a_0(x) := \sum_{j=1}^{M} a_j(x),
$$

where the compensator measure $q(x, dz)$ is atomistic in the stoichiometric vector set $Z$ and such that

$$q(x, z = \nu_j) = \mathbb{P}(z = \nu_j \mid X_t = x) = \frac{a_j(x)}{a_0(x)}, \quad j = 1, \ldots, M.$$

Although (2.1) and (2.2) are equivalent they may lead to different discretizations. In particular, the stochastic simulation algorithm (SSA) introduced by Gillespie [11] is the natural discretization scheme for (2.2). Moreover, the corresponding error estimates and error control algorithms behave differently.

Since (2.1) is driven by pure jumps with finite activity it is in principle possible to simulate trajectories of $X_t$ exactly; the SSA does precisely that. It only requires the sample of two random variables per time step: one to find the time of the next reaction and another to decide which is the reaction that is firing at that time. The drawback of this algorithm appears clearly as the sum of the intensity of all reactions, $a_0(x)$, gets large: since all the jump times have to be included in the time discretization the corresponding computational work may become unaffordable. Indeed, we have that the mean value of the number of jumps on the interval $(t, t + \tau)$ is approximately $a_0(X_t)\tau + o(\tau)$.

**Assumption 2.1 (Bounded population).** We here assume that species can only be transformed into other species or be consumed. This means that the state $X_t \in \mathbb{Z}_+$ will be bounded from above by a hyperplane intersecting the point $X_0$ and the coordinate axes, i.e.

$$
X_t \in \Pi(X_0, n) := \{x \in \mathbb{Z}_+^d : n \cdot (x - X_0) \leq 0\}.
$$

for some vector $n \in \mathbb{R}_+^d$ with strictly positive coordinates, i.e. $n > 0$.

In other words, all the stoichiometric vectors should satisfy

$$n \cdot \nu_j \leq 0, \quad j = 1, \ldots, M.$$
Remark 2.2 (Preventing negative populations). To prevent the state from becoming negative after a jump we must have that \( a_j(x) = 0 \) for \( x + \nu_j \notin \mathbb{Z}^d_+ \). For the same reason we also have that \( a_j(0) = 0 \). For common chemical reactions the propensity functions can be modeled as polynomials of the form

\[
a_j(x) := c_j \prod_{i=1}^{d} \frac{x_i!}{(x_i + \nu_{ij}^-)!} 1_{(x_i + \nu_{ij}^-) \geq 0},
\]

which satisfies the above criteria, see [2, 11]. Here, \( \nu_{ij}^- := \min(\nu_{ij}, 0) \). From the expression \( (2.3) \) it also follows that the propensity is monotone in \( \mathbb{Z}^d_+ \), i.e. the gradient of the polynomial function \( a_j \) is non-negative.

Remark 2.3 (Boundary values). From Remark 2.2 it follows that Equation \( (2.1) \) has a natural boundary condition at the boundaries where any component of the \( x \) vector is zero.

3. The tau-leap method

To avoid the computational drawback of the SSA, i.e. when many reactions occur during a short time interval, the tau-leap method was proposed in [10]: Given a population \( \bar{X}_t \), and a time step \( \tau > 0 \), the population at time \( t + \tau \) is generated by

\[
\bar{X}_{t+\tau} = \bar{X}_t + \sum_{j=1}^{M} \nu_j \mathcal{P}_j(a_j(\bar{X}_t)\tau),
\]

where \( \mathcal{P}(a_j(\bar{X}_t)\tau) \) is a sample value from the Poisson distribution with parameter \( a_j(\bar{X}_t)\tau \), indicating the sampled number of times that the reaction \( j \) fires during the \((t, t+\tau)\) interval.

The tau-leap method \( (3.1) \) is based on the observation that if the propensity is constant between \( t \) and \( t + \tau \), the firing probability in one reaction channel is independent of the other reaction channels. The total number of firings in each channel is then a Poisson distributed stochastic variable depending only on the initial population \( \bar{X}_t \). Also, Equation \( (3.1) \) is nothing else than a forward Euler discretization of the SDE corresponding to the Kolmogorov backward equation \( (2.1) \), (or the chemical master equation), driven by the Poisson random measure, cf. [17].

In the following we let \( X_t \) denote the exact process and \( \bar{X}_t \) the tau-leap approximation.

Remark 3.1. Although the path generated by \( (3.1) \) seems to only be defined for discrete time steps, it can be extended to the continuous time interval. Indeed, any intermediate time steps in the \((t, t+\tau)\) interval can be defined as a Poisson bridge with fixed endpoints \( \bar{X}_t, \bar{X}_{t+\tau} \) and fixed intensity \( \bar{a}_j := a_j(\bar{X}_t) \).

After freezing the propensity to \( a(\bar{X}_t) \) in each time step \([t, t+\tau]\), the error in the tau-leap method \( (3.1) \) comes from the variation of \( a(X_s) \) for \( s \in (t, t+\tau) \), where \( X_s \) is the true process starting at \( X_t = \bar{X}_t \). To take this into account it was in [10] proposed choosing local time steps following the leap condition

\[
|\Delta a_j(\bar{X}_t)| := |a_j(\bar{X}_{t+\tau}) - a_j(\bar{X}_t)| \leq \epsilon a_0(\bar{X}_t),
\]

for a given control parameter \( 0 < \epsilon \ll 1 \). In order to avoid unnecessary sampling of the Poisson random variable a pre-leap check can be done by first doing a Taylor
expansion
\[ \Delta a_j(\bar{X}_t) = a_j \left( \bar{X}_t + \sum_{i=1}^{M} \nu_i \mathcal{P}_i(a_i(\bar{X}_t) \tau) \right) - a_j(\bar{X}_t) \]
\[ \approx \nabla a_j(\bar{X}_t) \cdot \sum_{i=1}^{M} \nu_i \mathcal{P}_i(a_i(\bar{X}_t) \tau), \]
and approximating the mean and variance of \( \Delta a_j(x) \) by
\[ \frac{1}{\tau} \mathbb{E}[\Delta a_j(x)] \approx \sum_{i=1}^{M} a_i(x) (\nabla a_j(x) \cdot \nu_i) =: \mu_j(x), \quad j = 1, \ldots, M, \]
and
\[ \frac{1}{\tau} \text{Var}[\Delta a_j(x)] \approx \sum_{i=1}^{M} a_i(x) (\nabla a_j(x) \cdot \nu_i)^2 =: \sigma_j(x)^2, \quad j = 1, \ldots, M, \]
respectively, see [13]. The leap size is then chosen as
\[ \tau = \min_{j=1,\ldots,M} \min \left\{ \frac{\epsilon a_0(\bar{X}_t)}{|\mu_j(\bar{X}_t)|}, \frac{\epsilon^2 a_0(\bar{X}_t)^2}{\sigma_j(\bar{X}_t)^2} \right\}, \]
which implies that \( |\mathbb{E}[\Delta a_j]| \leq \epsilon a_0 \) and \( \text{Var}[\Delta a_j] \leq \epsilon^2 a_0^2 \), so that the leap condition (3.2) holds in some statistical sense. The leap size control (3.3) has the advantage that it can be computed before each step is taken; however, it relies on the ad hoc parameter \( \epsilon \) and only controls the local error.

Our goal is here to develop a rigorous \textit{a posteriori} global weak error estimate for (3.1), with computable leading order term, that can be used to control the error in a more systematic way than the leap condition (3.2), and that can in future work be used for efficient adaptive time stepping algorithms. In Section 3.1 we present a procedure that eliminates the possibility of negative populations \( \bar{X}_t \), similarly to [1], and in Section 4 we develop error estimates that are finally tested numerically in Section 5.

3.1. Avoiding negative population. The regular tau-leap approximation (3.1) suffers from the undesirable property that \( \bar{X}_t \) can become negative. To prevent such unphysical behavior, which is a result of the approximation and not the process itself, the idea is to adaptively adjust the time step \( \tau \) to avoid negative populations and at the same time leave the distribution of \( \bar{X}_t \) unchanged. Similarly to [1], this is done by post-leap checks such that if any component of \( \bar{X}_{t+\tau} \) becomes negative, a new step \( \bar{X}_{t+\tau/2} \) will be sampled using a conditional Poisson distribution, \textit{i.e.} a Poisson bridge. To describe this procedure, we first introduce independent unit rate Poisson processes \( Y_j(\cdot) \), and define their corresponding internal times as
\[ \lambda^j_t := \int_0^t a_j(X_s) \, ds, \quad j = 1, \ldots, M. \]
The state of the chemical system at time \( t \) then satisfies
\[ X_t = X_0 + \sum_{j=1}^{M} \nu_j Y_j(\lambda^j_t), \]
see [1], *i.e.* each reaction channel is described by a unit rate Poisson process with an internal time given by \( \lambda_i \). From the definition of \( Y_j \) we have Poisson distributed increments

\[
Y_j(\lambda_i, t+\tau) - Y_j(\lambda_i, t) = Y_j \left( \lambda_i \int_t^{t+\tau} a_j(X_s) \, ds \right) - Y_j(\lambda_i, t) = \mathcal{P}_j \left( \int_t^{t+\tau} a_j(X_s) \, ds \right),
\]

and since we have for each tau-leap step that \( Y_j \) the tau-leap method can be written in terms of increments in \( Y_j \), *i.e.*

\[
(3.5) \quad \Delta Y_j(\lambda_i) := \int_t^{t+\tau} a_j(X_s) \, ds = \bar{a}_j(\bar{X}_t) \tau := \Delta \lambda_i,
\]

the tau-leap method can be written in terms of increments in \( Y_j \), *i.e.*

\[
(3.6) \quad \Delta Y_j(\cdot) := \mathcal{P}_j (\cdot).
\]

As the tau-leap method steps forward in time we build up a history of samples for the driving process \( Y \), \( \{(\lambda_i^j, Y^j_i)\}_{i=0}^n \), such that \( 0 = \lambda_0 < \lambda_1 < \ldots < \lambda_{n_j} \), and \( 0 = Y_0^j \leq Y_1^j \leq \ldots \leq Y_n^j \), by summing increments \( (\Delta \lambda_i, \Delta Y_j(\Delta \lambda_i)) \). Starting at \( \bar{X}_t \) and at the last value \( (\lambda_i^j, Y_i^j) \) in the history, a regular tau-leap step samples an increment \( \Delta Y_j := \Delta Y_j(\Delta \lambda_i^j) \) and saves \( (\lambda_i^{j+1}, Y_i^{j+1} + \Delta Y_j^j) \) to the history. Let \( B(n, p) \) denote the binomial distribution. As soon as a negative population \( \bar{X}_{t+\tau} < 0 \) is encountered, a new step \( \bar{X}_{t+\tau/2} \) is calculated by the Poisson bridge

\[
\bar{X}_{t+\tau/2} = \bar{X}_t + \sum_{j=1}^M \nu_j B(\Delta Y_j^j, 0.5),
\]

and \( (\lambda_i^j + 0.5 \Delta \lambda_i^j, Y_i^{j+1} + B(\Delta Y_j^j, 0.5)) \) is added to the saved history. If \( \bar{X}_{t+\tau/2} \) is non-negative we move forward along the \( t \)-axis, otherwise the step is halved once again. When traversing the physical time axis \( t \) we have to check if there already exist samples to the right on the internal time axis \( \lambda_i \), *e.g.* given the position \( \lambda_i^{j+1} \) and a future value \( \lambda_i^{j+1} \) the physical time step \( \tau \) must be adjusted such that we end up on \( \lambda_i^{j+1} \) for at least one \( j \) and to the left of \( \lambda_i^{j+1} \) for the remaining \( j \). For the reaction \( j \) that ends up on \( \lambda_i^{j+1} \) we use the corresponding \( Y_i^{j+1} \), and for the other reactions, a bridge between \( (\lambda_i^j, Y_i^j) \) and \( (\lambda_i^{j+1}, Y_i^{j+1}) \) is sampled. Algorithm 3.1 describes in detail one step of the Poisson bridge tau-leap method in the interval \( (t, t+\tau) \). To speed up the algorithm we approximate, for large \( np \), the binomial distribution \( B(n, p) \) with the normal distribution \( \mathcal{N}(np, np(1-p)) \) rounded to integers and multiplied by the indicator function with support in \([0, n]\). We here apply this approximation whenever \( np > 10^4 \).

**Remark 3.2.** The post-leap check performed by the Poisson bridge tau-leap method in Algorithm 3.1 will guarantee non-negative sampled steps. There is however still a probability that components of the continuous tau-leap process may become negative.
we can introduce a pre-leap check that adjusts the time step $\tau$ at points between the sampled steps, as discussed in Remark 3.1. To limit this effect we can introduce a pre-leap check that adjusts the time step $\tau$ such that

\begin{equation}
\text{P}(X_{t+\tau}^{(i)} < 0 \mid \bar{X}_t) < \epsilon, \quad i = 1, \ldots, d,
\end{equation}
for some small $\epsilon > 0$, see [15] where the exit probability (3.7) is approximated by a normal approximation of the tau-leap step (3.1), leading to a quadratic inequality in $\tau$.

4. Accuracy and error estimation

To develop computable global error estimates for the Poisson bridge tau-leap method we start with the following (non-computable) error representation based on the backward Kolmogorov equation (2.1), along the continuous-time approximate tau-leap paths $\tilde{X}_t$, defined in (3.1) and Remark 3.1, and the difference in propensities:

**Lemma 4.1** (Error representation for the tau-leap method). Assume that $a_j$ and $u$ are defined for $x \in \mathbb{Z}^d$ and that $u$ solves the backward Kolmogorov equation (2.1) in $\mathbb{Z}^d_+ \times [0,T]$. For deterministic time steps we then have

$$
\mathbb{E} \left[ g(X_T) - g(\tilde{X}_T) \right] = \sum_{j=1}^{M} \mathbb{E} \left[ \int_0^T (a_j - \bar{a}_j)(\tilde{X}_t) \left( u(\tilde{X}_t + \nu_j, t) - u(\tilde{X}_t, t) \right) dt \right]
$$

$$
- \mathbb{E} \left[ \int_0^T \phi(\tilde{X}_t, t) 1_{(\tilde{X}_t \in \mathbb{Z}^d_-)} dt \right],
$$

where

$$
\phi(\tilde{X}_t, t) := \partial_t u(\tilde{X}_t, t) + \sum_{j=1}^{M} \bar{a}_j(\tilde{X}_t) \left( u(\tilde{X}_t + \nu_j, t) - u(\tilde{X}_t, t) \right),
$$

and $\mathbb{Z}^d_- := \mathbb{Z}^d \setminus \mathbb{Z}^d_+$ is the set where at least one component is negative.

**Proof.** Since $\tilde{X}_0 = X_0$ we have

$$
\mathbb{E} \left[ g(X_T) - g(\tilde{X}_T) \right] = \mathbb{E} \left[ u(\tilde{X}_0, 0) - u(\tilde{X}_T, T) \right]
$$

(4.1)

$$
= \mathbb{E} \left[ \int_0^T -(\partial_t + \mathcal{L}_{\tilde{X}})u(\tilde{X}_t, t) \ dt \right],
$$

where the "infinitesimal generator" for $\tilde{X}_t$ is defined as

$$
\mathcal{L}_{\tilde{X}} u(\tilde{X}_t, t) := \sum_{j=1}^{M} \bar{a}_j(\tilde{X}_t) \left( u(\tilde{X}_t + \nu_j, t) - u(\tilde{X}_t, t) \right).
$$

Note the abuse of notion here: $\bar{a}_j$, and correspondingly $\mathcal{L}_{\tilde{X}} u$, is from Remark 3.1 only defined along paths. Adding and subtracting

$$
\mathcal{L}_{\tilde{X}} u(\tilde{X}_t, t) := \sum_{j=1}^{M} a_j(\tilde{X}_t) \left( u(\tilde{X}_t + \nu_j, t) - u(\tilde{X}_t, t) \right),
$$

gives

$$
\mathbb{E} \left[ g(X_T) - g(\tilde{X}_T) \right] = \mathbb{E} \left[ \int_0^T \left( \mathcal{L}_{\tilde{X}} - \mathcal{L}_{\tilde{X}} \right) u(\tilde{X}_t, t) - \phi(\tilde{X}_t, t) dt \right]
$$

From the Kolmogorov backward equation (2.1) we have $\phi = 0$ for $\tilde{X}_t \in \mathbb{Z}^d_+$ which gives Lemma 4.1.

$\square$
4.1. Relative error. Assume that we have \( x \in \mathbb{Z}_+^d \) particles and propensities \( a_j(x) \). Introduce the scaling \( z := x/\gamma \) where the scaling factor \( \gamma > 0 \) is related to the initial number of particles \( X_0 \), e.g. by taking the Euclidean norm \( \gamma := \|X_0\| \).

The relative error can now be defined as
\[
\varepsilon := E[g(Z_T) - g(\hat{Z}_T)],
\]
where the scaled \( Z_t \)-process is represented by the Kolmogorov backward equation
\[
\partial_t \bar{u} + \sum_{j=1}^{M} \bar{a}_j(z) \left( \bar{u}(z + \bar{v}_j, t) - \bar{u}(z, t) \right) = 0, \quad \text{in } \mathbb{Z}_+^d / \gamma \times [0, T),
\]
and approximated by the rescaled tau-leap method
\[
Z_{t+\tau} = \bar{Z}_t + \sum_{j=1}^{M} \bar{v}_j P_j(\bar{a}_j(\bar{Z}_t)) \tau,
\]
with the scaled propensities \( \bar{a}_j(z) := a_j(x) = a_j(\gamma z) \) and jumps \( \bar{v}_j := v_j/\gamma \).

Example 4.2. Let \( g(x) = x^r := \prod_{i=1}^{d} x_i^{r_i} \) and \( |r| := \sum_{i=1}^{d} |r_i| \geq 1 \) where \( r \in \mathbb{Z}_+^d \) is a \( d \)-dimensional multi-index. Then
\[
E[g(Z_T) - g(\hat{Z}_T)] = E\left[\frac{g(X_T) - g(\hat{X}_T)}{g(X_0)}\right],
\]
for some \( \min_i X_0^{(i)} \leq \gamma \leq \max_i X_0^{(i)} \).

Assumption 4.3. Following Assumption 2.1 and Remark 2.2 we here assume that:

1. The process \( Z_t \in \mathbb{Z}_+^d / \gamma \) is bounded from above by a hyperplane passing through the point \( Z_0 \) and with normal \( n > 0 \), i.e.
   \[ Z_t \in \Pi(Z_0, n) := \Pi(\gamma X_0, n) / \gamma = \{ z \in \mathbb{Z}_+^d / \gamma : n \cdot (z - Z_0) \leq 0 \} \]. Consequently, the tau-leap process takes values in the larger set
   \[ \bar{Z}_t \in \bar{\Pi}(Z_0, n) := \{ z \in \mathbb{Z}_+^d / n \cdot (z - Z_0) \leq 0 \} \].

2. The propensity \( a_j : \mathbb{Z}_+^d \to \mathbb{R} \) is non-negative and non-decreasing in each component. Also, we have that \( a_j(0) = 0 \), and \( a_j(x) = 0 \) if \( x + \nu \notin \mathbb{Z}_+^d \).

The goal is now to show an a priori bound for the discretization error \( \varepsilon \) that is independent of the scaling factor \( \gamma \), see Theorem 4.4. The proof is based on a Taylor expansion and bounds on the value function \( \bar{u} \) and its derivatives.

Theorem 4.4 (Bound on relative error). Let the process \( Z_t \) and the propensities \( a_j \) satisfy Assumption 4.3. Assume polynomial propensity functions of order \( |p_j| \), with \( p_j \in \mathbb{Z}_+^d \), and let \( g \in C^2(\mathbb{R}^d) \). Also, assume that the value function \( \bar{u} \) given by (4.3) and its first two spacial derivatives are bounded in \( \bar{\Pi}(Z_0, n) \times [0, T] \), independently of the scaling factor \( \gamma \).

For a time step \( \tau = h/\gamma^\delta \), with \( h > 0 \) and \( \delta = \max_j (2|p_j| - 2) \), the relative error (4.2) for the Poisson bridge tau-leap method is then bounded by
\[
|\varepsilon| \leq C h,
\]
for some sufficiently large \( \gamma \) and where the constant \( C > 0 \) is independent of \( h \) and the scaling factor \( \gamma \).
Proof: Throughout the proof $C$ will denote a non-negative constant value, not necessarily the same at each instance. To show the theorem we note that from the error representation in Lemma 4.1, the relative error can be expressed as

$$
\varepsilon = \sum_{j=1}^{M} \sum_{n=0}^{N-1} \int_{t_n}^{t_{n+1}} \mathbb{E}\left[\left(\tilde{a}_j(\tilde{Z}_t) - \tilde{a}_j(\tilde{Z}_{tn})\right)D_j \tilde{u}(\tilde{Z}_t, t) \mid \tilde{Z}_{tn}\right]\, dt
$$

(4.5)

$$
- \sum_{n=0}^{N-1} \int_{t_n}^{t_{n+1}} \mathbb{E}\left[\left(A_n \tilde{u}(\tilde{Z}_t, t)\right) 1_{\{\tilde{Z}_t \in \mathbb{Z}^d_t/\gamma\}} \mid \tilde{Z}_{tn}\right] dt,
$$

where

$$
A_n := \partial_t + \sum_{j=1}^{M} \tilde{a}_j(\tilde{Z}_{tn})D_j.
$$

For the first term in (4.5), Taylor expanding the propensity $\tilde{a}$ around $\tilde{Z}_{tn}$ gives

$$
I_{j,n} = \sum_{|\alpha_j| = 1}^{|p|} \frac{\tilde{a}_j^{(\alpha_j)}(\tilde{Z}_{tn})}{\alpha_j!} \mathbb{E}\left[\left(\tilde{Z}_t - \tilde{Z}_{tn}\right)^{\alpha_j} D_j \tilde{u}(\tilde{Z}_t, t) \mid \tilde{Z}_{tn}\right],
$$

where $\alpha_j \in \mathbb{Z}^d_+$. According to Lemma 4.5 the value function and its two first spatial derivatives can be continuously extended to $\mathbb{R}^d \times [0, T]$. The mean value theorem then yields

$$
\bar{I}_{\alpha_j,n} = \mathbb{E}\left[\left(\bar{Z}_t - \tilde{Z}_{tn}\right)^{\alpha_j} \left(\bar{u}(\bar{Z}_t + \tilde{v}_j, t) - \bar{u}(\bar{Z}_t, t)\right) \mid \tilde{Z}_{tn}\right]
$$

$$
= \mathbb{E}\left[\left(\bar{Z}_t - \tilde{Z}_{tn}\right)^{\alpha_j} \left(\partial_{\tilde{v}_j} \bar{u}(\bar{Z}_t, t) \tilde{v}_j + \frac{1}{2} \tilde{v}_j^T \partial^2_{\tilde{v}} \bar{u}(\xi_1, t) \tilde{v}_j\right) \mid \tilde{Z}_{tn}\right]
$$

$$
= \mathbb{E}\left[\left(\bar{Z}_t - \tilde{Z}_{tn}\right)^{\alpha_j} \partial_{\tilde{v}_j} \bar{u}(\tilde{Z}_{tn}, s) \tilde{v}_j \mid \tilde{Z}_{tn}\right]
$$

$$
+ \frac{1}{2} \mathbb{E}\left[\left(\bar{Z}_t - \tilde{Z}_{tn}\right)^{\alpha_j} \left(\partial_{\tilde{v}_j} \bar{u}(\tilde{Z}_t, t) \tilde{v}_j\right) \mid \tilde{Z}_{tn}\right]
$$

$$
+ \frac{1}{2} \mathbb{E}\left[\tilde{v}_j^T (\bar{Z}_t - \tilde{Z}_{tn})^{\alpha_j} \partial^2_{\tilde{v}} \bar{u}(\xi_2, t) \tilde{v}_j \mid \tilde{Z}_{tn}\right]
$$

$$
= \bar{I}_{\alpha_j,n} + \bar{I}^{\alpha_j,n} + \bar{I}^{\alpha_j,n},
$$

for $\xi_1 = \alpha \bar{Z}_t + (1 - \alpha) \left(\bar{Z}_t + \tilde{v}_j\right)$ for some $\alpha \in [0, 1]$ and $\xi_2 = \beta \tilde{Z}_{tn} + (1 - \beta) \bar{Z}_t$ for some $\beta \in [0, 1]$. From the tau-leap approximation of the process $Z_t$ we have

$$
\mathbb{E}\left[\left(\bar{Z}_t - \tilde{Z}_{tn}\right)^{\alpha_j} \mid \tilde{Z}_{tn}\right] = \sum_{j=1}^{M} \mathbb{E}\left[P_j \left(\tilde{a}_j(\tilde{Z}_{tn})(t - t_n)\right)^{\alpha_j} \mid \tilde{Z}_{tn}\right]
$$

$$
= \sum_{j=1}^{M} \sum_{\beta_j = 1}^{\alpha_j} C_{\beta_j} \tilde{a}_j(\tilde{Z}_{tn})^{\beta_j} (t - t_n)^{\beta_j} \tilde{v}_j^{\alpha_j}
$$

$$
\leq \sum_{j=1}^{M} \sum_{\beta_j = 1}^{\alpha_j} C_{\beta_j} \tilde{a}_j(\tilde{Z}_{tn})^{\beta_j} \tau^{\beta_j} \tilde{v}_j^{\alpha_j},
$$
for some positive constants $C_{\beta_j}$ that do not depend on $\gamma$. Choosing $\tau = h^{\gamma-\delta}$ for $h, \delta > 0$, and without loss of generality assuming that the propensity is a monomial $a_j(x) = Cx^{p_j}$ with $C > 0$, $p_j \in \mathbb{Z}_+^4$ and $|p_j| \geq 1$, then

$$\tilde{a}_j(\bar{Z}_{tn})^{\beta_j} \tau^{\beta_j} |\tilde{p}^{\alpha_j}_j| = a_j(\gamma \bar{Z}_{tn})^{\beta_j} \tau^{\beta_j} |\tilde{p}^{\alpha_j}_j|$$

$$= a_j(\gamma \bar{Z}_{tn})^{\beta_j} h^{\beta_j} |\tilde{p}^{\alpha_j}_j| \gamma^{-\delta \beta_j - |\alpha_j|}$$

$$\leq C Z^\beta_j h^{\beta_j} |\tilde{p}^{\alpha_j}_j| \gamma^{-\delta (|p_j| - |\alpha_j|)}.$$

Using the continuous extension in Remark 4.6 and assuming the value function $\tilde{u}$ and its first two derivatives are bounded independently of $\gamma$ inside $\bar{\Pi}(Z_0, n) \times [0, T]$, i.e. neglecting the probability terms in the growth condition in Lemma 4.11, leads to continuity and boundedness in the extended domain $\{z \in \mathbb{R}^d : n \cdot (z - Z_0) \leq 0\}$. Together with $\delta = \max_j (2|p_j| - 2)$ and $h \leq 1$, this gives

$$\left| \sum_{|\alpha_j| = 1}^{\frac{|p_j|}{\alpha_j}} \tilde{a}_j^{(\alpha_j)}(\bar{Z}_{tn}) \Pi_{\alpha_j n} \right| \leq C \sum_{|\alpha_j| = 1}^{\frac{|p_j|}{\alpha_j}} \gamma^{\frac{|p_j|}{\alpha_j} + |\beta_j| (|p_j| - |\alpha_j|) - |\alpha_j| - 1} h^{\beta_j}$$

$$\leq C \sum_{|\alpha_j| = 1}^{\frac{|p_j|}{\alpha_j}} \gamma^{\max_j (|p_j|) - 2 + \beta_j (\max_j (|p_j|) - |\alpha_j|) h}$$

$$\leq C \sum_{|\alpha_j| = 1}^{\frac{|p_j|}{\alpha_j}} \gamma^{\max_j (|p_j|) - 2 + \beta_j (|p_j|)} h$$

for $\bar{Z}_{tn} \in \bar{\Pi}(Z_0, n)$.

Performing the same analysis on the error contribution from the terms $\Pi_{\alpha_j n}$ and $\Pi_{\alpha_j n}$ gives the estimate in Theorem 4.4. Note that the additional $(\bar{Z}_{tn} - \bar{Z}_{tn})$ term in $\Pi_{\alpha_j n}$ and the extra $\tilde{p}_j$ in $\Pi_{\alpha_j n}$ and $\Pi_{\alpha_j n}$ yields that $\bar{\Pi}_{\alpha_j n} = O(1)$, $\bar{\Pi}_{\alpha_j n} = O(\gamma^{-1})$ and $\Pi_{\alpha_j n} = O(\gamma^{-1})$, so for large $\gamma$ the first term in the Taylor expansion is dominant.

For the second term in (4.5) we have that since the value function and its derivatives are continuously extended and bounded in $\bar{\Pi}(Z_0, n)$

$$\Lambda_n \tilde{u}(\bar{Z}_t, t) = \left( \partial_t + \sum_{j=1}^{M} \tilde{a}_j(\bar{Z}_{tn}) D_j \right) \tilde{u}(\bar{Z}_t, t) \leq \gamma^{-1} \sum_{j=1}^{M} C_j \tilde{a}_j(\bar{Z}_{tn}).$$

and thus

$$\mathbb{E} \left[ \Lambda_n \tilde{u}(\bar{Z}_t, t) 1_{\bar{Z}_t \in \mathbb{Z}_d / \gamma} \right] \leq \gamma^{-1} \mathbb{E} \left[ 1_{\bar{Z}_t \in \mathbb{Z}_d / \gamma} \bar{Z}_{tn} \right] \sum_{j=1}^{M} C_j \tilde{a}_j(\bar{Z}_{tn})$$

$$= \gamma^{-1} \mathbb{P} \left( \bar{Z}_t \in \mathbb{Z}_d / \gamma \mid \bar{Z}_{tn} \right) \sum_{j=1}^{M} C_j \tilde{a}_j(\bar{Z}_{tn})$$

$$\leq \gamma^{-1} \sum_{i=1}^{d} \mathbb{P} \left( \bar{Z}_t^{(i)} < 0 \mid \bar{Z}_{tn} \right) \sum_{j=1}^{M} C_j \tilde{a}_j(\bar{Z}_{tn}).$$
Neglecting positive jumps we obtain
\[ \tilde{Z}_t^{(i)} = \tilde{Z}_{t_0}^{(i)} + \sum_{j=1}^M \tilde{\nu}_j^{(i)} P(\tilde{a}_j(\tilde{Z}_{t_0})(t - t_n)) \]
\[ \geq \tilde{Z}_{t_n}^{(i)} + \tilde{\nu}_j^{(i)} P(\tilde{a}_0(\tilde{Z}_{t_n})\tau) =: \tilde{Z}_t^{(i)}, \quad t \in (t_n, t_{n+1}), \]
where \( \tilde{\nu}_j^{(i)} := \min_j \{ \min(\tilde{\nu}_j^{(i)}, 0) \} < 0, \) and \( \tilde{a}_0 := \sum_{j=1}^M \tilde{a}_j. \) For \( \tilde{Z}_{t_n}^{(i)} > 0 \) the probability of negative populations in (4.6) can then be approximated by
\[ P(\tilde{Z}_t^{(i)} < 0 \mid \tilde{Z}_{t_n}) \leq P\left( \tilde{Z}_t^{(i)} < 0 \mid \tilde{Z}_{t_n}^{(i)} \right) \]
\[ \leq P\left( \tilde{a}_0(\tilde{Z}_{t_n})\tau > \frac{-\tilde{Z}_{t_n}^{(i)}/\tilde{\nu}_j^{(i)}}{=: q > 0} \right) \]
\[ = \sum_{k=[q]}^{\infty} \left( \frac{\tilde{a}_0(\tilde{Z}_{t_n})\tau}{k!} \right)^k e^{-\tilde{a}_0(\tilde{Z}_{t_n})\tau} \]
\[ = \sum_{k=0}^{\infty} \left( \frac{\tilde{a}_0(\tilde{Z}_{t_n})\tau}{[k + |q|]} \right)^k e^{-\tilde{a}_0(\tilde{Z}_{t_n})\tau} \]
\[ < \sum_{k=0}^{\infty} \left( \frac{\tilde{a}_0(\tilde{Z}_{t_n})\tau}{|q|} \right)^k \frac{\tilde{a}_0(\tilde{Z}_{t_n})\tau}{k!} e^{-\tilde{a}_0(\tilde{Z}_{t_n})\tau} \]
\[ \leq \frac{\tilde{a}_0(\tilde{Z}_{t_n})\tau}{(C\gamma)^!} \]
where \([::] \) denotes the ceiling and \( C \) is independent of \( \gamma. \) For \( \tilde{Z}_{t_n}^{(i)} = 0, \) the probability \( P(\tilde{Z}_t^{(i)} < 0 \mid \tilde{Z}_{t_n}) \) is zero since \( a_j(\tilde{Z}_{t_n}) = 0 \) if \( \tilde{\nu}_j^{(i)} < 0. \)

Combining (4.6) and (4.7), and using \( a_0(x) \leq C_a \max \{|p_j| \} \) and \( \tau = h\gamma^{2-2 \max \{|p_j| \}} \) gives
\[ E \left[ A_n \tilde{u}(\tilde{Z}_t, t) \mathbf{1}_{\{ \tilde{Z}_t \in \mathbb{R}^d / \gamma \}} \right] \leq C\gamma^{-1} \tilde{a}_0(\tilde{Z}_{t_n}) \left( \frac{a_0(\tilde{Z}_{t_n})\tau}{(C\gamma)!} \right) \]
\[ \leq C\gamma^{\max \{|p_j| \}} \left( \frac{Ch\gamma^{2-2 \max \{|p_j| \}}}{(C\gamma)!} \right) \]
\[ \approx C\gamma^{\max \{|p_j| \}} \left( \frac{Ch\gamma^{1-\max \{|p_j| \}}}{(C\gamma)!} \right), \]
so the remainder term (4.6) can be neglected.

In the theorem above we used that the relative value function \( \tilde{u} \) defined by (4.3) and its derivatives can be continuously extended to \( \mathbb{R}^d \times [0, T], \) and are bounded independently of \( \gamma \) in the domain \( \tilde{\Pi}(Z_0, n) \times [0, T]. \) In the remaining part of this section we will motivate why those assumptions make sense.

**Lemma 4.5** (Extension of the value function and its derivatives). Assume that the process \( \tilde{Z}_t \) and the propensities \( a_j \) satisfy Assumption 4.3, and that \( a_j \) and \( g \) are \( C^2 \) on \( \mathbb{R}^d. \) The solution \( \tilde{u} \) to the Kolmogorov backward equation (4.3) is then locally
bounded and smooth in time on \( \mathbb{Z}_+^{d}/\gamma \times [0, T] \) and can be continuously extended to \( \mathbb{R}^d \times [0, T] \). Also, the derivatives \( \partial_z \tilde{u} \) and \( \partial_z^2 \tilde{u} \) are locally bounded and smooth in time on the lattice \( \mathbb{Z}_+^{d}/\gamma \) and can be continuously extended to \( \mathbb{R}^d \times [0, T] \).

**Proof.** First, we continuously extend \( \tilde{a}_j \) such that it is non-negative, monotone in each component and \( C^2 \) on \( \mathbb{R}^d \), see e.g. Example 4.7 and 4.8 below. Given such an extension of the propensity, the value function \( \tilde{u} \) can be continuously extended to the domain \( \mathbb{R}^d \times [0, T] \) by solving the Kolmogorov backward equation (4.3) on the shifted lattice \( (\mathbb{Z}_+^{d} + \epsilon)/\gamma \times [0, T], \epsilon \in \mathbb{R}^d \).

Note that, for any point \( Z_t \in \mathbb{Z}_+^{d}/\gamma \) we know that \( Z_s \in \tilde{\Pi}(Z_t, n) \) for \( s \geq t \), and (4.3) can be understood as a linear constant coefficient system of ordinary differential equations on a finite lattice, with a unique bounded smooth solution \( \tilde{u} \).

The derivatives \( \tilde{v} := \partial_z \tilde{u} \in \mathbb{R}^d \) and \( \tilde{w} := \partial_z^2 \tilde{u} \in \mathbb{R}^{d \times d} \) can be defined on \( \mathbb{Z}_+^{d}/\gamma \times [0, T] \) and satisfy the equations

\[
(4.9) \quad \partial_t \tilde{v} + \sum_{j=1}^{M} \tilde{a}_j(z) D_j \tilde{v} = - \sum_{j=1}^{M} \nabla \tilde{a}_j(z) D_j \tilde{u}, \quad \text{in } \mathbb{Z}_+^{d}/\gamma \times [0, T),
\]

\[
\tilde{v} = \nabla g, \quad \text{in } \mathbb{Z}_+^{d}/\gamma \times \{ T \},
\]

and

\[
(4.10) \quad \partial_t \tilde{w} + \sum_{j=1}^{M} \tilde{a}_j(z) D_j \tilde{w} = - \sum_{j=1}^{M} \nabla^2 \tilde{a}_j(z) \left( D_j \tilde{v} - \nabla^2 \tilde{a}_j(z) D_j \tilde{u} \right), \quad \text{in } \mathbb{Z}_+^{d}/\gamma \times [0, T),
\]

\[
\tilde{w} = \nabla^2 g, \quad \text{in } \mathbb{Z}_+^{d}/\gamma \times \{ T \}.
\]

Using that \( g \in C^2(\mathbb{R}^d) \) and that \( \tilde{u} \) is locally bounded and smooth, we can by the same argument as for \( \tilde{u} \) above see that \( \tilde{v} \) and \( \tilde{w} \) are locally bounded and smooth in time.

By shifting the grid in the same manner as was done for \( \tilde{u} \), the solutions \( \tilde{v} \) and \( \tilde{w} \) can be continuously extended to \( \mathbb{R}^d \times [0, T] \).

\[\square\]

**Remark 4.6.** In addition to the above lemma we can also continuously extend the value function \( \tilde{u}(z, \cdot) \) to real negative values \( z \in \mathbb{R}^d_- \) such that \( \tilde{u}, \partial_z \tilde{u} \) and \( \partial_z^2 \tilde{u} \) vanish for \( z_i < -l < 0 \). This extension is used for the Taylor expansion in Lemma 4.4.

Without loss of generality consider the extension to the domain \( \mathbb{R}_-^d \), with subdomains \( A := \{ z \in (-l, 0) \times (0, \infty) \}, \quad B := \{ z \in (-l, 0)^2 \} \) and \( C := \{ z \in (0, \infty) \times (-l, 0) \} \).

First let \( \tilde{u}(z, \cdot) = 0 \) on \( z \in \mathbb{R}_-^d \setminus \{ A \cup B \cup C \} \). Next, extend the value function to the domain \( A \) by third degree polynomials in the \( z_1 \) direction, for all \( z_2 \geq 0 \), matching \( \tilde{u}, \partial_z \tilde{u} \) and \( \partial_z^2 \tilde{u} \) on \( z_1 = -L \) and \( z_1 = 0 \). Similarly, fit polynomials in the \( z_2 \) direction in domain \( C \). In the domain \( B \) a \( C^2 \)-extension can be made by transfinite interpolation using \( \tilde{u}, \partial_z \) and \( \partial_z^2 \tilde{u} \) on \( \partial B \), see e.g. [3, 14, 27].
Example 4.7. A natural extension to the propensity function $a_j(x) := x, x \in \mathbb{Z}$, is
\[
a_j(x) := \begin{cases} 
0, & x < 0, \\
\hat{a}_j(x), & 0 \leq x \leq 1, \\
x, & x > 1,
\end{cases}
\]
for $x \in \mathbb{R}$, where $\hat{a}_j$ is a positive and monotone $C^2$ function chosen such that $a_j \in C^2(\mathbb{R})$, e.g. $\hat{a}_j(x) := 6x^3 - 8x^4 + 3x^5$, see Figure 4.1.

Example 4.8. The propensity function $a(x) := x(x - 1)$ is negative in $(0, 1)$. A natural extension is thus to let
\[
a(x) := \begin{cases} 
0, & x < 1, \\
\hat{a}(x), & 1 \leq x < 2, \\
x(x - 1), & x \geq 2,
\end{cases}
\]
for $x \in \mathbb{R}$, where $\hat{a}$ is a positive and monotone $C^2$ function chosen such that $a \in C^2(\mathbb{R})$, e.g. $\hat{a}(x) := 9(x - 1)^3 - 11(x - 1)^4 + 4(x - 1)^5$, see Figure 4.1.

![Propensity](image1)

(a) Example 4.7

![Propensity](image2)

(b) Example 4.8

Figure 4.1. Extended propensity functions in Example 4.7 and 4.8.

In Lemma 4.5 we saw that $\tilde{u}$ and its first two derivatives are locally bounded in $\mathbb{R}^d \times [0, T]$, however, this bound depends on $\gamma$. The next step is to show under what conditions we can find a bound that does not depend on $\gamma$. First, we start by generalizing the polynomial form of the propensity (2.3) in Remark 2.2 into bounds:

Assumption 4.9. Given some multi-index $p_j \in \mathbb{Z}_+^d$ and positive constants $0 < C^i_L \leq C^i_U$, $0 < C'^i_L' \leq C'^i_U'$ and $0 < C''_L'' \leq C''_U''$, assume that the propensity has the bounds
\[
C^i_L(x + \zeta_j)^{p_j} \leq a_j(x) \leq C^i_U(x + \zeta_j)^{p_j},
\]
(4.11)
\[
C'^i_L(x + \zeta_j)^{p_j - e_i} \leq \partial_x a_j(x) \leq C'^i_U(x + \zeta_j)^{p_j - e_i},
\]
\[
C''_L(x + \zeta_j)^{p_j - e_i - e_k} \leq \partial_{x_k} a_j(x) \leq C''_U(x + \zeta_j)^{p_j - e_i - e_k},
\]
for $i = 1, \ldots, d$, $j = 1, \ldots, M$ and $x \in \mathbb{Z}_+^d$. Here, $(\cdot)_+ := \max(\cdot, 0)$, $\zeta_{ij} := (\nu_{ij} + 1)1_{\nu_{ij}<0}$, and $e_i$ indicate the unit basis vectors in $\mathbb{R}^d$. 
In the next step, we introduce a weight definition that in Lemma 4.11 will allow us to do find weighted estimates for the value function and its derivatives.

**Remark 4.10 (Weight definition).** From the Assumption 4.9 on boundedness of $Z_t$, there exists a vector $n > 0$ in $\mathbb{R}^d$ such that $\nu_j \cdot n < 0$ for $j = 1, \ldots, M$. Take a weight function $y(z) := \psi(n \cdot z) > 0$ where $\psi : (t_{\text{min}}, +\infty) \to \mathbb{R}^+$ is a smooth, strictly decreasing function. Observe that we have by construction $y(z + \nu_j) - y(z) \geq 0$, for all $z \in \Pi(Z_0, n)$. In particular, if $g$ has polynomial growth $g(z) \leq C(z \cdot n)^r_0(z \cdot n + 1)^r_1$ we can have the product $yg$ uniformly bounded, for instance by taking $\psi(t) = (t + t_0)^{-r_0}(t + 1)^{-r_1}$, with some $t_{\text{min}} = t_0 > 0$ and $r_0, r_1 \geq 0$.

Now we are ready to present weighted estimates that are uniform with respect to the scaling parameter $\gamma$, and on which Theorem 4.4 for the a priori relative error bound is based.

**Lemma 4.11 (Growth condition).** Assume that the assumptions on boundedness of $Z_t$ and the conditions on $a_j$ in Assumption 4.3 hold. Also, assume that the bounds (4.11) on the propensity and its derivatives in Assumption 4.9 are satisfied. Let $|p|$ be the maximum reaction order in the system, i.e. $|p| := \max_j |p_j|$ for the multi-indices in (4.11), and assume that for each of the components $x_i$, there exist a single component reaction whose propensity has order $|p|$. Finally, assume that $g$ is $C^2$ on $\mathbb{R}^d$, non-negative with $g(0) = 0$, and that for the weight functions

$$y(z) := \left( z \cdot n + \frac{1}{\gamma} \max_j |\nu_j \cdot n| \right)^{-r_0} (1 + z \cdot n)^{-r_1},$$

$$y_1(z) := y(z) \left( z \cdot n + \frac{1}{\gamma} \max_j |\nu_j \cdot n| \right),$$

$$y_2(z) := y_1(z) \left( z \cdot n + \frac{1}{\gamma} \max_j |\nu_j \cdot n| \right),$$

the quantities $| yg |, | y_1 \nabla g |$ and $| y_2 \nabla^2 g |$ are bounded.

We then have the bounds

$$| \tilde{u}(z,t) | \leq \frac{C}{y(z)},$$

$$| \partial_z \tilde{u}(z,t) | \leq \frac{C}{y_1(z)} + \frac{C'}{y_1(z)} (\gamma z \cdot n)^{|p|} P \left( \frac{\theta}{\gamma} < Z_T \cdot n < \eta \mid Z_t = z \right),$$

$$| \partial^2_z \tilde{u}(z,t) | \leq \frac{C}{y_2(z)} + \frac{C''}{y_2(z)} (\gamma z \cdot n)^{2|p|} P \left( \frac{\theta}{\gamma} < Z_T \cdot n < \eta \mid Z_t = z \right)^2,$$

for $(z,t) \in \Pi(Z_0, n) \times [0,T]$ , for some $\theta, \eta > 0$ and positive constants $C$, $C'$ and $C''$ that are independent of $\gamma$.

**Proof.** Throughout the proof $C$ will denote a constant value, not necessarily the same at each instance. Also, for simplicity we will assume that the propensity has the form $a_j(x) := C x^{\nu_j}$. In the general case with bounds (4.11), the proof is essentially the same. The proof is divided into three sections corresponding to the bounds in (4.12).

**Bound on $\tilde{u}$:** Let $U(z,t) := y(z) \tilde{u}(z,t)$. Since $g$ has polynomial growth we can take $y$ as in Remark 4.10 with $t_0 = \max_j |\tilde{\nu}_j \cdot n| := |\tilde{\nu}^* \cdot n|$. 


Also, since \( g(0) = 0 \) we have \( r_0 > 0 \). Then we have

\[
\partial_t U + \sum_{j=1}^{M} \tilde{a}_j \left( y \tilde{u}(z + \tilde{\nu}_j, t) - U \right) = 0, \quad \text{in } \tilde{\Pi}(Z_0, n) \times [0, T),
\]

\[
U = yg, \quad \text{on } \tilde{\Pi}(Z_0, n) \times \{T\},
\]

where \( \|U(\cdot, T)\|_\infty = \|y \tilde{u}(\cdot, T)\|_\infty = \|yg\|_\infty \) by definition is bounded. Adding and subtracting \( \sum_{j=1}^{M} \tilde{a}_j(z)U(z + \tilde{\nu}_j, t) \) yields

\[
\partial_t U + \sum_{j=1}^{M} \tilde{a}_j D_j U = \sum_{j=1}^{M} \tilde{a}_j \tilde{u}(z + \tilde{\nu}_j, t) D_j y,
\]

with the stochastic representation

\[
U(z, t) = E \left[ y(Z_T) g(Z_T) - \int_t^T \sum_{j=1}^{M} \tilde{a}_j(Z_s) \tilde{u}(Z_s + \tilde{\nu}_j, s) D_j y(Z_s) \right]_{Z_t = z \, ds}.
\]

Since the right hand side of (4.13) is non-negative we obtain

\[
\|U(\cdot, t)\|_\infty \leq \|U(\cdot, T)\|_\infty \leq C,
\]

and therefore

\[
\tilde{u}(z, t) \leq C y(z)^{-1} \leq C \left( z \cdot n + \frac{|\nu^* \cdot n|}{\gamma} \right)^{r_0} (1 + z \cdot n)^{r_1},
\]

which is the first estimate in (4.12).

**Bound on \( \partial \tilde{u} \):** For the bound on the first derivative \( \tilde{\nu} := \partial_z \tilde{u} \in \mathbb{R}^d \), we consider the weighted function \( V(z, t) := y_1(z) \tilde{v}(z, t) \in \mathbb{R}^d \) with the weight

\[
y_1(z) := y(z) \left( z \cdot n + \frac{|\nu^* \cdot n|}{\gamma} \right) = \left( z \cdot n + \frac{|\nu^* \cdot n|}{\gamma} \right)^{1-r_0} (1 + z \cdot n)^{-r_1} \in \mathbb{R},
\]

such that the product \( y_1 \nabla g \) is bounded uniformly in \( z \) and \( \gamma \). Define an auxiliary function

\[
R(z, t) = \sum_{j=1}^{M} \tilde{a}_j(z) \tilde{v}(z + \tilde{\nu}_j, t) D_j y_1(z).
\]

This yields

\[
\partial_t V + \sum_{j=1}^{M} \tilde{a}_j D_j V = R(z, t) - \sum_{j=1}^{M} \nabla \tilde{a}_j(z) y_1(z) D_j \tilde{u}(z, t), \quad \text{in } \tilde{\Pi}(Z_0, n) \times [0, T),
\]

\[
V = y_1 \nabla g, \quad \text{on } \tilde{\Pi}(Z_0, n) \times \{T\}.
\]

Denote

\[
\beta_j(z) := \tilde{a}_j(z) D_j y_1(z),
\]

(4.14)

\[
\beta(z) := \sum_{j=1}^{M} \beta_j(z),
\]

and observe that \( \beta_j(0) = 0 \) and \( \beta_j \geq 0 \). Since

\[
R(z, t) = \sum_{j=1}^{M} V(z + \tilde{\nu}_j, t) \beta_j(z),
\]
we have
\[ \partial_t V + \sum_{j=1}^{M} (\tilde{a}_j - \beta_j) D_j V - \beta V = -y_1 \sum_{j=1}^{M} \nabla \tilde{a}_j D_j \tilde{u}, \quad \text{in } \tilde{\Pi}(Z_0, n) \times [0, T), \]
\[ V = y_1 \nabla g, \quad \text{on } \tilde{\Pi}(Z_0, n) \times \{ T \}. \]

The solution \( V \) can now be stochastically represented as
\[ (4.15) \quad V(z, t) = E \left[ y_1(\hat{Z}_T) \nabla g(\hat{Z}_T) e^{-\int_t^T \beta(\hat{Z}_s) ds} \mid \hat{Z}_t = z \right] \]
\[ = V_1 + E \left[ \int_t^T y_1(\hat{Z}_s) e^{-\int_t^s \beta(\hat{Z}_u) du} \sum_{j=1}^{M} \nabla \tilde{a}_j(\hat{Z}_s) D_j \tilde{u}(\hat{Z}_s, s) ds \mid \hat{Z}_t = z \right], \]
where \( \hat{Z}_t \) is a modified jump process with smaller propensities
\[ \tilde{a}_j(z) := (\tilde{a}_j - \beta_j)(z) = \tilde{a}_j(z) \left( 1 - D_j y_1(z) y_1(z + \tilde{\nu}_j)^{-1} \right) = \tilde{a}_j(z) y_1(z) y_1(z + \tilde{\nu}_j)^{-1}. \]

Indeed, since \( y_1(z + \tilde{\nu}_j) \geq y_1(z) \geq 0 \) by definition, we have \( 0 \leq \tilde{a}_j(z) \leq \tilde{a}_j(z) \).

Observe that since the product \( |y_1 \nabla g| \) is bounded, we have \( |V_1| \leq C \). We now consider \( V_2 \), and first focus on a lower bound for the functions \( \beta_j \) defined in (4.14). From the assumption \( a_j(x) := C x^{p_j} \) we obtain
\[ \beta_j(z) = C \gamma \gamma^{|p_j| z^{p_j}} \xi_j(z), \]
and
\[ \xi_j(z \cdot n) := D_j y_1(z) y_1(z + \tilde{\nu}_j)^{-1} \]
\[ = 1 - \left( 1 - \frac{|\tilde{\nu}_j \cdot n|}{z \cdot n + |\tilde{\nu}^* \cdot n|} \right)^{r_0 - 1} \left( 1 - \frac{|\tilde{\nu}_j \cdot n|}{1 + z \cdot n} \right)^{r_1}. \]

Observe that \( \xi_j \) is strictly decreasing with respect to the product \( z \cdot n \) on \((0, +\infty)\), and that \( \xi_j(+\infty) = 0^+ \). Since the values \( z \in \tilde{\Pi}(Z_0, n) \) and \( \tilde{\nu} \) are bounded by assumption 2.1, we conclude that \( \xi_j(z) \geq \xi_0 > 0 \) and then
\[ \beta_j(z) \geq C \xi_0 \gamma \gamma^{|p_j| z^{p_j}}, \]
for all \( z \in \tilde{\Pi}(Z_0, n) \).

Given \( \eta > 0 \), let us now introduce a family of time intervals,
\[ I^\eta_t := \{ s \in [t, T] : \hat{Z}_s \cdot n \geq \eta \}. \]

Let
\[ |p| = \max_j |p_j|, \]
and observe that, thanks to the assumption on the existence of all the single component reactions with order \(|p|\),
\[ (4.16) \quad \int_t^T \beta(\hat{Z}_s) ds \geq \xi_0 C |I^\eta_t| (\gamma \eta)^{|p|}. \]
On the other hand, we have
\[ |\partial_z \tilde{a}_j(z)y_1(z)D_j \tilde{u}(z, s)| \leq C |\partial_z \tilde{a}_j(\gamma z)y_1(z)y(z)^{-1}| \]
\[ = C_1 \gamma e^{-\xi_0 C \gamma (\gamma z)^{\frac{1}{n}}} \left( z \cdot n + \frac{\nu^* \cdot n}{\gamma} \right) \]
\[ \leq C_1 \gamma e^{-\xi_0 C \gamma (\gamma z)^{\frac{1}{n}}} \left( z \cdot n + \frac{\nu^* \cdot n}{\gamma} \right). \]
(4.17)

Let \( 0 < \kappa < 1 \) denote a time fraction. Then thanks to (4.16) and (4.17) the term \( V_2 \) in (4.15) can be estimated as
\[ |V_2(z, t)| \leq C \int_t^T E \left[ \gamma |p| (\hat{Z}_s \cdot n)^{|p|} e^{-\xi_0 C \gamma (\gamma z)^{\frac{1}{n}}} |I_s^*| \bigg| \hat{Z}_t = z \right] ds \]
\[ \leq C \gamma |p| \int_t^T e^{-\xi_0 C \gamma (\gamma z)^{\frac{1}{n}}} s \]
\[ + C \gamma |p| E \left[ \int_t^T (\hat{Z}_s \cdot n)^{|p|} 1_{|I_s^*| < \kappa(T-t)} ds \bigg| \hat{Z}_t = z \right] \]
\[ \leq C \frac{1 - e^{-\xi_0 C \gamma (\gamma z)^{\frac{1}{n}}} s}{\xi_0 C \gamma (\gamma z)^{\frac{1}{n}}} + C \gamma |p| \int_t^T P(|I_s^*| < \kappa(T-t)|\hat{Z}_t = z) ds. \]

Observe, that since the process \( \hat{Z}_s \cdot n \) is non increasing, we have
\[ 1_{|I_s^*| < \kappa(T-s)} \leq 1_{|I_s^*| < \kappa(T-s)} \leq 1_{\hat{Z}_s \cdot n < \eta}, \] for \( s_1 \leq s_2 < T, \)
and then, for a given constant \( \theta > 1, \)
\[ \gamma |p| E \left[ \int_t^T (\hat{Z}_s \cdot n)^{|p|} 1_{|I_s^*| < \kappa(T-s)} ds \bigg| \hat{Z}_t = z \right] \]
\[ \leq \gamma |p| E \left[ \int_t^T (\hat{Z}_s \cdot n)^{|p|} 1_{\hat{Z}_s \cdot n < \eta} \left( 1_{\hat{Z}_s \cdot n < \frac{\xi}{2}} + 1_{\hat{Z}_s \cdot n > \frac{\xi}{2}} \right) ds \bigg| \hat{Z}_t = z \right] \]
\[ \leq \theta |p| E \left[ \int_t^T 1_{\hat{Z}_s \cdot n < \frac{\xi}{2}} ds \bigg| \hat{Z}_t = z \right] \]
\[ + \gamma |p| (\hat{Z}_s \cdot n)^{|p|} E \left[ \int_t^T 1_{\hat{Z}_s \cdot n < \eta} ds \bigg| \hat{Z}_t = z \right] \]
\[ \leq (T-t) \theta |p| P \left( \hat{Z}_T \cdot n \leq \frac{\theta}{\gamma} \bigg| \hat{Z}_t = z \right) \]
\[ + (T-t) \gamma |p| (\hat{Z}_s \cdot n)^{|p|} P \left( \frac{\theta}{\gamma} < \hat{Z}_T \cdot n < \eta \bigg| \hat{Z}_t = z \right). \]

Observe that when the process \( \hat{Z}_s \cdot n \) is within a distance \( O(1/\gamma) \) from zero there are only bounded contributions to the derivative of \( \tilde{u} \). Therefore, what really deteriorates the derivative estimate is the time spent between \( \theta/\gamma \) and \( \eta. \)

**Bound on \( \partial^2 \tilde{u} \):** Similar to the bound on \( \partial \tilde{u} \) we consider the weighted function
\[ W(z, t) := y_2(z) \tilde{w}(z, t) = y_2(z) \partial^2 \tilde{u}(z, t) \in \mathbb{R}^{d \times d} \text{ with the weight} \]
\[ y_2(z) = y_1(z) \left( z \cdot n + \frac{\nu^* \cdot n}{\gamma} \right) \in \mathbb{R}, \]
such that the product \( y_2 \nabla^2 g \) is bounded uniformly in \( z \) and \( \gamma \). Following the same procedure as for \( V \) we obtain from (4.10) that

\[
\partial_t W + \sum_{j=1}^{M} (\hat{a}_j - \beta_j) D_j W - \beta_j W = -R, \quad \text{in} \quad \tilde{\Pi}(Z_0, n) \times [0, T),
\]

\[
W = y_2 \nabla^2 g, \quad \text{on} \quad \tilde{\Pi}(Z_0, n) \times \{ T \},
\]

where

(4.19) \[
\beta(z) := \sum_{j=1}^{M} \beta_j(z), \quad \beta_j(z) := \hat{a}_j(z) D_j y_2(z) y_2(z + \hat{v}_j)^{-1},
\]

and

\[
R(z, t) = \sum_{j=1}^{M} 2 y_2(z) \nabla \hat{a}_j(z) \otimes D_j \hat{v}(z, t) + \nabla^2 \hat{a}_j(z) y_2(z) D_j \tilde{u}(z, t),
\]

with '\( \otimes \)' denoting the tensor product. This gives the stochastic representation formula

\[
W(z, t) = \mathbb{E} \left[ y_2(\hat{z}_T) \nabla^2 g(\hat{z}_T) e^{-\int_{\hat{z}_s}^{\hat{z}_t} \beta(\hat{z}_s) ds} \Big| \hat{z}_t = z \right] =: W_1
\]

\[
+ \mathbb{E} \left[ \int_{\hat{z}_s}^{\hat{z}_t} y_2(\hat{z}_s) e^{-\int_{\hat{z}_s}^{\hat{z}_t} \beta(\hat{z}_s) ds} R(\hat{z}_s, s) ds \Big| \hat{z}_t = z \right] =: W_2,
\]

where the modified process \( \hat{z}_t \) has propensity \( \hat{a}_j(z) := \hat{a}_j(z) - \beta_j(z) \).

Since \( |y_2 \nabla^2 g| \) is bounded we have that \( |W_1| \leq C \). For \( W_2 \) we note that (4.16) holds also for the new \( \beta \) in (4.19) and the new modified process \( \hat{z}_t \). Also, we have the bounds

\[
|\partial_z \hat{a}_j(z) y_2(z) D_j \hat{v}(z, s)| \leq C|\partial_z a_j(\gamma z) y_2(z)|
\]

\[
\leq \gamma |\nu| (z \cdot n)^{|p|} P \left( \theta_{\gamma^{-1}} < \hat{z}_T \cdot n < \eta \mid \hat{z}_s = z \right) y_1(z)^{-1}
\]

\[
= C \gamma |\nu| (z \cdot n)^{|p|} \left( z \cdot n + \frac{|\nu^* \cdot n|}{\gamma} \right)
\]

\[
\leq C \gamma^2 |\nu| (z \cdot n)^{2|p|} P \left( \theta_{\gamma^{-1}} < \hat{z}_T \cdot n < \eta \mid \hat{z}_s = z \right),
\]

and similarly

\[
|\partial_{z, \gamma} \hat{a}_j(z) y_2(z) D_j \tilde{u}(z, s)| \leq C|\partial_{z, \gamma} a_j(\gamma z) y_2(z)/y(z)|
\]

\[
= C \gamma |\nu| (z \cdot n + \frac{|\nu^* \cdot n|}{\gamma})^2
\]

\[
\leq C \gamma^2 |\nu| (z \cdot n)^{2|p|} (z \cdot n + \frac{|\nu^* \cdot n|}{\gamma})^2
\]

\[
\leq C \gamma^2 |\nu| (z \cdot n)^{|p|}.
\]
In the same manner as in (4.18) we obtain

\[
|W_2(z, t)| \leq C \int_t^T E \left[ \gamma^{|p|} (\hat{Z}_s \cdot n)^{|p|} e^{-\xi_0 C (\gamma n)^{|p|}|t_s^*|} | \hat{Z}_t = z \right] ds
\]

\[
+ C \int_t^T E \left[ \gamma^{2|p|} (\hat{Z}_s \cdot n)^{2|p|} | \theta_{\gamma^{-1}} < \hat{Z}_T \cdot n < \eta \mid \hat{Z}_s \cdot \hat{Z}_s' = \hat{Z}_s \right] ds
\]

\[
\leq C + C\gamma^{|p|} (z \cdot n)^{|p|} P \left( \frac{\theta_{\gamma^{-1}} < \hat{Z}_T \cdot n < \eta \mid \hat{Z}_s \cdot \hat{Z}_s = \hat{Z}_s} \right)
\]

and in particular if the quantity (4.21) is uniformly bounded in \(\gamma\) we have that \(|W| \leq C\).

\[\square\]

**Corollary 4.12.** Assume, in addition to the assumptions made in Lemma 4.11, that given \(z > 0\) there exists \(\eta(z)\) s.t. for a sufficiently small constant \(\theta > 0\) the quantity

\[(4.21) \quad \gamma^{|p|} (z \cdot n)^{|p|} P \left( \frac{\theta_{\gamma^{-1}} < \hat{Z}_T \cdot n < \eta \mid \hat{Z}_t = z} \right) < C,
\]

is uniformly bounded in \(\gamma\). Then

\[
|\hat{u}(z, t)| \leq C \left( z \cdot n + \max_j |\hat{u}_j \cdot n| \right)^{r_0} (1 + z \cdot n)^{r_1},
\]

\[
|\partial_z \hat{u}(z, t)| \leq C \left( z \cdot n + \max_j |\hat{u}_j \cdot n| \right)^{r_0-1} (1 + z \cdot n)^{r_1},
\]

\[
|\partial_z^2 \hat{u}(z, t)| \leq C \left( z \cdot n + \max_j |\hat{u}_j \cdot n| \right)^{r_0-2} (1 + z \cdot n)^{r_1},
\]

for \((z, t) \in \tilde{\Pi}(Z_0, n) \times [0, T]\).

The assumption (4.21) is trivially true whenever \(n \cdot \nu_j = 0\) for all \(j = 1, \ldots, M\), e.g. for a system with only reversible reactions of the form \(X_1 \rightleftharpoons X_2\). In that case the product \(\hat{Z}_t \cdot n = z \cdot n\) remains constant for all \(t \leq s \leq T\).

### 4.2. Computational work.

The results in the previous section now give us the possibility to judge in which regimes and for which propensities the Poisson bridge tau-leap method is expected to be more efficient than the SSA. As mentioned in Section 1, the computational work of the SSA is roughly inversely proportional to the total propensity, and becomes intractable as the number of particles grow. The tau-leap method, on the other hand, approximates the process by using fixed time steps, and may lose accuracy as the number of particles grow unless the step size is adjusted accordingly. A reasonable way to compare the two methods is thus to keep the required accuracy of the tau-leap method fixed.

From Theorem 4.4 we see that the computational work for the Poisson bridge tau-leap method to achieve a relative error \(\epsilon := E[g(\hat{Z}_T) - g(Z_T)]\), using the time
step $\tau = h\gamma^{2-2p}$, is

$$\text{(4.22) } \text{Work}_{TL} \approx \frac{C}{\tau} \approx \frac{C\gamma^{2p-2}}{\varepsilon}.$$ 

The comparable work for the SSA is

$$\text{Work}_{SSA} \approx \frac{C}{\tau_{SSA}} \approx C\tilde{a}(Z_0) = Ca(\gamma Z_0) \approx C\gamma^p Z_0^p,$$

and then we have

$$\text{(4.23) } \frac{\text{Work}_{SSA}}{\text{Work}_{TL}} \approx C\gamma^{2-p} Z_0^p \varepsilon.$$ 

Thus, asymptotically as $\gamma \to \infty$, for $p = 1$ the tau-leap method outperforms the SSA. For $p = 2$ the methods are comparable and for $p > 2$ the SSA seems to be the right choice. Note, that for $p = 1$ the step size $\tau = h$ is independent of the number of particles even though the time between reactions is of order $\gamma^{-p}$.

Remark 4.13. The estimated work (4.22) and consequently the comparison (4.23) is a worst case scenario. For a simple decaying reaction, $X \to \emptyset$, with propensity $a(x) = x^p$ for $p = 1, 2, 3$, stoichiometric number $\nu = -1$ and initial number of particles $\gamma$, the tau-leap method is

$$\bar{X}_{t_{n+1}} = \bar{X}_{t_n} - \mathcal{P}(\bar{X}_{t_n}^p \tau_n), \quad p = 1, 2, 3,$$

$$\bar{X}_{t_0} = \gamma.$$ 

Rewrite

$$\mathcal{P}(\bar{X}_{t_n}^p \tau_n) = \bar{X}_{t_n}^p \tau_n + \sqrt{\bar{X}_{t_n}^p \tau_n} \Delta W_{t_n},$$

where

$$\Delta W_{t_n} := \frac{\mathcal{P}(\bar{X}_{t_n}^p \tau_n) - \bar{X}_{t_n}^p \tau_n}{\sqrt{\bar{X}_{t_n}^p \tau_n}}.$$ 

The Berry-Essén theorem, see [8], implies that $\Delta W_{t_n}$ approaches a $N(0, \tau_n)$ distributed variable as the number of particles grow. Neglecting the (relatively decreasing) stochastic term the tau-leap method can thus be approximated by the mean field equation

$$\bar{X}_t' = -\bar{X}_t^p, \quad t \in (0, T], \quad p = 1, 2, 3,$$

$$\bar{X}_0 = \gamma.$$ 

with scaled solutions

$$\bar{Z}_t = e^{-t}, \quad \bar{Z}_t = \frac{1}{\gamma t + 1}, \quad \bar{Z}_t = \frac{1}{\sqrt{2\gamma^2 t + 1}},$$

for $p = 1, 2, 3$, respectively. Since $g(\bar{Z}_T)$ is essentially independent of $\gamma$ for $p = 1$, the work is also expected to be independent of $\gamma$, as indicated in (4.22). For $p = 2, 3$ the relative solution $\bar{Z}_T$ decays as $\gamma^{-1}$ and most of the decay happen in $\gamma^{-p}$ time, so for the interval $t \in (\gamma^{-p}, T)$ less work is required and using the time-step $\tau = h\gamma^{2-2p}$ in the interval $t \in (0, \gamma^{-p})$ implies that the estimate (4.22) gains at least one order of $p$.

Remark 4.14. In [2], the authors consider the case of constant density, by assuming that

$$c_j = C\gamma^{1-|\nu_j|}, \quad |\nu_j| := \sum_{i=1}^d |\nu_{ji}|,$$
in (2.3). This implies that the propensity can be written as
\[ \tilde{a}_j(z) = a_j(\gamma x) = \gamma A(x), \]
for some uniformly bounded function \( A \), and the ‘effective’ propensity is thus linear in terms of \( \gamma \). Using this assumption, the authors of [2] show that choosing \( \tau = \gamma^{-\beta} \), for some \( \beta \in (0,1) \), gives a relative error of the same order. Using the same constant density assumption would, with our analysis, lead to a step size \( \tau = h \), for some \( h > 0 \), and a relative error of the same order, which has the additional advantage that the step size is independent of \( \gamma \) and the unknown constant \( \beta \).

### 4.3. Dual approximation.
In Theorem 4.4 we showed an a priori estimate for the relative global error. For an a posteriori error estimate we have the following result:

**Theorem 4.15 (A posteriori error).** Assume that Lemma 4.5 and the growth condition in Corollary 4.12 hold. Given \( M_\omega \) sample paths \( \{X_{t_n}(\omega_i)\}_{i=1}^{M_\omega} \) from the Poisson bridge tau-leap method, with deterministic time steps \( t_n \), the relative error can be approximated by

\[
E[g(Z_T) - g(\bar{Z}_T)] = \frac{1}{M_\omega} \sum_{i=1}^{M_\omega} I(\omega_i) + O(\gamma^{-1/2} \tau_{\max}) + \varepsilon_d + \varepsilon_\omega,
\]

where
\[
I := \sum_{n=0}^{N-1} \frac{\tau_n}{2} \tilde{\varphi}_{t_n+1} \cdot \left( \sum_{j=1}^{M} \left( \tilde{a}_j(Z_{t_n+1}) - \bar{a}_j(Z_{t_n}) \right) \tilde{\nu}_j \right).
\]

Here, the time steps are \( \tau_n := t_{n+1} - t_n \) and the dual weight \( \tilde{\varphi}_{t_n} \in \mathbb{R}^d \) is defined by the backward problem
\[
\tilde{\varphi}_{t_n} = \hat{J}_n \tilde{\varphi}_{t_{n+1}}, \quad t_n = 0, \ldots, N - 1,
\]
\[
\tilde{\varphi}_T = g'(Z_T),
\]
with \( \hat{J}_n \in \mathbb{R}^{d \times d} \) defined by

\[
\hat{J}_n := \text{Id} + \sum_{j=1}^{M} \tilde{\nu}_j \cdot \nabla \bar{a}_j(Z_{t_n}) \left( \tau_n + \frac{1}{2\sqrt{\bar{a}_j(Z_{t_n})}} \Delta \bar{W}_{t_n}^j \right) 1_{\hat{a}(Z_{t_n}) > 0},
\]

where
\[
\Delta \bar{W}_{t_n}^j := \frac{\Delta Y_{t_n}^j / \bar{a}_j(Z_{t_n})}{\sqrt{\bar{a}_j(Z_{t_n})}},
\]
are approximate Wiener increments, defined for \( \hat{a}(Z_{t_n}) > 0 \). The process \( \bar{Z}_{t_n} \) has increments \( \Delta Y_{t_n}^j \), as described by (3.6) in Section 3.1.

Finally, \( \varepsilon_\omega \) is the standard Monte Carlo error with \( \text{Var}[\varepsilon_\omega] = M_\omega^{-1} \text{Var}[I] \), and \( \varepsilon_d \) is a remainder of diffusion type
\[
\varepsilon_d = \sum_{n=0}^{N-1} \frac{\tau_n}{2} \left( \partial_z \tilde{u}(Z_{t_{n+1}}, t_{n+1}) - E[\tilde{\varphi}_{t_{n+1}} \mid \mathcal{F}_{t_{n+1}}] \right) \cdot \sum_{j=1}^{M} \left( \tilde{a}_j(Z_{t_{n+1}}) - \bar{a}_j(Z_{t_n}) \right) \tilde{\nu}_j,
\]
where the \( \sigma \)-algebra \( \mathcal{F}_t \) is generated by the history of \( \bar{Z}_t \) up to time \( t \).
Proof. The proof of the above theorem comes from applying the Trapezoidal rule to the error representation formula in Lemma 4.1, Taylor expanding \( \tilde{u} \) as in the first part of the proof of Theorem 4.4, and using Corollary 4.12. For given time steps \( \tau_n \) this gives

\[
E[g(Z_T) - g(\bar{Z}_T)] = \sum_{j=1}^{M} \sum_{n=0}^{N-1} \int_{t_n}^{t_{n+1}} E\left[\left(\hat{a}_j(\bar{Z}_s) - \bar{a}_j(\bar{Z}_t)\right)\left(\hat{\bar{u}}(\bar{Z}_s + \tilde{\nu}_j, s) - \bar{\hat{u}}(\bar{Z}_s, s)\right)\right] ds
\]

\[
= \sum_{j=1}^{M} \sum_{n=0}^{N-1} \sum_{m=0}^{\tau_n} \tau_m E\left[\left(\hat{a}_j(\bar{Z}_{t_{n+1}}) - \bar{a}_j(\bar{Z}_t)\right)\partial_z \hat{\bar{u}}(\bar{Z}_{t_{n+1}}, t_{n+1}) \cdot \tilde{\nu}_j\right] + O\left(\left(\gamma^{-1}r_n^3\right) + \varepsilon_d\right)
\]

(4.28)

Remark 4.16. Note that (4.26) is the approximation of the first variation \( \partial X_{n+1}/\partial X_n \) for the chemical Langevin equation,

\[
(4.29)\quad X_{t_{n+1}} = X_{t_n} + \sum_{j=1}^{M} \nu_j \left(\tau_n a_j(X_{t_n}) + \Delta W^j_{t_n}\sqrt{a_j(X_{t_n})}\right),
\]

where \( \Delta W^j_{t_n} \sim N(0, \tau_n) \) are standard Wiener increments, and \( \hat{\varphi}_{t_n} \) is thus an approximation to the discrete dual for the corresponding value function. This means that the \( \varepsilon_d \) term contains errors from both approximating the value function and the dual for the Langevin equation.

5. Examples

The goal is here to numerically verify the error representation in Lemma 4.1 and the a posteriori error estimate in Theorem 4.15. This is a fundamental step for future work developing an appropriate adaptive algorithm for the Poisson bridge tau-leap method in the spirit of [20].

5.1. Testing the estimates. To test the error representation in Lemma 4.1 we use the approximation

\[
E[g(X_T) - g(\bar{X}_T)] = \sum_{n=0}^{N-1} \sum_{j=1}^{M} E[I_{j,n}] + O\left(\left(\tau_n^2\right) + O\left(\tau_{max}^2\right)\right),
\]
where
\begin{equation}
I_{j,n} = \frac{\tau_n}{2} \left( a_j(\bar{X}_{t_{n+1}}) - a_j(\bar{X}_{t_n}) \right) \times \left( u(\bar{X}_{t_{n+1}} + \nu_j, t_{n+1}) - u(\bar{X}_{t_{n+1}}, t_{n+1}) \right),
\end{equation}
and show that both lhs and rhs decay as $O(\tau_{\text{max}})$ asymptotically, and that the efficiency index $\frac{\text{lhs}}{\text{rhs}}$ approaches 1.

To estimate the true value function $u$, we solve the Kolmogorov backward equation (2.1), which by Assumption 2.1 will become a $\prod_{i=1}^{d}(X_{\text{max}}^{(i)} + 1)$ dimensional (stiff) system of ordinary differential equations, since the number of particles in the chemical system will either be constant or decrease over time, e.g. $X^{(i)}_t \in \{0, 1, \ldots, X_{\text{max}}^{(i)}\}$ for some upper bound $X_{\text{max}} \in \mathbb{R}^d$.

For large values of $X_{\text{max}}$ the discretization is chosen such that the system is solved for a subset of logarithmically distributed integers in $[0, X_{\text{max}}^{(i)}]$, see Figure 5.1. Of course, this distribution is in no sense optimal and ideally a spatially adaptive algorithm should be used, but it can be expected that points close to any $X^{(i)} = 0$ will have a greater contribution to the error.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{logarithmic_grid.png}
\caption{Example of logarithmic grid used for solving the backward Kolmogorov equation in $\mathbb{Z}^2_+$.}
\end{figure}

Calculating lhs with sufficient accuracy can be very demanding for problems with many species and a high number of particles. A less demanding way is to use the approximation
\[ lhs = E[g(X_T) - g(\bar{X}_T)] + E[g(\bar{X}_T) - g(\bar{X}_T)] \]
\[ = 2E[g(\bar{X}_T) - g(\bar{X}_T)] + O(\tau_{\text{max}}^{2}) \]
where the process $\bar{X}_t$ is generated by using half the step size of $X_t$ and the sample path $(\lambda, Y)$ generated by $X_t$. The estimate $lhs_{\text{approx}}$ does not use the value function
at all, and has the sample variance of order $\tau M^{-1}$ compared to $M^{-1}$ for lhs, see [17].

In practice, the estimate rhs in itself is not much of use since it requires knowledge of the value function $u$, and thus rhs must be approximated by computable quantities, e.g. as in Theorem 4.15. For this purpose, let

$$rhs_{dual} := E\left[\sum_{n=0}^{N-1} \sum_{j=1}^{M} \frac{\tau_n}{2} (a_j (\bar{X}_{n+1}) - a_j (\bar{X}_n)) \varphi_n \cdot \nu_j\right],$$

where the approximate discrete dual is given as in Theorem 4.15 but without the scaling factor $\gamma$. The accuracy of $rhs_{dual}$ is of great importance to construct a proper adaptive algorithm, see e.g. [20, 21, 25]. To show this we use the error density

$$\rho_{j,n} := \left| \frac{1}{2\tau_n} E[(a_j (X_{n+1}) - a_j (X_n)) \varphi_n \cdot \nu_j] \right|,$$

defined for the initial deterministic time steps, i.e. not the time steps given by the Poisson bridge tau-leap method in Section 3.1, see [22]. This gives the total error

$$\varepsilon := rhs_{dual} = \sum_{n=0}^{N-1} \sum_{j=1}^{M} \tau_n^2 \rho_{j,n},$$

and the current work $Work_{TL} := N$ is then compared with the estimated work to achieve the same error $\varepsilon$ for an optimal adaptive mesh

$$Work_u = T \sum_{n=0}^{N-1} \rho_n \tau_n.$$  

5.2. Reactive decay. In this example we have an irreversible reaction where molecules of a single species spontaneously disappear, possibly into another particle type. The chemical reaction for reactive decay (or isomerization) can be written as

$$X \rightarrow \emptyset$$

and is here described by the linear propensity function

$$a(x) = cx,$$

initial value $X(0) = X_0 \in \mathbb{Z}_+$, and stoichiometric number $\nu = -1$. We test four different cases: a high number of particles or a low number of particles, that becomes negative often or not so often, see Table 5.1. In Figure 5.2 a few realizations of $X_t$ for $t \in [0, 1]$ are shown for each example.

| Example | 1 | 2 | 3 | 4 |
|---------|---|---|---|---|
| $X_0$   | 10 | 10^6 | 10 | 10^6 |
| $c$     | 0.2 | 1.0 | 2.0 | 7.0 |

Table 5.1. Reactive decay, cf. (5.5) and (5.6).
As quantities of interest we take the first moments of $X$, i.e. $g(x) = x^{mom}$ for $mom = 1, 2, 3$ and with final time $T = 1$. In Figure 5.3, 5.4 and 5.5 the convergence of $\text{lhs}_{\text{approx}}$, $\text{rhs}$ and $\text{rhs}_{\text{dual}}$ can be seen for the different moments. In all cases we see a linear $O(\tau)$ convergence and in Figure 5.6, 5.7 and 5.8, we see that the corresponding efficiency indices stay close to 1, i.e. the computable error approximation in Theorem 4.15 agrees well with the error representation formula in Lemma 4.1. Comparing the current work $W$ with the work estimates for an adaptive mesh in (5.3), and a completely uniform mesh in (5.4), shows that for these relatively non-stiff examples adaptivity will not make any improvement, see Table 5.2. In this case, a uniform mesh is thus most suitable, and the examples are only run for verification purposes. Also note that the error in Example 2 and 4, i.e. for a high number of particles, is almost completely governed by the deterministic error and require few realizations to achieve a low statistical error of the estimates $\text{lhs}$, $\text{rhs}$ and $\text{rhs}_{\text{dual}}$.

Figure 5.2. A few realizations of reactive decay for Example 1 to 4. These examples are mostly suited for uniform meshes and adaptivity will thus not make any improvement.
Figure 5.3. Reactive decay: Convergence of the errors \( \text{lhs}_{\text{approx}} \), \( \text{rhs} \) and \( \text{rhs}_{\text{dual}} \) with respect to the maximum time step. Here, \( g(x) = x \) and the data is scaled by dividing with \( u(x_0, 0) \). For each data point the number of samples is controlled by the standard error such that \( 1.96 \times SE \leq 0.1 \mu \), where \( \mu \) is the sample mean and \( SE \) the standard error of the mean. Bars indicate the 95% confidence intervals.

| Example | 1 | 2 | 3 | 4 |
|---------|---|---|---|---|
| Number of realizations | \( 7.5 \times 10^4 \) | \( 4.0 \times 10^4 \) | \( 1.3 \times 10^5 \) | \( 3.6 \times 10^5 \) |
| Current work | 17 | 4097 | 513 | 11265 |
| Optimal work | 16 | 4096 | 512 | 10866 |
| Uniform work | 16 | 4096 | 512 | 10868 |
| Optimal work using dual | 16 | 4096 | 512 | 10867 |
| Uniform work using dual | 16 | 4096 | 512 | 10869 |

Table 5.2. Current and estimated work for first moment. Values corresponding to smallest \( \tau \) in Figure 5.3. Two error densities are here used: one using the dual as in (5.2) and one using the derivative of the true value function.
Figure 5.4. Reactive decay: convergence for second moment of $X$.

5.3. **Unstable dimer.** This stiff model was used in e.g. [1, 13] and has four reactions and three species. The reactions are

$$X_1 \rightarrow 0, \quad X_2 \rightarrow 2X_1,$$

$$2X_1 \rightarrow X_2, \quad X_2 \rightarrow X_3,$$

represented by the stoichiometric matrix and propensity function

$$\nu = \begin{pmatrix} -1 & -2 & 2 & 0 \\ 0 & 1 & -1 & -1 \\ 0 & 0 & 0 & 1 \end{pmatrix} \quad \text{and} \quad a(X) = \begin{pmatrix} X_1 \\ 0.001X_1(X_1 - 1) \\ 0.5X_2 \\ 0.04X_2 \end{pmatrix},$$

respectively. In Figure 5.9, where a few realizations of the path $X_t := (X_1, X_2, X_3)(t)$ are shown (in a log-lin scale), it can be noted that there is a large difference in time-scales; during a very short time most of the $X_1$-molecules will turn into $X_2$-molecules. This difference in time scales has several consequences: the step size during the transient phase may have a big effect on the error, and the tau-leap method will cause negative populations unless the step size is adjusted accordingly.

We here let $g(x) = x_1 + x_2 + x_3$, and the convergence of the corresponding error and efficiency index can be seen in Figure 5.10. As in the previous example we see
that the error decreases linearly with $\tau$, as expected, with error estimates being close to each other.

From Figure 5.11 we see that the error density here play a big role, and that the optimal time stepping is to choose very small time steps during the transient phase. To see if choosing a pre-leap check as in [12] will give a similar result we apply the leap-size condition (3.3) with $\epsilon = 0.05$, which turns out to give almost the same error density and proposed time steps. In Table 5.3 a comparison between the current and estimated work shows potential for great improvement using adaptive time stepping.

| Leap-check        | No  | Yes |
|-------------------|-----|-----|
| Current work      | 2628| 2637|
| Optimal work      | 573 | 575 |
| Uniform work      | 40480| 40501|
| Optimal work using dual | 529  | 531 |
| Uniform work using dual | 42362 | 42313 |

Table 5.3. Unstable dimer: Current and estimated work for 880 realizations. Values corresponding to smallest $\tau$ in Figure 5.10.
We have in this work shown a weak global error representation for the tau-leap method that can be accurately approximated by a computable leading order term using a discrete dual weighted propensity residual, see Lemma 4.1 and Theorem 4.15. This type of \emph{a posteriori} error estimates, using discrete dual functions, are the first for the tau-leap method and are important tools for the ongoing work on developing efficient adaptive time stepping algorithms, see \emph{e.g.} [22, 21]. Also, we have here shown an \emph{a priori} estimate on the relative error of the tau-leap method, that is of order $\tau$ independently of the number of particles in the system, see Theorem 4.4.

Our results are based on an error representation using the value function for the corresponding Kolmogorov backward equation, which for jump processes is defined on a discrete lattice. Using extensions from lattices onto real values and stochastic representations, we develop weighted estimators for the value function and its derivatives, see Lemma 4.5 and Lemma 4.11 respectively. The weighted estimators developed here give \emph{polynomial} bounds on the value function and its derivatives.
derivatives and improve similar $L$-infinity bounds in [16] that are exponential in the propensity function.

References

[1] David F. Anderson. Incorporating postleap checks in tau-leaping. *Journal of Chemical Physics*, 128(5), Feb 7 2008.
[2] David F. Anderson, Arnab Ganguly, and Thomas G. Kurtz. Error analysis of tau-leap simulation methods. arXiv: math.PR/0909.4790, September 2009.
[3] R.E. Barnhill. Coons’ Patches. *Computers in Industry*, 3(1-2):37–43, 1982.
[4] Y Cao, LR Petzold, M Rathinam, and DT Gillespie. The numerical stability of leaping methods for stochastic simulation of chemically reacting systems. *Journal of Chemical Physics*, 121(24):12169–12178, DEC 22 2004.
[5] Yang. Cao, Daniel T. Gillespie, and Linda R. Petzold. Avoiding negative populations in explicit Poisson tau-leaping. *Journal of Chemical Physics*, 123(5), Aug 1 2005.
[6] Yang Cao, Daniel T. Gillespie, and Linda R. Petzold. Efficient step size selection for the tau-leaping simulation method. *The Journal of Chemical Physics*, 124(4):044109, 2006.
[7] Abhijit Chatterjee, Dionisios G. Vlachos, and Markos A. Katsoulakis. Binomial distribution based tau-leap accelerated stochastic simulation. *The Journal of Chemical Physics*, 122(2):024112, 2005.
Figure 5.8. Reactive decay: Efficiency index for third moment of $X$.

Figure 5.9. Realizations for unstable dimer shown in different axis scales.

[8] Richard Durrett. *Probability: theory and examples*. Duxbury advanced series Probability: Theory & Examples. Duxbury Press, Belmont, CA, second edition, 1996.

[9] D. T. Gillespie. A rigorous derivation of the chemical master equation. *Physica A Statistical Mechanics and its Applications*, 188:404–425, September 1992.
Figure 5.10. Unstable dimer: Convergence and efficiency index.

Figure 5.11. Unstable dimer: Error densities and step sizes.

[10] D. T. Gillespie. Approximate accelerated stochastic simulation of chemically reacting systems. *Journal of Chemical Physics*, 115:1716–1733, July 2001.
[11] Daniel T. Gillespie. A general method for numerically simulating the stochastic time evolution of coupled chemical reactions. *Journal of Computational Physics*, 22:403–434, 1976.
[12] Daniel T. Gillespie and Linda R. Petzold. Improved leap-size selection for accelerated stochastic simulation. *The Journal of Chemical Physics*, 119(16):8229–8234, 2003.
[13] Daniel T. Gillespie and Linda R. Petzold. Improved leap-size selection for accelerated stochastic simulation. *Journal of Chemical Physics*, 119(16):8229–8234, 2003.
[14] WJ Gordon. Blending-Function Methods of Bivariate and Multivariate Interpolation and Approximation. *SIAM journal on numerical analysis*, 8(1):158–177, 1971.
[15] Jesper Karlsson, Markos Katsoulakis, Anders Szepessy, and Raul Tempone. Automatic Weak Global Error Control for the Tau-Leap Method. Working paper.
[16] Markos A. Katsoulakis, Petr Plecháč, and Alexandros Sopasakis. Error analysis of coarse-graining for stochastic lattice dynamics. *SIAM J. Numer. Anal.*, 44(6):2270–2296 (electronic), 2006.
[17] Tiejun Li. Analysis of explicit tau-leaping schemes for simulating chemically reacting systems. *Multiscale Model. Simul.*, 6(2):417–436 (electronic), 2007.
Kyoung-Sook Moon, Anders Szepessy, Raúl Tempone, and Georgios E. Zouraris. Convergence rates for adaptive approximation of ordinary differential equations. Numer. Math., 96(1):99–129, 2003.

Kyoung-Sook Moon, Anders Szepessy, Raúl Tempone, and Georgios E. Zouraris. A variational principle for adaptive approximation of ordinary differential equations. Numer. Math., 96(1):131–152, 2003.

Kyoung-Sook Moon, Anders Szepessy, Raúl Tempone, and Georgios E. Zouraris. Convergence rates for adaptive weak approximation of stochastic differential equations. Stoch. Anal. Appl., 23(3):511–558, 2005.

Kyoung-Sook Moon, Erik von Schwerin, Anders Szepessy, and Raúl Tempone. An adaptive algorithm for ordinary, stochastic and partial differential equations. In Recent advances in adaptive computation, volume 383 of Contemp. Math., pages 325–343. Amer. Math. Soc., Providence, RI, 2005.

E. Mordecki, A. Szepessy, R. Tempone, and G. E. Zouraris. Adaptive weak approximation of diffusions with jumps. SIAM J. Numer. Anal., 46(4):1732–1768, 2008.

Muruhan Rathinam, Linda R. Petzold, Yang Cao, and Daniel T. Gillespie. Stiffness in stochastic chemically reacting systems: The implicit tau-leaping method. The Journal of Chemical Physics, 119(24):12784–12794, 2003.

Muruhan Rathinam, Linda R. Petzold, Yang Cao, and Daniel T. Gillespie. Consistency and stability of tau-leaping schemes for chemical reaction systems. Multiscale Model. Simul., 4(3):867–895 (electronic), 2005.

Anders Szepessy, Raúl Tempone, and Georgios E. Zouraris. Adaptive weak approximation of stochastic differential equations. Comm. Pure Appl. Math., 54(10):1169–1214, 2001.

Tianhai Tian and Kevin Burrage. Binomial leap methods for simulating stochastic chemical kinetics. The Journal of Chemical Physics, 121(21):10356–10364, 2004.

A.J. Worsey. C2 interpolation over hypercubes. Computer Aided Geometric Design, 2(1-3):107–115, 1985.

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