Solving the chemical master equation for monomolecular reaction systems analytically: a Doi-Peliti path integral view

John J. Vastola
Department of Physics and Astronomy, Vanderbilt University, Nashville, Tennessee

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Abstract

The chemical master equation (CME) is a fundamental description of interacting molecules commonly used to model chemical kinetics and noisy gene regulatory networks. Exact time-dependent solutions of the CME—which typically consists of infinitely many coupled differential equations—are rare, and are valuable for numerical benchmarking and getting intuition for the behavior of more complicated systems. Jahnke and Huisinga’s landmark calculation of the exact time-dependent solution of the CME for monomolecular reaction systems is one of the most general analytic results known; however, it is hard to generalize, because it relies crucially on properties of monomolecular reactions. In this paper, we rederive Jahnke and Huisinga’s result on the time-dependent probability distribution and moments of monomolecular reaction systems using the Doi-Peliti path integral approach, which reduces solving the CME to evaluating many integrals. While the Doi-Peliti approach is less intuitive, it is also more mechanical, and hence easier to generalize. To illustrate how the Doi-Peliti approach can go beyond the method of Jahnke and Huisinga, we also find the exact time-dependent solution to a problem involving an autocatalytic reaction that Jahnke and Huisinga identified as not solvable using their method.
1 Introduction

The chemical master equation (CME) provides a fundamental description of well-mixed molecules interacting with each other via a set of chemical reactions \[1, 2, 3, 4, 5, 6, 7\]. It models dynamics that are discrete (the state of the system is a set of nonnegative integers) and stochastic (chemical reactions occur with some probability). The CME has recently enjoyed tremendous success as a framework for understanding noisy single cell data \[8, 9, 10, 11, 12, 13, 14\], particularly in simple model organisms like yeast where techniques like single-molecule Fluorescence in situ Hybridization (smFISH) allow RNA molecule numbers to be counted accurately \[15, 16, 17\]. Outside of cell and molecular biology, master equations have been successfully used to model population dynamics \[18, 19, 20\], traffic \[21, 22, 23\], and gas phase chemical kinetics \[24, 25, 26\], among other things.

Although it is very useful for defining discrete stochastic models, the CME generally cannot be solved directly. One typically resorts to an approximate approach, like using Gillespie’s algorithm \[27, 28\] to extract information from many brute force simulations, or using finite state projection \[29, 30, 10\], or partitioning the system (e.g. low versus high copy number, slow versus fast time scale) \[31, 32, 33, 34, 35, 36\], or solving a continuous approximation to the CME like the chemical Langevin equation \[3, 37, 38, 39\].

Unsurprisingly, exact time-dependent solutions (as opposed to steady state solutions) of the CME are particularly rare, and have only been computed for specific cases. McQuarrie \[1\] describes some of the early attempts: in 1940, Max Delbrück evaluated the CME for the autocatalytic reaction \[S \rightarrow S + S\] \[40\]; in 1954, Renyi solved the binding reaction \[A + B \rightarrow C\] \[41\]; in 1960, Ishida solved the death reaction \[S \rightarrow \emptyset\] and presented the first CME solution with time-dependent rates \[42\]; in 1963 and 1964, McQuarrie et al. solved many simple systems (including \[A + A \rightarrow B\] and \[A + B \rightarrow C\]) using the method of generating functions \[43, 44\].

The situation did not change appreciably until Jahnke and Huisinga’s landmark paper \[45\], more than forty years later. Their 2007 paper constituted a major advance in our collective understanding of the CME; they were able to solve the CME for a system with an arbitrary number of species experiencing an arbitrary number of reactions whose rates have arbitrary time-dependence, provided that the reactions consisted of some combination of birth (\[\emptyset \rightarrow S_k\]), death (\[S_j \rightarrow \emptyset\]), and conversion (\[S_j \rightarrow S_k\]). The shocking generality of their result, as well as the explicitness of the solution they wrote down (in Theorem 1 of that paper), was powerful.

Since 2007, there have been few new results of the same generality. Reis et al. \[46\] extend Jahnke and Huisinga’s result by considering hierarchical first-order reaction networks (which allow a certain subset of first-order reactions that is strictly larger than the set of monomolecular reactions). However, there is not (for example) any result on the solution to general first-order reactions, or general bimolecular reactions. At present, even finding the exact solutions of simple systems that involve bimolecular reactions is nontrivial: the work of Laurenzi (\[A + B \leftrightarrow C\]) \[47\], as well as Arslan and Laurenzi (\[A + B \leftrightarrow A + A\]) \[48\] are two examples.

One drawback of Jahnke and Huisinga’s paper is that it essentially relied on guessing the
solution. It was well-known that Poisson and multinomial distributions solved the CME in special cases, and that these distributions had certain desirable properties (e.g. a Poisson distribution stays a Poisson distribution, and a multinomial distribution stays a multinomial distribution; see Sec. 3 of their paper). To derive their Theorem 1, these properties were exploited, along with the fact that only monomolecular reactions were considered. Of course, their method completely breaks down for a system that is only slightly more complicated; as they point out in Sec. 6, adding an autocatalytic reaction $S \to S + S$ to a system they can easily solve manages to make it beyond the scope of their results.

Hence, it would be nice if there was a method to obtain their classic result that did not rely on systematic guessing. In this paper, we offer the Doi-Peliti path integral approach to solving the CME as one such method. The Doi-Peliti approach allows one to ‘turn the crank’, so to speak, and generate a time-dependent solution of the CME through a straightforward but difficult calculation. Importantly, it is system-agnostic: one does not need to know properties like ‘Poisson distributions stay Poisson’, or assume the solution takes a certain form.

Doi-Peliti field theory—which emerged from the pioneering papers of researchers like Doi [49, 50], Peliti [51, 52, 53], and Grassberger [54, 55, 56, 57]—reframes solving the CME as a field theory problem. This enables the use of powerful approximation schemes, like the renormalization group and diagrammatic perturbation theory [58, 59, 60, 61, 62, 63, 64, 65]. While Doi-Peliti field theory is still somewhat obscure in mathematical biology, it has seen the occasional application: e.g. to understand population dynamics given colored noise [66], age dependent branching processes [67, 68], and large deviations in gene regulatory networks [69, 20]. Although not Doi-Peliti, a qualitatively similar path integral has been used to solve the CME for a multistep transcription and translation process [70].

We will use Doi-Peliti field theory to rederive Jahnke and Huisinga’s Theorem 1. Moreover, in order to show that the Doi-Peliti path integral approach is strictly more powerful than the one used by Jahnke and Huisinga, we use it to exactly solve a problem they said their method could not. We solve this additional problem in complete generality, and obtain the exact time-dependent solution assuming rates with arbitrary time-dependence.

The paper is organized as follows. In Sec. 2 we review the monomolecular CME and state Jahnke and Huisinga’s solution of it. In Sec. 3 we define the generating function and show how the problem of solving the CME can be reframed as a problem in a certain Hilbert space. In Sec. 4 we describe the basic machinery of Doi-Peliti field theory, including coherent states, inner products, and how the transition probability and other information can be extracted from the generating function. In Sec. 5 we construct the Doi-Peliti path integral. In Sec. 6 we solve the Doi-Peliti path integral. In Sec. 7 we convert the path integral solution into a solution of the CME. In Sec. 8 we show how to convert the path integral solution directly into the time-dependent moments of the CME. In Sec. 9 we completely solve a problem Jahnke and Huisinga could not solve to demonstrate the flexibility of the Doi-Peliti approach. Finally, in Sec. 10 we discuss the merits and drawbacks of the Doi-Peliti approach to solving the CME, and speculate on how it could be further utilized.
2 Problem statement

We will consider a system with \( n \) species \( S_1, ..., S_n \), whose reaction list reads

\[
\begin{align*}
S_j \xrightarrow{c_{jk}} S_k & \quad j \neq k \\
\emptyset \xrightarrow{c_{0k}} S_k & \quad k = 1, ..., n \\
S_j \xrightarrow{c_{j0}} \emptyset & \quad j = 1, ..., n
\end{align*}
\]

(1)

i.e. all possible monomolecular reactions (birth, death, and conversion) are allowed. Note that the rates are allowed to have arbitrary time-dependence as long as \( c_{jk}(t) \geq 0 \) for all \( j, k \) and all times \( t \). The corresponding CME reads

\[
\frac{\partial P(x,t)}{\partial t} = \sum_{k=1}^{n} c_{0k}(t) [P(x - \epsilon_k, t) - P(x, t)]
\]

\[
+ \sum_{k=1}^{n} c_{k0}(t) [(x_k + 1)P(x + \epsilon_k, t) - x_kP(x, t)]
\]

\[
+ \sum_{j=1}^{n} \sum_{k=1}^{n} c_{jk}(t) [(x_j + 1)P(x + \epsilon_j - \epsilon_k, t) - x_jP(x, t)]
\]

(2)

where \( P(x, t) \) is the probability that the state of the system is \( x := (x_1, ..., x_n) \in \mathbb{N}^n \) at time \( t \geq t_0 \), and where \( \epsilon_k \) is the \( n \)-dimensional vector with a 1 in the \( k \)th place and zeros everywhere else.

The exact solution to Eq. 2 given the initial condition \( P(x, t_0) = \delta(x - \xi) \) for some vector \( \xi := (\xi_1, ..., \xi_n) \in \mathbb{N}^n \), is reported in Theorem 1 of Jahnke and Huisinga [45]. In order to state their solution, we will need some notation.

Define the matrix \( A(t) \) and vector \( b(t) \) by

\[
A_{jk}(t) := c_{kj}(t) \quad \text{for} \quad j \neq k \geq 1
\]

\[
A_{kk}(t) := -\sum_{j=0}^{n} c_{kj}(t) \quad \text{for} \quad 1 \leq k \leq n
\]

\[
b(t) := \begin{pmatrix} c_{01}(t) & c_{02}(t) & \cdots & c_{0n}(t) \end{pmatrix}^T.
\]

(3)

The deterministic reaction rate equations corresponding to our reaction list can be written in terms of \( A(t) \) and \( b(t) \) as

\[
\dot{x} = A(t)x + b(t).
\]

(4)

Because Eq. 4 is linear, the solution with initial condition \( \xi = (\xi_1, ..., \xi_n) \) can be written as

\[
x(t) = \sum_{k=1}^{n} \xi_k w^{(k)}(t) + \lambda(t)
\]

(5)
where the vectors $w^{(1)}(t), ..., w^{(n)}(t)$ and $\lambda(t)$ are defined as
\[\dot{w}^{(k)} = A(t)w^{(k)} , \quad w^{(k)}(t_0) = \epsilon_k \]
\[\lambda = A(t)\lambda + b(t) , \quad \lambda(t_0) = 0 .\]  
(6)

As we will shortly observe, the solution to the deterministic reaction rate equations is intimately related to the solution of the CME (at least for monomolecular reactions). Now define the 1-norm of a vector $x$ as
\[|x| := \sum_{k=1}^{n} |x_k| ,\]  
(7)
the product Poisson distribution as
\[p(x, \lambda) := \frac{\lambda_{x_1}^{x_1} \cdots \lambda_{x_n}^{x_n}}{x_1! \cdots x_n!} e^{-|\lambda|} = \frac{\lambda^x}{x!} e^{-|\lambda|} ,\]  
(8)
the multinomial distribution as
\[m(x, N, w) := \frac{N!}{(N-|w|)!} \frac{w_{x_1}^{x_1} \cdots w_{x_n}^{x_n}}{x_1! \cdots x_n!} e^{-|w|} \text{ if } |x| \leq N \text{ and } x \in \mathbb{N}^n \]
\[= \frac{N!}{(N-|x|)!} \frac{w^x}{x!} \text{ if } |x| \leq N \text{ and } x \in \mathbb{N}^n ,\]  
(9)
and the convolution of two probability distributions as
\[p_1(x) * p_2(x) := \sum_z p_1(z)p_2(x-z) = \sum_z p_1(x-z)p_2(z)\]  
(10)
where the sum is over all $z \in \mathbb{N}^n$ such that $x - z \in \mathbb{N}^n$. We can now state the solution to Eq. 2 with initial condition $P(x, t_0) = \delta(x - \xi)$; it is the $(n+1)$-fold convolution
\[P(x, t; \xi, t_0) = p(x, \lambda(t)) * m(x, \xi_1, w^{(1)}(t)) * \cdots * m(x, \xi_n, w^{(n)}(t))\]  
(11)
where $P(x, t; \xi, t_0)$ denotes the probability that the system transitions from state $\xi$ to state $x$ in time $T := t - t_0$. It is this result that we will derive using the Doi-Peliti path integral formalism.

3 Reframing the problem in Hilbert space

In order to apply the Doi-Peliti technique, we first need to rewrite Eq. 2 in terms of states and operators in a certain Hilbert space. Consider an infinite-dimensional Hilbert space spanned by the $|x\rangle$ states (where $x = (x_1, ..., x_n) \in \mathbb{N}^n$) in which an arbitrary state $|\phi\rangle$ is written
\[|\phi\rangle = \sum_{x_1=0}^{\infty} \cdots \sum_{x_n=0}^{\infty} c(x) |x\rangle\]  
(12)
for some generally complex-valued coefficients $c(x)$. To ease notation, we will write

$$
\sum_x := \sum_{x_1=0}^{\infty} \cdots \sum_{x_n=0}^{\infty}.
$$

(13)

The state we are principally interested in is the generating function

$$
|\psi(t)\rangle := \sum_x P(x, t) |x\rangle
$$

(14)

which, by construction, contains exactly the same information that the probability distribution $P(x, t)$ does. Define the annihilation and creation operators $\hat{a}_j$ and $\hat{\pi}_j$ for all $j = 1, \ldots, n$ by

$$
\hat{a}_j |x\rangle = x_j |x - \epsilon_j\rangle \\
\hat{\pi}_j |x\rangle = |x + \epsilon_j\rangle
$$

(15)

where we remind the reader that $\epsilon_j$ is the $n$-dimensional vector with a 1 in the $j$th place and zeros everywhere else. It is easy to show that these operators satisfy the commutation relations

$$
[\hat{a}_j, \hat{\pi}_k] = \delta_{jk}, \quad [\hat{a}_j, \hat{a}_k] = [\hat{\pi}_j, \hat{\pi}_k] = 0
$$

(16)

which are precisely the same as the commutation relations satisfied by the creation and annihilation operators familiar from quantum mechanics and quantum field theory [71, 72].

We would like an equation equivalent to the CME (Eq. 2) that is satisfied by the generating function $|\psi(t)\rangle$ (Eq. 14). To obtain such an equation, take the time derivative of $|\psi(t)\rangle$:

$$
\frac{\partial |\psi\rangle}{\partial t} = \sum_x \left\{ \sum_{k=1}^{n} c_{0k}(t) [P(x - \epsilon_k, t) - P(x, t)] \\
+ \sum_{k=1}^{n} c_{k0}(t) [(x_k + 1)P(x + \epsilon_k, t) - x_kP(x, t)] \\
+ \sum_{j=1}^{n} \sum_{k=1}^{n} c_{jk}(t) [(x_k + 1)P(x + \epsilon_j - \epsilon_k, t) - x_jP(x, t)] \right\} |x\rangle
$$

(17)

where we have used Eq. 2. Reindex the sums over $x$ so that this expression reads

$$
\frac{\partial |\psi\rangle}{\partial t} = \sum_x \left\{ \sum_{k=1}^{n} c_{0k}(t) [ |x + \epsilon_k\rangle - |x\rangle ] \\
+ \sum_{k=1}^{n} c_{k0}(t) [ x_k |x - \epsilon_k\rangle - x_k |x\rangle ] \\
+ \sum_{j=1}^{n} \sum_{k=1}^{n} c_{jk}(t) [ x_j |x - \epsilon_j + \epsilon_k\rangle - x_j |x\rangle ] \right\} P(x, t).
$$

(18)
Using the creation and annihilation operators we defined earlier, the right-hand side can be written as

$$
\sum_x \left\{ \sum_{k=1}^n c_{0k}(t) \left[ \hat{\pi}_k - 1 \right] + \sum_{k=1}^n c_{k0}(t) \left[ \hat{a}_k - \hat{\pi}_k \hat{a}_k \right] + \sum_{j=1}^n \sum_{k=1}^n c_{jk}(t) \left[ \hat{a}_j \hat{\pi}_k - \hat{\pi}_j \hat{a}_j \right] \right\} P(x, t | x). 
$$

(19)

If we define the Hamiltonian operator via

$$
\hat{H} := \sum_{k=1}^n c_{0k}(t) \left[ \hat{\pi}_k - 1 \right] - \sum_{k=1}^n c_{k0}(t) \left[ \hat{\pi}_k - 1 \right] \hat{a}_k + \sum_{j=1}^n \sum_{k=1}^n c_{jk}(t) \left[ \hat{\pi}_k - \hat{\pi}_j \right] \hat{a}_j
$$

(20)

we can write the equation of motion for \( |\psi(t)\rangle \) as

$$
\frac{\partial |\psi\rangle}{\partial t} = \hat{H} |\psi\rangle
$$

(21)

which is analogous to the equation of motion for a state in quantum mechanics. It is this equation that we will solve instead of the CME. As usual, Eq. 21 has the formal solution

$$
|\psi(t)\rangle = e^{\int_{t_0}^t \hat{H} dt} |\psi(t_0)\rangle = \hat{U}(t, t_0) |\psi(t_0)\rangle
$$

(22)

where we can define the time evolution operator \( \hat{U}(t_2, t_1) \) as

$$
\hat{U}(t_2, t_1) := e^{\int_{t_1}^{t_2} \hat{H} dt}
$$

(23)

for any two times \( t_1 \leq t_2 \). As in quantum mechanics, this operator has the composition property

$$
\hat{U}(t_2, t_1) = \hat{U}(t_2, t') \hat{U}(t', t_1)
$$

(24)

for any time \( t' \) with \( t_1 \leq t' \leq t_2 \).

4 Basic Doi-Peliti formalism

In essence, the Doi-Peliti approach to solving Eq. 21 involves using many coherent state resolutions of the identity to rewrite Eq. 22 as a coherent state path integral. Once that path integral is evaluated, quantities like moments and \( P(x, t) \) can be recovered by manipulating the path integral solution in specific ways. In order to follow this prescription, we will need to define coherent states, define inner products, and construct associated resolutions of the identity; that is our primary task in this section.

7
4.1 Coherent states

Just like in quantum mechanics, we define the coherent state as the state $|z\rangle$ that satisfies

$$\hat{a}_j |z\rangle = z_j |z\rangle$$

for all $j = 1, ..., n$, with $z = (z_1, ..., z_n) \in \mathbb{C}^n$. By imposing this constraint on an arbitrary state (Eq. 12), it is straightforward to show that the explicit form for $|z\rangle$ must be proportional to

$$|z\rangle = \sum_y z^y e^{-z \cdot 1} |y\rangle$$

where the factor $e^{-z \cdot 1}$ is a specific overall constant chosen for our later convenience, and where we again use the shorthand $x! := x_1! \cdots x_n!$ and $z^y := z_1^{y_1} \cdots z_n^{y_n}$ to ease notation. We can also write a coherent state as

$$|z\rangle = e^{z \cdot (\hat{\pi} - 1)} |0\rangle$$

where $\hat{\pi} := (\hat{\pi}_1, ..., \hat{\pi}_n)$.

4.2 Inner products

Now we will define two inner products on our Hilbert space: the exclusive product, and the Grassberger-Scheunert product. Both were introduced by Grassberger and Scheunert in a 1980 paper that clearly describes their motivation and properties [54]; we are calling their “inclusive” inner product the Grassberger-Scheunert product to recognize their contribution.

Briefly, the exclusive product is useful for computing $P(x,t)$, while the Grassberger-Scheunert product is useful for simplifying path integral calculations (specifically, we avoid having to perform a “Doi shift” [73, 74]; see Eq. 3.4 of Peliti [51] for an example of the Doi shift) and computing moments. We will use both inner products in solving Eq. 2.

Define the exclusive product of two basis states by

$$\langle x|y \rangle_{ex} := x! \delta_{xy}$$

for all basis vectors $|x\rangle$ and $|y\rangle$, so that the exclusive product of two arbitrary states reads

$$\langle \phi_2|\phi_1 \rangle_{ex} = \sum_x x! c_2^*(x) c_1(x) .$$

Using the notation $\hat{a} := (\hat{a}_1, ..., \hat{a}_n)$, define the Grassberger-Scheunert product of two basis states by

$$\langle x|y \rangle := \langle x|e^{\hat{\pi} - 1} e^{\hat{\pi} - 1} |y\rangle_{ex} = \sum_k \frac{x! y!}{(x-k)! (y-k)! k!}$$

for all basis vectors $|x\rangle$ and $|y\rangle$, where the sum on the right is over all values of $k \in \mathbb{N}^n$ with $k_j \leq \min(x_j, y_j)$ for all $j = 1, ..., n$. While it is not obvious just from looking at them,
it is straightforward to show that these two definitions are equivalent (see Grassberger and Scheunert [54] and the appendix to Peliti [51]). The Grassberger-Scheunert product of two arbitrary states reads

$$\langle \phi_2 | \phi_1 \rangle = \langle \phi_2 | e^{\hat{\pi} \cdot 1} e^{\hat{a} \cdot 1} | \phi_1 \rangle_{ex} .$$  (31)

With respect to the exclusive product, $\hat{a}_j$ and $\hat{\pi}_j$ are Hermitian conjugates of each other for all $j = 1, \ldots, n$, i.e.

$$\hat{a}_j \dagger = \hat{\pi}_j. \quad (32)$$

With respect to the Grassberger-Scheunert product, the Hermitian conjugate of $\hat{a}_j$ is

$$\hat{a}_j \dagger = \hat{\pi}_j - 1. \quad (33)$$

Let us compute some inner products that we will use later. First, the exclusive product of a basis state $|x\rangle$ with a coherent state $|z\rangle$ is

$$\langle x|z\rangle_{ex} = \sum_y e^{-z \cdot 1} \langle x|y\rangle_{ex} = \sum_y e^{-z \cdot 1} x! \delta_{xy} = z^x e^{-z \cdot 1}. \quad (34)$$

Next, the Grassberger-Scheunert product of a basis state $|x\rangle$ with a coherent state $|z\rangle$ is

$$\langle x|z\rangle_{ex} = \langle x|e^{\hat{\pi} \cdot 1} e^{\hat{a} \cdot 1} |z\rangle_{ex} = e^{(z \cdot 1)\cdot 1} \langle x|z + 1\rangle_{ex} = (1 + z)^x \quad (35)$$

where we have used that $|z\rangle$ is an eigenstate of the annihilation operators $\hat{a}_j$, the representation of $|z\rangle$ from Eq. 27 and Eq. 34. The exclusive product of two coherent states is

$$\langle p|z\rangle_{ex} = \langle p|e^{\hat{\pi} \cdot 1} e^{\hat{a} \cdot 1} |z\rangle_{ex} = e^{(z \cdot 1)\cdot 1} \langle p|z\rangle_{ex} = e^{p^* \cdot z - (p^* + z) \cdot 1}. \quad (36)$$

Finally, the Grassberger-Scheunert product of two coherent states is

$$\langle p|z\rangle = \langle p|e^{\hat{\pi} \cdot 1} e^{\hat{a} \cdot 1} |z\rangle_{ex} = e^{(p^* + z) \cdot 1} \langle p|z\rangle_{ex} = e^{p^* \cdot z} \quad (37)$$

where we have used Eq. 36.

### 4.3 Resolution of the identity

The coherent states we defined, along with the Grassberger-Scheunert product, can be used to construct a resolution of the identity. It is

$$1 = \int_{[0,\infty)^n} dz \int_{\mathbb{R}^n} \frac{dp}{(2\pi)^n} |z\rangle \langle -ip| e^{-iz \cdot p} \quad (38)$$
where \(|z\rangle\) and \(|p\rangle\) are coherent states, \(z\) is integrated over \([0, \infty)^N\), and \(p\) is integrated over \(\mathbb{R}^n\). To establish Eq. 38, first observe that

\[
\int_{[0, \infty)^n} \frac{dz}{z^n} \int_{\mathbb{R}^n} \frac{dp}{(2\pi)^n} |z\rangle \langle -ip| x^N e^{-iz \cdot p} = \sum \frac{1}{y!} |y\rangle \int_{[0, \infty)^n} dz \frac{dz}{z^n} \int_{\mathbb{R}^n} \frac{dp}{(2\pi)^n} (1 + iP)^x e^{-z \cdot (1+ip)}
\]

for all basis kets \(|x\rangle\), where we used the shorthand

\[
\left(\frac{d}{dz}\right)^x := \left(\frac{d}{dz_1}\right)^x \cdots \left(\frac{d}{dz_n}\right)^x
\]

(40)

to ease notation. Integrate the last line of Eq. 39 by parts to obtain

\[
\sum \frac{1}{y!} |y\rangle \int_{[0, \infty)^n} dz \left(\frac{d}{dz}\right)^x |z^y\rangle e^{-z} \delta(z)
\]

\[
= \sum \frac{1}{y!} |y\rangle x! \delta(y - x)
\]

(41)

which confirms that Eq. 38 is a resolution of the identity.

### 4.4 The Grassberger-Scheunert creation operator

As we noted in Sec. 4.2, the Hermitian conjugate of the annihilation operator \(\hat{a}_j\) with respect to the Grassberger-Scheunert product is \(\pi_j - 1\) for all \(j = 1, \ldots, n\). Motivated by this, define the Grassberger-Scheunert creation operator

\[
\hat{a}_j^+ := \pi_j - 1
\]

(42)

for all \(j = 1, \ldots, n\). In the rest of the article, we will take “creation operator” without qualification to mean this operator. The Hamiltonian can be written more compactly in terms of this operator:

\[
\hat{H} = \sum_{k=1}^{n} c_{0k}(t) \hat{a}_k^+ - \sum_{k=1}^{n} c_{k0}(t) \hat{a}_k^+ \hat{a}_k + \sum_{j=1}^{n} \sum_{k=1}^{n} c_{jk}(t) \left[ \hat{a}_k^+ - \hat{a}_j^+ \right] \hat{a}_j
\]

(43)
Note that this expression is ‘normal ordered’—all creation operators are to the left of all annihilation operators. For all (possibly time-dependent) operators $O(t)$ in this form, i.e.

$$O(t) := \sum_{n,m,j,k} d_{nmjk}(t) (\hat{a}_j^+)^m(\hat{a}_k)^n,$$

coherent state matrix elements are easily evaluated by exploiting that $(\hat{a}_j)^\dagger = \hat{a}_j^+$ and that the coherent states are eigenstates of the annihilation operators:

$$\langle p|O(t)|z \rangle = \langle p|z \rangle \sum_{n,m,j,k} d_{nmjk}(t) (p_j^*)^m(z_k)^n$$

$$= e^{p^\ast \cdot z} \sum_{n,m,j,k} d_{nmjk}(t) (p_j^*)^m(z_k)^n.$$

We will use this result in the next section to evaluate many matrix elements of the Hamiltonian operator.

### 4.5 Probability distribution and moments

We need some way to convert the generating function $|\psi(t)\rangle$ to a solution $P(x,t)$ of the CME (Eq. 2). We can achieve this using the exclusive product $[51]$:

$$P(x, t) = \frac{\langle x|\psi(t)\rangle_{ex}}{x!}.$$  

Factorial moments are easily obtained using the Grassberger-Scheunert product $[54]$. For example:

$$\langle x_j(t) \rangle = \langle 0|\hat{a}_j|\psi(t)\rangle$$

$$\langle x_j(t)x_k(t) \rangle = \langle 0|\hat{a}_j\hat{a}_k|\psi(t)\rangle$$

$$\langle x_j(t) [x_j(t) - 1] \rangle = \langle 0|\hat{a}_j^2|\psi(t)\rangle$$

$$\langle x_j(t)[x_j(t) - 1][x_j(t) - 2] \rangle = \langle 0|\hat{a}_j^3|\psi(t)\rangle.$$  

### 5 Doi-Peliti path integral construction

In this section, we will use the coherent state resolution of the identity (Eq. 38) constructed in the previous section to rewrite our formal solution for $|\psi(t)\rangle$ (Eq. 22). Applying it twice, we have

$$|\psi(t)\rangle = \int \frac{dz^f dp^f dz^0 dp^0}{(2\pi)^n} |z^f\rangle \langle -i p^f |\hat{U}(t, t_0)|z^0\rangle \langle -i p^0 |\psi(t_0)\rangle e^{-ip^0 \cdot z^0 - ip^f \cdot z^f}.$$  

11
Define the propagator
\[ U(i\mathbf{p}, \mathbf{z}^0) := \langle -i\mathbf{p} | \hat{U}(t, t_0) | \mathbf{z}^0 \rangle. \]  
(49)
We will construct a coherent state path integral expression for the propagator. To do this, first write the time evolution operator \( U(t, t_0) \) as a product of many time evolution operators using the composition property (Eq. 24):
\[ \hat{U}(t, t_0) = \hat{U}(t, t_{N-1}) \hat{U}(t_{N-1}, t_{N-2}) \cdots \hat{U}(t_1, t_0) \]  
(50)
where \( t_\ell := t_0 + \ell \Delta t \) for \( \ell = 0, \ldots, N \), and \( \Delta t := (t - t_0) / N \). Now insert \((N-1)\) resolutions of the identity to write
\[ U = \int \prod_{\ell=1}^{N-1} \frac{dz^\ell dp^\ell}{(2\pi)^n} \langle -i\mathbf{p} | \hat{U}(t, t_{N-1}) | \mathbf{z}^{\ell-1} \rangle \cdots \langle -i\mathbf{p} | \hat{U}(t_1, t_0) | \mathbf{z}^0 \rangle e^{-\sum_{\ell=1}^{N-1} p^\ell \cdot z^\ell}. \]  
(51)
To arrive at our desired path integral, all we must do is compute the matrix elements in the above equation. Assuming that \( N \) is large enough that \( \Delta t \) is very small, we have that
\[ \hat{U}(t_\ell, t_{\ell-1}) \approx e^{\int_{t_{\ell-1}}^{t_\ell} \hat{H} dt'} \approx 1 + \hat{H}(t_{\ell-1}) \Delta t \]  
i.e. \( \hat{U} \) is equal to its first order Taylor expansion. Moreover, this inequality becomes exact in the \( N \to \infty \) limit. Using this,
\[ \langle -i\mathbf{p} | \hat{U}(t_\ell, t_{\ell-1}) | \mathbf{z}^{\ell-1} \rangle \approx e^{i\mathbf{p} \cdot \mathbf{z}^{\ell-1}} + \Delta t \langle -i\mathbf{p} | \hat{H}(t_{\ell-1}) | \mathbf{z}^{\ell-1} \rangle. \]  
(53)
At this point, we can exploit the properties of coherent states described in the previous section. Using the fact that the Hamiltonian is normal ordered so that Eq. 15 applies (see Sec. 4.4), we have
\[ \langle -i\mathbf{p} | \hat{H}(t_{\ell-1}) | \mathbf{z}^{\ell-1} \rangle = e^{i\mathbf{p} \cdot \mathbf{z}^{\ell-1}} \mathcal{H}(i\mathbf{p}, \mathbf{z}^{\ell-1}, t_{\ell-1}) \]  
(54)
where the Hamiltonian kernel \( \mathcal{H} \) is defined as
\[ -i\mathcal{H}(i\mathbf{p}, \mathbf{z}^{\ell-1}, t_{\ell-1}) := \sum_{k=1}^n c_{0k}(t_{\ell-1}) p_k^0 - \sum_{k=1}^n c_{0k}(t_{\ell-1}) p_k^{\ell-1} \mathbf{z}_{k}^{\ell-1} + \sum_{j=1}^n \sum_{k=1}^n c_{jk}(t_{\ell-1}) [p_k^0 - p_j^0] \mathbf{z}_{j}^{\ell-1}. \]  
(55)
Hence,
\[ \langle -i\mathbf{p} | \hat{U}(t_\ell, t_{\ell-1}) | \mathbf{z}^{\ell-1} \rangle \approx e^{i\mathbf{p} \cdot \mathbf{z}^{\ell-1}} \left[ 1 + \mathcal{H}(i\mathbf{p}, \mathbf{z}^{\ell-1}, t_{\ell-1}) \Delta t \right] \approx e^{i\mathbf{p} \cdot \mathbf{z}^{\ell-1} + \Delta t \mathcal{H}(i\mathbf{p}, \mathbf{z}^{\ell-1}, t_{\ell-1})} \]  
(56)
where we have again used the fact that \( \Delta t \) is small. Putting all of these matrix elements together, our final coherent state path integral expression for \( U(i\mathbf{p}, \mathbf{z}^0) \) reads
\[ U = \lim_{N \to \infty} \int \prod_{\ell=1}^{N-1} \frac{dz^\ell dp^\ell}{(2\pi)^n} \exp \left\{ \sum_{\ell=1}^{N-1} -i\mathbf{p} \cdot (\mathbf{z}^\ell - \mathbf{z}^{\ell-1}) + \Delta t \mathcal{H}(i\mathbf{p}, \mathbf{z}^{\ell-1}, t_{\ell-1}) \right\} \]  
(57)
where the \( N \to \infty \) limit must be taken so that the approximation we made in Eq. 52 becomes exact.
6 Monomolecular propagator derivation

In this section, we will evaluate the path integral expression for the propagator \( U(i\mathbf{p}^f, z^0) \) (Eq. 57) given our specific dynamics, which are captured by the Hamiltonian kernel \( \mathcal{H} \) (Eq. 55).

Let us first integrate over the \( p^f_k \) (where \( \ell \in \{1, ..., N-1\} \) and \( k \in \{1, ..., n\} \)). For fixed \( \ell \) and \( k \), these integrals look like

\[
\int_{-\infty}^{\infty} \frac{dp^f_k}{2\pi} \exp \left\{ -ip^f_k \left[ (z^\ell_k - z^{\ell-1}_k) - \Delta t \left( \sum_{j=1}^{n} c_{jk}^{-1} z_{j-1} - c_{kj}^{-1} z_{k}^{\ell-1} \right) \right] \right\}
\]

(58)

where \( c_{jk}^{-1} \) is shorthand for \( c_{jk}(t_{\ell-1}) \). Using the usual integral representation of the Dirac delta function, these integrals are easily done to obtain \( n \cdot (N-1) \) delta function constraints:

\[
\delta \left[ (z^\ell_k - z^{\ell-1}_k) - \Delta t \left( \sum_{j=1}^{n} c_{jk}^{-1} z_{j-1} - c_{kj}^{-1} z_{k}^{\ell-1} \right) \right].
\]

(59)

Fortunately, that is exactly how many integrals we have left to do. Notice that the constraints force

\[
z^\ell_k = z^{\ell-1}_k + \Delta t \left( \sum_{j=1}^{n} c_{jk}^{-1} z_{j-1} - c_{kj}^{-1} z_{k}^{\ell-1} \right)
\]

(60)

which exactly corresponds to taking an Euler time step given the deterministic dynamics described by the reaction rate equations, Eq. 4. What remains of our calculation is to evaluate

\[
U = \lim_{N \to \infty} \exp \{ \Delta t \mathcal{H}(i\mathbf{p}^f, z^{N-1}, t_{\ell-1}) + i\mathbf{p}^f \cdot \mathbf{z}^{N-1} \}
\]

(61)

given Eq. 60 the constraint on \( z^{N-1} \) relating it (via \( N-1 \) Euler time steps) to \( z^0 \). We have

\[
i\mathbf{p}^f \cdot \mathbf{z}^{N-1} + \Delta t \mathcal{H}(i\mathbf{p}^f, z^{N-1}, t_{\ell-1})
\]

\[
i \sum_{k=1}^{n} p^f_k \left[ z^{N-1}_k + \Delta t \left( c_{0k}^{N-1} z^{N-1}_k - c_{k0}^{N-1} z^{N-1}_k \right) \right]
\]

\[
= i \sum_{k=1}^{n} p^f_k z^N_k
\]

(62)

where we define \( z^N_k \) as the result of taking \( N \) time steps of length \( \Delta t \) according to Eq. 60 given the initial condition \( z^0_k \). In the \( N \to \infty \) limit, \( z^N_k \to z_k(t) \), where \( z_k(t) \) is defined as the \( k \)th component of the solution to Eq. 4. As described in Sec. 2, \( z(t) \) can be decomposed as

\[
z(t) = \sum_{k=1}^{n} z^0_k w^{(k)}(t) + \lambda(t)
\]

(63)
Using Eq. 46 and Eq. 48, we have
\[ U(i\mathbf{p}^f, z^0) = e^{ip^f \cdot z(t)}. \] (64)

While it may seem that this path integral calculation was completely trivial, that is mostly because we put in the legwork to define and characterize the Grassberger-Scheunert product beforehand. Had we used the exclusive product to construct our path integral, we would either have to perform a hard to justify Doi shift, or deal with extra terms after enforcing the delta function constraints.

7 From the propagator to the transition probability

Now that we have computed \( U(i\mathbf{p}^f, z^0) \), we can relate it to \( |\psi(t)\rangle \) using Eq. 48. Then, using the result from Sec. 4.5, \( P(x, t) \) can be found by calculating \( \langle x|\psi(t)\rangle \). Because this last calculation is somewhat involved, we will first present it for a one species system.

7.1 One species derivation

Since \( P(x, t_0) = \delta(x - \xi) \) for some \( \xi \geq 0 \),
\[ |\psi(t_0)\rangle = |\xi\rangle. \] (65)

Using Eq. 46 and Eq. 48, we have
\[ P(x, t; \xi, t_0) = \frac{1}{x!} \int \frac{d\xi}{2\pi} \frac{d\lambda}{2\pi} \langle x | \xi \rangle \langle \xi | \psi(t_0) \rangle e^{-ip^f z^0 - ip^f z^f} \]
\[ = \frac{1}{x!} \int \frac{d\xi}{2\pi} \frac{d\lambda}{2\pi} (\xi^f)^x e^{-ip^f z^f} (1 + ip^0)^\xi e^{-ip^0 z^0 - ip^f z^f}. \] (66)

The integral over \( p^f \) is easily done:
\[ \int_{-\infty}^{\infty} \frac{dp^f}{2\pi} e^{ip^f [z(t) - z^f]} = \delta(z(t) - z^f). \] (67)

Enforcing the delta function constraint removes the integral over \( z^f \). Since \( z(t) = z^0 w(t) + \lambda(t) \),
\[ P = \frac{1}{x!} \int \frac{d\xi}{2\pi} \frac{d\lambda}{2\pi} [z^0 w(t) + \lambda(t)]^x e^{z^0 [w(t) + \lambda(t)]} (1 + ip^0)^\xi e^{-ip^0 z^0} \]
\[ = \frac{e^{-\lambda(t)}}{x!} \int \frac{d\xi}{2\pi} \frac{d\lambda}{2\pi} [z^0 w(t) + \lambda(t)]^x e^{z^0 [1 - w(t)]} (1 + ip^0)^\xi e^{-z^0 [1 + ip^0]} \] (68)

This can be rewritten as
\[ P = \frac{e^{-\lambda(t)}}{x!} \int \frac{d\xi}{2\pi} \frac{d\lambda}{2\pi} \left[ \frac{d}{dz^0} \right]^\xi \left\{ [z^0 w(t) + \lambda(t)]^x e^{z^0 [1 - w(t)]} \right\} e^{-z^0 [1 + ip^0]} \]
\[ = \frac{e^{-\lambda(t)}}{x!} \int \frac{d\xi}{2\pi} \frac{d\lambda}{2\pi} \left\{ \frac{d}{dz^0} \right]^\xi \left\{ [z^0 w(t) + \lambda(t)]^x e^{z^0 [1 - w(t)]} \right\} e^{-z^0 [1 + ip^0]} \] (69)
where we integrated by parts in the second step. The $p^0$ integral can now be done:

$$
\int_{-\infty}^{\infty} \frac{dp^0}{2\pi} e^{-ip^0 z^0} = \delta(z^0) .
$$

We now have

$$
P = \frac{e^{-\lambda(t)}}{x!} \int_0^\infty dz^0 \left( \frac{d}{dz^0} \right)^\xi \left\{ [z^0 w(t) + \lambda(t)]^x e^{z^0[1-w(t)]} \right\} e^{-z^0} \delta(z^0) .
$$

If we can evaluate the derivative, then we can easily evaluate the integral using the delta function. Using the binomial theorem,

$$
[z^0 w(t) + \lambda(t)]^x = \sum_{k=0}^{x} \binom{x}{k} w(t)^k \lambda(t)^{x-k} (z^0)^k .
$$

Since

$$
(z^0)^k e^{z^0[1-w(t)]} = \sum_{j=0}^{\infty} (z^0)^{j+k} \frac{[1-w(t)]^j}{j!} ,
$$

the derivative of a specific term is

$$
\left( \frac{d}{dz^0} \right)^\xi \left\{ (z^0)^k e^{z^0[1-w(t)]} \right\} = \sum_{j=0}^{\infty} \frac{(j+k)(j+k-1) \cdots (j+k-\xi+1)}{j!} (z^0)^{j+k-\xi} \frac{[1-w(t)]^j}{j!} .
$$

When enforcing the delta function constraint that $z^0 = 0$, all terms will disappear from this series except for the constant term. The constant term is the term with $j + k = \xi$, which reads

$$
\frac{\xi!}{(\xi - k)!} [1-w(t)]^{\xi-k} \theta(\xi - k)
$$

where the step function $\theta$, defined as

$$
\theta(\xi - k) := \begin{cases} 
1 & k \leq \xi \\
0 & k > \xi
\end{cases}
$$

must be there since the result will be zero if $k > \xi$. Hence,

$$
P = \frac{e^{-\lambda(t)}}{x!} \sum_{k=0}^{x} \binom{x}{k} w(t)^k \lambda(t)^{x-k} \frac{\xi!}{(\xi - k)!} [1-w(t)]^{\xi-k} \theta(\xi - k)
$$

$$
= e^{-\lambda(t)} \sum_{k=0}^{\min(x,\xi)} \binom{\xi}{k} w(t)^k \lambda(t)^{x-k} \frac{1}{(x-k)!} [1-w(t)]^{\xi-k}
$$

$$
= \sum_{k=0}^{\min(x,\xi)} \left[ \frac{\lambda(t)^{x-k} e^{-\lambda(t)}}{(x-k)!} \right] \left[ \binom{\xi}{k} w(t)^k [1-w(t)]^{\xi-k} \right]
$$

$$
= P(x, \lambda(t)) \ast M(x, \xi, w(t))
$$

as desired.
7.2 General derivation

The general case proceeds analogously to the one species case. The main difference is that we must do the appropriate multivariable generalization of each of the steps in the previous subsection (e.g., use the multinomial theorem instead of the binomial theorem). Since \( P(x, t_0) = \delta(x - \xi) \),

\[
|\psi(t_0)\rangle = |\xi\rangle . \tag{78}
\]

Using Eq. 46 and Eq. 48,

\[
P(x, t; \xi, t_0) = \frac{1}{x!} \int \frac{dz f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} e^{-i\xi f \cdot \xi f} U(i\xi f, \xi f) \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} . \tag{79}
\]

The integrals over \( p f \), ..., \( p f \) yield delta functions:

\[
\int \frac{d\xi f}{{(2\pi)}^n} e^{i\xi f \cdot (\xi f - \xi f)} = \delta(z_1(t) - z_1(t)) \cdot \delta(z_n(t) - z_n(t)) = \delta(z(t) - z(t)) . \tag{80}
\]

Enforcing the delta function constraints removes the integrals over \( z_1(t), ..., z_n(t) \). Using Eq. 63

\[
P = \frac{1}{x!} \int \frac{dz f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} . \tag{81}
\]

Reusing the notation we used earlier to denote many derivatives with respect to each variable (Eq. 40), we can rewrite this result as

\[
P = \frac{e^{-|\xi(t)|}}{x!} \int \frac{dz f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} . \tag{82}
\]

where we integrated by parts many times in the second step. The \( p f, ..., p f \) integrals can now be done:

\[
\int \frac{d\xi f}{{(2\pi)}^n} e^{-i\xi f \cdot \xi f} = \delta(z f) \cdot \delta(z f) = \delta(z f) . \tag{83}
\]

We now have

\[
P = \frac{e^{-|\xi(t)|}}{x!} \int \frac{dz f}{{(2\pi)}^n} \left\{ \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} \int \frac{d\xi f}{{(2\pi)}^n} e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} \cdot \langle -i\xi f | \psi(t_0) \rangle e^{-i\xi f \cdot \xi f} \right\} . \tag{84}
\]
If we can evaluate the derivative, then we can easily evaluate the integral using the delta function. Recall that
\[
\left[ \sum_{k=1}^{n} z_k^0 w_j^{(k)} + \lambda_j \right]^{x_j} = \left[ \sum_{k=1}^{n} z_k^0 w_1^{(k)} + \lambda_1 \right]^{x_1} \cdots \left[ \sum_{k=1}^{n} z_k^0 w_n^{(k)} + \lambda_n \right]^{x_n}.
\]
(85)

Using the multinomial theorem,
\[
\left[ \sum_{k=1}^{n} z_k^0 w_j^{(k)} + \lambda_j \right]^{x_j} = \sum_{v_1 \cdots v_{n+1} = x_j} \left( v_1^{x_1} \cdots v_{n+1}^{x_{n+1}} \right) \left[ z_1^0 w_j^{(1)} \right]^{v_1} \cdots \left[ z_n^0 w_j^{(n)} \right]^{v_n} \lambda_j^{v_{n+1}}
\]
(86)
for each \( j = 1, \ldots, n \). Write \( |v_\ell| := v_1^\ell + \cdots + v_n^\ell \). Putting these multinomial expansions together, our integral now involves computing \( n \) expressions of the form
\[
\frac{e^{-|v_\ell|}}{x!} \sum_{v_k^\ell} \left\{ \prod_{j=1}^{n} \left( v_1^{x_j} \cdots v_{n+1}^{x_{n+1}} \right) \left[ w_j^{(1)} \right]^{v_1} \cdots \left[ w_j^{(n)} \right]^{v_n} \lambda_j^{v_{n+1}} \xi_k! \frac{\xi_k! (1 - |w_j^{(k)}|)^{\xi_k - |v_k|}}{(\xi_k - |v_k|)!} \theta(\xi_k - |v_k|) \right\}
\]
(88)

where we have used the result from earlier (Eq. 75) to evaluate it. When enforcing the delta function constraint that \( z_k^0 = 0 \) for all \( \ell = 1, \ldots, n \), we get
\[
\frac{e^{-|\lambda(t)|}}{x!} \prod_{j=1}^{n} \left[ \frac{\lambda_j^{v_{n+1}}}{v_{n+1}!} \right] = \frac{\lambda(t)^{v_{n+1}}}{v_{n+1}!} e^{-|\lambda(t)|} = P(v_{n+1}, \lambda(t)).
\]
(89)

Also,
\[
\frac{\xi_k! (1 - |w_j^{(k)}|)^{\xi_k - |v_k|}}{(\xi_k - |v_k|)!} \theta(\xi_k - |v_k|) \prod_{j=1}^{n} \frac{\left[ w_j^{(k)} \right]^{v_k}}{v_k!} = \frac{\xi_k! (1 - |w_j^{(k)}|)^{\xi_k - |v_k|}}{(\xi_k - |v_k|)!} \theta(\xi_k - |v_k|) \frac{\left[ w_j^{(k)} \right]^{v_k}}{v_k!} = M(v_k, \xi_k, w_j^{(k)}).
\]
(90)

We are left with
\[
P = \sum_{v_k^\ell} P(v_{n+1}, \lambda(t)) \cdot M(v_1, \xi_1, w_j^{(1)}) \cdots M(v_n, \xi_n, w_j^{(n)})
\]
\[
= \sum_{v_k^\ell} P(x-v_1, \ldots, v_n, \lambda(t)) \cdot M(v_1, \xi_1, w_j^{(1)}) \cdots M(v_n, \xi_n, w_j^{(n)})
\]
(91)
\[
= P(x, \lambda(t)) \cdot M(x, \xi_1, w_j^{(1)}(t)) \cdots M(x, \xi_n, w_j^{(n)}(t))
\]
(92)
which matches Eq. 11.

8 From the propagator to moments

If we wanted to compute the moments of \( P(x,t) \), we could just use Eq. 11 and carry out the calculation as usual; however, the Doi-Peliti approach offers a way to compute moments which bypasses \( P(x,t) \) completely. In other words, if we are only interested in moments, the work from the previous section is unnecessary. Instead, we can use Eq. 47 from Sec. 4.5.

As in the previous section, we will warm up with the one species case before treating the general case.

8.1 One species moments

Using Eq. 47,

\[
\langle x(t) \rangle = \langle 0|\hat{a}|\psi(t)\rangle = \int \frac{dz^f dp^f}{2\pi} \int \frac{dz^0 dp^0}{2\pi} \langle 0|\hat{a}|z^f \rangle \langle -ip^0|z^0 \rangle e^{-ip^0 z^0 - ip^t z^f} \left( z^f \right)^2 e^{i p^f z(t)} (1 + ip^0)^\xi e^{-ip^0 z^0 - ip^f z^f}.
\]

The \( p^f, z^f, \) and \( p^0 \) integrals can be done as in Sec. 7.1, leaving

\[
\langle x(t) \rangle = \int_0^\infty dz^0 \left( \frac{d}{dz^0} \right)^\xi \left\{ [z^0 w(t) + \lambda(t)] e^{z^0} \right\} e^{-z^0} \delta(z^0).
\]

The derivative is easily evaluated, and we obtain

\[
\langle x(t) \rangle = \int_0^\infty dz^0 \left[ \xi w(t) e^{z^0} + z(t) e^{z^0} \right] e^{-z^0} \delta(z^0) = \xi w(t) + \lambda(t)
\]

which is just the solution to the one species reaction rate equation with \( x(t_0) = \xi \), just as expected. The second factorial moment can be computed in similar fashion:

\[
\langle x(t)[x(t) - 1] \rangle = \langle 0|\hat{a}^2|\psi(t)\rangle = \int \frac{dz^f dp^f}{2\pi} \int \frac{dz^0 dp^0}{2\pi} \left( z^f \right)^2 e^{i p^f z(t)} (1 + ip^0)^\xi e^{-ip^0 z^0 - ip^f z^f}
\]

\[
= \int_0^\infty dz^0 \left( \frac{d}{dz^0} \right)^\xi \left\{ [z^0 w(t) + \lambda(t)] e^{z^0} \right\} e^{-z^0} \delta(z^0)
\]

\[
= w(t)^2 \xi (\xi - 1) + 2\lambda(t) w(t) \xi + \lambda(t)^2.
\]

Higher factorial moments can be computed in exactly the same way.
8.2 General moments

Unlike in the one species case, there are many first moments: \( \langle x_1(t) \rangle, \ldots, \langle x_n(t) \rangle \). Picking a specific \( x_j \) and using Eq. 47, we have

\[
\langle x_j(t) \rangle = \langle 0 | \hat{a}_j \hat{a}_j | \psi(t) \rangle = \int \frac{dz^f dp^f dz^0 dp^0}{(2\pi)^n} \langle 0 | \hat{a}_j \hat{a}_j | z^f \rangle U(i p^f, z^0) \langle -i p^0 | \psi(t_0) \rangle e^{-ip^0z^0-ip^f z^f}
\]

\[
= \int \frac{dz^f dp^f dz^0 dp^0}{(2\pi)^n} z^f_j e^{ip^f z(t)} (1 + i p^0) \xi e^{-ip^0z^0-ip^f z^f}.
\]

The \( p^f, z^f \), and \( p^0 \) integrals can be done as in Sec. 7.2 yielding

\[
\langle x_j(t) \rangle = \int dz^0 \left( \frac{d}{dz^0} \right)^\xi \left\{ \sum_{k=1}^n z^0_k w^{(k)}_j + \lambda_j \right\} e^{z^0 \cdot 1} \left( \frac{d}{dz^0} \right)^{-1} \delta(z^0)
\]

\[
= \sum_{k=1}^n \xi_k w^{(k)}_j(t) + \lambda_j(t)
\]

which is the \( j \)th component of the solution to Eq. 4 with \( x(t_0) = \xi \).

Let us compute \( \langle x_j(t)x_\ell(t) \rangle \) for \( j \neq \ell \). To start off,

\[
\langle x_j(t)x_\ell(t) \rangle = \langle 0 | \hat{a}_j \hat{a}_\ell | \psi(t) \rangle = \int \frac{dz^f dp^f dz^0 dp^0}{(2\pi)^n} \langle 0 | \hat{a}_j \hat{a}_\ell | z^f \rangle U(i p^f, z^0) \langle -i p^0 | \psi(t_0) \rangle e^{-ip^0z^0-ip^f z^f}
\]

\[
= \int \frac{dz^f dp^f dz^0 dp^0}{(2\pi)^n} z^f_j z^\ell \ e^{ip^f z(t)} (1 + i p^0) \xi e^{-ip^0z^0-ip^f z^f}.
\]

Proceeding as we just did, we obtain

\[
\langle x_j x_\ell \rangle = \int dz^0 \left( \frac{d}{dz^0} \right)^\xi \left\{ \sum_{k=1}^n z^0_k w^{(k)}_j + \lambda_j \right\} \left\{ \sum_{k'=1}^n z^0_{k'} w^{(k')}_\ell + \lambda_\ell \right\} e^{z^0 \cdot 1} \left( \frac{d}{dz^0} \right)^{-1} \delta(z^0)
\]

\[
= \sum_{k=1}^n \sum_{k'=1}^n \xi_k \xi_{k'} w^{(k)}_j w^{(k')}_\ell + \sum_{k=1}^n \xi_k \left[ w^{(k)}_j \lambda_\ell + w^{(k')}_\ell \lambda_j - w^{(k)}_j w^{(k')}_\ell \right] + \lambda_j \lambda_\ell.
\]

For the similar case \( j = \ell \), we obtain

\[
\langle x_j(x_j(t) - 1) \rangle = \int dz^0 \left( \frac{d}{dz^0} \right)^\xi \left\{ \sum_{k=1}^n z^0_k w^{(k)}_j + \lambda_j \right\}^2 e^{z^0 \cdot 1} \left( \frac{d}{dz^0} \right)^{-1} \delta(z^0)
\]

\[
= \sum_{k=1}^n \sum_{k'=1}^n \xi_k \xi_{k'} w^{(k)}_j w^{(k')}_j + \sum_{k=1}^n \xi_k \left[ 2 w^{(k)}_j \lambda_j - \left( w^{(k)}_j \right)^2 \right] + \lambda_j^2.
\]
Putting these results together, we find that the covariance of \( x_j \) and \( x_\ell \) is

\[
\text{Cov}(x_j, x_\ell) = \sum_{k=1}^{n} \xi_k w_j^{(k)} \left( 1 - w_j^{(k)} \right) + \lambda_j \quad j = \ell
\]

\[
- \sum_{k=1}^{n} \xi_k w_\ell^{(k)} w_j^{(k)} \quad j \neq \ell
\]

\( (101) \)

Hence, we have recovered the moment results from Sec. 4.2 of Jahnke and Huisinga.

9 A new result on autocatalytic reactions

In section 6 of their classic paper \[45\], Jahnke and Huisinga solve the CME corresponding to the autocatalytic reaction \( S \rightarrow S + S \) exactly; however, they note that adding birth and death reactions yields a system not amenable to their approach. In this section, we present the exact time-dependent solution to this problem, whose reactions read

\[
\begin{align*}
\emptyset & \xrightarrow{k} S \\
S & \xrightarrow{\gamma} \emptyset \\
S & \xrightarrow{c} S + S
\end{align*}
\]

(102)

where the rates of birth, death, and autocatalysis are all allowed to have arbitrary time-dependence as long as they are nonnegative for all times. The CME reads

\[
\frac{\partial P(x,t)}{\partial t} = k(t) [P(x-1,t)-P(x,t)]
\]

\[
+ \gamma(t) [(x+1)P(x+1,t)-xP(x,t)]
\]

\[
+ c(t) [(x-1)P(x-1,t)-xP(x,t)]
\]

(103)

where \( P(x,t) \) is the probability that the state of the system is \( x \in \mathbb{N} \) at time \( t \geq t_0 \).

9.1 Deriving the propagator

The Hamiltonian operator corresponding to this problem is

\[
\hat{H} := \hat{a}^+ \left[ k + (c-\gamma)\hat{a} + c \; \hat{a}^+ \hat{a} \right]
\]

(104)

in terms of the Grassberger-Scheunert creation and annihilation operators. The Hamiltonian kernel \( \mathcal{H} \) is

\[
\mathcal{H}(ip, z, t) := ip \left[ k + (c-\gamma)z \right] - c \; p^2 \; z
\]

(105)

Constructing the coherent state path integral just as in Sec. \[5\] the propagator \( U(ip_f, z_0) \) is

\[
U(ip_f, z_0) = \lim_{N \rightarrow \infty} \int \prod_{\ell=1}^{N-1} \frac{dz_\ell dp_\ell}{2\pi} \exp \left\{ \sum_{\ell=1}^{N-1} -ip_\ell(z_\ell - z_{\ell-1}) + \Delta t \mathcal{H}(ip_\ell, z_{\ell-1}, t_{\ell-1}) \right. \\
+ \left. \Delta t \mathcal{H}(ip_f, z_{N-1}, t_{N-1}) + ip_f z_{N-1} \right\}
\]

(106)
where we have used slightly different notation than before since there is only one chemical species. In order to evaluate this path integral, first integrate over each \( z_\ell \), and then integrate over each \( p_\ell \). Collecting terms containing \( z_\ell \), the integral over each \( z_\ell \) looks like

\[
\int_0^\infty \frac{dz_\ell}{2\pi} \exp \left\{ z_\ell \left[ -c_\ell \Delta t \, p_{\ell+1}^2 + i(c_\ell - \gamma_\ell) \Delta t \, p_{\ell+1} - i(p_\ell - p_{\ell+1}) \right] \right\} = \frac{1}{2\pi i} \int_\infty^\infty dp_\ell \frac{1}{(p_\ell - p_{\ell+1}) - \Delta t \left[ (c_\ell - \gamma_\ell) \, p_{\ell+1} + ic_\ell \, p_{\ell+1}^2 \right]} \quad (107)
\]

The integrals over \( p_\ell \) can now be done—but they must be done in a specific order. Do the integral over \( p_{N-1} \), then \( p_{N-2} \), and so on, until the integral over \( p_1 \) has been done. Each of these integrals is schematically

\[
\frac{1}{2\pi i} \int_\infty^\infty dp_\ell \frac{f(p_\ell)}{(p_\ell - p_{\ell+1}) - \Delta t \left[ (c_\ell - \gamma_\ell) \, p_{\ell+1} + ic_\ell \, p_{\ell+1}^2 \right]} \quad (108)
\]

where the function \( f(p_\ell) \) has no poles. This means that each integral can be evaluated using Cauchy’s integral formula, so that the net effect of doing them is to enforce the \((N - 1)\) constraints

\[
p_\ell = p_{\ell+1} + \Delta t \left[ (c_\ell - \gamma_\ell) \, p_{\ell+1} + ic_\ell \, p_{\ell+1}^2 \right] \quad (109)
\]

on the \( p_\ell \) for \( \ell = 1, ..., N - 1 \). There are no more integrals to do, so all that remains is to evaluate what’s left of the propagator using these constraints. Eq. (109) looks like an Euler time step, although it is ‘backwards’—we go from \( p_{\ell+1} \) to \( p_\ell \) instead of the other way around. Define \( q_{N-\ell} := p_\ell \) so that it reads

\[
q_{N-\ell} = q_{N-\ell-1} + \Delta t \left[ (c_{N-n} - \gamma_{N-n}) \, q_{n-1} + ic_{N-n} \, q_{n-1}^2 \right] \quad (110)
\]

Choosing \( \ell = N - n \), we find

\[
q_n = q_{n-1} + \Delta t \left[ (c_{N-n} - \gamma_{N-n}) \, q_{n-1} + ic_{N-n} \, q_{n-1}^2 \right] \quad (111)
\]

This corresponds to dynamics

\[
\dot{q}(s) = [c(t - s + t_0) - \gamma(t - s + t_0)] \, q(s) + ic(t - s + t_0) \, q(s)^2 \quad (112)
\]

where \( s \in [t_0, t] \) and \( q(t_0) = p_f \). As can be verified by substitution, Eq. (112) is solved by

\[
q(s) = \frac{w(s)}{p_f - i \int_{t_0}^s c(t - t') + t_0)w(t') \, dt'} \quad (113)
\]

where \( w(t) \) is the solution to

\[
\dot{w}(s) = [c(t - s + t_0) - \gamma(t - s + t_0)] \, w(s) \quad (114)
\]

with \( w(t_0) = 1 \) (c.f. Eq. 6), i.e.

\[
w(s) = e^{\int_{t_0}^s c(t - t' + t_0) - \gamma(t - t' + t_0) \, dt'} \quad (115)
\]
The continuous limit of Eq. (109) is then \( p(s) := q(t - s + t_0) \). With that done, the propagator with most terms integrated out reads

\[
U(ip_f, z_0) = \lim_{N \to \infty} \exp \left\{ i \sum_{\ell=1}^{N-1} k_{\ell-1} p_{\ell} \Delta t + i p_1 z_0 + \Delta t \left[ i p_1 (c_0 - \gamma_0) z_0 - c_0 p_1^2 z_0 \right] \right\}. \tag{116}
\]

The term on the right is just another Euler time step, so we can write it as

\[
iz_0 \left\{ p_1 + \Delta t \left[ p_1 (c_0 - \gamma_0) - c_0 p_1^2 \right] \right\} = iz_0 p_0
\]

where we define

\[
p_0 := p_1 + \Delta t \left[ p_1 (c_0 - \gamma_0) - c_0 p_1^2 \right]. \tag{118}
\]

In the limit as \( N \to \infty \), \( p_0 \to p(t_0) = q(t) \). The term on the left is just a Riemann sum:

\[
\sum_{\ell=1}^{N-1} k_{\ell-1} p_{\ell} \Delta t \approx \int_{t_0}^{t} k(s) p(s) \, ds = \int_{t_0}^{t} k(s) q(t - s + t_0) \, ds. \tag{119}
\]

Hence, our final answer for the propagator \( U \) is

\[
U(ip_f, z_0) = \exp \left\{ iz_0 q(t) + i \int_{t_0}^{t} k(s) q(t - s + t_0) \, ds \right\}. \tag{120}
\]

As an aside, we note that this calculation closely resembles the Martin-Siggia-Rose-Janssen-De Dominicis path integral computation from our earlier paper [75]: in particular, many applications of Cauchy’s integral formula and another ‘backwards’ Euler time step constraint are both involved.

### 9.2 Deriving the transition probability

As in Sec. [7.1], we will use the propagator derived in the previous section to derive an expression for the transition probability \( P(x, t; \xi, t_0) \). Since \( P(x, t_0) = \delta(x - \xi) \), we have \( |\psi_0 \rangle = |\xi \rangle \). Using Eq. (46) and Eq. (48)

\[
\begin{align*}
P(x, t; \xi, t_0) &= \frac{1}{x!} \int \frac{dz_f dp_f}{2\pi} \frac{dz_0 dp_0}{2\pi} \langle x | z_f \rangle \, \langle z_f | \rangle \, U(ip_f, z_0) \langle -ip_0 | \psi(t_0) \rangle \, e^{-ip_0 z_0 - ip_f z_f} \\
&= \frac{1}{x!} \int \frac{dz_f dp_f}{2\pi} \frac{dz_0 dp_0}{2\pi} \langle z_f | \rangle \, e^{-z_f} \, e^{i z_0 q(t) + i \int_{t_0}^{t} k(s) q(t - s + t_0) \, ds} (1 + ip_0)^{\xi} \, e^{-ip_0 z_0 - ip_f z_f}.
\end{align*}
\]

The integral over \( z_0 \) is

\[
\int_0^{\infty} \frac{dz_0}{2\pi} \, e^{-iz_0 [p_0 - q(t)]} = \frac{1}{2\pi i} \frac{1}{p_0 - q(t)}. \tag{122}
\]

The integral over \( p_0 \) can be performed using Cauchy’s integral formula:

\[
\frac{1}{2\pi i} \int_{-\infty}^{\infty} dp_0 \, \frac{(1 + ip_0)^{\xi}}{p_0 - q(t)} = \left[ 1 + iq(t) \right]^\xi. \tag{123}
\]
The integral over \( z_f \) can be recognized as a Laplace transform:

\[
\int_{0}^{\infty} dz_f \ (z_f)^x e^{-z_f[1+ip_f]} = \frac{x!}{(1+i p_f)^{x+1}}. \tag{124}
\]

Putting these results together, we obtain

\[
P(x, t; \xi, t_0) = \frac{1}{2\pi} \int_{-\infty}^{\infty} dp_f \frac{[1 + iq(t)]^\xi e^{i \int_{t_0}^{t} k(s) q(t-s) + t_0) ds}}{(1 + i p_f)^{x+1}}. \tag{125}
\]

We will leave our solution in this form, since it is difficult to evaluate the contour integral without knowing the explicit time-dependence of the rates. In the next few sections, we will examine a few special cases.

### 9.3 Time-independent rates

Assume \( k, \gamma, \) and \( c \) are all constant. In this case, \( q(t) \) reads

\[
q(t) = \frac{[c - \gamma] q + ic q^2}{e^{(c-\gamma)T}} = \frac{w(t)}{\frac{1}{p_f} - \frac{i c}{c-\gamma} [e^{(c-\gamma)T} - 1]} = \frac{w(t)}{\frac{1}{p_f} - \frac{i c}{c-\gamma} [w(t) - 1]} \tag{126}
\]

where \( T := t - t_0 \). We have

\[
\int_{t_0}^{t} q(s) \ ds = \frac{i}{c} \log \left\{ 1 - \frac{i c}{c-\gamma} \left[ e^{(c-\gamma)T} - 1 \right] p_f \right\} \tag{127}
\]

so that the convolution term from the propagator reads

\[
e^{ik \int_{t_0}^{t} q(s) \ ds} = \frac{1}{\left[ 1 - \frac{i c}{c-\gamma} \left[ e^{(c-\gamma)T} - 1 \right] p_f \right]^{k/c}} = \left[ 1 - iB(t)p_f \right]^{k/c} \tag{128}
\]

where we define

\[
B(t) := \frac{c}{c-\gamma} [w(t) - 1]. \tag{129}
\]

It is important to note that Eq. (128) has no poles in the upper half-plane (the region around which we are integrating), regardless of whether \( c - \gamma > 0, \ c - \gamma < 0, \) or \( c = \gamma \). Next,

\[
1 + iq(t) = 1 + \frac{i w(t)p_f}{1 - iB(t)p_f} = \left[ 1 - \frac{w(t)}{B(t)} \right] + \frac{w(t)}{B(t)} \frac{1}{1 - iB(t)p_f} \tag{130}
\]

so that

\[
[1 + iq(t)]^\xi = \sum_{j=0}^{\xi} \binom{\xi}{j} \left[ 1 - \frac{w(t)}{B(t)} \right]^{\xi-j} \left( \frac{w(t)}{B(t)} \right)^j \frac{1}{\left[ 1 - iB(t)p_f \right]^j} \tag{131}
\]
Putting all these results together, our expression for the transition probability is

\[ P = \sum_{j=0}^{\xi} \left( \frac{\xi}{j} \right) \left[ 1 - \frac{w(t)}{B(t)} \right]^{\xi-j} \left( \frac{w(t)}{B(t)} \right)^j \frac{1}{x!} \int_{-\infty}^{\infty} \frac{1}{[1 - iB(t)\gamma/c]^{j+k/c}} \left( \frac{x!}{(pf-i)^x} \right) \right]. \]

(132)

Since

\[ \frac{d^x}{dp_f^x} \left[ \frac{1}{[1 - iB(t)\gamma/c]^{j+k/c+x}} \right]_{p=i} = \frac{i^x B(t)^x}{[1 + B(t)]^{j+k/c+x}} \left( j + \frac{k}{c} \right) \left( j + \frac{k}{c} + 1 \right) \cdots \left( j + \frac{k}{c} + x - 1 \right) \]

we have

\[ P = \sum_{j=0}^{\xi} \left( \frac{\xi}{j} \right) \left[ 1 - \frac{w(t)}{B(t)} \right]^{\xi-j} \left( \frac{w(t)}{B(t)} \right)^j \frac{1}{x!} \frac{B(t)^x}{[1 + B(t)]^{j+k/c+x}} \]

\[ = \left( \frac{1 - \frac{\xi}{\gamma}}{w - \frac{\xi}{c}} \right)^{k/c} \frac{w - 1}{w - \frac{\xi}{c}} \sum_{j=0}^{\xi} \left( \frac{\xi}{j} \right) \left( j + \frac{k}{c} \right) \left( j + \frac{k}{c} + 1 \right) \cdots \left( j + \frac{k}{c} + x - 1 \right) \]

\[ \left[ 1 - \left( 1 - \frac{\gamma}{c} \right) \frac{w}{w - 1} \right]^{-\xi} \left[ \frac{w \left( 1 - \frac{\xi}{\gamma} \right)^2}{(w - 1)(w - \frac{\xi}{c})} \right] \]

(134)

where \((y)_x := (y)(y+1) \cdots (y+x-1)\) is the Pochhammer symbol/rising factorial. This can also be written in terms of the hypergeometric function \(_2F_1(a, b; c; x)\). Assuming that \(\gamma > c\), taking the time length \(T \to \infty\) yields the steady state solution

\[ P_{ss}(x) = \left( \frac{\gamma - c}{\gamma} \right)^{k/c} \frac{\left( \frac{\xi}{\gamma} \right)^x}{x!} \frac{\left( \frac{k}{c} \right)}{x}. \]

(135)

It is easy to check that this solution is normalized and solves the (steady state) CME. In the limit as \(c \to 0\), we have a birth-death process, and the steady state probability distribution becomes

\[ P_{ss}(x) = \frac{\left( \frac{k}{c} \right)^x e^{-k/\gamma}}{x!} \]

(136)

which is Poisson, as expected. In the limit taking \(k \to 0\) (while keeping \(\gamma\) and \(c\) finite), we have \(P_{ss}(x) = \delta(x)\), which is also expected (a system with only autocatalytic and death reactions, with \(\gamma > c\), has all of its probability concentrated in \(x = 0\) at steady state).

### 9.4 Binomial distribution special cases

Return to the original contour integral for time-dependent rates (Eq. 125), and set \(k = c = 0\), but leave the time-dependence of \(\gamma(t)\) arbitrary. We have

\[ w(t) := \exp \left[ - \int_{t_0}^{t} \gamma(t') dt' \right] \]

(137)
\[ q(t) = w(t)p_f \]  
\[ P(x, t; \xi, t_0) = \frac{1}{2\pi} \int_{-\infty}^{\infty} dp_f \frac{[1 + iw(t)p_f]^{\xi}}{(1 + ip_f)^{x+1}}. \]

The function in the numerator has no poles, so the contour integral can easily be evaluated using Cauchy’s integral formula. The result is

\[ P(x, t; \xi, t_0) = \left( \frac{\xi}{x} \right) [w(t)]^{x} [1 - w(t)]^{\xi-x} \]

for \( x \leq \xi \) and 0 otherwise, i.e. a binomial distribution.

### 9.5 Poisson distribution special case

Return to the original contour integral for time-dependent rates (Eq. 125), and set \( \gamma = c = 0 \), but leave the time-dependence of \( k(t) \) arbitrary. We have

\[ \lambda(t) := \int_{t_0}^{t} k(t') dt' \]
\[ q(t) = p_f \]
\[ P(x, t; \xi, t_0) = \frac{1}{2\pi} \int_{-\infty}^{\infty} dp_f \frac{e^{i\lambda(t)p_f}}{(1 + ip_f)^{x+1}}. \]

This contour integral can be evaluated using either Cauchy’s integral formula or a table of integrals (c.f. Gradshteyn and Ryzhik [76] ET I 118(3), in section 3.382, on pg. 365). The result is

\[ P(x, t; \xi, t_0) = \frac{\lambda(t)^{x-\xi}e^{-\lambda(t)}}{(x-\xi)!} \]

for \( x \geq \xi \) and 0 otherwise, i.e. a (shifted) Poisson distribution.

### 9.6 Negative binomial distribution special case

Return to the original contour integral for time-dependent rates (Eq. 125), and set \( k = c = 0 \), but leave the time-dependence of \( c(t) \) arbitrary. In this case, we will define \( w(t) \) differently from before as

\[ w(t) := \exp \left[ - \int_{t_0}^{t} c(t') dt' \right] \]

i.e. as the reciprocal of what we previously called \( w(t) \). This is to match the result from Jahnke and Huisinga. Now we have

\[ q(t) = \frac{1}{p_f} - \frac{1}{i [w(t)^{-1}] - 1} \]
\[ P(x, t; \xi, t_0) = \frac{1}{2\pi} \int_{-\infty}^{\infty} dp f \frac{1}{(1 + ip)^{x-\xi+1}} \frac{1}{[1 - i(w(t)^{-1} - 1)p]^\xi}. \tag{147} \]

The term on the right has no poles in the upper half-plane, so we can evaluate it using Cauchy’s formula to find
\[ P(x, t; \xi, t_0) = \left( \frac{x - 1}{\xi - 1} \right) [w(t)]^\xi [1 - w(t)]^{x-\xi} \tag{148} \]

which is nonzero only for \( x \geq \xi \). As Jahnke and Huisinga note in Sec. 6, this is a shifted negative binomial distribution.

## 10 Discussion

The strength of the Doi-Peliti approach—that calculations require nothing more clever than evaluating many integrals—is probably also its primary weakness. In Jahnke and Huisinga’s original paper, they began with proofs of partial results that offered intuition for why their main result is true: in short, Poisson remains Poisson, and multinomial remains multinomial. In contrast, our calculation does not seem to offer such insight en route to the full solution. This may make it easier to generalize to other kinds of systems (as we did in Sec. 9), but it is a little unsatisfying.

Still, the Doi-Peliti approach was able to generate a solution in a nontrivial case where Jahnke and Huisinga’s approach broke down. As they noted at the end of their Sec. 6, it interpolates between Poisson \((\gamma = c = 0)\), binomial \((k = c = 0)\), and negative binomial \((k = \gamma = 0)\). While the calculation is likely to be tedious, it seems possible that the Doi-Peliti approach could also work on some generalization of the system we considered in Sec. 9 like one that involves many autocatalytic, birth, and death reactions.

Another obvious objection to the Doi-Peliti approach is that it is not entirely mathematically rigorous: in rederiving Jahnke and Huisinga’s result, we freely swapped many improper integrals, frequently utilized the integral representation of the Dirac delta function, and so on. But we did get answers, and the method is likely to yield answers for problems that other methods cannot currently solve. If nothing else, the Doi-Peliti approach can be used as a tool to generate answers, which can be justified as rigorously correct using some other method (e.g. by showing that they solve the CME directly).

While we did not resort to approximations in this paper, it is worth noting that utilizing Doi-Peliti path integrals enables the use of powerful perturbative and asymptotic expansions. For most systems of interest in mathematical biology (e.g. gene networks with many species and interactions), this is the way in which the Doi-Peliti approach can be practically applied. See Weber and Frey [74], and Assaf and Meerson [20], for recent reviews discussing approximation techniques related to path integral descriptions of the CME.

The Doi-Peliti path integral is just one example of a stochastic path integral [74, 77]. The Onsager-Machlup [78, 79, 80, 81] and Martin-Siggia-Rose-Janssen-De Dominicis [82, 83, 84, 85, 81] path integrals are two other examples, which offer an alternative to the Fokker-Planck
equation in the same way the Doi-Peliti path integral is an alternative to the CME. While exact computations of these path integrals are also tedious, they are just as mechanical—one can ‘turn the crank’ and generate answer, without relying on (for example) a priori knowledge of special functions to solve differential equations [86, 75].

11 Conclusion

We rederived Jahnke and Huisinga’s classic result on monomolecular reaction systems using the Doi-Peliti coherent state path integral approach, which reduces solving the CME to the computation of many integrals. In addition to deriving the explicit form of the transition probability and moments for monomolecular reaction systems, we also presented the exact time-dependent solution to a problem involving an autocatalytic reaction that was beyond the scope of Jahnke and Huisinga’s method. We hope that our calculation, as well as our detailed description of the Doi-Peliti formalism, helps make the Doi-Peliti method more accessible to mathematical biologists studying the CME.

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