Spectral theory of metastability and extinction in birth-death systems

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We suggest a general spectral method for calculating statistics of multi-step birth-death processes and chemical reactions of the type $mA \rightarrow nA$ ($m$ and $n$ are positive integers) which possess an absorbing state. The method employs the generating-function formalism in conjunction with the Sturm-Liouville theory of linear differential operators. It yields accurate results for the extinction statistics and for the quasi-stationary probability distribution, including large deviations, of the metastable state. The power of the method is demonstrated on the example of binary annihilation and triple branching reactions $2A \rightarrow \emptyset$, $A \rightarrow 3A$, representative of the rather general class of dissociation-recombination reactions.

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Since the pioneering works of Delbrück [1], Bartholomay [2] and McQuarrie [3], kinetics of systems of birth-death type, containing a large but finite number of agents (such as molecules, bacteria, cells, animals or even humans), have attracted much attention in different areas of science and become a paradigm of theory of stochastic processes [4, 5]. Birth-death models are extensively discussed in chemistry, astrochemistry, epidemiology, population biology, cell biochemistry, etc. They are also well known in non-equilibrium physics, and can be viewed in the context of reaction-limited kinetics on a lattice, as opposed to more extensively studied diffusion-limited kinetics [6]. While the behavior of the average number of particles in such systems may be describable, at not too long times, by (mean-field) rate equations, fluctuations may lead to important quantitative or even qualitative differences. This necessitates using the more general master equation which deals with the probability of having a certain number of particles of each type at time $t$. The master equation is rarely solvable analytically, and various approximations, often uncontrolled, are in use [4, 5], such as the Fokker-Planck equation which may suffice unless one has to deal with large deviations or extinction phenomena [7, 8, 9]. Not much is known beyond the Fokker-Planck description, though in particular cases the statistics were determined by using approximations in the master equation [10] or, alternatively, by introducing a generating function [11, 12, 13], see below, and developing different approximations in the equation describing its evolution [14, 15, 16].

In this work we advance the generating function technique by marrying it with the Sturm-Liouville theory of linear differential operators. This yields a general and robust spectral formalism, capable of providing accurate, and often analytical, results for extreme statistics in a variety of (not necessarily single-step) birth-death systems and chemical reactions. We demonstrate the power of our method by a simple reaction of binary annihilation and triple branching. An example of such a reaction is recombination of two atoms $A$ and dissociation of the molecule $A_2$: $A + A \rightarrow A_2$, and $A_2 + A \rightarrow 3A$, assuming that the $A_2$ molecules are always at hand [11]. For $H$ or $N$ atoms this reaction occurs at high temperatures [17]. We calculate the extinction probability as a function of time, the mean time to extinction and the complete quasi-stationary probability distribution of the long-lived metastable state, intrinsic to this problem.

Rate equation, master equation, generating function and spectral theory. Consider the binary annihilation and triple branching reactions $2A \rightarrow \emptyset$, and $A \rightarrow 3A$ where $\mu, \lambda > 0$ are rate constants. The rate equation (or the mean field theory) of this simple system, $dn/ dt = 2\lambda n - \mu n^2$, describes a nontrivial attracting steady state $n_* = 2\lambda/\mu$, where $\lambda = \mu/\mu$. Fluctuations, caused by discreteness of particles, invalidate this mean-field result owing to the existence of the absorbing state $n = 0$: a state from which there is a zero probability of exiting. At $\Omega \gg 1$, however, a long-lived (and therefore quasi-stationary) fluctuating metastable state is observed, once the initial population is not too sparse. The statistics of the quasi-stationary state and of the extinction times are the subjects of our interest here.

To account for discreteness of particles, we assume that the evolution of the probability $P_n(t)$ to find $n$ particles at time $t$ is described, for $n > 1$, by the master equation

$$\frac{d}{dt} P_n(t) = \mu \left[(n+2)(n+1)P_{n+2}(t) - n(n-1)P_n(t)\right] + \lambda [(n-2)P_{n-2}(t) - nP_n(t)].$$

(1)

Let us introduce the generating function $G(x, t)$

$$G(x, t) = \sum_{n=0}^{\infty} x^n P_n(t),$$

(2)

where $x$ is an auxiliary variable. $G(x, t)$ encodes all the probabilities:

$$P_n(t) = \frac{1}{n!} \frac{\partial^n G(x, t)}{\partial x^n} \bigg|_{x=0}.$$  

(3)

Obviously, $G(x = 1, t) = 1$. Equations (11) and (12) yield a partial differential equation (PDE) for $G(x, t)$:

$$\frac{\partial G}{\partial t} = \mu \left(1 - x^2\right) \frac{\partial^2 G}{\partial x^2} + \lambda x(x^2 - 1) \frac{\partial G}{\partial x}.$$  

(4)
As the reaction we are dealing with conserves parity, 
\( G(x, t) \) can be written as

\[
G(x, t) = c_1 G_{\text{even}}(x, t) + c_2 G_{\text{odd}}(x, t),
\]

where \( c_1 = \sum_{0}^{\infty} P_{2m}(t = 0) \), and \( c_2 = 1 - c_1 \). Therefore, 
\( G_{\text{even}}(x = \pm t, t) = 1 \) and \( G_{\text{odd}}(x = \pm t, t) = 1 \). The steady state solution of Eq. (4) is

\[
G_{st}(x, t) = c_1 + c_2 \frac{erfi(\sqrt{\Omega}x)}{erfi(\sqrt{\Omega})},
\]

where \( erfi(x) = (2/\sqrt{\pi}) \int_{0}^{x} e^{t^{2}} dt \). Let the number of particles at \( t = 0 \) be even: \( n_0 = 2k_0 \), where \( k_0 \) is integer. In this case the parity conservation yields \( c_1 = 1 \) and \( c_2 = 0 \), so \( G_{st}(x) = 1 \), and the only true steady state is the empty state: \( P_0 = 1 \), while the rest of \( P_n \) are zero \[20\].

To see how the population of \( n_0 = 2k_0 \) particles at \( t = 0 \) becomes extinct, we introduce a new function \( g(x, t) = G(x, t) - G_{st}(x) = G(x, t) - 1 \) which obeys Eq. (4) with homogenous boundary conditions \( g(x = \pm 1, t) = 0 \). Substituting \( g(x, t) = e^{-\gamma t} \varphi(x) \), we obtain

\[
(1 - x^2)\varphi''(x) + 2\Omega x(x^2 - 1)\varphi'(x) + 2E\varphi(x) = 0, \tag{7}
\]

where \( E = \gamma/\mu \). Rewriting this ordinary differential equation in a self-adjoint form,

\[
\left[\varphi'(x)\exp(-\Omega x^2)\right]' + E w(x)\varphi(x) = 0, \tag{8}
\]

with the weight function \( w(x) = 2\exp(-\Omega x^2)(1 - x^2)^{-1} \), we arrive at a standard eigenvalue problem of the Sturm-Liouville theory \[21\]. Once we have found the complete set of orthogonal eigenfunctions \( \varphi_k(x) \) (which are all even), and the real eigenvalues \( E_k \), \( k = 1, 2, \ldots \), we can solve the time-dependent problem:

\[
G(x, t) = 1 + \infty \sum_{k=1}^{\infty} a_k \varphi_k(x)e^{-\mu E_k t}, \tag{9}
\]

where

\[
a_k = \int_{0}^{1} G(x, t = 0) - 1 |\varphi_k(x)| w(x) dx \int_{0}^{1} \varphi_k(x) w(x) dx, \tag{10}
\]

and \( G(x, t = 0) = x^{2k_0} \).

As all \( E_k \) > 0, Eq. (9) describes decay of initially populated states \( k = 1, 2, \ldots \), and the system approaches the empty state \( G(x, t \to \infty) = 1 \). We are interested in the case of \( \Omega \gg 1 \), where the metastable state is expected to be long-lived. Elgart and Kamenev \[22\] showed that the eigenvalues \( E_2, E_3, \ldots \) scale like \( O(\Omega) \gg 1 \). In contrast to these, the “ground state” eigenvalue \( E_1 \) is exponentially small, as will be proved a posteriori. We will be interested in sufficiently long times \( \mu \Omega t = \lambda t \gg 1 \), when the contribution from the “excited” states to \( G(x, t) \) becomes negligible, and we can write

\[
G(x, t) = 1 + a_1 \varphi_1(x) e^{-\mu E_1 t}. \tag{11}
\]

Let us proceed to the ground state calculations.

**Ground state calculations.** As \( \varphi_1(x) \equiv \varphi(x) \) is an even function, it suffices to consider the interval \( 0 \leq x \leq 1 \). We will employ the strong inequality \( \Omega \gg 1 \) and find the (very small) eigenvalue \( E_1 \) and the corresponding eigenfunction of Eq. (7) by a matched asymptotic expansion, see e.g. Ref. \[23\]. In most of the region \( 0 \leq x < 1 \) (the bulk) we can treat the last term in Eq. (7) perturbatively. In the zero order we put \( E_1 = 0 \) and arrive at the steady state equation \( \varphi''_b(x) - 2\Omega x \varphi'_b(x) = 0 \), whose even solution is \( \varphi_b^{(0)} = 1 \). Now we put \( \varphi_b(x) = 1 + \delta \varphi_b(x) \), where \( \delta \varphi_b(x) \ll 1 \), and obtain in the first order

\[
\delta \varphi'_b(x) - 2\Omega x \delta \varphi_b(x) = -2E_1(1 - x^2)^{-1}. \tag{12}
\]

The solution for \( \varphi_b(x) \) takes the form:

\[
\varphi_b(x) = 1 - 2E_1 \int_{0}^{x} e^{\Omega x^2} ds \int_{0}^{s} e^{-\Omega r^2} 1 - r^2 dr. \tag{13}
\]

As \( \Omega \gg 1 \), we can omit the \( r^2 \) term in the denominator of the inner integral in Eq. (13) (this omission is illegitimate too close to \( x = 1 \), but the bulk solution is invalid there anyway, see below). We obtain

\[
\varphi_b(x) \simeq 1 - 2E_1 \int_{0}^{x} e^{\Omega x^2} ds \int_{0}^{s} e^{-\Omega r^2} 1 - r^2 dr
\]

\[
= 1 - E_1 x^2 2F_2 \left(1, 1; \frac{3}{2}; \Omega x^2 \right), \tag{14}
\]

where \( 2F_2(a_1, a_2; b_1, b_2; x) \) is the generalized hypergeometric function \[21\], while \( E_1 \) is yet unknown. It is easy to check that the bulk solution is valid \( \delta \varphi_b(x) \ll 1 \) as long as \( 1 - x \ll 1/\Omega \).

In the boundary layer \( 1 - x \ll 1 \) we can again disregard, at \( \Omega \gg 1 \), the (exponentially small) last term in Eq. (7). The resulting equation is again \( \varphi''_b(x) - 2\Omega x \varphi'_b(x) = 0 \), its non-trivial solution, obeying the boundary condition at \( x = 1 \), is

\[
\varphi_l(x) = C \int_{x}^{1} e^{\Omega s^2} ds \simeq C e^{\Omega/2N} \left[1 - e^{-\Omega(1 - x^2)}\right], \tag{15}
\]

where \( C \) is a yet unknown constant.

Now we demand that, in the common region \( 1/\Omega \ll 1 - x \ll 1 \), the proper asymptote of the bulk solution \[14\], obtained by moving to infinity the upper limit in the inner integral of Eq. (14):

\[
\varphi_b(x) \simeq 1 - \frac{\sqrt{\pi} E_1}{\sqrt{\Omega}} \int_{0}^{x} e^{\Omega s^2} ds \simeq 1 - \frac{\sqrt{\pi} E_1}{2\Omega^{3/2}} e^{\Omega x^2}, \tag{16}
\]
that the term appearing in the nominator of Eq. (10), we notice that the main contributions come from the bulk region $1 - x^2 \gg 1/\Omega$, and the standard deviation $\sigma = 2\Omega e^{-\Omega}$.\textsuperscript{16} As expected, the lowest eigenvalue $E_1$ is exponentially small in $\Omega$. The respective eigenfunction is

$$E_1 = \frac{2\Omega^{3/2}}{\sqrt{\pi}} e^{-\Omega} \quad \text{and} \quad C = 2\Omega e^{-\Omega}. \quad (17)$$

Now we use Eq. (10) to calculate the coefficient $a_1$ entering Eq. (11). While evaluating the integrals, we notice that the main contributions come from the bulk region $1 - x^2 \gg 1/\Omega$, and it suffices to take the eigenfunction $\varphi_0(x)$ in the zeroth order, that is $\varphi_0^{(0)}(x) \approx 1$. Evaluating the integral in the nominator of Eq. (10), we notice that, the term $x^{2k_0}$ under the integral is negligible compared to 1. As a result, the integrals in the nominator and denominator become identical up to a minus sign. Therefore, $a_1 \approx -1$ which completes our solution (11).

Statistics of the quasi-stationary state. We start this part with calculating the average number of particles $\bar{n}$ and the standard deviation $\sigma$ at intermediate times $\Omega^{-1} \ll \mu t \ll E_1^{-1}$. Using Eq. (10), we obtain

$$\bar{n} = \partial_x G |_{x=1} = 2\Omega, \quad (19)$$

which coincides with the mean field result. Furthermore,

$$\sigma^2 = \bar{n}^2 - \bar{n}^2 = \left[ \partial_{xx} G + \partial_x G - (\partial_x G)^2 \right] |_{x=1} = 4\Omega. \quad (20)$$

where we have used for $\varphi(x)$ its boundary layer asymptote $\varphi(x)$ from Eq. (12). One can see that, at intermediate times $\Omega^{-1} \ll \mu t \ll E_1^{-1}$, the system stays in the (weakly fluctuating) quasi-stationary state. What is the complete probability distribution $P_n(t)$ of the quasi-stationary state at these times? For $n = 0$ we obtain

$$P_0(t) = G(x = 0, t) = 1 - e^{-\mu E_1 t} \quad (21)$$

which, at $\mu E_1 t \ll 1$, is very small. For (even) nonzero values of $n$, Eqs. (9) and (11) yield

$$P_n(t) = \frac{2E_1(4\Omega)^{n/2-1}(n/2-1)!}{n!} e^{-\mu E_1 t}. \quad (22)$$

For $n \gg 1$ we can use Stirling’s formula and obtain

$$P_n(t) \approx \frac{E_1}{\sqrt{2\pi n\Omega}} e^{-\frac{\bar{n}}{2} - n \ln \frac{\bar{n}}{n\Omega} - \mu E_1 t}. \quad (23)$$

Notably, all of the probabilities $P_n(t)$ ($n > 0$) decay with time, while $P_0(t)$ grows. One can check that the most probable state coincides with $\bar{n} = 2\Omega$. In the vicinity of $n = \bar{n}$, $P_n(t)$ from Eq. (22) can be approximated by a normal distribution with the mean $\bar{n}$ and standard deviation $\sigma$, given by Eqs. (10) and (20), respectively. The tails of the true distribution, however, are strongly non-Gaussian. A comparison between our analytic result (22), the large-$n$ approximation (23), and the normal distribution is shown in Fig. 1. One can see that Eq. (22) is very accurate, whereas the gaussian approximation strongly overpopulates the low-$n$ tail and underpopulates the high-$n$ tail.

![FIG. 1: (Color online) The natural logarithms of the probability distribution (22) (the blue solid line), of its large-$n$ asymptotics (23) (the green dotted line), and of the normal distribution with $\bar{n}$ and $\sigma$ from Eqs. (10) and (20) (the red dashed line), for $\Omega = 10$ and $\mu E_1 t \ll 1$.](image)

Figure 2 compares our analytic result (22) with a numerical solution of the (truncated) master equation (11) with $\langle d/dt \rangle P_n(t)$ replaced by zeros and $P_0 = 0$. The two curves are almost indistinguishable for $\Omega = 10$. In fact, rapid agreement is observed already for $\Omega = O(1)$, and it rapidly improves further as $\Omega$ increases.

![FIG. 2: (Color online) The natural logarithm of the probability distribution (22) at $\mu E_1 t \ll 1$. The blue solid line: a numerical solution of the master equation (11), see text. The parameters are $\Omega = 10$, $n_0 = 2k_0 = 40$.](image)
Extinction time statistics. The quantity $P_0(t)$ is the probability of extinction at time $t$. The extinction probability density is $p(t) = dP_0(t)/dt$. Using Eq. (23), we obtain an exponential distribution:

$$p(t) \simeq \mu E_1 e^{-\mu E_1 t} \text{ at } \lambda t \gg 1. \quad (24)$$

The average time to extinction, $\tau = \int_0^\infty tp(t) dt \simeq (\mu E_1)^{-1}$, is exponentially large, at $\Omega \gg 1$, as expected. Figure 3 compares the analytical result (23) for $P_0(t)$ with $G(0,t)$ found by solving Eq. (1) numerically with the boundary conditions $G(\pm 1,t) = 1$ and the initial condition $G(x, t = 0) = x^{-2k_0}$. The inset compares the analytical and numerical ground state eigenvalues, and good agreement is observed.

Final comments. The spectral formalism yields accurate extinction time statistics and a complete quasi-stationary probability distribution of the metastable state for a wide class of birth-death processes which possess an absorbing state and are describable by a master equation. In this formalism, the problem of computing these statistics is reduced to a problem (familiar to every physicist) of finding a ground-state eigenfunction and eigenvalue of a linear differential operator. We have demonstrated the formalism by an example of binary annihilation and triple branching, but the formalism is general and can be used for a variety of kinetics. In most interesting cases of long-lived metastable states, a large parameter (the average number of particles in the metastable state) is always present in the problem. This paves the way to a perturbative treatment, like in the example we have considered.

The spectral formalism should be also efficient when the absorbing state is at infinity, rather than at zero. For systems of this type the rate equation yields a stable non-empty steady state, but an account of fluctuations brings about an unlimited population growth, see e.g. Ref. 3. In that case the ground-state eigenvalue is expected to be negative. Finally, the use of spectral formalism is not at all limited to systems possessing an absorbing state. 17.

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