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Residence time densities for non-Markovian systems. (II). The N-state system

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Abstract

In the preceding paper (Boguñá et al., Physica A 282 (2000) 475), we developed formalism to calculate a probability density for the cumulative time spent in one out of a two-state non-Markovian system of the form $S_1 \rightleftarrows S_2$ when the system is observed continuously for a time T. The asymptotic form for the probability density was shown to be Gaussian. In this paper we indicate how to reduce any reacting nearest-neighbor system, i.e., $S_1 \rightleftarrows S_2 \rightleftarrows \cdots \rightleftarrows S_N$ to an equivalent two-state system. This also shows that the probability density for the cumulative residence time in a single state is asymptotic to a Gaussian. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

Dynamical systems undergoing random transitions among their internal states are ubiquitous in chemistry and physics [1,2]. The simplest illustrative example of this type of system is the isomerization reaction, in which a molecule can exist in either of two states, transitions between them being described by the kinetic scheme

$$S_1 \underset{k_2}{\overset{k_1}{\rightleftarrows}} S_2 \,, \tag{1.1}$$

where k_1 and k_2 are rate constants. This is equivalent to saying that the probability densities for the duration of a single sojourn in each of the states are exponential, i.e., $\psi_i(t) = k_i\,\mathrm{e}^{-k_i t}$, $i = 1, 2$. The kinetics of such simple reactions are generally analyzed by finding the probability, at time t, for the molecule to be in one state or the other. In chemical terms this is equivalent to calculating the concentrations of the two species.

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In mathematical terms it is an example of a Markov process, the state probabilities being functionals of the random trajectories. The terminology “random trajectory” is defined to be the record of the succession of states of the system for time T. Although a knowledge of the state probabilities or concentrations for the system in Eq. (1.1) suffices for most purposes for the chemist, other random functionals can also be useful in applications. One example of these is the cumulative residence time. By this we mean the total amount of time τ_i spent in state i (S_i), out of the total observation time T. Our interest in this functional was stimulated by an analysis of recently developed experimental techniques generally referred to as single-molecule spectroscopy (SMS) [3–8]. In the case of the first-order isomerization reaction of Eq. (1.1) the probability densities for the random variables τ_i conditioned on the observation time T are known exactly [9].

An obvious generalization replaces the Markov process in Eq. (1.1) by a non-Markovian one, in effect allowing the probability densities for a single sojourn, the $\psi_i(t)$, to differ from single exponentials. When the $\psi_i(t)$ are single exponentials the state probabilities can be found by solving a set of two linear differential equations. When they are not, the differential equations for the state probabilities must be replaced by integral equations solvable in terms of Laplace transforms. A general approach allowing one to evaluate the cumulative residence time for such systems was first derived by Takács [10].

Of course, chemical reactions generally take much more varied forms than that shown in Eq. (1.1). One might ask whether there are any universal properties that might be invoked to calculate the probability density of the cumulative residence time τ. At values of T for which the system can be expected to pass through the target state many times, the central-limit theorem can be applied, allowing the inference that at sufficiently long times the cumulative sojourn time in any state has a Gaussian distribution. That such is the case has been demonstrated by a number of authors who analyzed specific reaction schemes in the context of SMS experiments, cf., for example [11,12], and a recent related investigation [13].

In the preceding paper [14], we generalized our analysis of the isomerization reaction to allow for the two states in Eq. (1.1) to be non-Markovian. It was shown that in this class of models it is only possible to find the Fourier–Laplace transforms of the desired probability densities rather than their forms in the time domain. These results were shown to lead to an asymptotic Gaussian form for the probability density of the cumulative sojourn time in either of the states. The parameters of the Gaussians are expressed in terms of the first two moments of the duration of a single sojourn in each of the states.

Isomerization reactions can obviously be more complicated than the simple reaction in Eq. (1.1). In the present paper we consider the kinetics associated with a more general set of reactions which we term “nearest-neighbor” reactions, which have the form

$$S_1 \rightleftarrows S_2 \rightleftarrows S_3 \rightleftarrows \cdots \rightleftarrows S_N \tag{1.2}$$

in which the residence-time (by which is meant the time spent in a single sojourn in any one of the states) densities can either have a negative exponential, or a more general non-Markovian form, which might, for example, be a consequence of the existence of substates for a given state. The important feature of the class of reactions in Eq. (1.2) is that it can be regarded as being one dimensional, which simplifies the analysis to a considerable extent. The results to be derived here are exact for non-Markovian systems. In Ref. [15] we developed a theory for a network of Markovian elements that could be more general than Eq. (1.2).

In the present paper we show that if only the cumulative sojourn time in one of the states in Eq. (1.2) is of interest, one can always map the N-state non-Markovian system into a simpler two-state non-Markovian system. This allows us to use the theory in Ref. [14] to conclude that the asymptotic form of the probability density of the cumulative sojourn time is Gaussian.

2. The three-state system

In this section we demonstrate, by example, the reduction of a three-state system to an equivalent two-state system. By equivalence we mean that the probability density for residence time in the state of interest remains invariant under the transformation. The two-state formalism of Boguñá et al. [14] can then be applied to find the probability density for the cumulative time spent in any state, during an observation time T. The significance of such a reduction is that we can immediately infer that the long-time behavior of the probability density for the cumulative residence time in either one of the states is Gaussian, provided that the state is visited sufficiently often during the total observation time. It will be shown, in the following subsection, that the reaction scheme for a finite N-state nearest-neighbor system can be reduced to that of a two-state system by systematically applying the technique used to reduce the three-state system to a two-state system.

We begin by examining how the three-state non-Markovian system, which we represent schematically by

$$S_1 \underset{a_{21}(t)}{\overset{\psi_{12}(t)}{\rightleftarrows}} S_2 \underset{\psi_{32}(t)}{\overset{a_{23}(t)}{\rightleftarrows}} S_3 \tag{2.1}$$

can be converted to an equivalent two-state system. Notice that a different notation has been used for the sojourn time densities for transitions into and out of S_2 in the reaction in Eq. (2.1). This is done to emphasize the fact that $\psi_{12}(t)$ and $\psi_{32}(t)$ are genuine sojourn-time densities in the sense that they satisfy the normalization conditions

$$\int_0^\infty \psi_{i2}(t)\,\mathrm{d}t = 1, \quad i = 1,3\,. \tag{2.2}$$

In contrast, the $a_{2i}(t)$, $i = 1,3$ are to be interpreted as joint probability–probability densities. This means, for example, that $a_{23}(t)\,\mathrm{d}t$ is the joint probability that the time spent a single sojourn in state in S_2 is between t and $t + \mathrm{d}t$ and the immediately following transition is made to S_3. Consequently, the integral $\theta_i = \int_0^\infty a_{2i}(t)\,\mathrm{d}t$ is the probability that when the system leaves S_2 it moves to S_i, $i=1,3$. The two probabilities obviously satisfy $\theta_1 + \theta_3 = 1$.

Even in the relatively simple system of Eq. (2.1) there are two separate cases to be analyzed, depending on whether the state of specific interest is S_1 or S_2. In the first case S_2 and S_3 are to be combined into a composite state Γ, while in the second case the new composite state is comprised of S_1 and S_3.

2.1. $\Gamma = S_2 + S_3$

Consider first the case in which $\Gamma = S_2 + S_3$, which is to be transformed to an equivalent reaction scheme

$$S_1 \underset{\rho_{\Gamma 1}(t)}{\overset{\rho_{1\Gamma}(t)}{\rightleftarrows}} \Gamma\,, \tag{2.3}$$

where both $\rho_{1\Gamma}(t)$ and $\rho_{\Gamma 1}(t)$ are probability densities for their corresponding sojourn times. These are to be calculated in terms of the $\psi_{ij}(t)$ and $a_{2i}(t)$ that appear in Eq. (2.1). We will see that the relationship is most easily found in the Laplace transform domain. A comparison of Eqs. (2.1) and (2.3) shows that $\rho_{1\Gamma}(t) = \psi_{12}(t)$ so only the expression for $\rho_{\Gamma 1}(t)$ is needed to complete a calculation of the equivalent two-state system.

Recall that $\rho_{\Gamma 1}(t)$ can be regarded as the probability density for the system to leave the composite state Γ for the first time given that it entered Γ at $t=0$. This function can be found in terms of general formalism developed in Ref. [16], but we here analyze the problem by showing that it satisfies a convolution integral equation and is therefore solvable in terms of Laplace transforms.

The integral equation for $\rho_{\Gamma 1}(t)$ is derived by observing that either the jump from S_2 to S_1 is the first such transition, or the first transition takes the system to S_3. Hence, the probability density $\rho_{\Gamma 1}(t)$ in Eq. (2.3) can be written as a sum of two terms:

$$\rho_{\Gamma 1}(t) = a_{21}(t) + \int_0^t \rho_{\Gamma 1}(t-\xi)\,\mathrm{d}\xi \int_0^\xi a_{23}(\xi')\psi_{32}(\xi-\xi')\,\mathrm{d}\xi'\,. \tag{2.4}$$

The first term on the right-hand side accounts for a direct transition 2 → 1, while the second term accounts for an initial transition 2 → 3 which is necessarily followed by the transition 3 → 2 at which point the process is regenerated.

If we set

$$u(\xi) = \int_0^\xi a_{23}(\xi')\psi_{32}(\xi-\xi')\,\mathrm{d}\xi' \tag{2.5}$$

and take the Laplace transform of Eq. (2.4) we obtain the equality

$$\hat{\rho}_{\Gamma 1}(s) = \frac{\hat{a}_{21}(s)}{1-\hat{u}(s)} = \frac{\hat{a}_{21}(s)}{1-\hat{a}_{23}(s)\hat{\psi}_{32}(s)}\,. \tag{2.6}$$

Since $\hat{\psi}_{32}(0) = 1$, $\hat{a}_{21}(0) = \theta_1$, and $\hat{a}_{23}(0) = \theta_3$ it follows that $\hat{\rho}_{\Gamma 1}(0) = 1$. This shows that $\rho_{\Gamma 1}(t)$ is properly normalized. Moments of $\rho_{\Gamma 1}(t)$ can be generated exactly and can be expressed in terms of successive derivatives of Eq. (2.6) with the value of s set equal to zero.

As a simple example of this formalism we allow all of the reactions scheme to satisfy first-order kinetics by setting

$$\psi_{ij}(t) = k_{ij}\,\mathrm{e}^{-k_{ij}t}\,, \tag{2.7}$$

so that

$$a_{23}(t) = k_{23}\,\mathrm{e}^{-(k_{23}+k_{21})t}, \qquad a_{21}(t) = k_{21}\,\mathrm{e}^{-(k_{23}+k_{21})t}. \tag{2.8}$$

By an earlier remark $\rho_{1\Gamma}(t) = k_{12}\exp(-k_{12}t)$. On substituting the Laplace transforms of the functions in Eqs. (2.7) and (2.8) into Eq. (2.6) we find

$$\hat{\rho}_{\Gamma 1}(s) = \frac{k_{21}(s+k_{32})}{s^2 + s(k_{21}+k_{23}+k_{32}) + k_{21}k_{32}}\,. \tag{2.9}$$

An inversion of this expression shows that $\rho_{\Gamma 1}(t)$ is a linear combination of two exponentials. Even in this simplest of cases the two-state system has one non-Markovian component.

2.2. $\Gamma = S_1 + S_3$

The second case to be considered is one in which S_2 is the state whose occupancy properties are sought. This means that the two states S_1 and S_3 are now to be combined into a single state which we schematically indicate as

$$S_2 \underset{\rho_{\Gamma 2}(t)}{\overset{\rho_{2\Gamma}(t)}{\rightleftarrows}} \Gamma\,, \tag{2.10}$$

where now the composite state is $\Gamma = S_1 + S_3$. Now both $\rho_{2\Gamma}(t)$ and $\rho_{\Gamma 2}(t)$ are to be found. A comparison of Eqs. (2.1) and (2.10) allows us to obtain $\rho_{2\Gamma}(t)$ immediately as

$$\rho_{2\Gamma}(t) = a_{21}(t) + a_{23}(t)\,. \tag{2.11}$$

We next calculate the Laplace transform of $\rho_{\Gamma 2}(t)$. For this purpose assume that $t = 0$ corresponds to the beginning of a stay in S_2 and let $\rho_{2\Gamma 2}(t)$ be the probability density for the sojourn time in S_2 plus the immediately following sojourn time in Γ. That is

$$\rho_{2\Gamma 2}(t) = \int_0^t a_{23}(\xi)\psi_{32}(t-\xi)\,\mathrm{d}\xi + \int_0^t a_{21}(\xi)\psi_{12}(t-\xi)\,\mathrm{d}\xi\,. \tag{2.12}$$

But this sequence of two sojourns can be decomposed into a sum of the sojourn time in S_2 and a single one in Γ. That is,

$$\rho_{2\Gamma 2}(t) = \int_0^t \rho_{2\Gamma}(\xi)\rho_{\Gamma 2}(t-\xi)\,\mathrm{d}\xi \tag{2.13}$$

from which it follows that the transform of $\rho_{\Gamma 2}(t)$ is

$$\hat{\rho}_{\Gamma 2}(s) = \frac{\hat{\rho}_{2\Gamma 2}(s)}{\hat{\rho}_{2\Gamma}(s)} = \frac{\hat{a}_{21}(s)\hat{\psi}_{12}(s) + \hat{a}_{23}(s)\hat{\psi}_{32}(s)}{\hat{a}_{21}(s) + \hat{a}_{23}(s)}\,. \tag{2.14}$$

That $\rho_{\Gamma 2}(t)$ is properly normalized can be verified by setting $s = 0$ in its transform. The integrals can be evaluated explicitly when all of the probability densities for the sojourn time are exponential, and lead to the result that $\rho_{\Gamma 2}(t)$ is a linear combination of two exponentials, just as in the case defined by Eq. (2.3).

3. The N-state system

A solution for the equivalent reaction for the nearest-neighbor system shown in Eq. (2.2) can be found in the general case by systematically exploiting the technique developed in the context of the three-state system. In this treatment the probability densities for the transition $i \to j$ are: $\psi_{12}(t)$ for the transition $S_1 \to S_2$ and $\psi_{N,N-1}(t)$ for $S_N \to S_{N-1}$. The remaining densities will be denoted by $a_{ij}(t)$ so that, for example, the case of a system with four possible states will be written as

$$S_1 \underset{a_{21}(t)}{\overset{\psi_{12}(t)}{\rightleftarrows}} S_2 \underset{a_{32}(t)}{\overset{a_{23}(t)}{\rightleftarrows}} S_3 \underset{\psi_{43}(t)}{\overset{a_{34}(t)}{\rightleftarrows}} S_4 \,. \tag{3.1}$$

In the last section we demonstrated that a three-state nearest-neighbor model is always reducible to an equivalent two-state model. By extension we reduce the four-state model in Eq. (3.1) to an equivalent two-state model. By induction it will follow that an N-state system can always be reduced to an equivalent two-state model.

This case requires us to convert the four-state system to the equivalent three-state system

$$S_1 \underset{a_{21}(t)}{\overset{\psi_{12}(t)}{\rightleftarrows}} S_2 \underset{\rho_{\Gamma 2}(t)}{\overset{\rho_{2\Gamma}(t)}{\rightleftarrows}} \Gamma \,, \tag{3.2}$$

where $\Gamma = S_3 + S_4$. By a comparison of Eqs. (3.1) and (3.2) one can immediately infer that $\rho_{2\Gamma}(t) = a_{23}(t)$. Thus, there remains only the job of finding the probability density $\rho_{\Gamma 2}(t)$. The significance of the reduction indicated in Eqs. (3.1) and (3.2) is that it provides a blueprint for systematically reducing an arbitrary N-state nearest-neighbor system to an equivalent $N-1$-state system. Observe first that $\rho_{\Gamma 2}(t)$ is a properly normalized probability density for the first-passage time for a transition from Γ to S_2 given that the system entered Γ at $t = 0$. Hence, following the argument used to derive Eq. (2.6), we find

$$\hat{\rho}_{\Gamma 2}(s) = \frac{\hat{a}_{32}(s)}{1 - \hat{a}_{34}(s)\hat{\psi}_{43}(s)} \,. \tag{3.3}$$

In reducing the N-state system to the two-state system one combines the outermost two states into a single state as we have done for the four-state system. Although we have carried out the analysis for a system in which S_1 is an end state of the reaction chain, no further extension of the analysis is required when S_1 is in the middle of the chain since the induction step can be used to reduce either of the two end sites until the reaction scheme $\Gamma \rightleftarrows S_1 \rightleftarrows \Gamma'$ is reached, at which time the analysis related to Eq. (2.10) can be invoked.

The preceding analysis can be systematized and leads to a representation of the Laplace transform in terms as a sum of two continued fractions. Let the number of states defining the system be N, and define the functions

$$a_n(t) = a_{n,n-1}(t) + a_{n,n+1}(t), \qquad \hat{b}_n(s) = \hat{a}_{n,n+1}(s)\hat{a}_{n+1,n}(s)\,, \tag{3.4}$$

where the functions on the right-hand side of the definition of $a_n(t)$ are analogous to the ones defined in Eq. (2.1). Suppose that the state of interest is S_n where $1 \leqslant n \leqslant N$. Then the Laplace transform of the probability density for a single sojourn time in the set of states complementary to n can be expressed as

$$\hat{\psi}_{\Gamma,n}(s) = \frac{1}{\hat{a}_n(s)}[U_{n,N-1}(s) + U_{n-1,1}(s)]\,, \tag{3.5}$$

where the $U's$ are the continued fractions

$$U_{n,N-1}(s) = \cfrac{\hat{b}_n(s)}{1 - \cfrac{\hat{b}_{n+1}(s)}{1 - \cfrac{\hat{b}_{n+2}(s)}{\ddots\, 1 - \hat{b}_{N-1}(s)}}}, \qquad U_{n-1,1}(s) = \cfrac{\hat{b}_{n-1}(s)}{1 - \cfrac{\hat{b}_{n-2}(s)}{1 - \cfrac{\hat{b}_{n-3}(s)}{\ddots\, 1 - \hat{b}_1(s)}}}\,. \tag{3.6}$$

Application of this formalism to the three-state system leads to the results derived earlier.

Since Eq. (3.5) is a Laplace transform it allows one to calculate the mean time spent in the composite state Γ. A first step in this procedure is to define the probability that the system moves from S_i to $S_{i\pm1}$. in a single step. Further, we define the probability that a random walker in S_i moves to $i+1$, $\theta_{i,i+1}$ which is given by

$$\theta_{i,i+1} = \int_0^\infty a_{i,i+1}(t)\,\mathrm{d}t\,. \tag{3.7}$$

The objective of the calculation is to find a small-s expansion of the term $U_{n,N-1}(s) + U_{n-1,1}(s)$. For mathematical brevity we define the functions

$$\Omega_{ni} = \theta_{n,n+1}\theta_{n+1,n+2}\cdots\theta_{i-1,i} \tag{3.8}$$

which is the probability for moving from S_n to S_i in a series of consecutive steps. We see first that the expansion of $\hat{a}_i(s)$, to lowest order near $s = 0$ is

$$\hat{a}_{i,i\pm1}(s) = \theta_{i,i\pm1} - \tau_{i,i\pm1}s + \cdots \tag{3.9}$$

in which $\tau_{i,i\pm1}$ is a mean time for the transition $i \to i\pm1$. The expansion of $U_{n,N-1}(s) + U_{n-1,1}(s)$ to the term linear in s is

$$U_{n,N-1}(s) + U_{n-1,1}(s) \approx 1 - \left\{ \langle t_n \rangle + \sum_{i \neq n} \frac{\Omega_{ni}}{\Omega_{in}} \langle t_i \rangle \right\} s\,, \tag{3.10}$$

where we have made use of the identities

$$\theta_{n,n+1} + \theta_{n+1,n} = 1, \qquad \tau_{n,n-1} + \tau_{n,n+1} = \langle t_n \rangle\,. \tag{3.11}$$

After some easy algebra we obtain the identity

$$\langle t_\Gamma \rangle = \sum_{i \neq n} \frac{\Omega_{ni}}{\Omega_{in}} \langle t_i \rangle \, . \tag{3.12}$$

One can use the same formalism to find expressions for higher-order moments when these are finite.

4. Discussion

In this paper we have shown how to systematically derive two-state non-Markovian systems equivalent to the class of nearest-neighbor systems in Eq. (1.2). This enables one to invoke all of the results known for two-state systems [14]. In fact, when there is only a single state being observed, any finite system of reactions can be reduced to an equivalent two-state non-Markovian system, but, with few exceptions the result of such a reduction is expressed in terms of determinants and therefore awkward to work with. The only universal property that appears to exist for such non-Markovian systems is that at sufficiently long observation times the probability density for the cumulative residence time becomes Gaussian. However, since we obtain results for probability densities that are given in the form of Laplace transforms it is possible to find exact expressions for the associated moments. These can be used to calculate corrections to the Gaussian density. We expect these to decrease in terms of powers of $T^{-1/2}$ by analogy with central-limit law calculations in which corrections decrease as $n^{-1/2}$ [17], where n is the number of random variables whose sum approaches the Gaussian.

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