Simplified approach for calculating moments of action for linear reaction-diffusion equations

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The mean action time is the mean of a probability density function that can be interpreted as a critical time, which is a finite estimate of the time taken for the transient solution of a reaction-diffusion equation to effectively reach steady state. For high-variance distributions, the mean action time underapproximates the critical time since it neglects to account for the spread about the mean. We can improve our estimate of the critical time by calculating the higher moments of the probability density function, called the moments of action, which provide additional information regarding the spread about the mean. Existing methods for calculating the nth moment of action require the solution of n nonhomogeneous boundary value problems which can be difficult and tedious to solve exactly. Here we present a simplified approach using Laplace transforms which allows us to calculate the nth moment of action without solving this family of boundary value problems and also without solving for the transient solution of the underlying reaction-diffusion problem. We demonstrate the generality of our method by calculating exact expressions for the moments of action for three problems from the biophysics literature. While the first problem we consider can be solved using existing methods, the second problem, which is readily solved using our approach, is intractable using previous techniques. The third problem illustrates how the Laplace transform approach can be used to study coupled linear reaction-diffusion equations.

I. INTRODUCTION

The transient solution of a reaction-diffusion process takes an infinitely long time to asymptote to the corresponding steady solution. To determine whether it is appropriate to work with such steady state solutions, we must decide whether a sufficient amount of time has passed so that the transient solution has effectively reached steady state. Several definitions of critical time have been proposed for this purpose [1–7]. One such definition, the mean action time (MAT) [3–8], also known as the local accumulation time [9–12], is the mean of a probability density function (PDF) associated with the linear reaction-diffusion problem of interest. The MAT is an objective definition of the critical time which can be determined without solving for the transient solution of the reaction-diffusion equation. For high-variance PDFs, the MAT underapproximates the critical time since it neglects to account for the spread about the mean [5,6,13]. To address this limitation we can calculate the higher moments of the PDF, also known as the moments of action [6]. We anticipate that an improved estimate of the critical time for high-variance PDFs would be the MAT plus one standard deviation of the PDF [6,13,14]. Additional higher moments of the PDF, such as the third and fourth moments, are related to the skew and kurtosis [15], which provide further information about the shape of the PDF.

Existing techniques for calculating the moments of action can be tedious to implement. Solving for the nth moment of action using existing techniques requires the solution of n nonhomogeneous boundary value problems that become increasingly complicated as n increases. This approach is not always possible for practical problems. In this manuscript we show how to calculate the MAT and the moments of action using Laplace transforms. This technique does not depend on solving

for the transient solution of the underlying linear reaction-diffusion equation and it allows us to determine the MAT and the moments of action for a much wider class of problems. We outline the Laplace transform method and apply it to three problems from the biophysics literature. The first problem we consider confirms that the Laplace transform method recovers previously established results more easily, while the second problem we consider illustrates how the approach can be used to find the moments of action for a reaction-diffusion problem that is intractable using previous techniques. We conclude with a third example demonstrating how the approach can be used to study coupled linear reaction-diffusion problems.

By way of illustration, we consider a general linear reaction-diffusion equation

$$\frac{\partial c}{\partial t} = \nabla \cdot (D\nabla c - vc) - k_1 c + k_2, \tag{1}$$

where D is the diffusivity, v is the advective velocity, and k_1 and k_2 are rate constants. Such reaction-diffusion equations are widely used in the biophysics literature, including the study of morphogen gradients [10,11], the distribution of nutrients in cells [16,17], and collective cell migration [18,19]. Furthermore, such reaction-diffusion equations are routinely used in other areas of physics, applied mathematics, and engineering [13,20]. To illustrate our approach, we define

$$F(t;\mathbf{x}) = 1 - \frac{c(\mathbf{x},t) - c_\infty(\mathbf{x})}{c_0(\mathbf{x}) - c_\infty(\mathbf{x})}, \tag{2}$$

where $c_0(\mathbf{x}) = c(\mathbf{x},0)$ is the initial condition and $c_\infty(\mathbf{x}) = \lim_{t\to\infty} c(\mathbf{x},t)$ is the steady solution of Eq. (1). For a wide class of problems, $F(t;\mathbf{x})$ increases monotonically from $F = 0$ at $t = 0$, to $F \to 1^-$ as $t \to \infty$ [5–7]. We

can therefore interpret $F(t;\mathbf{x})$ as a cumulative distribution function which measures the progress of $c(\mathbf{x},t)$ towards $c_\infty(\mathbf{x})$. The corresponding PDF is

$$f(t;\mathbf{x}) = -\frac{\partial}{\partial t}\left[\frac{c(\mathbf{x},t) - c_\infty(\mathbf{x})}{c_0(\mathbf{x}) - c_\infty(\mathbf{x})}\right], \qquad (3)$$

with which we can associate a mean, or the MAT [3–5,8],

$$T(\mathbf{x}) = \int_0^\infty t\, f(t;\mathbf{x})\,dt,$$
$$= \int_0^\infty \frac{c(\mathbf{x},t) - c_\infty(\mathbf{x})}{c_0(\mathbf{x}) - c_\infty(\mathbf{x})}\,dt, \qquad (4)$$

where we have used the fact that $c(\mathbf{x},t) - c_\infty(\mathbf{x}) = o(t^{-1})$ as $t \to \infty$. This condition is always satisfied for linear reaction-diffusion processes, since $c(\mathbf{x},t)$ approaches $c_\infty(\mathbf{x})$ exponentially fast as $t \to \infty$ [21].

To find the moments of action, we begin by defining the nth moment [15]:

$$S_n(\mathbf{x}) = \int_0^\infty t^n \frac{\partial c}{\partial t}\,dt, \qquad (5)$$
$$= -n\int_0^\infty t^{n-1}[c(\mathbf{x},t) - c_\infty(\mathbf{x},t)]\,dt. \qquad (6)$$

The central moments of $f(t;x)$ are given by [6]

$$M_n(\mathbf{x}) = \frac{1}{g(\mathbf{x})}\int_0^\infty [t - T(\mathbf{x})]^n \frac{\partial c}{\partial t}\,dt, \qquad (7)$$

where $g(\mathbf{x}) = c_\infty(\mathbf{x}) - c_0(\mathbf{x})$. Equation (7) can be rewritten using the binomial theorem and the resulting integrals can be re-expressed to provide a recurrence relationship for the moments of action, $M_n(\mathbf{x})$:

$$M_n(\mathbf{x}) = \frac{S_n(\mathbf{x})}{g(\mathbf{x})} + \sum_{k=0}^{n-1}\binom{n}{k}[-T(\mathbf{x})]^{n-k}\frac{S_k(\mathbf{x})}{g(\mathbf{x})}. \qquad (8)$$

Therefore one approach to calculate the moments of action is to solve for $S_n(\mathbf{x})$, and then use Eq. (8) to calculate $M_n(\mathbf{x})$.

We note that four separate methods for calculating the MAT have appeared previously in the literature. The first method involves solving Eq. (1) for $c(\mathbf{x},t)$ and $c_\infty(\mathbf{x})$, and then directly evaluating Eq. (4) [9]. Since this method requires that we must first solve for the transient solution of Eq. (1), it is not straightforward to apply in general. The second method involves treating Eq. (4) as an integral transform with which we can transform Eq. (1) into a boundary value problem for $T(\mathbf{x})$ [5]. The second method is more versatile than the first since it does not require $c(\mathbf{x},t)$. The third method involves calculating the Laplace transform of the Green's function for Eq. (1), $G(\mathbf{x},s)$, where s denotes the transform variable, and then calculating the limit of $-dG/ds$ as $s \to 0$ [11]. Since the Green's function may be complicated or difficult to find an exact expression for, this method suffers similar disadvantages as the first. More recently, Berezhkovskii and co-workers [22] observed that $T(\mathbf{x})$ is related to the Laplace transform of $c(\mathbf{x},t) - c_\infty(\mathbf{x})$ according to

$$T(\mathbf{x})g(\mathbf{x}) = -\lim_{s\to 0}\tilde{C}(\mathbf{x},s), \qquad (9)$$

where $\tilde{C}(\mathbf{x},s)$ denotes the Laplace transform of the transient solution minus the steady state solution [23]:

$$\tilde{C}(\mathbf{x},s) = \mathcal{L}\{c(\mathbf{x},t) - c_\infty(\mathbf{x})\}, \qquad (10)$$
$$= \int_0^\infty [c(\mathbf{x},t) - c_\infty(\mathbf{x})]e^{-st}\,dt. \qquad (11)$$

To date, only one method to calculate the moments of action has been proposed [6]. This involves treating Eq. (6) as an integral transform to derive a nonhomogeneous boundary value problem for $S_n(\mathbf{x})$, whose forcing term is proportional to $S_{n-1}(\mathbf{x})$. In general, if we know $S_0(\mathbf{x})$, then solving for $S_n(\mathbf{x})$ means that we must solve n nonhomogeneous boundary value problems recursively to give $S_1(\mathbf{x}), S_2(\mathbf{x}), S_3(\mathbf{x}), \ldots, S_n(\mathbf{x})$, from which we can evaluate $M_n(\mathbf{x})$ using Eq. (8). We note that the family of boundary value problems that we must solve becomes increasingly complicated as n increases. While in principle it may be possible to proceed in this fashion, this approach is often impractical since it can become increasingly difficult to determine appropriate particular solutions as n increases.

II. RESULTS

In this section we outline a general method for calculating $S_n(\mathbf{x})$ and then apply this approach to three examples.

To solve for $S_n(\mathbf{x})$ we consider the identity [23]

$$\mathcal{L}\{t^n[c(\mathbf{x},t) - c_\infty(\mathbf{x})]\} = (-1)^n\frac{\partial^n \tilde{C}}{\partial s^n}. \qquad (12)$$

Since

$$S_n(\mathbf{x}) = -n\lim_{s\to 0}\mathcal{L}\{t^{n-1}[c(\mathbf{x},t) - c_\infty(\mathbf{x})]\}, \qquad (13)$$

it follows that

$$S_n(\mathbf{x}) = (-1)^n n\lim_{s\to 0}\frac{\partial^{n-1}\tilde{C}}{\partial s^{n-1}}. \qquad (14)$$

Equation (14), which includes Eq. (9) as a special case for $n = 1$, allows us to calculate $S_n(\mathbf{x})$ given $\mathcal{L}[c(\mathbf{x},t) - c_\infty(\mathbf{x})]$. Therefore a key aspect of our method is that we must compute the Laplace transform of $c(\mathbf{x},t) - c_\infty(\mathbf{x})$, which is possible without solving for the transient solution of the underlying linear reaction-diffusion equation. Once we have obtained this expression, we can then calculate $S_n(\mathbf{x})$ very simply by repeatedly differentiating with respect to s and then evaluating a limit as $s \to 0$. In practice, this procedure can be automated using standard symbolic software.

A. Example 1: Morphogen gradient formation

As an example of our more general approach to calculating the moments of action, we consider a linear reaction-diffusion problem governing the distribution of some morphogen density $c(x,t)$, which can be written as

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} - k_1 c, \quad 0 < x < \infty, \qquad (15)$$

$$c(x,0) = 0, \quad \left.\frac{\partial c}{\partial x}\right|_{x=0} = -\frac{Q}{D}, \quad \lim_{x\to\infty}c(x,t) = 0, \qquad (16)$$

where Q is the flux of the morphogen at $x = 0$. Equation (15), with boundary conditions and initial conditions described

by Eq. (16), has been widely used to model the formation of morphogen gradients [9–11,22,24]. The steady solution is $c_\infty(x) = Qe^{-\gamma_1 x}/(\gamma_1 D)$, where $\gamma_1 = \sqrt{k_1/D}$. Taking the Laplace transform of Eqs. (15) and (16) gives us

$$D\frac{\partial^2 \tilde{c}}{\partial x^2} - (k_1 + s)\tilde{c} = 0, \qquad (17)$$

$$\left.\frac{\partial \tilde{c}}{\partial x}\right|_{x=0} = -\frac{Q}{Ds}, \quad \lim_{x\to\infty}\tilde{c}(x,s) = 0, \qquad (18)$$

where $\tilde{c}(x,s) = \mathcal{L}\{c(x,t)\}$. Equation (17), with boundary conditions described by Eq. (18), can be solved using standard methods to find $\tilde{c}(x,s)$ [23], which in turn gives

$$\tilde{C}(x,s) = \mathcal{L}\{c(x,t) - c_\infty(x)\},$$
$$= \frac{Q}{s\sqrt{D(s+k_1)}}e^{-\sqrt{\frac{s+k_1}{D}}x} - \frac{Q}{\gamma_1 Ds}e^{-\gamma_1 x}. \quad (19)$$

From $\tilde{C}(x,s)$ we can derive an expression for the MAT and the higher central moments using Eqs. (8), (9), and (14). The first four moments are

$$T(x) = \frac{1}{2k_1} + \frac{x}{2\gamma_1 D}, \qquad (20)$$

$$M_2(x) = \frac{1}{2k_1^2} + \frac{x}{4k_1\gamma_1 D}, \qquad (21)$$

$$M_3(x) = \frac{1}{k_1^3} + \frac{3x}{8k_1^2\gamma_1 D}, \qquad (22)$$

$$M_4(x) = \frac{15}{4k_1^4} + \frac{27x}{16k_1^3\gamma_1 D} + \frac{3x^2}{16k_1^3 D}. \qquad (23)$$

We note that Eqs. (20) and (21) coincide with previously published results [14]; however, these previous studies neglected to calculate $M_3(x)$ and $M_4(x)$.

B. Example 2: Oxygen uptake in a spherical cell

We now consider a more complicated problem which is related to a mathematical model proposed by Lin and McElwain [16,17,25], who considered a reaction-diffusion model describing the distribution of oxygen in a spherical

cell. The model is

$$\frac{\partial c}{\partial t} = \frac{D}{r^2}\frac{\partial}{\partial r}\left[r^2\frac{\partial c}{\partial r}\right] - k_1 c + k_2, \quad 0 < r < R,$$

$$c(r,0) = 0, \quad \left.\frac{\partial c}{\partial r}\right|_{r=0} = 0, \qquad (24)$$

$$\left.\frac{\partial c}{\partial r}\right|_{r=R} = H[c_{\max} - c(R,t)],$$

where H is a positive constant representing the permeability of the cell membrane at $r = R$. The model assumes that the distribution of oxygen is spherically symmetric, with a symmetry condition imposed at the center of the cell ($r = 0$) and that the flux of oxygen at the cell surface ($r = R$) is proportional to the difference between the oxygen concentration at the surface and some maximum oxygen concentration, $c_{\max}$. We consider the simplest possible initial condition, which is that there is no oxygen in the cell, $c(r,0) = 0$. The Laplace transform of $c(r,t)$ for this problem can be found using a standard technique [23], with the result

$$\mathcal{L}\{c(r,t)\} = \frac{HR^2[c_{\max}(s+k_1) - k_2]\sinh(\alpha r)}{sr(s+k_1)[\alpha R\cosh(\alpha R) + (HR-1)\sinh(\alpha R)]}$$
$$+ \frac{k_2}{s(s+k_1)}, \qquad (25)$$

where $\alpha = \sqrt{(s+k_1)/D}$. We can recover the steady state solution, $c_\infty(r)$, using the final value theorem [26]

$$c_\infty(r) = \lim_{s\to 0}[s\tilde{c}(r,s)],$$
$$= \frac{\delta}{k_1\gamma}\frac{\sinh(\beta r)}{r} + \frac{k_2}{k_1}, \qquad (26)$$

where $\beta = \sqrt{k_1/D}$, $\gamma = \beta R\cosh(\beta R) + (HR-1)\sinh(\beta R)$, and $\delta = HR^2(c_{\max}k_1 - k_2)$. The Laplace transform of $c(r,t) - c_\infty(r)$ can be found by combining Eq. (25) with the Laplace transform of Eq. (26), from which we can evaluate the following expressions:

$$T(r) = \frac{k_1\gamma r}{\delta\sinh(\beta r) + k_2\gamma r}\left(\frac{k_2}{k_1^2} - \frac{\delta\beta}{2\gamma k_1^2}\cosh(\beta r) - \frac{HR^2 c_{\max}}{\gamma k_1}\frac{\sinh(\beta r)}{r}\right.$$
$$\left. + \frac{\delta e^{\beta R}[(2\beta R + HR^2\beta)\cosh(\beta R) + (\beta^2 R^2 + 2HR - 2)\sinh(\beta R)]}{\gamma k_1^2[\beta R(e^{2\beta R}+1) + (HR-1)(e^{2\beta R}-1)]}\frac{\sinh(\beta r)}{r}\right), \qquad (27)$$

$$S_2(r) = \frac{2k_2}{D^2\beta^4 k_1} + \frac{\delta}{4k_1\gamma D^2\beta^2}r\sinh(\beta r) - \left(\frac{\delta}{4k_1\gamma D^2\beta^3} + \frac{R^2[\delta\beta^2\sinh(\beta R) + H\delta\beta\cosh(\beta R) - 2Hk_2\gamma]}{2k_1\gamma^2 D^2\beta^3}\right)\cosh(\beta r)$$
$$+ \frac{R^2}{4D^2\beta^4 k_1\gamma^3}\{H\gamma[\beta\delta\cosh(\beta R) - 8\gamma k_2] - (\delta\beta^2 + 4H^2 Rk_2)R\gamma\beta\cosh(\beta R) - (4Rk_2 + \delta)RH\beta^2\gamma\sinh(\beta R)$$
$$+ 2\delta R^2\beta^2[\beta\sinh(\beta R) + H\cosh(\beta R)]^2\}\frac{\sinh(\beta r)}{r}. \qquad (28)$$

We note that it is possible to calculate further higher moments and the associated central moments for this problem; however, the resulting expressions are cumbersome and so we do not include them here.

To demonstrate the importance of calculating the moments of action for this problem, we apply the model using parameters related to those reported by McElwain [16,25], which are $H = 0.5$, $c_{\max} = D = R = 1$, $k_1 = 0.38065$, and $k_2 = 0$.
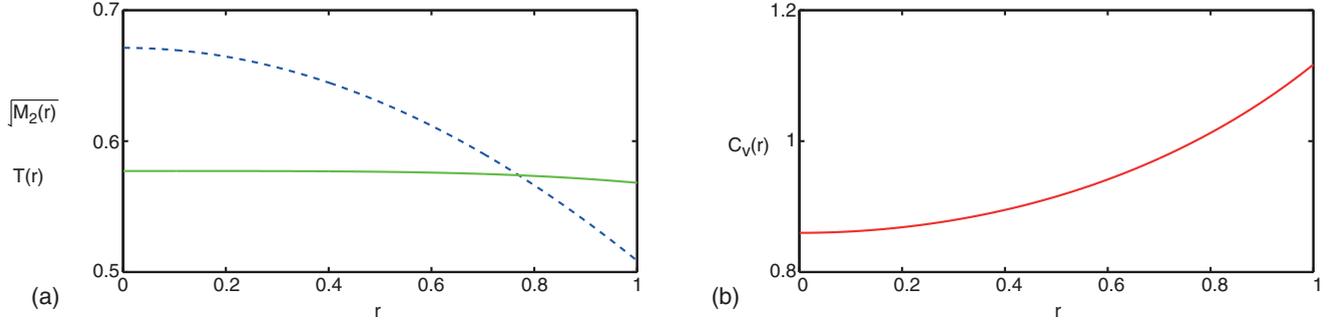
FIG. 1. (Color online) (a) $T(r)$ (dashed blue) and $\sqrt{M_2(r)}$ (solid green) for Eq. (24) with $H = 0.5$, $c_{\max} = D = R = 1$, $k_1 = 0.38065$, and $k_2 = 0$, for $0 < r < 1$. Results in (b) show the spatial distribution of the coefficient of variation, $C_v(r) = \sqrt{M_2(r)}/T(r)$, for the same problem.

Results in Fig. 1(a) show $T(r)$ and $\sqrt{M_2(r)}$. In (b) we show the coefficient of variation, $C_v(r) = \sqrt{M_2(r)}/T(r)$ [6]. We note that PDFs with $C_v > 1$ can be classified as high variance, whereas PDFs with $C_v < 1$ can be classified as low variance [6]. At $r = 1$ we have $T(1) = 0.509$, which we can interpret as an estimate of the critical time that neglects the spread about the mean of the associated PDF. To improve our estimate we can use Eqs. (8) and (28) to calculate the variance, $M_2(1) = 0.323$. This additional information gives us an improved estimate of the critical time, $T(1) + \sqrt{M_2(1)} = 1.08$. Incorporating information about the second moment is important for this application at $r = 1$, since we are dealing with a high-variance PDF with $C_v > 1$ [6,13].

C. Example 3: Coupled reaction-diffusion problems

We now show how our results can be used to inform us about the moments of action for coupled linear reaction-diffusion problems. To demonstrate these ideas we consider a two-species model:

$$\frac{\partial c_1}{\partial t} = D\frac{\partial^2 c_1}{\partial x^2} - k_1 c_1, \quad 0 < x < \infty, \tag{29}$$

$$\frac{\partial c_2}{\partial t} = D\frac{\partial^2 c_2}{\partial x^2} + k_1 c_1 - k_2 c_2, \quad 0 < x < \infty, \tag{30}$$

$$c_1(x,0) = 0, \quad c_2(x,0) = 0, \tag{31}$$

$$c_1(0,t) = 1, \quad c_2(0,t) = 0, \tag{32}$$

$$\lim_{x \to \infty} c_1(x,t) = 0, \quad \lim_{x \to \infty} c_2(x,t) = 0. \tag{33}$$

This kind of coupled model has applications in several areas of biophysics, including the study of the collective motion of a subpopulation of cells, with density $c_1(x,t)$, which differentiate to produce a second subpopulation, $c_2(x,t)$ [27]. Another application is the study of the motion and biodegradation of dissolved organic contaminants in a saturated porous medium [28,29]. In this setting Eqs. (29) and (30) can be used to represent the molar concentration of a particular contaminant $c_1(x,t)$, which is biologically degraded into another type of contaminant $c_2(x,t)$, which then decays at a different rate [28].

To study the moments of action for this coupled problem, we first consider the steady state solutions of Eqs. (29)–(33):

$$c_{1\infty}(x) = e^{-x\gamma_1}, \tag{34}$$

$$c_{2\infty}(x) = \frac{k_1(e^{-x\gamma_1} - e^{-x\gamma_2})}{k_2 - k_1}, \tag{35}$$

where $\gamma_1 = \sqrt{k_1/D}$, $\gamma_2 = \sqrt{k_2/D}$, and $k_1 \neq k_2$. The Laplace transforms of $c_1(x,t)$ and $c_{1\infty}(x)$ can be found using standard techniques [23], leading to

$$\tilde{C}_1(x,s) = \mathcal{L}\{c_1(x,t) - c_{1\infty}(x)\},$$
$$= \frac{1}{s}e^{-x\sqrt{\frac{s+k_1}{D}}} - \frac{1}{s}e^{-\gamma_1 x}. \tag{36}$$

From $\tilde{C}_1(x,s)$ we can derive an expression for the MAT and the higher central moments using Eqs. (8), (9), and (14). The first four moments for $c_1(x,t)$ are

$$T(x) = \frac{x\gamma_1}{2k_1}, \tag{37}$$

$$M_2(x) = \frac{x\gamma_1}{4k_1^2}, \tag{38}$$

$$M_3(x) = \frac{3x\gamma_1}{8k_1^3}, \tag{39}$$

$$M_4(x) = \frac{15x\gamma_1}{16k_1^4} + \frac{3x^2\gamma_1^2}{16k_1^4}. \tag{40}$$

To analyze the moments of action for the $c_2(x,t)$, we refer to our previous work [7] which showed that Eq. (4) cannot be applied directly to Eq. (30), since $F(t;x)$ is not a monotonically increasing function of t for $c_2(x,t)$. To overcome this we introduce a new variable, $\sigma(x,t) = c_1(x,t) + c_2(x,t)$, which leads to

$$\frac{\partial \sigma}{\partial t} = D\frac{\partial^2 \sigma}{\partial x^2} - k_2 c_2, \quad 0 < x < \infty, \tag{41}$$

$$\sigma(x,0) = 0, \quad \sigma(0,t) = 1, \quad \lim_{x \to \infty} \sigma(x,t) = 0, \tag{42}$$

$$\sigma_\infty(x) = \frac{k_2 e^{-x\gamma_1} - k_1 e^{-x\gamma_2}}{k_2 - k_1}. \tag{43}$$

The Laplace transforms of $\sigma(x,t)$ and $\sigma_\infty(x)$ can be found using standard techniques [23], leading to

$$\tilde{\Sigma}(x,s) = \mathcal{L}\{\sigma(x,t) - \sigma_\infty(x)\},$$
$$= \frac{1}{s(k_1 - k_2)}\Big[k_1\big(e^{-\sqrt{\frac{s+k_2}{D}}x} - e^{-\gamma_2 x}\big)$$
$$- k_2\big(e^{-\sqrt{\frac{s+k_1}{D}}x} - e^{-\gamma_1 x}\big)\Big]. \tag{44}$$

From $\tilde{\Sigma}(x,s)$ we can derive an expression for the MAT and the higher central moments using Eqs. (8), (9), and (14). The first two moments for $\sigma(x,t)$ are

$$T(x) = \frac{x}{2\sqrt{k_1 k_2 D}} \frac{k_1^{3/2} e^{-\gamma_2 x} - k_2^{3/2} e^{-\gamma_1 x}}{k_1 e^{-\gamma_2 x} - k_2 e^{-\gamma_1 x}}, \quad (45)$$

$$\begin{aligned}
M_2(x) = {} & \frac{x}{4 k_1^{3/2} k_2^{3/2} D^{3/2} (k_1 e^{\gamma_1 x} - k_2 e^{\gamma_2 x})^2} \\
& \times \left[k_1^{7/2} D e^{2\gamma_1 x} + k_2^{7/2} D e^{2\gamma_2 x} - k_1 k_2 D \left(k_1^{3/2} + k_2^{3/2} \right) \right. \\
& \left. \times e^{(\gamma_1 + \gamma_2)x} - x \sqrt{D} k_1^{3/2} k_2^{3/2} (\sqrt{k_1} - \sqrt{k_2})^2 e^{(\gamma_1 + \gamma_2)x} \right],
\end{aligned} \quad (46)$$

and further higher moments, which can be calculated in exactly the same way, have been neglected owing to algebraic complexity.

III. DISCUSSION AND CONCLUSION

We conclude with a few general remarks about our approach. For many reaction-diffusion problems $T(\mathbf{x})$ and $M_n(\mathbf{x})$ are complicated algebraic expressions. For example,

Gordon and co-workers considered a reaction-diffusion model on the outside of an infinite cylinder or sphere for which $T(\mathbf{x})$ involved modified Bessel functions [14,30]. Calculating $M_n(\mathbf{x})$ for this problem using existing methods requires the solution of n nonhomogeneous boundary value problems, in which the forcing term becomes increasingly algebraically complicated as n increases, making this approach difficult to implement. In comparison, our method allows us to calculate $S_n(\mathbf{x})$ without calculating $S_{n-1}(\mathbf{x}), S_{n-2}(\mathbf{x}), \ldots, S_0(\mathbf{x})$ first.

For a wide class of practical problems, such as reaction-diffusion equations in polar and spherical coordinate systems [14], or for reaction-diffusion equations where the diffusivity, advective velocity, or reaction rates are spatially variable [13,31], the governing partial differential equation has coefficients that are a function of the independent variable(s). The advantages of the Laplace transform technique become clear when applied to these problems.

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