Local accumulation times for source, diffusion, and degradation models in two and three dimensions

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We analyze the transient dynamics leading to the establishment of a steady state in reaction-diffusion problems that model several important processes in cell and developmental biology and account for the diffusion and degradation of locally produced chemical species. We derive expressions for the local accumulation time, a convenient characterization of the time scale of the transient at a given location, in two- and three-dimensional systems with first-order degradation kinetics, and analyze their dependence on the model parameters. We also study the relevance of the local accumulation time as a single measure of timing for the transient and demonstrate that, while it may be sufficient for describing the local concentration dynamics far from the source, a more delicate multi-scale description of the transient is needed near a tightly localized source in two and three dimensions.
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I. INTRODUCTION

Several problems in biophysics of cells and tissues require an analysis of reaction-diffusion equations that model the concentrations of molecules involved in intra- and extracellular processes. In addition to describing the spatial patterns of concentrations of these molecules across the domain modeling a cell or a tissue, one is commonly interested in the kinetics of concentrations at a given location within the system. Here, we consider single-variable problems in which the concentration starts from zero and monotonically approaches a steady state distribution. This dynamics is predicted by the so-called source, diffusion, and degradation (SDD) models that account for the diffusion and degradation of locally produced chemical signals.[1–9] Let $C(r, t)$ and $C_s(r)$ denote the instantaneous and the steady state concentrations at distance r from a radially symmetric source, respectively. The approach of $C(r, t)$ to its steady state level $C_s(r)$ at a given location can be completely characterized using the local relaxation function

$$\rho(r,t) = \frac{C_s(r) - C(r,t)}{C_s(r)}, \tag{1}$$

which starts from the value of unity and approaches zero for all locations. The difference between the values of this function at two consecutive times $t_1 < t_2$, $\rho(r, t_1) - \rho(r, t_2)$, can be viewed as the fraction of the steady state level that has been accumulated between t_1 and t_2. Clearly, the time derivative of the relaxation function is related to the fraction of the steady state level accumulated between t and $t + dt$, this fraction equals $-(\partial\rho(r, t)/\partial t)dt$. Based on this observation, Berezhkovskii *et al.* defined the local accumulation time $\tau(r)$, which provides a time scale for accumulation of the steady state level at a given location:[10,11]

$$\tau(r) = -\int_0^\infty t\,\frac{\partial\rho(r,t)}{\partial t}\,dt. \tag{2}$$

Local accumulation times were calculated for a number of biophysical models, resulting in convenient characterizations of the concentration dynamics as a function of position and problem parameters, such as the rate constants of diffusion and degradation.[10–14]

All the previous works mentioned above analyzed several kinds of SDD models in one space dimension. Here, we evaluate the local accumulation times for linear SDD models in two and three dimensions and compare the results with those in one dimension. We demonstrate that the local accumulation time provides a meaningful characterization of the local kinetics when the size of the source is much larger than the length scale for signal degradation and/or when this length scale is much smaller than the distance from the point of interest to the boundary of the source. However, a more detailed description of the kinetics based on the analysis of the relaxation function is required when these conditions are not satisfied.

Our paper is organized as follows: In Sec. II, we write down the SDD models in which a diffusible chemical is produced at the boundary of circular or spherical sources. Next, in Secs. III and IV, we derive local accumulation times for these problems and analyze their dependence on the size of the source. Following this, in Sec. V, we ask a more general question related to the extent to which local accumulation times can be used to characterize local relaxation kinetics in SDD problems. Finally, in Sec. VI, we summarize our findings and draw conclusions.

II. RADIAL SDD MODEL

The simplest multidimensional generalization of the canonical linear one-dimensional SDD model is given by the following initial boundary value problem:

$$\begin{cases} \dfrac{\partial C}{\partial t} = D\left(\dfrac{\partial^2 C}{\partial r^2} + \dfrac{n-1}{r}\dfrac{\partial C}{\partial r}\right) - kC, \\ -D\dfrac{\partial C}{\partial r}(R,t) = Q, \\ C(r,0) = 0. \end{cases} \tag{3}$$

Here, D is the diffusion coefficient, Q is the flux at the boundary of an n-dimensional radially symmetric source, k is the linear degradation rate, $r \geq R$ and $t \geq 0$. Throughout the rest of the paper, we assume that the flux Q is time-independent, which can be interpreted as an instantaneous establishment of constant ligand secretion rate from the surface of a spherical cell.[1]

As we mentioned in the Introduction, at long times the solution of the problem in (3) approaches the steady state, which is described by the following problem:

$$\begin{cases} D\left(\dfrac{d^2 C_s}{dr^2} + \dfrac{n-1}{r}\dfrac{dC_s}{dr}\right) - kC_s = 0, \\ -D\dfrac{\partial C_s}{\partial r}(R) = Q, \quad C_s(\infty) = 0. \end{cases} \tag{4}$$

Moreover, for each r the concentration $C(r, t)$ approaches its steady state value $C_s(r)$ monotonically from below. The time scale of this approach, however, depends in a rather non-trivial way on the position r and parameters k and D. The analysis that follows aims to quantify these dependencies.

III. LOCAL ACCUMULATION TIMES

In this section, we derive local accumulation times for solutions of (3) in different space dimensions. In the case of $n = 1$, the result was first obtained in Ref. 10 and reads

$$\tau_{n=1}(r) = \frac{r-R}{2\sqrt{Dk}} + \frac{1}{2k}. \tag{5}$$

For a reference, we also give the well known expression for the stationary profile of concentration:

$$C_{s,n=1}(r) = \frac{Q}{\sqrt{Dk}} \exp(\sqrt{k}(R-r)/\sqrt{D}). \tag{6}$$

In what follows, we will use an alternative definition of local accumulation time

$$\tau(r) = \int_0^\infty \rho(r,t)dt, \tag{7}$$

which can be obtained from the original one by integration by parts and is somehow more convenient for the analysis.

We now present a basic formalism for obtaining the local accumulation time in arbitrary dimension. Let $w(r, t) = C_s(r, t) - C(r, t)$. Then from (3) and (4), we have

$$\begin{cases} \dfrac{\partial w}{\partial t} = D\left(\dfrac{\partial^2 w}{\partial r^2} + \dfrac{n-1}{r}\dfrac{\partial w}{\partial r}\right) - kw, \\ \dfrac{\partial w}{\partial r}(R,t) = 0, \\ w(r,0) = C_s(r). \end{cases} \tag{8}$$

Next, we set

$$W(r) = \int_0^\infty w(r,t)dt, \tag{9}$$

which is well defined because of exponential decay of the integrand for each r. Then, the local accumulation time takes the form

$$\tau(r) = \frac{W(r)}{C_s(r)}. \tag{10}$$

Integrating (8) with respect to time and taking into account that $w(r, t)$ approaches zero as $t \to \infty$, we obtain the following boundary value problem:

$$\begin{cases} D\left(\dfrac{d^2 W}{dr^2} + \dfrac{n-1}{r}\dfrac{dW}{dr}\right) - kW = -C_s, \\ \dfrac{dW}{dr}(R) = 0, \quad W(\infty) = 0. \end{cases} \tag{11}$$

Solving problems (4) and (11) and substituting the result into (10), we obtain the local accumulation time as a function of r and all the model parameters.

Let us now apply this formalism to the case of dimensions two and three. In the case of $n = 2$, we obtain, after some tedious algebra, the following expressions for the stationary concentration profile and the local accumulation time, respectively:

$$C_{s,n=2}(r) = \frac{Q}{\sqrt{Dk}} \frac{K_0(\sqrt{k}r/\sqrt{D})}{K_1(\sqrt{k}R/\sqrt{D})}, \tag{12}$$

and

$$\begin{aligned} \tau_{n=2}(r) = {} & \frac{R}{2\sqrt{Dk}}\left(\frac{K_1^2(\sqrt{k}R/\sqrt{D}) - K_0^2(\sqrt{k}R/\sqrt{D})}{K_1(\sqrt{k}R/\sqrt{D})K_0(\sqrt{k}R/\sqrt{D})}\right) \\ & + \frac{1}{2k}\int_{\sqrt{k}R/\sqrt{D}}^{\sqrt{k}r/\sqrt{D}} s\left(\left(\frac{K_1(s)}{K_0(s)}\right)^2 - 1\right) ds, \end{aligned} \tag{13}$$

where $K_0(r)$, $K_1(r)$ are modified Bessel function of the second kind.[15] This expression may be approximated with an accuracy better than 2% by the following simpler expression for all values of the parameters:

$$\begin{aligned} \tau_{n=2}(r) \approx {} & \frac{1}{2k}\big(1/\ln[e + 2\sqrt{D}e^{-\gamma}/(\sqrt{k}R)] \\ & + (1 + \sqrt{k}r/(4\sqrt{D}))/\ln[e^{1/4} + 2\sqrt{D}e^{-\gamma}/(\sqrt{k}r)] \\ & - (1 + \sqrt{k}R/(4\sqrt{D}))/\ln[e^{1/4} + 2\sqrt{D}e^{-\gamma}/(\sqrt{k}R)]\big), \end{aligned} \tag{14}$$

where $\gamma \approx 0.5772$ is the Euler's constant. A simpler approximate expression can further be obtained for $\tau_{n=2}(r)$ for not

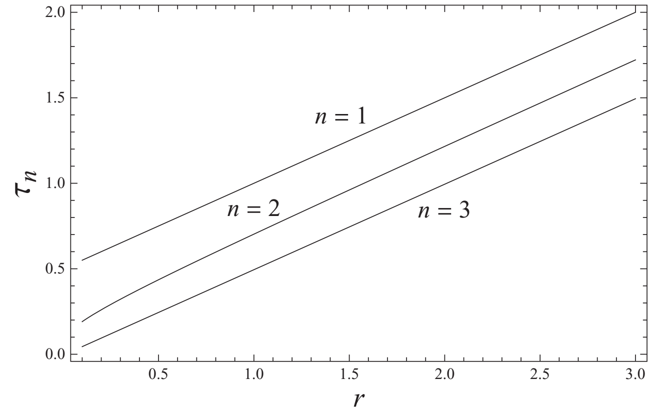

FIG. 1. Dependence of the local accumulation time on r in different space dimensions obtained from (5), (13), and (17) with $D = 1$, $k = 1$, and $R = 0.1$.

too small values of r:

$$\tau_{n=2}(r) \approx \frac{r - R}{2\sqrt{Dk}} + \frac{R + 0.31\sqrt{D/k}}{2k(R + 0.62\sqrt{D/k})}, \tag{15}$$

which gives the asymptotic behavior of $\tau_{n=2}(r)$ as $r \to \infty$ to within 1% accuracy. In practice, this formula also gives a good approximation to $\tau_{n=2}(r)$ in the whole range of $r \geq R$ for $R \gtrsim 0.1\sqrt{D/k}$.

In turn, in the case of $n = 3$ we have, after some algebra,

$$C_{s,n=3}(r) = \frac{QR^2 \exp(\sqrt{k}(R - r)/\sqrt{D})}{rD(1 + \sqrt{k}R/\sqrt{D})}, \tag{16}$$

and

$$\tau_{n=3}(r) = \frac{r - R}{2\sqrt{Dk}} + \frac{R}{2k(R + \sqrt{D/k})}. \tag{17}$$

The obtained expressions for $\tau(r)$ are plotted in Fig. 1, as functions of r for a particular value of R which is equal to one-tenth of the diffusion length $\sqrt{D/k}$. Note that the curves corresponding to $\tau_{n=1}(r)$ and $\tau_{n=3}(r)$ are straight lines with the slope $(4Dk)^{-1/2}$, and the curve $\tau_{n=2}(r)$ essentially coincides with a straight line with the same slope. The latter conclusion remains valid for all larger values of R, while for smaller R some deviations from a linear dependence develop for extremely small r and R compared with the diffusion length. We also find that the graphs of $\tau(r)$ for different n remain ordered for all values of R, i.e., we have $\tau_{n=3}(r) < \tau_{n=2}(r) < \tau_{n=1}(r)$ for all $r \geq R$ and all other parameters fixed.

IV. DEPENDENCE OF THE LOCAL ACCUMULATION TIME ON THE PARAMETERS OF THE SDD MODEL

In this section, we discuss the dependence of local accumulation times obtained in Sec. III on the parameters of the model and give a biophysical interpretation of these results.

As one might expect, for points located sufficiently far from the boundary the local accumulation time is asymptotically the same irrespectively of the dimension. Indeed, from (5), (13), and (17) we have for all n

$$\tau_n(r) \approx \bar{\tau}(r) = \frac{r}{2\sqrt{Dk}}, \qquad r \gg R \text{ and } r \gg \sqrt{D/k}. \tag{18}$$

This can be explained by the fact that for distances exceeding the diffusion length $\sqrt{D/k}$ away from the boundary the dynamics of concentration is effectively one-dimensional. Alternatively, from the probabilistic point of view a particle that is created at the boundary at time $T > 0$ will reach a neighborhood around a point at distance $r \gg R$ away from the boundary at time $T + t$ with probability approximately

$$P \propto e^{-kt - R^2/(4Dt)}, \tag{19}$$

where the first term in the exponent gives the survival probability of the particle at time $T + t$ and the second term gives the approximate conditional probability of finding a Brownian particle at distance r at time $T + t$, given that the particle was at the boundary at time T.

Clearly, for $r \gg \sqrt{D/k}$ the right-hand side of (19) is sharply peaked precisely around $\bar{\tau}$ given by (18). This implies that for $t < \bar{\tau}$ no particle will yet have a chance to reach the neighborhood of the point and, hence, the concentration will be far from the steady state value. On the other hand, when $t > \bar{\tau}$ with high probability there will always be a particle starting at time $T = t - \bar{\tau}$ and finishing at time t in the neighborhood of the considered point. Hence, $\bar{\tau}$ given by (18) provides the characteristic time of the establishment of the steady concentration. We note that for discrete stochastic SDD models a similar observation was recently made in Ref. 13.

However, the local accumulation time in the vicinity of the boundary depends crucially on the dimensionality of the problem. For example, at the boundary, i.e., when $r = R$, we have the following expression for the local accumulation time in one space dimension:

$$\tau_{n=1}(R) = \frac{1}{2k}. \tag{20}$$

Note that this expression is independent of both the diffusion constant D and the radius R of the boundary, and is simply proportional to the degradation time. At the same time, in two and three space dimensions, the local accumulation time depends rather sensitively on all the parameters of the problem, including the boundary radius. Indeed, for the most biophysically interesting case of $n = 2$ the local accumulation time at the boundary is given by

$$\begin{aligned} \tau_{n=2}(R) &= \frac{R}{2\sqrt{Dk}} \left(\frac{K_1^2(\sqrt{k}R/\sqrt{D}) - K_0^2(\sqrt{k}R/\sqrt{D})}{K_1(\sqrt{k}R/\sqrt{D})K_0(\sqrt{k}R/\sqrt{D})} \right) \\ &\approx \frac{1}{2k \ln[e + 2\sqrt{D}e^{-\gamma}/(\sqrt{k}R)]}. \end{aligned} \tag{21}$$

From this expression, one can see that the local accumulation time is proportional to $1/|\ln R|$ when $R \lesssim \sqrt{D/k}$, while, as expected, the dependence on R becomes weak for $R \gtrsim \sqrt{D/k}$ and, to the leading order, coincides with (20). Similarly, in the case of three space dimensions we have

$$\tau_{n=3}(R) = \frac{R}{2\sqrt{k}(\sqrt{D} + \sqrt{k}R)}, \tag{22}$$

and so the local accumulation time is proportional to R for $R \lesssim \sqrt{D/k}$, while for $R \gtrsim \sqrt{D/k}$ it becomes independent of R and coincides with the expression in one space dimension. The dependencies of $\tau_n(R)$ in all the three cases are shown

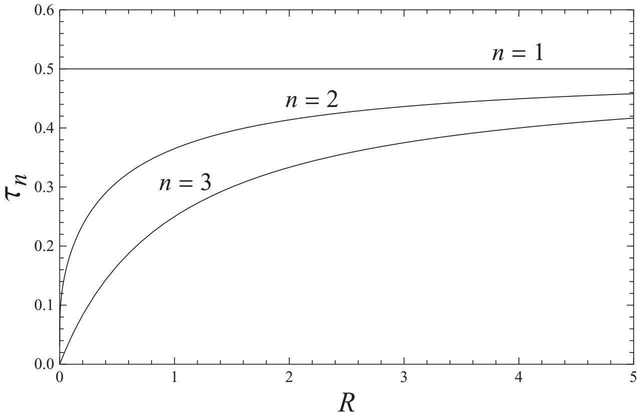

FIG. 2. Dependence of the local accumulation time on R at the source boundary in different space dimensions obtained from (20), (21), and (22) with $D = 1$ and $k = 1$.

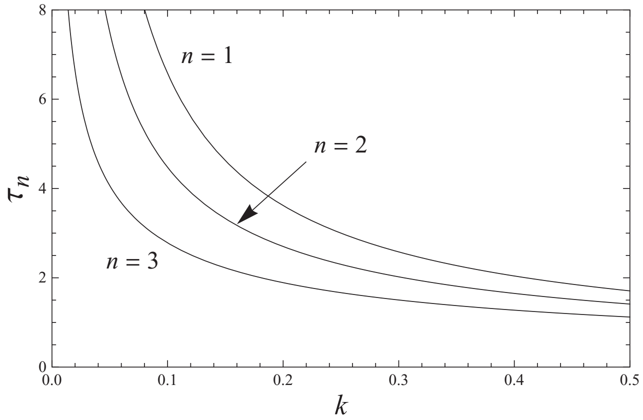

FIG. 3. Dependence of the local accumulation time on the degradation rate for $D = 1$, $R = 1$, and $r = 2$ in different dimensionalities.

graphically in Fig. 2, where without loss of generality we put $D = 1$ and $k = 1$.

It is clear from the above discussion and Fig. 2 that when the boundary radius is much smaller than the diffusion length, $R \ll \sqrt{D/k}$, the concentration almost immediately reaches its steady state profile at the boundary in two and three space dimensions. This is in contrast to the one-dimensional case, where the local accumulation time at the boundary is independent of R and, hence, remains finite for all R. Moreover, the behavior of the local accumulation time for fixed r as $R \to 0$, i.e., when the boundary can be replaced by a point source, is rather sensitive to the dimensionality of the problem and is rather non-trivial. According to (13), in two space dimensions we have

$$\tau_{n=2}(r) \approx \frac{1}{2k\ln(2\sqrt{D}e^{-\gamma}/(\sqrt{k}r))}, \qquad r \lesssim \sqrt{D/k}, \tag{23}$$

which implies, in particular, that the local accumulation time is proportional to $1/|\ln r|$ as a function of the distance to the point source sufficiently close to the source. At the same time, in three space dimensions, we have

$$\tau_{n=3}(r) = \frac{r}{2\sqrt{Dk}}, \tag{24}$$

which is valid for all values of the parameters. Surprisingly, this formula coincides with (18) obtained earlier as the asymptotic limit of the local accumulation time for $r \to \infty$ for the entire range of r. We will get back to this issue in Sec. V.

Similarly, the dependence of the local accumulation time on the degradation rate k is far from obvious. According to (5), (15), and (17), in the limit of large values of k the local accumulation time is independent of the dimension. On the other hand, for small values of k the result sensitively depends on the dimensionality. In one space dimension we have, according to (5), that $\tau_{n=1}$ obeys (20), implying that $\tau_{n=1} \propto k^{-1}$ asymptotically as $k \to 0$ with all other parameters fixed. For $n = 3$, on the other hand, we have $\tau_{n=3} \propto k^{-1/2}$. The most intricate case turns out to be $n = 2$, in which, according to (13), we have $\tau_{n=2} \propto k^{-1}|\ln k|^{-1}$. These results are summarized in Fig. 3 for a particular choice of r and R.

V. A MORE DETAILED CHARACTERIZATION OF THE LOCAL KINETICS IN THE SDD MODEL

In Sec. III, we have obtained closed form analytical expressions for the local accumulation time in the radially-symmetric SDD model. We found that the dependence of this quantity on the model parameters can be quite different for different spatial dimensionalities. In particular, when the radius of the boundary is smaller than the diffusion length $\sqrt{D/k}$, the dependence of the local accumulation time on the distance to the boundary given by (20), (21), and (22) to the leading order is very different in one, two, and three dimensions, and also different from the expected diffusive behavior $\tau_D \sim (r - R)^2/D$ near the boundary. Therefore, further understanding of the relaxation process occurring in this situation is necessary.

Let us examine the behavior of the relaxation function $\rho(r, t)$ on t for fixed $r \geq R$ in more detail. In the case of $n = 1$, one can, in fact, obtain a closed form expression[10] for $\rho(r, t)$, which can be written using the definition in (18) as follows:

$$\rho(r, t) = \frac{1}{2}\operatorname{erfc}\left\{\sqrt{kt}\left(1 - \frac{\bar{\tau}(r - R)}{t}\right)\right\} + \frac{e^{4k\bar{\tau}(r-R)}}{2}\operatorname{erfc}\left\{\sqrt{kt}\left(1 + \frac{\bar{\tau}(r - R)}{t}\right)\right\}, \tag{25}$$

where $\operatorname{erfc}(x)$ is the complementary error function.[15] The graphs of $\rho(r, t)$ as a function of t for different values of $r = r_0$ fixed are presented in Fig. 4. It is not difficult to see from (25) that when $r_0 - R \lesssim \sqrt{D/k}$, we have $\rho(r_0, t) \approx \operatorname{erfc}(\sqrt{kt})$. In particular, in this regime the relaxation function depends only weakly on r_0 and its characteristic time scale coincides with $\tau_{n=1}$, which depends only on k to the leading order.

On the other hand, when $r_0 - R \gtrsim \sqrt{D/k}$, the situation changes qualitatively. Indeed, as can be seen from Fig. 4, for large enough values of r_0 there exists a *delay* of order $\bar{\tau}(r - R)$ in the onset of the establishment of the steady profile of concentration. Furthermore, the dynamics occurs within a time window of order $\sqrt{\bar{\tau}/k} \lesssim \bar{\tau}$. As the value of r_0 is increased, the transition from $\rho(r_0, t) \approx 1$ to $\rho(r_0, t) \approx 0$ becomes sharply concentrated around $t = \bar{\tau}$. The latter can be seen from (25) by realizing that for large values of r_0 the

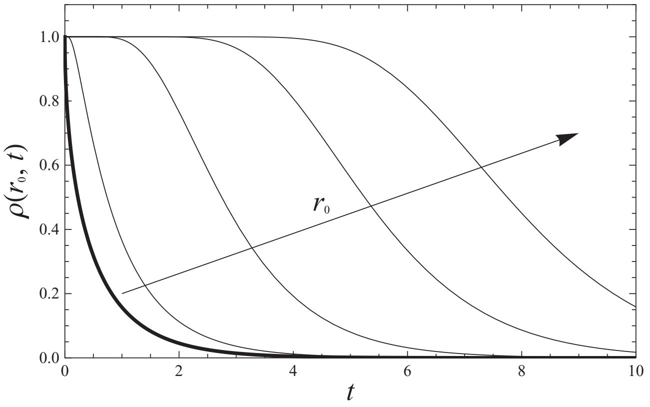

FIG. 4. Dependence of the relaxation function $\rho(r_0, t)$ on time for $r_0 = 0$, 1, 5, 10, 15 in one space dimension, obtained from (25) for $R = 0$, $D = 1$, and $k = 1$.

second term in the curly brackets becomes negligible, and the first term approximates a step function with the threshold at $t = \bar{\tau}$. Thus, the onset of the steady concentration profile sufficiently far from the boundary has an on/off character, with the switching time given by $\bar{\tau} \approx \tau_{n=1}$. Therefore, far from the boundary (in comparison with the diffusion length $\sqrt{D/k}$), the quantity $\tau_{n=1}$ gives a *sharp* time of the establishment of the steady concentration.

Note that the expression for $\tau_{n=1}$ when $r - R \gg \sqrt{D/k}$ coincides with the corresponding expressions for $\tau_{n=2}$ and $\tau_{n=3}$ to the leading order, see (18). In fact, as we explained in Sec. IV, the probabilistic reason for this phenomenon is common in all dimensions. Therefore, for $r - R \gtrsim \sqrt{D/k}$ the relaxation process to the steady morphogen concentration profile will have the same on/off character as in one space dimension. This can also be seen from the diffusion-transport equation satisfied by ρ:

$$\rho_t + \mathbf{v} \cdot \nabla \rho = D \nabla^2 \rho, \quad \mathbf{v} = -2D \nabla \ln C_s, \tag{26}$$

which follows directly from (3) and (4). Indeed, by (6), (12), and (16), we have $C_s \propto \exp(-\sqrt{k}(r - R)/\sqrt{D})$ for $r - R \gtrsim \sqrt{D/k}$, which implies that $|\mathbf{v}| \approx 2\sqrt{Dk}$ there. Therefore, for large values of r the level sets of ρ are advected with constant velocity $2\sqrt{Dk} = r/\bar{\tau}$ away from the source.

Let us now consider the other regime of r, $R \lesssim \sqrt{D/k}$ in dimensions two and three. When $R \to 0$, the solution for $\rho(r, t)$ may be easily found in integral form using Fourier techniques. Figure 5 shows the dependence of $\rho(r, t)$ on t for some $r = r_0 \ll \sqrt{D/k}$ fixed in three dimensions. From this figure, one can see that the character of the relaxation to the steady state in this case is quite different from the one-dimensional case (compare with the thick line in Fig. 4). The value of $\rho(r_0, t)$ quickly drops from 1 on the *diffusive* time scale $\tau_D \sim r_0^2/D$. Following that, the relaxation proceeds slowly up to the reaction time scale $\tau_k \sim k^{-1}$. During this period, we have $\rho(r_0, t) \sim (\tau_D/t)^{1/2}$ (see the dashed line in Fig. 5). In other words, in contrast to the one-dimensional case the dynamics of the level set $\rho(r_0, t) = 0.5$ may be very different from that of, say, $\rho(r_0, t) = 0.05$. This is why in this case, the local accumulation time is not representative of the time scale of the dynamics of the level set $\rho(r, t) = 0.5$. For the parameters of Fig. 5, the time $t = \tau_{n=3}$ corresponds to $\rho(r_0, t)$ reaching the value of about 0.1, i.e., to 90% of the steady concentration. Thus, in three dimensions the relaxation process is characterized by the presence of multiple time scales.

In the considered regime in three dimensions, the relaxation proceeds first by establishing a diffusion-dominated quasi-steady state at distance of order $\sqrt{Dt}$ around the source, followed by the expansion of this region up to the diffusion length $\sqrt{D/k}$. This is due to the fact that, in contrast to one and two dimensions, in three dimensions there exists a steady state for (3) even in the absence of degradation. The fact that $\tau_{n=3} \gg \tau_D$ has to do with the heavy tail of the distribution of the probability density $\phi = -\partial\rho/\partial t \propto t^{-3/2}$ for $\tau_D \ll t \ll \tau_k$. More than one time scale is, therefore, necessary to describe the approach of the concentration to its steady state at long times in the considered case.

In two dimensions, the situation is even more complicated, since in this case no steady state exists for (3) in the absence of degradation. Consider again the most delicate case of $R \to 0$. As in three dimensions, $\rho(r_0, t)$ first quickly drops from unity on the diffusive time scale τ_D. After that, in the range of $\tau_D \ll t \ll \tau_k$ the function $\rho(r, t)$ reaches a

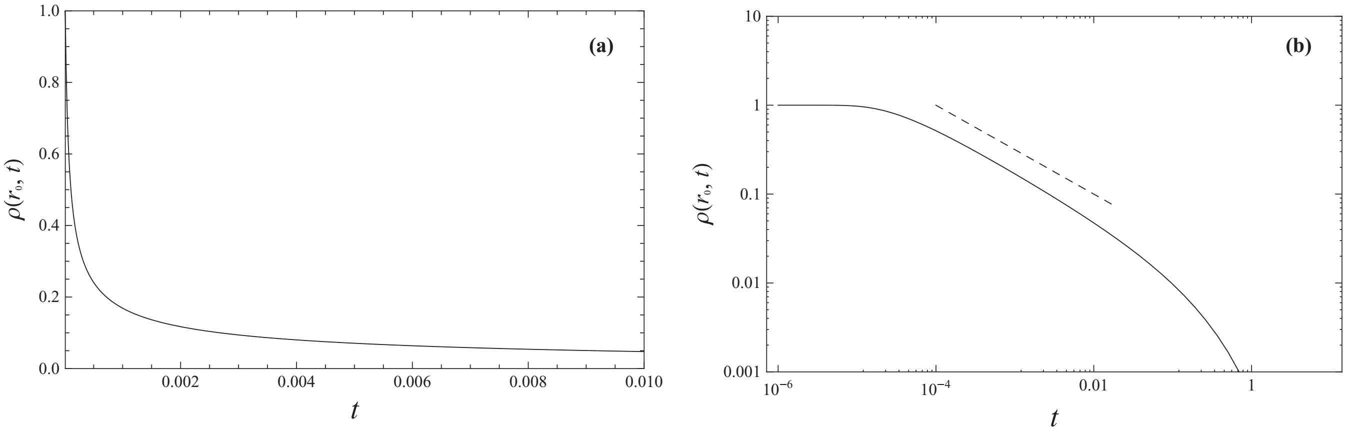

FIG. 5. Dependence of the relaxation function $\rho(r_0, t)$ on time for $r_0 = 0.01$ in three space dimensions, obtained from the numerical solution of (3) with $D = 1$ and $k = 1$. In (a), $\rho(r_0, t)$ is plotted on the linear scale. In (b), $\rho(r_0, t)$ is plotted on the log-log scale. The dashed line in (b) indicates the $t^{-1/2}$ dependence.

quasi-steady state, which vanishes beyond the length scale of order $\sqrt{Dt}$. Hence, the solution at point r_0 fixed is expected to behave as

$$\rho(r_0, t) \approx \frac{\ln(kt)}{\ln(kr_0^2/D)}, \quad \tau_D \ll t \ll \tau_k. \tag{27}$$

Indeed, at time $t \gtrsim \tau_D$ the concentration profile will be $C(r,t) \approx -\frac{1}{2\pi} \ln(r/\sqrt{Dt})$. At the same, from (12) we have $C_s(r) \approx -\frac{1}{2\pi} \ln(\sqrt{k}r/\sqrt{D})$ for $r \lesssim \sqrt{D/k}$. Substituting these expressions into the definition of ρ in (1), we obtain (27). Then, it is clear from (27) that the decay of $\rho(r_0, t)$ is extremely slow. Furthermore, the value of ρ corresponding to $t = \tau_{n=2}$ is, therefore, $\rho \approx \ln|\ln(kr_0^2/D)|/|\ln(kr_0^2/D)|$. This value is intermediate between the one-dimensional case (where $\rho \sim 1$ for $t = \tau_{n=1}$) and the three-dimensional case (where $\rho \sim r_0^{1/2} k^{1/4}/D^{1/4}$ for $t = \tau_{n=3}$). The probability density $\phi = -\partial\rho/\partial t$ in this case is given by $\phi \approx 1/(t|\ln(kr_0^2/D)|)$ which, once again, has a heavy tail.

VI. CONCLUSIONS

In conclusion, we have extended the results of Refs. 10 and 11 to higher-dimensional SDD models under an assumption of radial symmetry. We obtained exact closed form expressions for the local accumulation times in the SDD models and analyzed their dependences on the model parameters. We found that when the radius of the source boundary R is not too small when $n = 2$, and for every R when $n = 1$ or $n = 3$, the local accumulation time in n dimensions is essentially given by the following expression:

$$\tau(r) \approx \frac{1}{2k}\left[\frac{r-R}{\lambda} + \eta_n\left(\frac{R}{\lambda}\right)\right], \quad \lambda = \sqrt{\frac{D}{k}}, \tag{28}$$

where λ is the diffusion length and $0 \leq \eta_n(x) \leq 1$ are some explicit functions, see (5), (15), and (17). Moreover, when the distance from a given point to the source boundary exceeds the diffusion length λ, the expressions for the local accumulation times in higher dimensions essentially coincide with that for the one-dimensional problem, regardless of the size of the source. Furthermore, we found that in this case the relaxation function $\rho(r, t)$ at a fixed position r behaves approximately as a step function in t, and thus in the limit of large distances from the source boundary the steady state profile is established in an essentially on-off manner at time $\tau(r)$. Therefore, in this regime the local accumulation time $\tau(r)$ provides a good measure of the timing for the establishment of the steady state at a given location r.

At the same time, when the size of the source is smaller than λ and the location of the point is also within λ from the source boundary, the kinetics of the concentration at a given location is more complicated and cannot in general be described using a single time scale. In this regime, the kinetics consists of three stages: first, a quasi steady-state is established on a diffusive time scale r^2/D, then the relaxation proceeds algebraically in three dimensions or logarithmically in two dimensions until the time scale of the reaction is reached, finally, an exponential relaxation to the steady state occurs beyond the reaction time scale k^{-1}. This is in contrast with one-dimensional linear SDD problems, in which the relaxation is always exponential near the source boundary. Thus, dimensionality may play a different role for the relaxation kinetics in one, two, and three space dimensions.

Finally, we note that while the relaxation kinetics in the problems with first order degradation may, in principle, be completely characterized via the exact solution of the corresponding linear parabolic problem (although this may not be very practical), the situation becomes considerably more complicated in the presence of nonlinear feedbacks. In fact, as we showed in the case of one-dimensional problems with higher-order degradation kinetics,[14] the character of the dependence of the local accumulation time on the model parameters may change dramatically in nonlinear problems. Furthermore, in contrast to the linear models considered in this paper, the relaxation to the steady state for models with higher order degradation occurs in a self-similar fashion far from the source.[16–18]

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[1] S. Shvartsman and R. Baker, WIREs Dev. Biol. **1**, 715 (2012).

[2] H. G. Othmer, K. Painter, D. Umulis, and C. Xue, Math. Model. Nat. Phenom. **4**, 3 (2009).

[3] A. Kicheva, P. Pantazis, T. Bollenbach, Y. Kalaidzidis, T. Bittig, F. Julicher, and M. Gonzalez-Gaitan, Science **315**, 521 (2007).

[4] A. D. Lander, Cell **128**, 245 (2007).

[5] O. Grimm, M. Coppey, and E. Wieschaus, Development **137**, 2253 (2010).

[6] J. A. Drocco, O. Grimm, D. W. Tank, and E. Wieschaus, Biophys. J. **101**, 1807 (2011).

[7] S. R. Yu, M. Burkhardt, M. Nowak, J. Ries, Z. Petrasek, S. Scholpp, P. Schwille, and M. Brand, Nature (London) **461**, 533 (2009).

[8] O. Wartlick, A. Kicheva, and M. Gonzalez-Gaitan, Cold Spring Harbor Perspect. Biol. **1**, a001255 (2009).

[9] S. B. Yuste, E. Abad, and K. Lindenberg, Phys. Rev. E **82**, 061123 (2010).

[10] A. M. Berezhkovskii, C. Sample, and S. Y. Shvartsman, Biophys. J. **99**, L59 (2010).

[11] A. Berezhkovskii, C. Sample, and S. Shvartsman, Phys. Rev. E **83**, 051906 (2011).

[12] A. Berezhkovskii and S. Shvartsman, J. Chem. Phys. **135**, 154115 (2011).

[13] A. B. Kolomeisky, J. Phys. Chem. Lett. **2**, 1502 (2011).

[14] P. V. Gordon, C. Sample, A. M. Berezhkovskii, C. B. Muratov, and S. Y. Shvartsman, Proc. Natl. Acad. Sci. U.S.A. **108**, 6157 (2011).

[15] *Handbook of Mathematical Functions*, edited by M. Abramowitz and I. Stegun (National Bureau of Standards, 1964).

[16] C. B. Muratov, P. V. Gordon, and S. Y. Shvartsman, Phys. Rev. E **84**, 041916–1 (2011).

[17] P. V. Gordon and C. B. Muratov, Networks Heterog. Media **7**, 767 (2012).

[18] P. V. Gordon and C. B. Muratov, "Eventual self-similarity of solutions for diffusion-absorption equations with a singular source in $\mathbb{R}^n$" (unpublished).