Collective motion of dimers

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We consider a discrete agent-based model on a one-dimensional lattice and a two-dimensional square lattice, where each agent is a dimer occupying two sites. Agents move by vacating one occupied site in favor of a nearest-neighbor site and obey either a strict simple exclusion rule or a weaker constraint that permits partial overlaps between dimers. Using indicator variables and careful probability arguments, a discrete-time master equation for these processes is derived systematically within a mean-field approximation. In the continuum limit, nonlinear diffusion equations that describe the average agent occupancy of the dimer population are obtained. In addition, we show that multiple species of interacting subpopulations give rise to advection-diffusion equations. Averaged discrete simulation data compares very well with the solution to the continuum partial differential equation models. Since many cell types are elongated rather than circular, this work offers insight into population-level behavior of collective cellular motion.

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I. INTRODUCTION

For many biological and physical processes, two levels of understanding are required: both a local understanding of the behavior of individuals and a global understanding of properties of the group [1,2]. Therefore, there has been much interest in converting stochastic agent-based models of local movement into a partial differential equation (PDE) description for the agent density or occupancy as a continuous function [3–8]. Many of these approaches, however, do not consider the shape of the agents; in many biological contexts, cells or microorganisms to be modelled as agents do have a shape, for example, being elongated rather than nominally spherical. Although there has been considerable work on modeling extended objects using a Potts model formalism [9,10], this is not the approach that we follow here.

A reasonably reliable methodology for mean-field treatment of monomer agents has emerged, validated by comparison of simulation against the solution of mean-field derived partial differential equations (PDEs) [11–13]. Across a broad range of models, the PDEs work well up to modest densities and sometimes better than one might expect at high densities. In contrast, there appears to be very little work on mean-field treatments of extended agents, with the exception of Simpson *et al.* [14] and Baker and Simpson [15] on the motion of rod-shaped agents with length L (agents that cover L adjacent sites). When exclusion effects are included in the model, the rod-shaped agents are more subtle. For example, an optimistic independence approximation between L adjacent sites [14] leads to the porous media-type PDE that works well at higher densities but does not match at low densities (a counterintuitive result for mean-field theories that neglect correlations), whereas a more careful analysis [15] produces a different PDE that is better at low densities.

The primary objective of the present paper is to study the performance of mean-field analysis of several models of interacting dimer agents in one and two dimensions and to that end, PDEs obtained from discrete models via mean-field techniques are compared with simulations. Mean-field arguments are essentially either arguments about approximate independence of events or arguments in which functions of indicator variables (random variables which take the values 0 or 1 only) are replaced by their averages. The point at which a mean-field argument is invoked and how it is implemented can have significant effects on the quality of the resulting approximation (see, e.g., Ref. [15]). We present careful arguments involving conditional probabilities, in which mean-field approximations are delayed in the analysis as long as possible and given as small a role as possible. Such an approach may be helpful in other contexts in developing a best-practice approach to mean-field approximation.

Although we address only dimers, the basic ideas can, in principle, be generalized to polymeric agents that occupy L lattice sites, although the algebraic complexity that ensues in dimensions greater than 1 may prove inconvenient. However, as we show for the dimer problem, a mapping to an equivalent problem of monomer motion on an associated covering lattice leads to considerable simplifications.

The one-dimensional lattice and the two-dimensional square lattice are considered, although the models can be defined on all standard lattices in two or three dimensions. The extension of the analysis to these cases would be relatively straightforward. We shall generally work with a finite fragment of the lattice, which carries N dimers. We discuss both a strict exclusion process and a partial overlapping process. In this latter model, two agents are permitted to occupy the same site, although only one of the two sites a given agent occupies may also be occupied by another agent at the same time. Such a model may be useful in the context of biological cells, which are deformable and can change shape to allow another cell to fit, within limits.

For dimer movement in two dimensions, changes in orientation (for example, from horizontal to vertical) must be taken into account. There are two different means for such a change of orientation. Either the agent can undergo a rigid rotation around a site [14] or it can undertake a right-angle turn by reptation in the sense of de Gennes [16]. Here we consider the latter type. In this case, only one site must be unoccupied

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for any given move to take place and any successful move empties exactly one site.

We now describe a discrete time and discrete space simulation method and the associated probabilistic model, which within a mean-field approximation and on taking a continuum limit, produces a PDE. If there are N agents on the lattice, then for each time step of duration τ, N agents are selected, one at a time, and given the opportunity to move. An agent selected as a candidate to move chooses to attempt to move with probability P. If the attempted move is permitted, then it takes place; however, if the move is not permitted (for example, the move does not satisfy exclusion rules or partial overlap rules), then the attempt is aborted and the agent must wait until the next occasion on which it is selected. In both one and two dimensions, a successful agent move empties one previously occupied site and causes a new site to be occupied.

There are two ways in which the selection of N agents to be offered moves at a given time step can be made and both are considered in our simulations. This can be performed using the random sequential update method [17], where, on average, each agent is chosen once. We call this method "random choice." This is the choice predominantly explored in the literature [6,11–15]. Alternatively, each agent can be chosen exactly once per time step but in a random sequence. We call this method "random order" [18]. Here we implement both methods and compare the simulation results with solutions to the continuum limit PDE.

In transitioning from a probabilistic model to a continuum model, it is usual to discuss lattice site occupancy. However, since we are working with agents which occupy more than a single lattice site, care must be taken when defining and discussing occupancy. Here we will determine *agent occupancy* by either keeping account of the site occupancy of the one end of the dimer agent (either right or left for horizontal agents or top or bottom for vertical agents) or by keeping account of their centers. With this meaning, occupancy is equivalent to the number of dimer agents in a given area and not on whether a given site is occupied by an agent.

In Sec. II we discuss dimers with strict exclusion in one dimension. The analysis, which produces the same result as one of the approaches in Baker and Simpson [15], is based on a careful consideration of conditional probabilities and has been written out in sufficient detail to serve as a simple introduction to the more complicated analyses that follow later in the paper. The mean-field treatment predicts a diffusivity that is linear in density and approaches a constant in the low-density limit. In Sec. III, we allow one-dimensional dimer agents to overlap partially and predict that the diffusivity is no longer a linear function of the density.

These processes are extended to dimer motion on the square lattice. First, in Sec. IV, we impose a strict exclusion and permit the dimers to attempt to move parallel to their current orientation (a translation) or to change orientation by reptation. Then, in Sec. V, we allow partial overlap.

It has long been known that in a simple exclusion process for monomers without directional preference, the continuum limit is classical diffusion for the system as a whole, while the effective diffusivity for a single tagged particle is density dependent. Some light has been shed on this by the study of multispecies exclusion processes [6,13], where transport terms that are suppressed for the population as a whole, but active for components of the population, are revealed. For this reason, in Sec. VI, we discuss exclusion processes for dimer systems containing two species.

Concerning notation, throughout the paper $\mathbb{P}(E)$ denotes the probability of the event E; the union of two events E and F is written for brevity as E, F; conditional probabilities $\mathbb{P}(E \mid F) = \mathbb{P}(E, F)/\mathbb{P}(F)$ are used extensively; angle brackets denote averages; and $\mathbb{Z}$, $\mathbb{Z}^2$ are the usual linear chain and square lattice with bonds of unit length and integer site coordinates.

Our analysis is directed towards producing PDEs to be compared with simulation data in which only moves involving a single agent occur at any instant, and either each agent is offered only one chance to attempt to move at discrete time n or the expected number of opportunities offered is 1. Therefore, in all probability arguments written down, only events involving single agent attempts to move are considered. Subject to that caveat, all probability arguments are exact up to the point where it is stated explicitly that a mean-field approximation is being made.

II. SIMPLE EXCLUSION: 1D LATTICE

We begin by considering dimer agents on a one-dimensional lattice moving randomly, with the restriction that each site may be occupied by at most one agent. Figure 1 shows examples of an allowed and a disallowed position of neighboring dimers.

A. Probabilistic model

We consider a one-dimensional lattice separated by bonds of length Δ, with a generic site x and we write $i = \Delta^{-1}x$ with $i \in \mathbb{Z}$. There are N dimer agents of length 2Δ placed without overlap on the lattice. The dimers move on the lattice making only nearest-neighbor steps.

For horizontal agents moving on a line, the site occupancy of the *right-hand side* of the dimer agent will be determined using indicator variables.

At each time step, we choose an agent randomly and suppose that the agent will attempt to move with probability

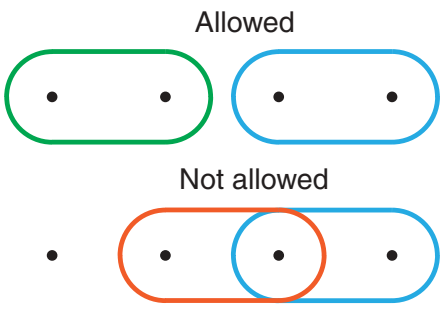

FIG. 1. (Color online) Dimers with simple exclusion in 1D: A dimer may occupy a neighboring pair of sites to another dimer (top row) but two dimers may not occupy the same site (bottom row). The dots are lattice sites.

P. We consider the indicator function

$$\gamma_n(i) = \begin{cases} 1 & \text{if site } i \text{ is occupied by the } \textit{right side} \\ & \text{of an agent after } n \text{ time-steps,} \\ 0 & \text{otherwise.} \end{cases} \quad (1)$$

We set out to calculate the change in the probability of occupancy of site i from time step n to time step $n+1$. There are only three ways that a single agent move can change the occupancy status of site i: (i) there is (the right side of) a dimer at i and that dimer moves to vacate site i, (ii) there is no (right side of a) dimer at i and invasion of i from the left occurs, and (iii) there is no (right side of a) dimer at i and invasion of i from the right occurs. For notational brevity, it is to be understood that in any event containing $\gamma_n(j) = 1$, it is the agent whose right side is at j that is being invited to attempt to move. We have

$$\begin{aligned} \mathbb{P}(\gamma_{n+1}(i) = 1) &= \mathbb{P}(\gamma_{n+1}(i) = 1, \gamma_n(i) = 1) + \mathbb{P}(\gamma_{n+1}(i) = 1, \gamma_n(i) = 0) \\ &= \mathbb{P}(\gamma_{n+1}(i) = 1, \gamma_n(i) = 1) + \sum_{s=\pm 1} \mathbb{P}(\gamma_{n+1}(i) = 1, \gamma_n(i) = 0, \gamma_{n+1}(i+s) = 0, \gamma_n(i+s) = 1). \end{aligned} \quad (2)$$

Under the strict exclusion condition, $\gamma_n(i+s) = 1$ for $s = \pm 1$ guarantees that $\gamma_n(i) = 0$, while $\gamma_{n+1}(i) = 1$ guarantees that $\gamma_{n+1}(i+s) = 0$, so we may write simply

$$\mathbb{P}(\gamma_{n+1}(i) = 1) = \mathbb{P}(\gamma_{n+1}(i) = 1, \gamma_n(i) = 1) + \sum_{s=\pm 1} \mathbb{P}(\gamma_{n+1}(i) = 1, \gamma_n(i+s) = 1).$$

Next we note that

$$\mathbb{P}(\gamma_{n+1}(i) = 1, \gamma_n(i) = 1) = \mathbb{P}(\gamma_n(i) = 1) - \sum_{s=\pm 1} \mathbb{P}(\gamma_{n+1}(i) = 0, \gamma_n(i) = 1, \gamma_{n+1}(i+s) = 1, \gamma_n(i+s) = 0), \quad (3)$$

$$= \mathbb{P}(\gamma_n(i) = 1) - \sum_{s=\pm 1} \mathbb{P}(\gamma_n(i) = 1, \gamma_{n+1}(i+s) = 1). \quad (4)$$

In conditional probability notation, we have

$$\begin{aligned} \mathbb{P}(\gamma_{n+1}(i) = 1) - \mathbb{P}(\gamma_n(i) = 1) = &\sum_{s=\pm 1} \mathbb{P}(\gamma_{n+1}(i) = 1 \mid \gamma_n(i+s) = 1)\mathbb{P}(\gamma_n(i+s) = 1) \\ &- \sum_{s=\pm 1} \mathbb{P}(\gamma_{n+1}(i+s) = 1 \mid \gamma_n(i) = 1)\mathbb{P}(\gamma_n(i) = 1). \end{aligned} \quad (5)$$

We assume that a selected agent attempts to move with probability P and does so in either direction with probability $1/2$, independently of the current local situation. However, if one of the sites it is trying to occupy is already occupied by part of another agent, then the move is aborted. Hence, in Eq. (5) for $s = \pm 1$ we have

$$\begin{aligned} \mathbb{P}(\gamma_{n+1}(i) = 1 \mid \gamma_n(i+s) = 1) &= \frac{P}{2}\mathbb{P}(\gamma_n(i-s) = 0, \gamma_n(i) = 0 \mid \gamma_n(i+s) = 1) \\ &= \frac{P}{2}\mathbb{P}(\gamma_n(i-s) = 0 \mid \gamma_n(i+s) = 1). \end{aligned} \quad (6)$$

Similar arguments [19] give an expression for the conditional probability in the second sum in Eq. (5).

In order to use a mean-field approach, we must make an approximation of independence, as we require probabilities of occupancy by the right sides of dimers at a single site without reference to its neighbors.

Approximation 1. The probability of a site j being occupied is independent of the occupancy of the sites $j \pm 2$.

By way of example, for $s = \pm 1$ and any site j,

$$\mathbb{P}(\gamma_n(j-s) = 1 \mid \gamma_n(j+s) = 1) \approx \mathbb{P}(\gamma_n(j-s) = 1).$$

If we write

$$r_n(i) = \langle \gamma_n(i) \rangle = \mathbb{P}(\gamma_n(i) = 1), \quad (7)$$

then within the mean-field approximation, Eq. (5) can be written as a discrete-time master equation,

$$r_{n+1}(i) - r_n(i) = \frac{P}{2}\left\{ -r_n(i) \sum_{s=\pm 1} (1 - r_n(i+2s)) + \sum_{s=\pm 1} r_n(i+s)(1 - r_n(i-s)) \right\}. \quad (8)$$

B. Continuum limit

One could compare the solutions of the master equation (8) directly with simulations, but as the ultimate goal is to obtain a PDE description that matches simulations, we proceed to take the appropriate continuum limit, as the distance Δ between lattice sites and the time τ between consecutive time steps tends to zero. To that end, we now return to $x = \Delta i$ and define $t = n\tau$, and we write $r_n(i) = R(x,t)$, where $R(x,t)$ is a continuous variable representing the *local average right-side occupancy*. Supposing R is sufficiently smooth, we use a Taylor expansion,

$$r_n(i+k) = R + k\Delta \frac{\partial R}{\partial x} + \frac{(k\Delta)^2}{2}\frac{\partial^2 R}{\partial x^2} + o(\Delta^2), \quad (9)$$

where R and its spatial derivatives are evaluated at (x,t). Equation (8) then can be rewritten as

$$\tau\frac{\partial R}{\partial t}+o(\tau)=\frac{P}{2}\Delta^2\left[(1+2R)\frac{\partial^2 R}{\partial x^2}+2\left(\frac{\partial R}{\partial x}\right)^2\right]+o(\Delta^2). \tag{10}$$

Taking the limit $\Delta,\tau\to 0$ simultaneously while keeping the ratio Δ^2/τ constant leads to the nonlinear diffusion equation

$$\frac{\partial R}{\partial t}=D_0^{(1)}\frac{\partial}{\partial x}\left[(1+2R)\frac{\partial R}{\partial x}\right], \tag{11}$$

where

$$D_0^{(1)}=\frac{P}{2}\lim_{\Delta,\tau\to 0}\frac{\Delta^2}{\tau}. \tag{12}$$

It is worth noting that if the calculations are repeated for agents of length L, with an equivalent independence approximation we obtain the equation for the *average right-side occupancy* as

$$\frac{\partial R}{\partial t}=D_0^{(1)}\frac{\partial}{\partial x}\left[(1+2(L-1)R)\frac{\partial R}{\partial x}\right], \tag{13}$$

with $D_0^{(1)}$ defined by Eq. (12). Both of Eqs. (11) and (13) behave as expected in the limit as the agent density becomes small ($R\to 0$), namely the PDEs reduce to linear diffusion equations. The continuum limit (11) was derived by different means in Baker and Simpson [15].

C. Simulation results

Simulations are performed on a lattice with $1\leqslant x\leqslant 300$. The N agents are initially placed in an interval J in the center of the lattice, corresponding to a density $d>0$, with details given in Appendix A. Here $J=[130,171]$, $P=1,\Delta=1,\tau=1$, and zero-flux boundary conditions are implemented.

We compare the average *right-side* occupancy obtained from the simulation with solutions to the nonlinear diffusion equation (11) for three values of the density d and random choice and random order method of choosing the N agents at each time step (Fig. 2). Note that $d=1/2$ corresponds to close packed dimer agents, since the right sides of the agents (determining R) occupy half the sites and the left sides of the agents occupy the remaining half of the sites. In both the discrete and continuous profiles, the agents or density spread out with time. Visually, we observe that the average discrete simulation and the PDE profiles fit better at the lower values of density d and the random choice fits better than the random order of agents. The fit is quantified by total squared error in Table I in Appendix C. For both methods, the fit improves as time increases. In particular, we note that the PDE captures the position of the front and and small density profile (where $R\approx 0$) well. The accuracy of the independence approximation given by Approximation 1 is determined. Certainly the approximation is excellent for small agent occupancy but the results detailed in Appendix D show that the approximation is relatively good even for moderate values of the agent occupancy (for example, up to 0.3). The discrepancies observed in Fig. 2 for the larger initial condition ($d=1/2$) can be mostly attributed to the limitations in Approximation 1.

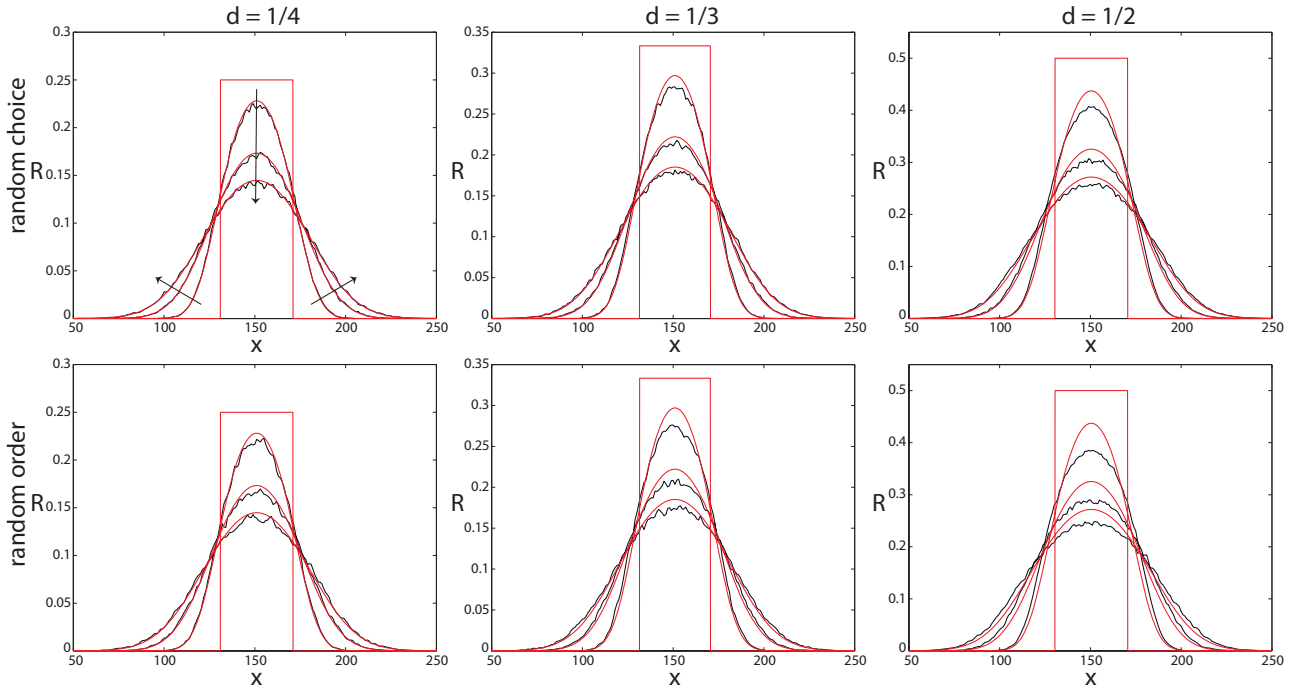

FIG. 2. (Color online) Dimers with simple exclusion in 1D: Solutions of Eq. (11) [red (medium gray)] and the right-side occupancy averaged over 10 000 realizations (black) with the initial density $d=1/4,1/3,1/2$ for $130\leqslant x\leqslant 171$ at times $t=100$, 300, and 500. The initial condition is also shown [red (medium gray)]. Here $P=1,\Delta=1,\tau=1$ for the simulations and MATLAB pdepe with $\delta x=0.1$ for solving Eq. (11). (Top row) Random choice of agents. (Bottom row) Random order of agents. The arrows (indicated in the first subfigure only) indicate the direction of increasing time. Note the different vertical scales.

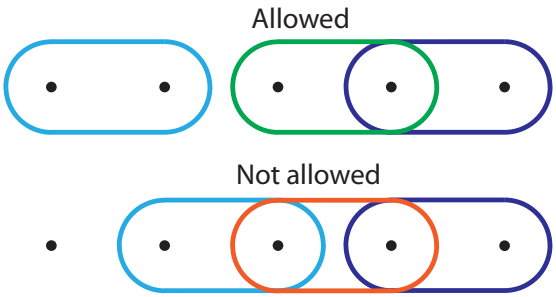

FIG. 3. (Color online) Dimers with partial overlaps in 1D: A dimer may overlap one other dimer (top row), but a dimer may not overlap two others (bottom row). Dimers also may not occupy the same two sites as another dimer. The dots are lattice sites.

III. PARTIAL OVERLAPS: 1D LATTICE

In this section we continue to consider dimers on the same one-dimensional lattice (described in Sec. II), but now we weaken the volume exclusion constraint. Instead, we now allow a dimer agent to have a partial overlap with another dimer. More precisely, each site can be occupied at most by two agents and each agent can share at most one site with at most one other agent. Figure 3 illustrates an example of an allowed and a disallowed configuration. Of course, partial overlapping means that two agents cannot be on top of each other, that is, one site cannot be occupied by right sides of two agents.

The aim of this model is to make allowances for cell deformation: cells can change shape (up to a limit) to allow another cell to pass them. By allowing an overlap on one side but not the other, we can model a cell that can reduce in size and shape to occupy only 3/4 of its original size but no smaller than that.

A. Probabilistic model

As in Sec. II, the dimers are permitted to make only nearest-neighbor steps and when we refer to occupancy we mean the occupancy by the right side of a dimer, with $\gamma_n(i)$ the indicator variable defined by Eq. (1).

We can now express $\mathbb{P}(\gamma_{n+1}(i)=1)$ in terms of the situation at time step n, exactly as in Eq. (2). Again we only need to consider events in which one dimer is offered the opportunity to attempt to move. As in Sec. II, in any event containing $\gamma_n(j)=1$, it is the agent whose right side is at j that is being invited to attempt to move. Unlike in Sec. II, now it is not the case that the right sides of agents must be at least two sites apart, so we cannot replace a compound event $\gamma_n(i)=1, \gamma_n(1+s)=0$ by the simpler-looking event $\gamma_n(i)=1$. However, we still have from Eq. (2) that

$$\mathbb{P}(\gamma_{n+1}(i)=1) = \mathbb{P}(\gamma_{n+1}(i)=1, \gamma_n(i)=1) + \sum_{s=\pm1} \mathbb{P}(\gamma_{n+1}(i)=1, \gamma_{n+1}(i+s)=0 \,|\, \gamma_n(i)=0, \gamma_n(i+s)=1)\mathbb{P}(\gamma_n(i)=0, \gamma_n(i+s)=1). \tag{14}$$

Although Eq. (4) is not valid, we can use Eq. (3) to write

$$\mathbb{P}(\gamma_{n+1}(i)=1, \gamma_n(i)=1) = \mathbb{P}(\gamma_n(i)=1) - \sum_{s=\pm1} \mathbb{P}(\gamma_{n+1}(i)=0, \gamma_{n+1}(i+s)=1 \,|\, \gamma_n(i)=1, \gamma_n(i+s)=0)\mathbb{P}(\gamma_n(i)=1, \gamma_n(i+s)=0). \tag{15}$$

Thus, our discrete-time master equation becomes

$$\begin{aligned}\mathbb{P}(\gamma_{n+1}(i)=1) - \mathbb{P}(\gamma_n(i)=1) &= \sum_{s=\pm1} \mathbb{P}(\gamma_{n+1}(i)=1, \gamma_{n+1}(i+s)=0 \,|\, \gamma_n(i)=0, \gamma_n(i+s)=1)\mathbb{P}(\gamma_n(i)=0, \gamma_n(i+s)=1) \\ &\quad - \sum_{s=\pm1} \mathbb{P}(\gamma_{n+1}(i)=0, \gamma_{n+1}(i+s)=1 \,|\, \gamma_n(i)=1, \gamma_n(i+s)=0)\mathbb{P}(\gamma_n(i)=1, \gamma_n(i+s)=0).\end{aligned} \tag{16}$$

We assume that an agent tries to move in either direction with probability $P/2$, independently of the current local situation, and the move is aborted if it would violate the partial overlap constraint. Thus, the event $\gamma_{n+1}(i)=1, \gamma_{n+1}(i+s)=0$ can follow from the event $\gamma_n(i)=0, \gamma_n(i+s)=1$ if and only if we have $\gamma_n(i-s)=0$ or $\gamma_n(i-2s)=0$. Hence,

$$\mathbb{P}(\gamma_{n+1}(i)=1, \gamma_{n+1}(i+s)=0 \,|\, \gamma_n(i)=0, \gamma_n(i+s)=1) = \frac{P}{2}[1 - \mathbb{P}(\gamma_n(i-s)=1, \gamma_n(i-2s)=1 \,|\, \gamma_n(i)=0, \gamma_n(i+s)=1)]. \tag{17}$$

Therefore the right-hand side of Eq. (16) can be written in terms of events at time n only.

For the strict exclusion case, a single simplifying approximation was needed to obtain an equation for $\mathbb{P}(\gamma_n(i)=1)$. However, in the present partial overlapping case, two approximations are required: one to deal with the compound event probabilities $\mathbb{P}(\gamma_n(i)=0, \gamma_n(i+s)=1)$ when $s=\pm1$ appearing in Eq. (16) and one to deal with the conditional probabilities involving four events in Eq. (16).

Approximation 2. The probability that a site j is occupied and a specified neighbor (one of sites $j \pm s$ for $s = \pm 1$) is unoccupied is equal to the product of the probabilities that site j is occupied and site $j \pm s$ is unoccupied.

That is, for $s = \pm 1$, and any site j,

$$\mathbb{P}(\gamma_n(j) = 1, \gamma_n(j+s) = 0) \approx \mathbb{P}(\gamma_n(j) = 1)\mathbb{P}(\gamma_n(j+s) = 0). \quad (18)$$

Note that this approximation is used only for this specific combination of events.

Approximation 3. For $s = \pm 1$, the probability that two neighboring sites j and $j - s$ are both occupied when site $j + s$ is unoccupied and site $j + 2s$ is occupied is equal to the product of the probabilities that sites j and $j - s$ are occupied divided by the probability that site $j + s$ is unoccupied.

That is, for $s = \pm 1$ and any site j,

$$\mathbb{P}(\gamma_n(j) = 1, \gamma_n(j-s) = 1 \,|\, \gamma_n(j+s) = 0, \gamma_n(j+2s) = 1) \approx \frac{\mathbb{P}(\gamma_n(j) = 1)\,\mathbb{P}(\gamma_n(j-s) = 1)}{\mathbb{P}(\gamma_n(j+s) = 0)}. \quad (19)$$

This approximation allows us to be consistent with Approximation 1 for the nonoverlapping strict exclusion dimer case: for $s = \pm 1$ we do not want the probability that sites j and $j - s$ are occupied when site $j + s$ is unoccupied to depend on the occupancy of site $j + 2s$, which is not adjacent to either of the occupied sites j and $j - s$. Approximation 3 is the only approximation consistent with this requirement in addition to Approximation 2 and the law of total probability over the occupancy of three neighboring sites.

Using $r_n(i)$ for the average right-side occupancy [Eq. (7)], then with Approximations 2 and 3 and Eq. (17), we can write Eq. (16) as a discrete-time master equation:

$$r_{n+1}(i) - r_n(i) = \frac{P}{2}\left\{ \sum_{s=\pm 1} r_n(i+s)[1 - r_n(i) - r_n(i-s)\,r_n(i-2s)] - r_n(i) \sum_{s=\pm 1} [1 - r_n(i+s) - r_n(i+2s)\,r_n(i+3s)] \right\}. \quad (20)$$

This mean-field approximate master equation based on the particular choice of independence approximations is not the only approximate master equation that could be obtained for the model. Different independence assumptions, and especially approximations made earlier in the analysis with less attention to the constraints, would yield different results. We have made the Approximations 2 and 3 for the following reasons: they are consistent with the approximations with strict volume exclusion, they are made as late as possible in the analysis, and they provide good results.

B. Continuum limit

As in Sec. II B, we now consider continuous variables $x = i\Delta$, $t = n\tau$, and $r_n(i) = R(x,t)$, where R represents the *local average right-side occupancy*. Assuming R is sufficiently smooth, we use a Taylor expansion as in Eq. (9) and derive the equation

$$\tau \frac{\partial R}{\partial t} + o(\tau) = \frac{P}{2}\Delta^2 \left[(1 + 7R^2)\frac{\partial^2 R}{\partial x^2} + 14R\left(\frac{\partial R}{\partial x}\right)^2 \right] + o(\Delta^2). \quad (21)$$

Letting $\Delta, \tau \to 0$ simultaneously while keeping the ratio Δ^2/τ constant, we obtain the nonlinear diffusion equation

$$\frac{\partial R}{\partial t} = D_0^{(1)} \frac{\partial}{\partial x}\left[(1 + 7R^2)\frac{\partial R}{\partial x} \right], \quad (22)$$

with $D_0^{(1)}$ given by Eq. (12). Equation (22) behaves as expected at very low density, where the PDE reduces to a linear diffusion equation.

C. Simulation results

Simulations are performed on a lattice with $1 \leqslant x \leqslant 300$. The N agents are initially placed in an interval J in the center of the lattice, corresponding to a density $d > 0$, with details given in Appendix A. Here $J \approx [130, 171]$ for the values of d chosen. Here $P = 1, \Delta = 1, \tau = 1$ and zero-flux boundary conditions are implemented.

We compare the average *right-side* occupancy obtained from the simulation with solutions to the nonlinear diffusion equation (22) for three values of the density d, and random choice and random order method of choosing the N agents at each time step (Fig. 4). Note that $d = 2/3$ corresponds to close packed dimer agents with maximum partial overlapping.

The discrete and continuous profiles spread out with time. Visually, we observe that the average discrete simulation and the PDE profiles fit reasonably well for all values of density d. For this case, it is not clear which method of simulation matches the solution to the nonlinear diffusion equation more closely: the random order method diffuses slightly faster than the PDE solution and the random choice method diffuses slightly slower. That being said, both simulations are very close to each other and the PDE solution. At earlier times the PDE matches the random choice simulations slightly better, whereas at later times the match for the random order method appears a little better (see total squared error in Table II in Appendix C). It is worth noting that there is more variability in the simulation results at lower values of the density, perhaps because there is an increase in motility due to fewer prohibited moves at lower values d.

IV. SIMPLE EXCLUSION: 2D LATTICE

We now return to the original volume exclusion constraint preventing agents from changing their size or overlapping with

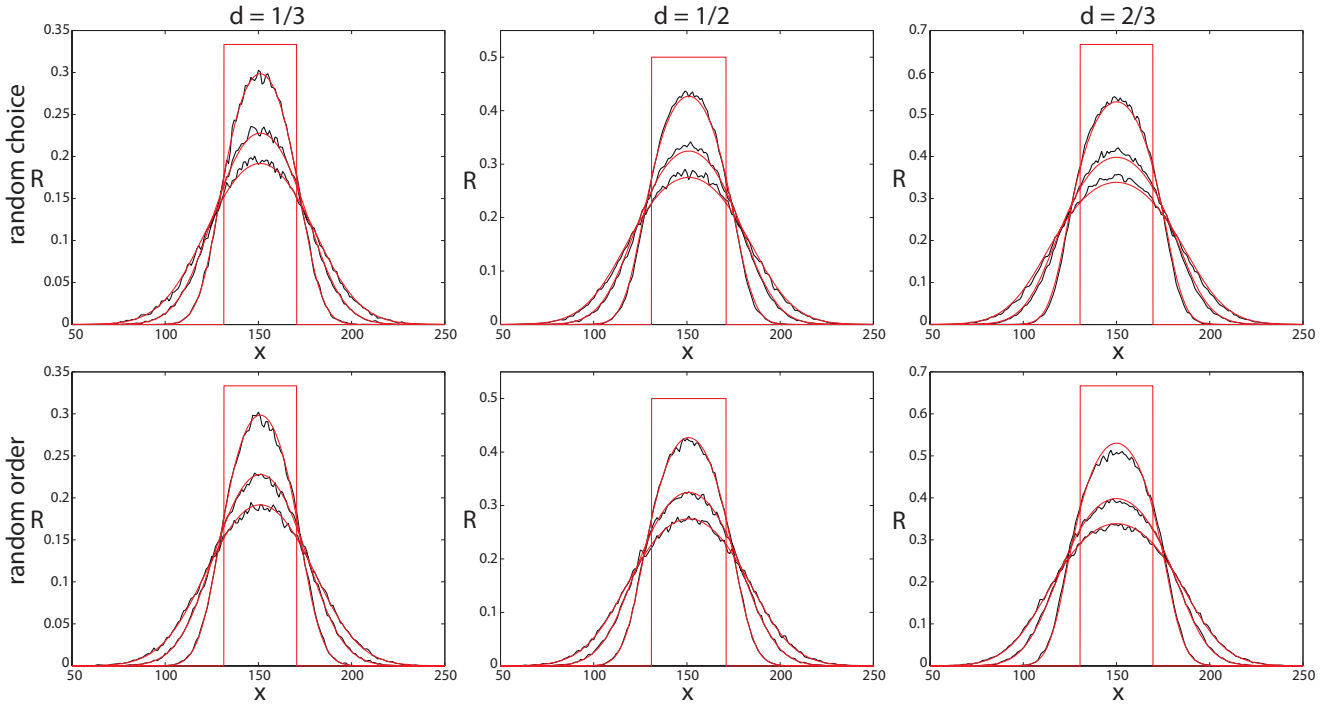

FIG. 4. (Color online) Dimers with partial overlaps in 1D: Solutions of Eq. (22) [red (medium gray)] and the right-side occupancy averaged over 10 000 realizations (black) with the initial density $d = 1/3, 1/2$, for $130 \leqslant x \leqslant 171$ and $d = 2/3$ for $130 \leqslant x \leqslant 170$ ($d = 2/3$ is the maximum density) at times $t = 100$, 300, and 500. The initial condition is also shown [red (medium gray)]. Here $P = 1, \Delta = 1, \tau = 1$ for the simulations and MATLAB pdepe with $\delta x = 0.1$ for solving Eq. (22). (Top row) Random choice of agents. (Bottom row) Random order of agents. Note the different vertical scales.

each other but extend the problem to two dimensions. This allows the model to predict more realistic cell movement, as cells are rarely only able to move in one dimension. However, this also adds more complexity to the problem as the agents can now be oriented horizontally or vertically on the lattice and move between the two orientations. We allow these changes to occur by reptation (snaking). Figure 5 illustrates a dimer moving from a vertical orientation to a horizontal orientation.

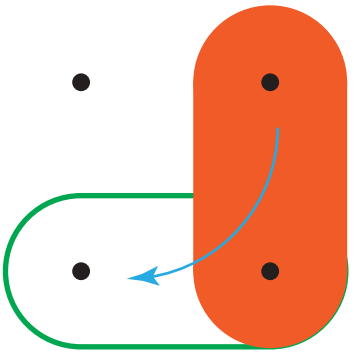

FIG. 5. (Color online) Example of a reptation movement in 2D: The vertical dimer moves to the horizontal position shown in outline. The dots are lattice sites. Although it is shown as unoccupied, the lattice site in the top left corner does not have to be unoccupied for a reptation event in order for the move to take place. (A rigid body rotation around the lower right site would require the top left site to also be unoccupied [14].)

A. Probabilistic model

We consider a two-dimensional square lattice for which all bonds are of length Δ, with a generic site $\mathbf{x} = (x, y)$. Again, all agents are of length 2Δ and move with simple exclusion, but this is complicated by the fact that there are now two orientations labeled H (horizontal) and V (vertical). Initially, we write $(i, j) = \Delta^{-1}\mathbf{x}$ so $(i, j) \in \mathbb{Z}^2$ is a site on a lattice with bonds of unit length, although eventually we will return to the original lattice and consider the limit $\Delta \to 0$.

When a selected agent attempts to move, it can do so in one of six possible ways, two of which preserve orientation and four of which change it. A horizontal agent occupying sites (i, j) and $(i + 1, j)$ can attempt to move horizontally to sites $(i - 1, j)$ and (i, j) or to sites $(i + 1, j)$ and $(i + 2, j)$, or as shown in Fig. 6 it can attempt to change orientation to occupy one of the pairs of sites (i, j) and $(i, j + 1)$; $(i, j - 1)$ and (i, j); $(i + 1, j)$ and $(i + 1, j + 1)$; or $(i + 1, j - 1)$ and $(i + 1, j)$. A vertical agent similarly has six possibly moves to attempt. Each of the possible moves vacates one site and occupies one new site, and if the new site is already occupied the attempted move is aborted. [Note that if dimers change orientation by rigid rotation rather than by reptation, there are two sites rather than only one that need to be vacant for an attempted orientation change to be allowed [14] (Fig. 5).]

For the present, a selected agent attempts to move with probability P and does so in six possible ways each with probability 1/6. This simplest case is worked through in detail for clarity. In Appendix D, corresponding results are summarized for the more general model in which the two

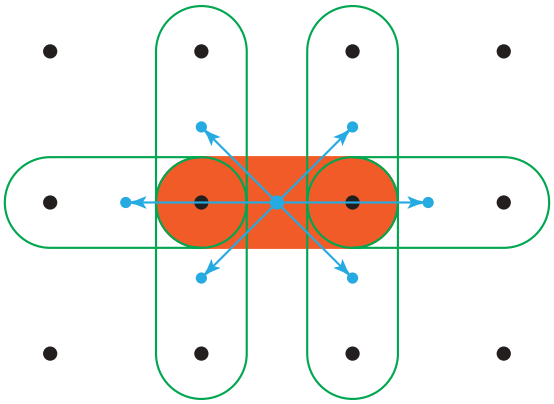

FIG. 6. (Color online) Six possible dimer movement operations. The horizontal agent [red (medium gray) at sites (i,j) and $(i+1,j)$] has six possible moves to attempt, to the positions shown in outline. The dots are lattice sites. The center of the agent [blue (light gray)] correspondingly moves to one of six possible new positions shown [blue (light gray) arrows], each of which uniquely describes the new position of the agent.

moves that keep the same orientation each have probability $\mu/6$ and the four moves that lead to a different orientation each have probability $\rho/6$.

The model in two dimensions is more complicated than the model for one dimension, partly because there are two possible orientations for each agent and the allowed moves depend on whether the agent is currently horizontal or vertical. However, if an agent is horizontal its center will be at position $(a+\frac{1}{2},b)$ for some integers a, b, but if the agent is vertical its center will be at position $(a,b+\frac{1}{2})$, which cannot be the center of a horizontal agent. The position of the agent's center therefore tells us the position of both its ends and whether it is horizontal or vertical (Fig. 7). Therefore, we can simplify the analysis by replacing the motion of dimers on the square lattice by the equivalent problem of motion of monomers on a new lattice. In the context of percolation theory, this would be described as the covering lattice of the square lattice [20].

To construct the covering lattice we first define its sites to be the midpoints of bonds of the original lattice. Then any two sites of the covering lattice are deemed joined by a bond of the covering lattice if the corresponding bonds of the original lattice share a common site. The covering lattice is a new square lattice with bonds of length $\sqrt{2}/2$ inclined at an angle of $\pi/4$ to the original lattice (Fig. 7), but half of its faces are crossed by two diagonal bonds of length 1, which are regarded as nonintersecting, giving a lattice of coordination number 6.

The dimer agent problem for any lattice can be turned into an equivalent monomer problem in the same way, but we confine our attention to the square lattice. The strict exclusion requirement on the original lattice becomes the requirement that all six nearest-neighbor sites of an occupied site on the covering lattice must be unoccupied. We shall denote a generic site of the covering lattice by $\mathbf{u}$ and we introduce the indicator function

$$\gamma_n(\mathbf{u}) = \begin{cases} 1 & \text{if site } \mathbf{u} \text{ is occupied at time step } n \\ 0 & \text{otherwise.} \end{cases}$$

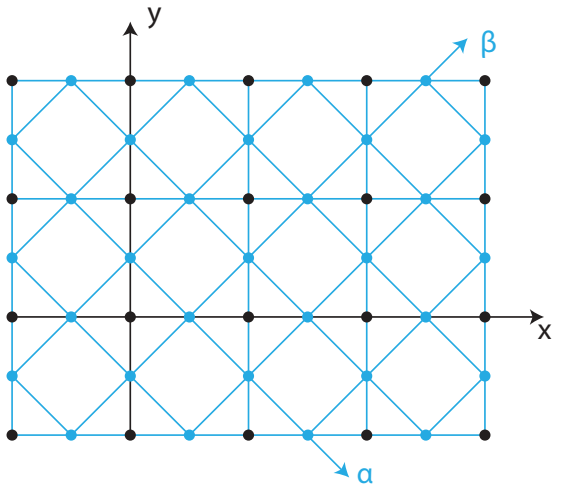

FIG. 7. (Color online) Original lattice and covering lattice: The original lattice sites (black) with directions x and y, compared to the new lattice site [blue (light gray)] with directions α and β. Agents can move to any of the six sites connected to the current site by a line, either through one of the black site (movement without changing orientation) or not (movement changing the orientation). The blue (light gray) square lattice, together with a pair of diagonal bonds regarded as nonintersecting in every second square, is the covering lattice of the square lattice.

The neighbors of $\mathbf{u}$ are denoted by $\mathcal{N}(\mathbf{u})$ and we write $\mathcal{M}(\mathbf{u}) = \mathcal{N}(\mathbf{u}) \cup \{\mathbf{u}\}$.

We now calculate $\mathbb{P}(\gamma_{n+1}(\mathbf{u})=1)$ in terms of the conditions at time step n. Since the exclusion condition tells us that at time step n at most one site of $\mathcal{M}(\mathbf{u})$ can be occupied, we can write

$$\mathbb{P}(\gamma_{n+1}(\mathbf{u})=1) = \sum_{\mathbf{v}\in\mathcal{M}(\mathbf{u})} \mathbb{P}(\gamma_{n+1}(\mathbf{u})=1 \mid \gamma_n(\mathbf{v})=1)\mathbb{P}(\gamma_n(\mathbf{v})=1). \quad (23)$$

The exclusion constraint also tells us that an agent cannot move to one of its neighboring sites unless the new site and all of its neighbors are unoccupied, so for $\mathbf{v}\in\mathcal{N}(\mathbf{u})$,

$$\begin{aligned}\mathbb{P}(\gamma_{n+1}(\mathbf{u})=1 \mid \gamma_n(\mathbf{v})=1) &= \frac{P}{6}\mathbb{P}(\{\gamma_n(\mathbf{w})=0\}_{\mathbf{w}\in\mathcal{M}(\mathbf{u})\setminus\mathbf{v}} \mid \gamma_n(\mathbf{v})=1) \\ &= \frac{P}{6}\mathbb{P}(\{\gamma_n(\mathbf{w})=0\}_{\mathbf{w}\in\mathcal{N}(\mathbf{u})\setminus\mathcal{M}(\mathbf{v})} \mid \gamma_n(\mathbf{v})=1), \quad (24)\end{aligned}$$

where $\mathcal{N}(\mathbf{u})\setminus\mathcal{M}(\mathbf{v})$ denotes the set of sites in $\mathcal{N}(\mathbf{u})$ that are not also sites of $\mathcal{M}(\mathbf{v})$, since we know that all sites in $\mathcal{N}(\mathbf{v})$ must be unoccupied when $\gamma_n(\mathbf{v})=1$. Further simplification is possible. By checking the two cases in which the bond joining the sites $\mathbf{u}$ and $\mathbf{v}$ has length $\sqrt{2}/2$ or length 1, we readily verify that there are only three sites in $\mathcal{N}(\mathbf{u})\setminus\mathcal{M}(\mathbf{v})$ and the exclusion constraint ensures that at most one of these can be occupied at the same time. Hence,

$$\mathbb{P}(\{\gamma_n(\mathbf{w})=0\}_{\mathbf{w}\in\mathcal{N}(\mathbf{u})\setminus\mathcal{M}(\mathbf{v})} \mid \gamma_n(\mathbf{v})=1) = 1 - \sum_{\mathbf{w}\in\mathcal{N}(\mathbf{u})\setminus\mathcal{M}(\mathbf{v})} \mathbb{P}(\gamma_n(\mathbf{w})=1 \mid \gamma_n(\mathbf{v})=1). \quad (25)$$

To compute $\mathbb{P}(\gamma_{n+1}(\mathbf{u}) = 1 \mid \gamma_n(\mathbf{u}) = 1)$ we note that if $\gamma_n(\mathbf{u}) = 1$, the only way that the event $\gamma_{n+1}(\mathbf{u}) = 1$ can be stopped from occurring by a single agent move is if the agent at $\mathbf{u}$ chooses to move to a site $\mathbf{v}$ which is unoccupied and has appropriate vacant neighbors, giving

$$\mathbb{P}(\gamma_{n+1}(\mathbf{u}) = 1 \mid \gamma_n(\mathbf{u}) = 1) = 1 - \frac{P}{6} \sum_{\mathbf{v}\in\mathcal{N}(\mathbf{u})} \left(1 - \sum_{\mathbf{w}\in\mathcal{N}(\mathbf{v})\setminus\mathcal{M}(\mathbf{u})} \mathbb{P}(\gamma_n(\mathbf{w}) = 1 \mid \gamma_n(\mathbf{u}) = 1)\right). \tag{26}$$

Up to this point, no approximations have been made in our analysis of probabilities of events involving a single agent move. We now make a mean-field approximation.

Approximation 4. The probability of site $\mathbf{u}$ being occupied is independent of the occupancy of the sites $\mathbf{w} \notin \mathcal{M}(\mathbf{u})$.

From Eqs. (24)–(26) we obtain an equation (under the mean-field approximation) for the evolution of

$$\mathbb{P}(\gamma_n(\mathbf{u}) = 1) = \langle\gamma_n(\mathbf{u})\rangle,$$

where angle brackets denote expectation, namely

$$\mathbb{P}(\gamma_{n+1}(\mathbf{u}) = 1) - \mathbb{P}(\gamma_n(\mathbf{u}) = 1) = \frac{P}{6}\Bigg\{ - \mathbb{P}(\gamma_n(\mathbf{u}) = 1) \sum_{\mathbf{v}\in\mathcal{N}(\mathbf{u})} \left(1 - \sum_{\mathbf{w}\in\mathcal{N}(\mathbf{v})\setminus\mathcal{M}(\mathbf{u})} \mathbb{P}(\gamma_n(\mathbf{w}) = 1)\right) + \sum_{\mathbf{v}\in\mathcal{N}(\mathbf{u})} \mathbb{P}(\gamma_n(\mathbf{v}) = 1)\left(1 - \sum_{\mathbf{w}\in\mathcal{N}(\mathbf{u})\setminus\mathcal{M}(\mathbf{v})} \mathbb{P}(\gamma_n(\mathbf{w}) = 1)\right)\Bigg\}. \tag{27}$$

B. Continuum limit

We take the continuum limit of Eq. (27) which is in terms sites of the covering lattice, but retaining the meaning of Δ as the lattice spacing on the original lattice. As before, $t = n\tau$. If we write $\mathbf{x}$ for the position of a generic site $\mathbf{u}$ of the covering lattice, then we note that the site $\mathbf{u}$ is of one of two types: type H if the associated dimer orientation is horizontal and the corresponding step possibilities on the covering lattice are an orientation change with the four displacements $(\pm\Delta/2, \pm\Delta/2)$ and horizontal translations with $(\pm\Delta,0)$ and type V if the associated dimer orientation is vertical, and the corresponding step possibilities on the covering lattice are an orientation change with the four displacements $(\pm\Delta/2, \pm\Delta/2)$, and vertical translations with $(0, \pm\Delta)$. We write

$$\langle\gamma_n(\mathbf{u})\rangle = \begin{cases} H(\mathbf{x},t) & \text{if site } \mathbf{u} \text{ is type H} \\ V(\mathbf{x},t) & \text{if site } \mathbf{u} \text{ is type V} \end{cases},$$

where $H(\mathbf{x},t)$, $V(\mathbf{x},t) \in [0,\frac{1}{2}]$ are the local average horizontal and vertical agent densities, respectively. The maximum density is $1/2$ because the agents are length 2, as in one dimension.

To take the continuum limit, we consider Eq. (27) twice, once when site $\mathbf{u}$ is of type H and once when site $\mathbf{u}$ is of type V. By reference to Fig. 7 for each of these cases, we can locate and classify by type the sites $\mathbf{v} \in \mathcal{N}(\mathbf{u})$ and $\mathbf{w} \in \mathcal{N}(\mathbf{u})\setminus\mathcal{M}(\mathbf{v})$. This process is tedious but straightforward. Using a Taylor expansion of first order in time for the left-hand side of Eq. (27) and a Taylor expansion of second order in space on the right, we obtain

$$\tau\frac{\partial H}{\partial t} + o(\tau) = P\big[Q_0^H(H,V) + \Delta Q_1^H(H,V) + \Delta^2 Q_2^H(H,V) + o(\Delta^2)\big], \tag{28}$$

$$\tau\frac{\partial V}{\partial t} + o(\tau) = P\big[Q_0^V(H,V) + \Delta Q_1^V(H,V) + \Delta^2 Q_2^V(H,V) + o(\Delta^2)\big], \tag{29}$$

where $Q_k^H(H,V)$ and $Q_k^V(H,V)$ contain spatial partial derivatives of order up to k. It is easy to show that the terms $Q_1^H(H,V)$ and $Q_1^V(H,V)$ vanish and that

$$Q_0^H(H,V) = -Q_0^V(H,V) = \tfrac{2}{3}(V - H)(1 - 2H - 2V).$$

Rather than solving for the subpopulations with each orientation, we focus on the total agent occupancy $T \in [0,\frac{1}{2}]$ and the orientation imbalance $S \in [-\frac{1}{2},\frac{1}{2}]$ defined by

$$T = H + V, \qquad S = H - V. \tag{30}$$

For $\ell = 0$ or 2 let $Q_\ell^T(T,S) = Q_\ell^H(H,V) + Q_\ell^V(H,V)$ and $Q_\ell^S(T,S) = Q_\ell^H(H,V) - Q_\ell^V(H,V)$, so $Q_0^T(T,S) = 0$ and

$$Q_0^S(T,S) = -\tfrac{4}{3}S(1 - 2T). \tag{31}$$

Then Eqs. (28) and (29) give

$$\tau\frac{\partial T}{\partial t} + o(\tau) = P\big[\Delta^2 Q_2^T(T,S) + o(\Delta^2)\big], \tag{32}$$

$$\tau\frac{\partial S}{\partial t} + o(\tau) = P\big[Q_0^S(T,S) + \Delta^2 Q_2^S(T,S) + o(\Delta^2)\big]. \tag{33}$$

We attempt to take the usual continuum limit $\Delta,\tau \to 0$ with the ratio Δ^2/τ held constant. Equation (32) says that $\partial T/\partial t$ are $\mathcal{O}(\Delta^2/\tau)$, but Eq. (33) behaves very differently; its dominant behavior is

$$\frac{\partial S}{\partial t} \sim -\frac{4}{3\tau}S(1 - 2T),$$

so the imbalance between horizontal and vertical agent densities decays exponentially rapidly to zero, with decay rate proportional to $(1 - 2T)/\tau$. So long as the lattice is not at maximal density ($T = 1/2$, in which case the agents cannot move at all) at $t = 0$, for all positive times we should take $S \approx 0$, and we can, therefore, replace $Q_2^T(T,S)$ with $Q_2^T(T,0)$ in Eq. (32) when taking the limit $\Delta,\tau \to 0$ with Δ^2/τ constant. We find that

$$\frac{\partial T}{\partial t} = D_0^{(2)}\nabla\cdot[(1 + 2T)\nabla T], \tag{34}$$

where

$$D_0^{(2)} = \frac{P}{6} \lim_{\Delta,\tau\to 0} \frac{\Delta^2}{\tau}. \tag{35}$$

We observe that Eq. (34) is the two-dimensional version of Eq. (11).

The diffusivity constant $D_0^{(2)}$ includes the factor $P/6$ because there are six possible moves an agent can attempt each time step, illustrated in Fig. 6. This not the same as for agents with length 1 where there are only four moves [6]. An extension to the problem, where the probability of moving to a position with a different orientation is not equal to the probability of moving to a position with the same orientation, is described in detail in Appendix E.

C. Simulation results

Simulations are performed on a lattice with $1 \leqslant x \leqslant 300$ and $1 \leqslant y \leqslant 20$. The N agents are initially placed in a region $J \times 20$ in the center of the lattice (with an equal number of vertical and horizontal agents), corresponding to a density $d > 0$, with details given in Appendix A. Here $J \approx [130,171]$, $P = 1, \Delta = 1, \tau = 1$. The simulations are implemented with zero-flux boundary conditions at the vertical ends and periodic boundary conditions on the horizontal boundaries. Although the simulations are in two dimensions, we reduce the results to one dimension by taking an average of the column occupancy of agents (see Appendix B).

We compare the average total agent occupancy T (equivalent to right-side and top-end occupancy) obtained from the simulation with solutions of the nonlinear diffusion equation (34) for two values of the density d, and random choice and random order method of choosing the N agents at each time step (Fig. 8). Again, $d = 1/2$ corresponds to close packed dimer agents. The PDE solution matches the simulated results extremely well for all values of x for both methods. There is some variation in the simulated results, which of course decreases when more realizations are performed and averaged. Other starting densities also produce similar results with good fits to the solution of Eq. (34). The fit is quantified by total squared error in Table III in Appendix C.

The accuracy of the independence approximation given by Approximation 4 is determined and given in Appendix D. The results show the approximation is reasonable for all values of the agent occupancy and excellent up to relatively high occupancies. This is in contrast to the 1D case. For this reason, the 2D comparisons given in Fig. 8 are excellent for the full range of initial densities.

To confirm that orientation imbalance rapidly becomes small (and, therefore, ignoring terms in S is an appropriate assumption), we repeated the simulations starting with an initial condition entirely made up of horizontal agents and measured the total difference across the lattice (Fig. 9). The difference decreases rapidly provided the density is not at its maximum, and the decrease is faster the lower the initial density. The speed of decrease in S is significantly slower with

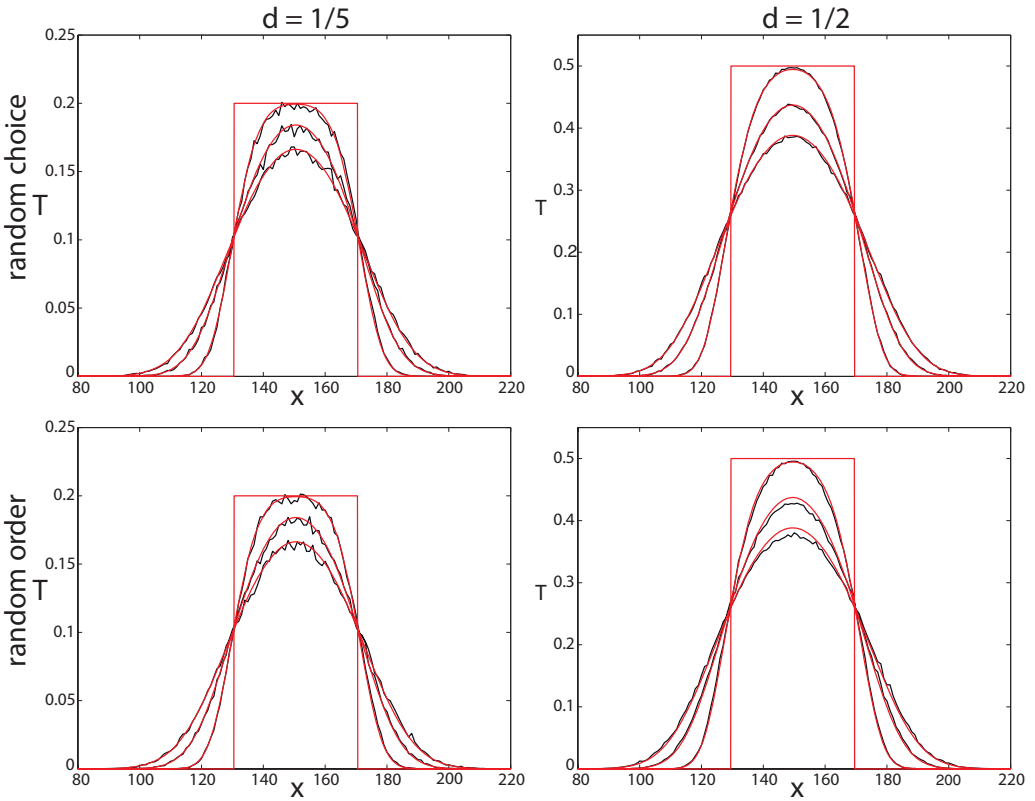

FIG. 8. (Color online) Dimers with simple exclusion in 2D: Solutions of Eq. (34) [red (medium gray)] and the column average of total agent occupancy T averaged over 500 realizations with the initial density $d = 0.2, 0.5$ (maximum density) (black) at times $t = 100$, 300, and 500. The initial condition is also shown [red (medium gray)]. Here $P = 1, \Delta = 1, \tau = 1$ for the simulations and MATLAB pdepe with $\delta x = 0.1$ for solving Eq. (34). (Top row) Random choice of agents. (Bottom row) Random order of agents. Note the different vertical scales.

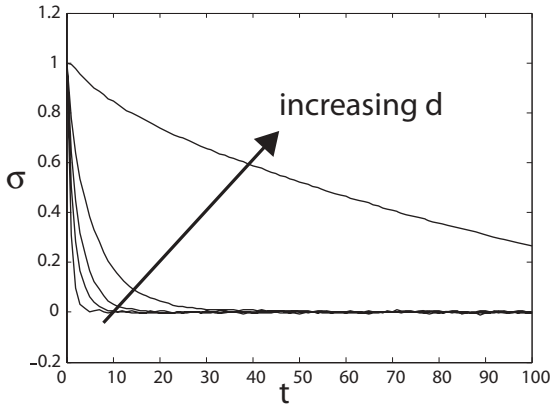

FIG. 9. Dimers with simple exclusion in 2D: The normalized orientation imbalance versus time ($\sigma = \int S dx dy / \int T dx dy$), for different initial density $d = 0.1, 0.2, 0.3, 0.4$, and 0.5 placed in the central region, as in Fig. 8. The initial population is made up of horizontal dimer agents only. The time taken for $\sigma \to 0$ increases as d increases, since there is initially very little opportunity for the agents to move and change their orientation when $d \to 0.5$ from below). Here $P = 1, \Delta = 1, \tau = 1$.

maximum density ($d = 0.5$), since the change in orientation must wait until unoccupied sites have appeared near all of the agents. However, even for this case, when S is a maximum value of $1/2$ initially, the averaged simulation data fit the solution to Eq. (34) just as well as illustrated in Fig. 8.

V. PARTIAL OVERLAPS: 2D LATTICE

We can naturally extend the two-dimensional simple exclusion process described above by allowing agents to overlap by (at most) one site, analogously to the one-dimensional case. We have not worked through a detailed mean-field analysis for this case. Instead, guided by the relation between the PDEs obtained for strict exclusion in one and two dimensions, we consider the natural generalization of Eq. (22), namely

$$\frac{\partial T}{\partial t} = D_0^{(2)} \nabla \cdot [(1 + 7T^2) \nabla T], \tag{36}$$

where $D_0^{(2)}$ is given by Eq. (35). The average total agent occupancy T obtained from the simulation with solutions to the nonlinear diffusion equation (36) compares very well for all values of initial starting density (two examples in Fig. 10), and is good even for the maximum density ($d = 2/3$). The fit is quantified by total squared error in Table IV in Appendix C.

VI. MULTISPECIES DIMERS

The models discussed in Secs. II–IV can be generalized to model multiple species of agents that all move with the appropriate simple exclusion or partial overlap rules. We consider m species of dimer agents, indexed by an integer k ($1 \leqslant k \leqslant m$), moving on a lattice in either one or two dimensions. We may think of k as corresponding to the color of the dimer. The probability that a dimer of species k selected for potential movement chooses to attempt to move is P_k, that is, we allow each species to have its own propensity to try to move. However, when we impose either a strict exclusion rule or allow partial overlapping, our definitions are color blind: A dimer of species k considers a neighboring site to be occupied by another dimer if another dimer of any species rests on it.

It is only necessary to work through the analysis focusing on a single species (species k), distinguishing carefully between indicator variables for occupancy by species k and indicator variables for occupancy by any species. We write

$$\gamma_{k,n}(i) = \begin{cases} 1 & \text{if site } i \text{ is occupied by the right side of} \\ & \text{an agent of species } k \text{ after } n \text{ time steps} \\ 0 & \text{otherwise} \end{cases}$$

and

$$\gamma_n(i) = \begin{cases} 1 & \text{if site } i \text{ is occupied by the right side of an} \\ & \text{agent of } \textit{any} \text{ species after } n \text{ time steps} \\ 0 & \text{otherwise} \end{cases}$$

for the one-dimensional lattice, and indicator variables for the two-dimensional lattice are defined similarly.

A. 1D lattices

1. Simple exclusion case

A similar method to that used in Sec. II (with an equivalent mean-field approximation) gives an equation equivalent to Eq. (8). If we write

$$r_n(i) = \mathbb{P}(\gamma_n(i) = 1) \qquad r_{k,n}(i) = \mathbb{P}(\gamma_{k,n}(i) = 1), \tag{37}$$

we determine the discrete-time master equation

$$r_{k,n+1}(i) - r_{k,n}(i) = \frac{P_k}{2} \Bigg\{ \sum_{s=\pm 1} r_{k,n}(i+s)(1 - r_n(i-s)) - r_{k,n}(i) \sum_{s=\pm 1} (1 - r_n(i+2s)) \Bigg\}. \tag{38}$$

We return to the original lattice with $x = \Delta i$ and $t = n\tau$ and consider as continuous functions the average local right-side occupancy $R(x,t)$ over all species and the average local right-side occupancy $R_k(x,t)$ of species k. Taking the limit $\Delta, \tau \to 0$ simultaneously while keeping the ratio Δ^2/τ constant leads to the advection-diffusion equation

$$\frac{\partial R_k}{\partial t} = D_{k,0}^{(1)} \frac{\partial}{\partial x} \left[(1 - R) \frac{\partial R_k}{\partial x} + 3 R_k \frac{\partial R}{\partial x} \right], \tag{39}$$

where

$$D_{k,0}^{(1)} = \frac{P_k}{2} \lim_{\Delta, \tau \to 0} \frac{\Delta^2}{\tau}.$$

2. Partial overlap case

Following the same methods as in Sec. III, we obtain in the limit $\Delta, \tau \to 0$ the advection-diffusion equation

$$\frac{\partial R_k}{\partial t} = D_{k,0}^{(1)} \frac{\partial}{\partial x} \left[(1 - R - R^2) \frac{\partial R_k}{\partial x} + R_k (1 + 8R) \frac{\partial R}{\partial x} \right], \tag{40}$$

where $D_{k,0}^{(1)}$ is defined above.

In both the simple exclusion and the partial overlap models, if the parameters P_k are not the same for all species, then Eq. (39) or Eq. (40) cannot be summed over k to yield a

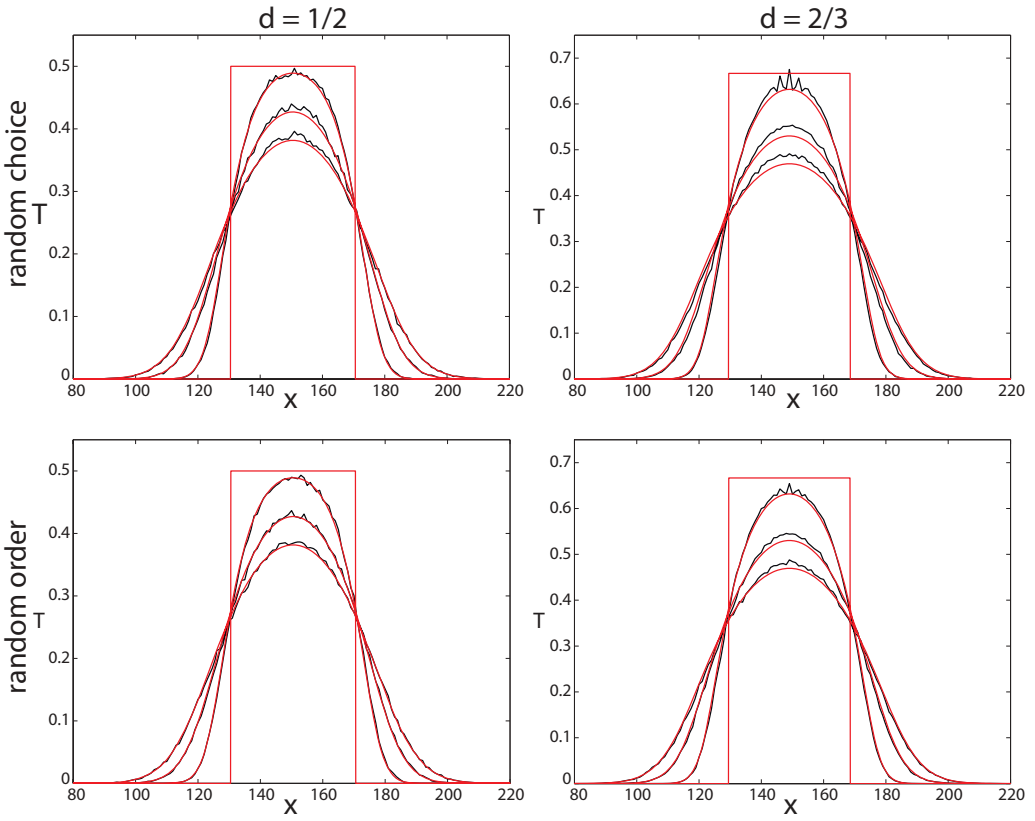

FIG. 10. (Color online) Dimers with partial exclusion in 2D: Solutions of Eq. (36) [red (medium gray)] and the column average of total agent occupancy T averaged over 500 realizations with the initial density $d = 1/2, 2/3$ (the maximum density) (black) at times $t = 100$, 300, and 500. The initial condition is also shown [red (medium gray)]. Here $P = 1, \Delta = 1, \tau = 1$ for the simulations and MATLAB pdepe with $\delta x = 0.1$ for solving Eq. (36). (Top row) Random choice of agents. (Bottom row) Random order of agents. Note the different vertical scales.

single PDE in which only $R = \sum_{k=1}^{m} R_k$ appears. However, if all species are identical, then $P_k = P$ for all species k, and summing over k in Eq. (39) or Eq. (40) yields (as it should) Eq. (11) or Eq. (22), respectively.

B. 2D lattices

For two dimensions we discuss only the multispecies extension of the simple exclusion model of Sec. IV. We define functions H, V, T, and S as in Sec. IV for occupancy irrespective of species. Their analogs for occupancy by species k are H_k, V_k, T_k, and S_k. The continuous evolution equation for the orientation imbalance S_k of species k is

$$\tau \frac{\partial S_k}{\partial t} + o(\tau) = -\frac{2}{3} P_k [S_k(2 - 3\,T) - S\,T_k] + o(\Delta), \qquad (41)$$

cf. Eq. (31) for a single species. The set of simultaneous equations (41) for all $1 \leqslant k \leqslant m$ form a system with a single steady state at zero. The Routh-Hurwitz Criteria [21] determine if a steady state is stable and, therefore, if the solution will move towards it. We have proved that this is the case for up to four species ($m \leqslant 4$); a more general result is difficult to obtain. When this is the case, then S_k and S become small at larger times and, therefore, the equation governing the total population of species k in the limit $\Delta, \tau \to 0$ becomes

$$\frac{\partial T_k}{\partial t} = D_{k,0}^{(2)} \nabla \cdot \left[\left(1 - \frac{3}{2}\,T \right) \nabla T_k + \frac{7}{2}\,T_k \nabla T \right], \qquad (42)$$

where

$$D_{k,0}^{(2)} = \frac{P_k}{6} \lim_{\Delta,\tau \to 0} \frac{\Delta^2}{\tau}.$$

We observe that while for a single species the nonlinear diffusion equations are the same (apart from the constant) in one and two dimensions [Eqs. (11) and (34)], for multiple species this is no longer the case. However, in the case where all the species are identical ($P_k = P$ for all species k), the total agent occupancy obeys Eq. (34) as the differences cancel out when summing all species. This perhaps unexpected result was confirmed by introducing a separate probability of movement when moving with the same orientation or changing orientation (Appendix E) to ensure that this result matches the result for a single species.

We compare the average total agent occupancy of two species T_1 and T_2 obtained from the simulation with solutions of the nonlinear diffusion equation (42) for two initial conditions (Fig. 11). Starting with a difference of two unit step functions with $d = 0.2$ for both species, the PDE solutions match the simulated results relatively well for most of the region [Fig. 11(a)]. As the value of d is increased to its maximum of $1/2$, the fit in central region is no longer very good. However, if instead two triangular profiles are used as an initial condition [Fig. 11(b)], the fit is good across all the domain.

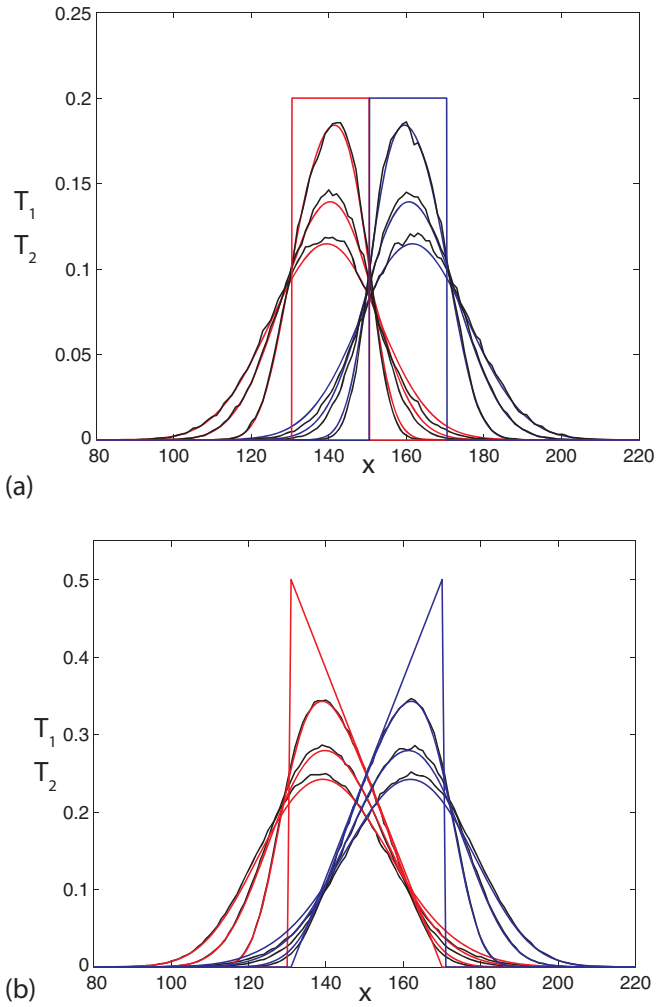

FIG. 11. (Color online) Two species of dimers with simple exclusion in 2D: Solutions of Eq. (42) [red (medium gray) and blue (dark gray)] and the column average of total agent occupancy T_1 and T_2 averaged over 2000 realizations with the initial density shown [red (medium gray) and blue (dark gray)]. (a) $d = 0.2$; (b) mirrored triangle distributions at times $t = 100, 300$, and 500. Here $P_1 = P_2 = 1, \Delta = 1, \tau = 1$ for the simulations and a Crank-Nicholson method with Picard linearization is used for solving Eq. (42). Random choice of agents is implemented. Note the different vertical scales.

VII. DISCUSSION

We have demonstrated that consideration of systematic probabilistic arguments before invoking mean-field approximations give rise to a reliable PDE description of the agent occupancy for probabilistic models for dimers with strict exclusion and allowing for partial overlaps. The PDE is a nonlinear diffusion equation when there is only one species of dimer and an advection-diffusion equation when there are multiple species. Numerical simulations have shown that PDE solutions are a good representation of the random walk movement of dimers.

In two dimensions, we have demonstrated a new model of dimer movement using reptation and shown that averaged simulation data match closely a nonlinear diffusion equation. The effect of allowing dimers to overlap with another agent has also been investigated. This is biologically useful as cells have the ability to deform (within limits) in order to move past other cells, and this is often not included in mathematical models. We have shown how this model (in both one and two dimensions) can also be approximated by a nonlinear diffusion equation with a good fit to the simulation data.

In comparing average simulation data to solution of PDEs, we found that the fit is much better in two dimensions than in one dimension. This is an interesting result. We hypothesize that the reason may be that the mean-field approximations are more accurate in two dimensions, as dimers can pass each other. Indeed, in one dimension the dimers must always remain in the order they started in, and so if one dimer does not move, then its neighbors are limited in their movements.

For the single-species models, the functional form of the diffusivity in one dimension is the same as that in two dimensions, but for multiple species this is not true. This difference is intriguing and may require further study. At present the reasons for it are not clear.

Whether we impose strict exclusion or allow limited overlap, the predicted diffusivity remains positive. There is no density at which the dimers tend to aggregate. We know that within a general class of interacting random walks of singlets (agents of length 1) [8], it is possible to obtain mean-field predicted diffusivities that are negative in an interval. It is probable that with a more complicated prescription of dimer interactions in a local environment, for example, one which favors dimer adhesion, dimer aggregation could be generated, but we have not pursued this matter.

Two methods of randomly choosing the N dimer agents have been implemented: random choice and random order. The quality of agreement between PDEs derived by mean-field arguments and averaged simulation data shows some sensitivity to whether random choice or random order agent selection is used. The random order method always results in the dimers diffusing faster because dimers are less likely to block the movement of other dimers in the surrounding area, particularly in one dimension when dimers cannot pass each other. For both one and two dimensions, generally the random choice method fits the nonlinear diffusion equations better for models without overlap, while the random order method fits the nonlinear diffusion equations better for the models with overlaps, although in some cases the differences between the results of the two simulation protocols are quite small. It is not clear why this is the case or which method is more realistic: The mean-field method used for finding the PDEs only considers the small part of a time step when only one dimer attempts to move.

Biological cells in motion are not structureless objects, nor are they rigid structures unable to accommodate, to a limited extent, encroachment on their personal space by neighboring cells. The models studied here show that at the mean-field level, the basic idea of a nonlinear diffusion equation as a model for cellular motion is robust to the insertion of some structural detail and some compliance, but the functional form of the diffusivities depends on the structural detail and in the multispecies case, convective terms will be needed. Although it will seldom, if ever, be the case that mean-field arguments yield exact results, numerical studies have shown that their range of usefulness as an approximation is significant.

ACKNOWLEDGMENTS

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APPENDIX A: SIMULATION INITIAL CONDITIONS

For many of the simulations, a decision must be made about how to initially arrange the dimer agents. There is a range of possibilities between (i) placing agents randomly with a given probability so the *average* density is the required one, but each simulation will typically involve a different number of agents, and (ii) placing each agent in a set position, making the spacing between adjacent agents as uniform as possible, so each simulation begins with exactly the same initial condition.

1. 1D simulations

The agents are initially placed in an interval J in the center of the lattice, corresponding to a density $d > 0$.

a. Lower than maximum density

For d lower than the maximal density, a fixed number of agents are randomly placed in $J = [130,171]$. The initial condition is, therefore, close to the "random" one, except that the number of agents is the same in all realizations. Of course, we ensure that the simple exclusion or partial overlap rules (whichever is appropriate) are obeyed. We place $N = 10$ agents for density $1/4$, $N = 13$ agents for density $1/3$, and $N = 20$ agents for density $1/2$.

b. Maximal density

When the initial density is maximal (i.e., $1/2$ for the simple exclusion process and $2/3$ for the partial overlap process), the dimer agents must be placed in an organized manner. For the simple exclusion case, we place $N = 20$ agents next to each other in $J = [130,169]$,$[131,170]$, or $[132,171]$. Each of these initial conditions is used the same number of times. For the partial overlap process, we place $N = 26$ agents in $J = [130,168]$,$[131,169]$, or $[132,170]$. The initial alignment can be divided into triples, where two sites are occupied by a right side of an agent and the third one is unoccupied (by a right-hand side). We interpret this triple as two overlapping agents.

2. 2D simulations

a. Lower than maximal density

The agents are distributed analogously to the one-dimensional case. Following the exclusion or partial overlap rules, a fixed number of dimers were randomly placed at sites inside the rectangle $[130,171] \times [0,20]$. For example, density $d = 1/5$ corresponds to $N = 160$ agents for the simple exclusion case, while $d = 1/2$ corresponds to $N = 400$ agents for the partial overlap case.

b. Maximal density

For the simple exclusion process, the initial placement of agents is implemented as follows: columns are grouped to form pairs of adjacent "double columns." In order to fill any chosen double column, we consider 10 "boxes," each 2×2 sites in size, 5 of them containing two horizontal agents and 5 containing two vertical agents. We then distribute these boxes randomly in the previously chosen double column. In total, $N = 400$ agents are placed between the sites 130 and 169.

For the partial overlaps case, and initial density $d = 2/3$, the columns are grouped in threes ("triple columns") and we create six boxes of size 3×3, three of them containing six horizontal agents and the other three containing six vertical agents. For a given triple column, we order these six boxes randomly and place them between the first and eighteenth rows. The two remaining rows of each triple column are filled by a box of size 2×3 containing four horizontal agents. The density $d = 2/3$ between the sites 130 and 168 corresponds to 520 agents.

APPENDIX B: SIMULATION OCCUPANCY AND AVERAGE OCCUPANCY

In determining agent occupancy at each site, the number of right-side agents is used in our probabilistic model and in the mean-field approximation. This, of course, can be done in the simulations as well. Alternatively, we can also split the unit mass between the two sites that an agent occupies. Hence, we can count both the left- and right-hand sides of the agents with the weight $1/2$ at each of the two sites. Both methods were implemented, with very little difference between the two. However, since the number of simulations we used are not very large, we find that the splitting method makes the mass more distributed and the simulation curves smoother than if we enumerate only the right-hand sides of the agents. However, we emphasize that there is little difference between the two methods.

Simulations are averaged over many statistically identical realizations, and so the occupancy at a site is averaged over realizations. In two dimensions, there are two averages to perform: First, the column average is performed and then the average over the realizations.

APPENDIX C: COMPARISON OF RESULTS

In order to quantify the errors between our simulation results and solutions of the corresponding PDEs, we calculate the total squared errors. These are shown in Tables I–IV.

TABLE I. Total squared error for the simple exclusion process in one dimension.

	Random choice			Random order		
	$t = 100$	$t = 300$	$t = 500$	$t = 100$	$t = 300$	$t = 500$
$d = 1/4$	0.000 76	0.000 55	0.000 46	0.0019	0.0016	0.0014
$d = 1/3$	0.0048	0.0019	0.0012	0.0133	0.0066	0.0041
$d = 1/2$	0.027	0.0142	0.0073	0.0793	0.0435	0.0268

TABLE II. Total squared error for partial overlap process in one dimension.

	Random choice			Random order		
	$t = 100$	$t = 300$	$t = 500$	$t = 100$	$t = 300$	$t = 500$
$d = 1/3$	0.0012	0.0018	0.0019	0.0015	0.0009	0.0011
$d = 1/2$	0.0032	0.0042	0.0051	0.0016	0.0020	0.0017
$d = 2/3$	0.0067	0.0104	0.0098	0.0141	0.0030	0.0024

TABLE III. Total squared error for the simple exclusion process in two dimensions.

	Random choice			Random order		
	$t = 100$	$t = 300$	$t = 500$	$t = 100$	$t = 300$	$t = 500$
$d = 1/5$	0.000 52	0.000 55	0.000 42	0.000 32	0.000 47	0.000 53
$d = 1/2$	0.000 44	0.000 54	0.000 84	0.0019	0.0035	0.0042

TABLE IV. Total squared error for partial overlap process in two dimensions.

	Random choice			Random order		
	$t = 100$	$t = 300$	$t = 500$	$t = 100$	$t = 300$	$t = 500$
$d = 1/2$	0.0014	0.0030	0.0027	0.0010	0.0010	0.0012
$d = 2/3$	0.0121	0.0149	0.0123	0.0045	0.0052	0.0043

APPENDIX D: ACCURACY OF APPROXIMATION 1 and 4

The accuracy of simple exclusion 1D Approximation 1 and 2D Approximation 4 are checked by using realizations of the discrete model starting with a random placement of the agents (at various densities) and data on agent positions are collected after 200 time steps. The proportion of agents with another agent in a neighboring position is compared with the proportion of positions occupied by an agent. These proportions were averaged over 10 000 and 500 realizations for the 1D and 2D cases, respectively. The standard errors in the means were very small (less than 10^{-3} for both cases). A lattice of length 100 and a lattice of size 100×20 are used for the 1D and 2D cases, respectively.

Figure 12 illustrates the approximation (straight lines) compared to the data (red crosses). Note that due to the difficulty of randomly placing agents at a higher density and the lengthy computational times, we did not collect data at higher values of density. However, for the maximum value of the agent occupancy ($1/2$ for 1D case and $1/4$ for 2D case), the conditional probabilities can be determined theoretically to be unity and $1/3$, respectively. The curve of best fit, namely cubic polynomials, are calculated with Mathematica, using the data points plus the two theoretical end points. The goodness-of-fit values, given by R^2, are excellent. The differences between the points and the best-fit curve are less than 10^{-2} for Approximation 1 and less than 10^{-3} for Approximation 4 (the size of the standard error in the mean).

It is interesting to observe that the approximation is much more accurate in two dimensions than one dimension, mirroring the improved accuracy in two dimensions seen in the PDE description, illustrated in Fig. 8 compared to Fig. 2.

APPENDIX E: REPTATION PROBABILITIES

To generalize the model in two dimensions, an agent attempts to move with probability P, and now we assign different weights for translation and reptation events. Let $\mu/6$ be the probability of each translation event, while $\rho/6$ is

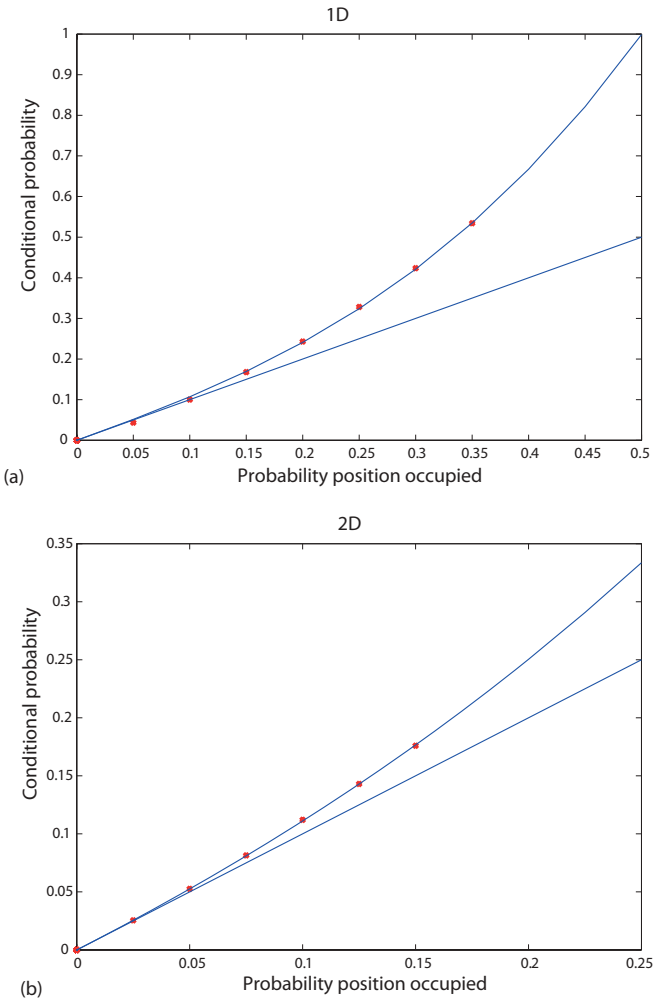

FIG. 12. (Color online) Accuracy of independence assumptions in Approximation 1 and Approximation 4 for simple exclusion case. (a) 1D case. Approximation 1 (straight line) compared to the actual probability for different agent occupancies. Simulated results [red (medium gray) crosses] and the curve of best fit given by a cubic equation ($y = x + 0.37x^2 + 3.25x^3$, with goodness-of-fit parameter $R^2 = 0.999\,86\,4$). (b) 2D case. Approximation 4 (straight line) compared to the actual probability for different densities. Simulated results [red (medium gray) crosses] and the curve of best fit given by a cubic equation ($y = x + 0.95x^2 + 1.55x^3$ with $R^2 = 0.999\,99\,1$). The theoretical maximum values were used for the curve fitting.

probability of each reptation event. For example, in Secs. IV and V, we have $\mu = \rho = 1$, so there is equal probability of moving in one of the six directions. The parameters μ and ρ are subject to the constraints $\mu \geqslant 0$, $\rho \geqslant 0$, and $2\mu + 4\rho = 6$, so hereafter we replace μ by $3 - 2\rho$, where $0 \leqslant \rho \leqslant 3/2$.

For a single species, using the same method as in Sec. IV, we obtain partial differential equations for the total population $T = H + V$ and the imbalance $S = H - V$. At first order,

$$\tau \frac{\partial S}{\partial t} + O(\tau^2) = -\frac{4\rho P}{3} S(1 - 2T) + O(\Delta^2).$$

The dominant behavior of S is exponential decay, as in Eq. (41), and in the continuum limit we can take $S \approx 0$. In the limit $\Delta, \tau \to 0$ with $\rho > 0$, the total population of dimers,

T, obeys the nonlinear diffusion equation

$$\frac{\partial T}{\partial t} = \frac{(3-\rho)P}{12}\left(\lim_{\Delta,\tau\to 0}\frac{\Delta^2}{\tau}\right)\nabla\cdot((1+2\,T)\,\nabla T).$$

When all translation and reptation moves are equally weighted (which corresponds to $\rho = 1$), this equation reduces to Eq. (34) as expected, while if reptation is turned off ($\rho \to 0$), we obtain formally what looks like diffusion of monomers in two dimensions, but of course we need $\rho > 0$ to allow the horizontal and vertical orientations to equilibrate so the limit $\rho \to 0$ is a singular one, with $\rho = 0$ having to be described by coupled advection-diffusion equations.

When there are multiple dimer species on the lattice, the orientation imbalance S_k in species k, obeys the following equation for at first order:

$$\tau\frac{\partial S_k}{\partial t} + O(\tau^2) = -\frac{2\rho P_k}{3}(S_k\,(2-3\,T) - S\,T_k) + O(\Delta^2),$$

which can be evaluated in the same way as Eq. (41) provided that $\rho \geqslant 0$ as above.

In the limit $\Delta,\tau \to 0$ with $\rho \geqslant 0$, the total population of T_k of dimers species k obeys the nonlinear PDE,

$$\frac{\partial T_k}{\partial t} = \frac{(3-\rho)P_k}{12}\left(\lim_{\Delta,\tau\to 0}\frac{\Delta^2}{\tau}\right)\nabla\cdot\left[\left(1-\frac{3}{2}T\right)\nabla T_k + \frac{7}{2}T_k\nabla T\right].$$

When $\rho = 1$, this reduces to Eq. (42) as expected.

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