The importance of the Voronoi domain partition for position-jump reaction-diffusion processes on non-uniform rectilinear lattices

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Abstract

Position-jump processes are used for the mathematical modelling of spatially extended chemical and biological systems with increasing frequency. A large subset of the literature concerning such processes is concerned with modelling the effect of stochasticity on reaction-diffusion systems. Traditionally, computational domains have been divided into regular voxels. Molecules are assumed well-mixed within each of these voxels and are allowed to react with other molecules within the same voxel or to jump to neighbouring voxels with predefined transition rates.

For a variety of reasons implementing position-jump processes on irregular grids is becoming increasingly important. However, it is not immediately clear what form an appropriate irregular partition of the domain should take if it is to allow the derivation of mean molecular concentrations that agree with a given partial differential equation for molecular concentrations. It has been demonstrated, in one dimension, that the Voronoi domain partition is the appropriate method with which to divide the computational domain.

In this report, we investigate theoretically the propriety of the Voronoi domain partition as an appropriate method to partition domains for position-jump models in higher dimensions. We also provide simulations of diffusion processes in two dimensions in order to corroborate our results.

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I. INTRODUCTION

Spatial reaction-diffusion models have been employed to describe many emergent phenomena in biological systems, including spatial ecology [1], animal coat patterning [2], limb/digit formation [3, 4] and tumour growth [5]. Of particular interest to mathematical biologists in recent years have been the effects of noise on those systems which form patterns via diffusion-driven instability [6].

In order to investigate the effects of stochasticity in these spatially extended reaction-diffusion systems we will consider 'compartment-based' or 'mesoscopic' models. Such models are characterised by a discretisation of the computational domain into a grid/lattice of discrete voxels between which molecules can move. These movements may represent diffusion or some other form of active transport. Molecules are considered to be well-mixed in each of the voxels and can react stochastically with other molecules in their voxel with prescribed rates. By far the simplest grids with which to partition the domain are uniform, with each voxel a regular $2d$-sided polytope of the same size (where d is the dimension of the domain). Since particle numbers and particle concentration scale by a constant factor on the uniform Cartesian grid it is a simple matter to convert from one to the other. In addition, for simple isotropic diffusion, the transition rates between intervals are independent of the interval under consideration since all intervals are the same size.

In recent work [7] we demonstrated (using a one-dimensional model) that there is a choice to be made when partitioning the domain into a *non-uniform* rectilinear grid. The two natural choices are referred to as the Voronoi and interval-centred partitions, respectively. In the Voronoi partition molecular positions (x_i for voxel $i = 1, \ldots, k$) are chosen and are associated with each voxel. The voxel edges are then naturally defined in a Voronoi neighbourhood sense: a point on the domain is defined to lie in the interval i if it is nearer to x_i than any other x_j for $j = 1, \ldots, k$, $j \neq i$. In the interval-centred partition the desired mesh of voxels is specified first and molecular positions defined to be the centroid of each voxel. Given a partial differential equation (PDE) such as the diffusion equation, we demonstrated that, in one dimension, only the Voronoi partition will permit the derivation of transition rates which give mean-field molecular *concentrations* consistent with the PDE [7].

As a confirmatory example of the propriety of the Voronoi domain partition, Fig. 1 of the supplementary material (SM) [8] compares molecular concentrations for the position-jump model on the Voronoi domain partition with the deterministic PDE counterpart concentrations for an example morphogen gradient formation system in one dimension. Good agreement is exhibited between the molecular concentrations given by the stochastic and deterministic models.

In the next section we compare two potential partitions for regular polytopal rectilinear grids in higher dimensions and demonstrate that only on the Voronoi partition is it possible to rederive the associated mean-field PDE for molecular concentrations. We also provide confirmatory numerical simulations which compare molecular concentrations given by the two partitions. We conclude in Section III by discussing the potential implications of our results.

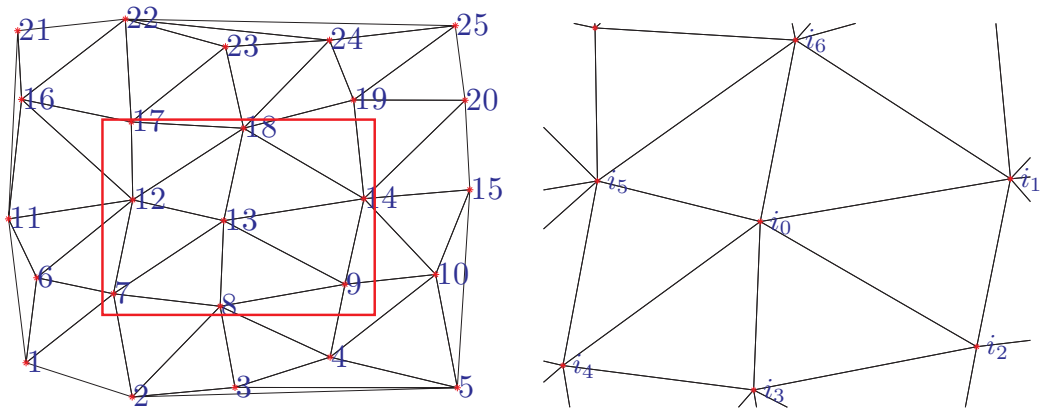
II. POSITION-JUMP PROCESSES ON NON-UNIFORM GRIDS IN TWO DIMENSIONS

A pertinent question to ask, given our previous work in one-dimension [7], is 'What role does the Voronoi partition play for unstructured grids higher dimensions?'

A. General unstructured grids

In order to answer this question we begin by considering molecules moving between nodes on a general triangularised lattice. In what follows, for ease of working and readability, we will derive results for a two-dimensional domain, but note that results can trivially be extended to higher dimensions. Associated with each node of the lattice is a voxel which encloses the node. The set of voxels forms a tessellation of the domain [9]. Molecules reside at the nodes and are able to move between elements along the edges of the lattice. We introduce a global numbering system in which all the nodes of the lattice take a number from 1 to k (Fig. 1 (a)). We also introduce a local labelling system whereby the neighbouring nodes of a central node with global label $i = i_0$ are labelled $i_1, i_2, \ldots, i_{J(i_0)}$, where $J(i_0)$ is the number

of neighbours of node i_0 (Fig. 1 (b)). Although, for ease of representation, we have chosen to realise our general unstructured grid in two dimensions, the same grid definition will hold in higher dimensions.



(a) (b)

FIG. 1. *(Color online) (a) Global node labelling from* 1 *to* $k = 25$*. (b) Local node labelling starting with the central node,* i_0*, and proceeding clockwise to* $i_{J(i_0)}$*, where* $J(i_0) = 6$ *is the number of neighbours of node* i_0*. The domain plotted in (b) corresponds to the area enclosed by the red rectangle in (a).*

The vectors connecting vertex i_0 to its neighbours are labelled locally as $\boldsymbol{r}_1, \boldsymbol{r}_2, \ldots, \boldsymbol{r}_{J(i_0)}$ and, in two dimensions, can be expressed in Cartesian coordinate form as (x_1, y_1), (x_2, y_2),..., $(x_{J(i_0)}, y_{J(i_0)})$. We denote the transition rates to go from node i_0 to one of its neighbours, i_j, for $j = 1, \ldots, J(i_0)$, as $T_{i_0}^{i_j}$ and the transition rate from that neighbour back to node i_0 as $T_{i_j}^{i_0}$. A vector specifying the number of molecules at each node can be written as follows:

$$\boldsymbol{n} = (n_1, n_2, \ldots, n_{i0}, \ldots, n_{i_{J(i_0)}}, \ldots, n_k), \tag{1}$$

where we have replaced some of the global labels with their local counterparts (with respect to central node i_0) for ease of notation in what follows [10]. Define operators $L_{i_0}^{i_j}$ for central node i_0 and neighbouring nodes i_j, $j = 1, \ldots, J(i_0)$ by their actions on the vector $\boldsymbol{n}$, as follows:

$$L_{i_0}^{i_j}\boldsymbol{n} = (n_1, n_2, \ldots, n_{i0} + 1, \ldots, n_{i_j} - 1, \ldots, n_{i_{J(i_0)}}, \ldots, n_k). \tag{2}$$

Operator $L_{i_0}^{i_j}$ takes a molecule from neighbouring node i_j and moves it to central node i_0. Let $\Pr(\boldsymbol{n}, t)$ denote the probability that the molecules take the configuration $\boldsymbol{n}$ at time t. Then we can write down a reaction diffusion master equation (RDME) as follows:

$$\frac{\mathrm{d}\Pr(\boldsymbol{n},t)}{\mathrm{d}t} = \sum_{i_0=1}^{k}\sum_{j=1}^{J(i_0)}\left\{(n_{i_0}+1)T_{i_0}^{i_j}\Pr(L_{i_0}^{i_j}\boldsymbol{n}) - n_{i_0}T_{i_0}^{i_j}\Pr(\boldsymbol{n},t)\right\}. \tag{3}$$

We note that this RDME is independent of the dimension in which the grid is embedded and, as such, it holds for all dimensions.

In order to find an equation for the evolution of the mean number of molecules at general node l_0 in terms of the mean numbers of molecules at its neighbouring nodes we multiply equation (3) by n_{l_0} and sum over all the possible values the vector of molecular concentrations can take. Upon simplification we derive the following equations

$$\frac{\mathrm{d}\langle n_{l_0}\rangle}{\mathrm{d}t} = \sum_{j=1}^{J(l_0)}\left\{\langle n_{l_j}\rangle T_{l_j}^{l_0} - \langle n_{l_0}\rangle T_{l_0}^{l_j}\right\}, \qquad \text{for} \qquad l_0 = 1,\ldots,k, \tag{4}$$

where $\langle n_{l_0}\rangle$ denotes the mean number of molecules at node l_0 and $\langle n_{l_j}\rangle$ is defined similarly. In order to find an equation for the evolution of molecular *concentration* rather than molecular *numbers* we use the relationship between numbers, concentration and area/volume of a voxel (denoted A_{l_j} for node/voxel l_j). Equation (4) becomes

$$\frac{\mathrm{d}u_{l_0}}{\mathrm{d}t} = \frac{1}{A_{l_0}}\sum_{j=1}^{J(l_0)}\left\{u_{l_j}A_{l_j}T_{l_j}^{l_0} - u_{l_0}A_{l_0}T_{l_0}^{l_j}\right\}, \qquad \text{for} \qquad l_0 = 1,\ldots,k, \tag{5}$$

where $u_{l_0} = \langle n_{l_0}\rangle / A_{l_0}$ is the mean molecular concentration in interval l_0 with u_{l_j} defined similarly for $j = 1,\ldots,J(l_0)$. Given transition rates and the appropriate grid geometry, by Taylor expanding these concentrations about l_0 in Eq. (5), we can theoretically determine whether the individual-level model corresponds to a population-level PDE in any dimension. Additionally, we can use Eq. (5) to derive the appropriate transition rates corresponding to a particular PDE.

For example, if we want to find transition rates which correspond to the diffusion equation in two dimensions then, after Taylor expansion of the appropriate concentration terms, u_{l_j}, we can equate the coefficients of the derivatives of u_{l_0} to find a

system of equations which must be satisfid by the transition rates:

$$\sum_{j=1}^{J(l_0)} \left\{ A_{l_j} T_{l_j}^{l_0} - A_{l_0} T_{l_0}^{l_j} \right\} = 0, \tag{6}$$

$$\sum_{j=1}^{J(l_0)} A_{l_j} T_{l_j}^{l_0} x_j = 0, \tag{7}$$

$$\sum_{j=1}^{J(l_0)} A_{l_j} T_{l_j}^{l_0} y_j = 0, \tag{8}$$

$$\sum_{j=1}^{J(l_0)} A_{l_j} T_{l_j}^{l_0} x_j^2 = 2DA_{l_0}, \tag{9}$$

$$\sum_{j=1}^{J(l_0)} A_{l_j} T_{l_j}^{l_0} x_j y_j = 0, \tag{10}$$

$$\sum_{j=1}^{J(l_0)} A_{l_j} T_{l_j}^{l_0} y_j^2 = 2DA_{l_0}. \tag{11}$$

Specifically Eq. (6) is derived by equating coefficients of the zeroth derivative, u_{l_0}, Eqs. (7) and (8), to coefficients of the first derivatives and Eqs. (9)-(11) to coefficients of the second derivatives.

Although on a general irregular lattice it may not be possible to use Eqs. (6)-(11) to derive consistent transition rates which allow for the molecular concentrations expected due to diffusion, there are special and informative cases in which we can derive the transition rates explicitly. In particular, for the domain tessellations shown in Fig. 2 (below) and Fig. 4 of the SM it is possible to derive consistent transition rates for which the mean molecular concentrations correspond to the concentrations given by the diffusion equation.

B. The non-uniform rectilinear domain partition

Consider the rectilinear domain partition. Using Eqs. (6)-(11) in an analogous manner to the method used in [7], it is possible to show that the necessary rectilinear domain tessellation is a Voronoi tessellation (Fig. 2). Using Eqs. (7)-(11) we can derive transition rates for the diffusion equation consistent with this tessellation. Denote the non-zero component of the vector from l_0 to l_1, l_2, l_3 and l_4 (respectively) as $r_{l_0}^r$, $r_{l_0}^d$, $r_{l_0}^l$ and $r_{l_0}^u$ (respectively) where the superscripts r, d, l and u (respectively)

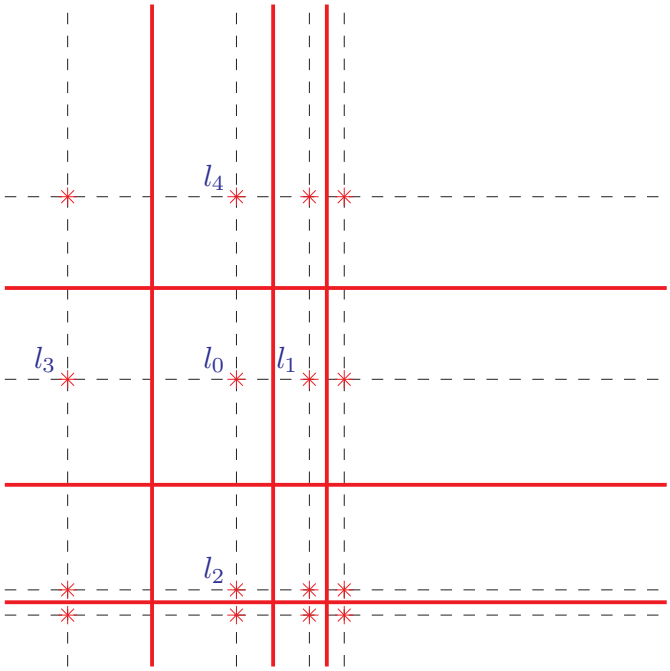


FIG. 2. *(Color online) The rectilinear domain tessellations. Voxel boundaries are demarcated in red, the grid on which the molecules move is displayed using a dashed black line and the points at which the molecules reside in each element are represented by red stars (*).*

stand for right, down, left and up (respectively). We define $r^i_{l_j}$ for $j = 1, \ldots, 4$ and $i = r, d, l, u$ analogously but note that there is some redundancy in this notation (e.g. $r^r_{l_0} = -r^l_{l_1}$). Equation (10) is satisfied automatically due to the rectilinear nature of the grid. Combining Eqs. (7) and (9) defines the transition rates $T^{l_0}_{l_1}$ and $T^{l_0}_{l_3}$ as

$$T^{l_0}_{l_1} = \frac{2DA_{l_0}}{A_{l_1} r^r_{l_0}(r^r_{l_0} - r^l_{l_0})}, \tag{12}$$

$$T^{l_0}_{l_3} = -\frac{2DA_{l_0}}{A_{l_3} r^l_{l_0}(r^r_{l_0} - r^l_{l_0})}, \tag{13}$$

where, as before, A_{l_j} denotes the area of voxel j. In a similar manner we can employ Eqs. (8) and (11) to find the transition rates $T^{l_0}_{l_2}$ and $T^{l_0}_{l_4}$:

$$T^{l_0}_{l_2} = -\frac{2DA_{l_0}}{A_{l_2} r^d_{l_0}(r^u_{l_0} - r^d_{l_0})}, \tag{14}$$

$$T^{l_0}_{l_4} = \frac{2DA_{l_0}}{A_{l_4} r^u_{l_0}(r^u_{l_0} - r^d_{l_0})}. \tag{15}$$

Using a simple index shift we can use the transition rates given in Eqs. (12)-(15) to find the transition rates $T_{l_0}^{l_1}$, $T_{l_0}^{l_2}$, $T_{l_0}^{l_3}$ and $T_{l_0}^{l_4}$:

$$T_{l_0}^{l_1} = \frac{2DA_{l_1}}{A_{l_0} r_{l_0}^r (r_{l_1}^r - r_{l_1}^l)}, \tag{16}$$

$$T_{l_0}^{l_2} = -\frac{2DA_{l_2}}{A_{l_0} r_{l_0}^d (r_{l_2}^u - r_{l_2}^d)}, \tag{17}$$

$$T_{l_0}^{l_3} = -\frac{2DA_{l_3}}{A_{l_0} r_{l_0}^l (r_{l_3}^r - r_{l_3}^l)}, \tag{18}$$

$$T_{l_0}^{l_4} = \frac{2DA_{l_4}}{A_{l_0} r_{l_0}^u (r_{l_4}^u - r_{l_4}^d)}. \tag{19}$$

These transition rates imply that Eq. (6) can only be satisfied if

$$A_{l_j} = \alpha (r_{l_j}^r - r_{l_j}^l)(r_{l_u}^r - r_{l_j}^d). \tag{20}$$

Using the argument that the contiguous elements must span the domain (as in one dimension), we find $\alpha = 1/4$. Only the Voronoi partition is consistent with the voxel areas and transition rates determined by Eqs. (6)-(11). It is of comfort to note that, in the special case of a regular grid consisting of squares, the transition rates are as we might expect: $T = D/h^2$, where h is the distance between neighbouring nodes and, consequently, also the length of the sides of the squares.

In Section II of the SM we provide example simulations which compare molecular concentrations for the individual-based models and their PDE counterparts for the Voronoi and interval-centred domain partitions. These examples clearly demonstrate the propriety of the Voronoi domain partition. In addition, in Section III A of the SM we use Eqs. (6)-(11) in order to derive appropriate transition rates for two other regular domain partitions.

Although the Voronoi partition has been shown to be crucial on the rectilinear grid in order to derive the transition rates which give molecular concentrations that correspond to the expected mean-field PDE, the two examples given in Section III B of the SM demonstrate that, in general, for a non-uniform grid in dimension $d > 1$, the Voronoi partition is neither a necessary nor a sufficient condition for the derivation of appropriate transition rates.

III. DISCUSSION

By initially considering a general unstructured domain tessellation, we demonstrated that the Voronoi partition was necessary when considering non-uniform rectilinear domain tessellations in higher dimensions. We corroborated our findings with numerical simulations demonstrating clearly the propriety of the Voronoi partition over its interval-centred counterpart. We also demonstrated that consistent transition rates can be found for other regular domain tessellations such as the triangular and hexagonal tessellations and also for semi-regular domain tessellations (see Section III of the SM). This latter case is important since it demonstrates that, in general, in higher dimensions, the Voronoi partition is not necessary in order to derive consistent transition probabilities. In addition, we presented an example of a Voronoi partition which did not support the derivation of consistent transition rates. We should, therefore, not expect a Voronoi partition to be either a necessary or sufficient condition for the derivation of consistent transition rates on a general unstructured grid.

In a wider context, we have highlighted the importance of considering molecular *concentrations* when attempting to draw comparisons between individual-based models and deterministic counterparts, rather than simply considering molecular copy numbers.

Acknowledgements

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[8] . See Supplemental Material at [URL will be inserted by publisher] for an example of the formation of a morphogen gradient on a non-uniform domain, a confirmatory example of the propriety of the Voronoi domain partition for rectilinear lattices and the consideration of some alternative structured domain partitions.

[9] . Alternatively we could have posed this as a (possibly irregular) tessellation of the domain, each element of which has a node (between which molecules move) associated with it.

[10] . The global ordering we have used in Eq. (1) is purely for notational convenience. Generally, locally neighbouring nodes will not appear consecutively in the globally ordered vector of molecule numbers.