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Relationship between the reaction–diffusion master equation and particle tracking models

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Abstract
The reaction–diffusion master equation (RDME) is a model for chemical systems in which both noise in the chemical reaction process and the diffusion of molecules are important. It extends the chemical master equation for well-mixed chemical reactions by discretizing space into a collection of voxels. In this work, we show how the RDME may be rewritten as an equivalent 'particle tracking' model following the motion and interaction of individual molecules on a lattice. This new representation can be interpreted as a discrete version of the spatially-continuous 'probability distribution function' stochastic reaction–diffusion model studied by Doi. We show how this new representation can be mapped to a quantum field theory, complementing the existing work by Peliti mapping the RDME, and Doi mapping his spatially continuous model, to quantum field theories. The *formal* continuum limit, as the voxel size approaches zero, of the 'particle tracking' representation is studied to consider the question of whether the RDME approximates any spatially continuous model.

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1. Introduction

The reaction–diffusion master equation (RDME) models stochastic reaction–diffusion systems where both noise in the chemical reaction process and diffusion of molecules are important. In the RDME formulation, the chemical master equation [14] for well-mixed chemical reactions is extended by discretizing space into a collection of voxels. The state of the chemical system is then given by the number of each chemical species within each voxel. Molecules are assumed locally well mixed so that within a given mesh voxel reactions occur as if in an isolated well-mixed container. Diffusion of individual molecules is modeled as a continuous-time random walk between voxels. The RDME model goes back as far as the work of [8].

Until recently, there was an unanswered question as to how solutions to the RDME, for systems containing bimolecular reactions, depend on the voxel size. In particular, a common physical argument, see for example [10] or the supplement to [6], suggests the RDME is a reasonable physical model for bimolecular reactions only for mesh spacings that are neither too large or too small. It is important to note that this argument gives no suggestion as to an underlying microscopic physical model or spatially-continuous model that the RDME is an approximation to. In [10], we studied the dependence of the RDME on mesh spacing for the bimolecular reaction $\mathrm{A}+\mathrm{B} \to \varnothing$, in a system initially containing one molecule of each species. There it was proven that in the continuum limit of the mesh spacing approaching zero the two molecules never react, and simply diffuse relative to each other. Note that we only considered the standard scaling, inversely proportional to mesh voxel volume, of the bimolecular reaction rate. While bimolecular reaction effects are lost in the continuum limit of the RDME model, we also showed that with the standard reaction-rate scaling the mesh spacing can be chosen sufficiently large, though not too large, that the RDME can be thought of as an asymptotic approximation to the diffusion limited chemical reaction model of Smoluchowski [17]. (In this spatially continuous model, molecules undergo Brownian Motion, and react instantaneously when they approach within a specified reaction radius).

In this work, we consider the case of the more general bimolecular reaction $\mathrm{A} + \mathrm{B} \leftrightarrows \mathrm{C}$, with an arbitrary number of each chemical species initially. We restrict our attention to the standard scaling of the bimolecular reaction rate, where it varies as the inverse volume of a mesh voxel. In section 2, we show how to covert the reaction–diffusion master equation for this chemical system to an equivalent ‘particle tracking’ formulation. Our state variables switch from the number of molecules of each species in each voxel to the *total* number of molecules of each species in the system, and the locations of each individual molecule. (Here the location of a molecule corresponds to the index of the voxel containing it). The particle tracking formulation corresponds to a discrete version of the spatially-continuous ‘distribution function’ stochastic reaction–diffusion model of Doi ([4], section 5, equation (51)), and has the benefit of clearly showing the pair-wise interactions between molecules for bimolecular reactions.

In section 4, we show that the formal continuum limit of the particle tracking formulation is a coupled set of partial differential equations with delta-function coefficients. Since the RDME is equivalent to the discrete particle tracking model, the solutions to the RDME for fixed mesh spacings approximate the solutions to these PDEs. Based on the results of [10], we expect the approximation to only be asymptotic in nature, with reasonable agreement for mesh spacings that are neither too large or too small.

In section 3, we show that the particle tracking representation may be mapped to a quantum field theory, complementing both the work of Peliti [15] mapping the RDME, and the work of Doi [4] mapping his ‘distribution function’ model, to quantum field theories. The effective Hamiltonian we derive is of the same form that would be obtained when mapping the RDME directly to a quantum field theory. Peliti’s quantum field theory representation for the RDME has been studied by many authors; we refer the reader to [3, 12] and the reviews [13, 18] for references to the existing literature. When using the quantum field theory representation of the solution to the RDME, it is common to perform calculations using a formal continuum field theory limit. We restrict our attention herein to the discrete-space field theory formulation, and only consider spatial continuum limits in the context of the particle tracking representation. By making this choice the formal continuum model we obtain is changed from a functional integral based field representation to PDEs with singular coefficients.

2. Reformulation of the RDME to a particle tracking model

We now show how to convert the reaction–diffusion master equation to a form where the position of each individual molecule is explicitly tracked. For notational simplicity, we restrict the chemical system we study to the reaction $\mathrm{A}+\mathrm{B} \rightleftarrows \mathrm{C}$. An introduction to the general RDME for arbitrary chemical systems is available in [10, 11], and a recent review of stochastic-reaction diffusion models, including the RDME, is provided in [7]. Denote by k_+ the forward reaction rate with units volume time^{-1}, and the reverse reaction rate with units time^{-1} by k_-. The domain in which the reaction may occur is taken to be all of $\Omega = \mathbb{R}^3$.

We divide Ω into a standard Cartesian mesh, comprised of cubes with sides of length h. Let

$$\boldsymbol{i} = (i_1, i_2, i_3) \in \mathbb{Z}^3$$

be the multi-index labeling a given voxel in Ω, with $\mathbb{Z}^3$ representing the three-dimensional integer index space. We denote by $a_{\boldsymbol{i}}$ the number of molecules of chemical species A at location $\boldsymbol{i}$, and define

$$\boldsymbol{a} = \{a_{\boldsymbol{i}} \mid \boldsymbol{i} \in \mathbb{Z}^3\}.$$

(We similarly define $\boldsymbol{b}$ and $\boldsymbol{c}$.) The notation $\boldsymbol{a} + 1_{\boldsymbol{i}}$ will represent $\boldsymbol{a}$ with one added to $a_{\boldsymbol{i}}$. The diffusive jump rate for species A, from voxel $\boldsymbol{j}$ to voxel $\boldsymbol{i}$, is denoted by $k^{\mathrm{A}}_{\boldsymbol{ij}}$, with $k^{\mathrm{B}}_{\boldsymbol{ij}}$ and $k^{\mathrm{C}}_{\boldsymbol{ij}}$ defined similarly. Using these definitions, the reaction–diffusion master equation can be written as

$$\frac{\mathrm{d}P}{\mathrm{d}t}(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t) = (L_h P + R_h P)(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t), \tag{1}$$

where the diffusion operator, L_h, is

$$\begin{aligned}
&(L_h P)(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t) \\
&\quad = \sum_{\boldsymbol{i}\in\mathbb{Z}^3} \sum_{\boldsymbol{i}'\in\mathbb{Z}^3} \Big(\big[k^{\mathrm{A}}_{\boldsymbol{ii}'} (a_{\boldsymbol{i}'} + 1)\, P(\boldsymbol{a} + 1_{\boldsymbol{i}'} - 1_{\boldsymbol{i}}, \boldsymbol{b}, \boldsymbol{c}, t) - k^{\mathrm{A}}_{\boldsymbol{i}'\boldsymbol{i}} a_{\boldsymbol{i}} P(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t) \big] \\
&\qquad + \big[k^{\mathrm{B}}_{\boldsymbol{ii}'} (b_{\boldsymbol{i}'} + 1)\, P(\boldsymbol{a}, \boldsymbol{b} + 1_{\boldsymbol{i}'} - 1_{\boldsymbol{i}}, \boldsymbol{c}, t) - k^{\mathrm{B}}_{\boldsymbol{i}'\boldsymbol{i}} b_{\boldsymbol{i}} P(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t) \big] \\
&\qquad + \big[k^{\mathrm{C}}_{\boldsymbol{ii}'} (c_{\boldsymbol{i}'} + 1)\, P(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c} + 1_{\boldsymbol{i}'} - 1_{\boldsymbol{i}}, t) - k^{\mathrm{C}}_{\boldsymbol{i}'\boldsymbol{i}} c_{\boldsymbol{i}} P(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t) \big] \Big),
\end{aligned}$$

and the reaction operator, R_h, is

$$\begin{aligned}
&(R_h P)(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t) \\
&\quad = \sum_{\boldsymbol{i}\in\mathbb{Z}^3} \left(\frac{k_+ (a_{\boldsymbol{i}} + 1)(b_{\boldsymbol{i}} + 1)}{h^3} P(\boldsymbol{a} + 1_{\boldsymbol{i}}, \boldsymbol{b} + 1_{\boldsymbol{i}}, \boldsymbol{c} - 1_{\boldsymbol{i}}, t) - \frac{k_+ a_{\boldsymbol{i}} b_{\boldsymbol{i}}}{h^3} P(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t) \right. \\
&\qquad \left. + k_- (c_{\boldsymbol{i}} + 1) P(\boldsymbol{a} - 1_{\boldsymbol{i}}, \boldsymbol{b} - 1_{\boldsymbol{i}}, \boldsymbol{c} + 1_{\boldsymbol{i}}, t) - k_- c_{\boldsymbol{i}} P(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t) \right).
\end{aligned}$$

Note that (1) is a coupled system of ODEs over all possible states $(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c})$.

We now change variables to convert to the our new particle tracking representation, a spatially-discrete version of the spatially-continuous probability distribution function representation used in [4]. Denote by a the *total* number of molecules of chemical species A within Ω, i.e.

$$a = \sum_{\boldsymbol{i}\in\mathbb{Z}^3} a_{\boldsymbol{i}}.$$

(Define b and c similarly.) We introduce a new set of variables, $\boldsymbol{j}^a = \big(\boldsymbol{j}^a_1, \ldots, \boldsymbol{j}^a_a\big)$, where $\boldsymbol{j}^a_l \in \mathbb{Z}^3$ labels the voxel in which the lth molecule of chemical species A is located. Note that we use a as a superscript to indicate that there are a total *vectors*, $\boldsymbol{j}_l^a$, that comprise the components of $\boldsymbol{j}^a$. $\boldsymbol{j}^a$ is therefore a vector in $\mathbb{Z}^{3a}$. With $\boldsymbol{j}^b$ and $\boldsymbol{j}^c$ defined similarly, let $f^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t)$ denote the probability that at time t there are a molecules of species A located within the voxels given by $\boldsymbol{j}^a$, b molecules of species B located within the voxels given by $\boldsymbol{j}^b$ and c molecules of species C located within the mesh voxels given by $\boldsymbol{j}^c$. Note that the molecules are assumed to be labeled so that each $\boldsymbol{j}_l^a$ always represents the same molecule.

The set of all permutations of the index vectors comprising $\boldsymbol{j}^a$ is defined as

$$\sigma(\boldsymbol{j}^a) = \left\{ \left(\boldsymbol{j}_{\sigma_1}^a, \ldots, \boldsymbol{j}_{\sigma_a}^a\right) \,\middle|\, (\sigma_1, \ldots, \sigma_a) \text{ is any permutation of } (1, \ldots, a) \right\},$$

with $\sigma(\boldsymbol{j}^b)$ and $\sigma(\boldsymbol{j}^c)$ defined similarly. With these definitions, we now symmetrize $f^{(a,b,c)}$. Physically, this assumption means that molecules of the same chemical species are assumed identical, and hence the order in which such molecules are labeled is irrelevant. Note that this assumption is implicit in the reaction–diffusion master equation (1). The symmetrized probability is defined as

$$F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) = \sum_{\substack{\tilde{\boldsymbol{j}}^a \in \sigma(\boldsymbol{j}^a), \\ \tilde{\boldsymbol{j}}^b \in \sigma(\boldsymbol{j}^b), \\ \tilde{\boldsymbol{j}}^c \in \sigma(\boldsymbol{j}^c)}} f^{(a,b,c)}(\tilde{\boldsymbol{j}}^a, \tilde{\boldsymbol{j}}^b, \tilde{\boldsymbol{j}}^c, t). \tag{2}$$

$F^{(a,b,c)}$ is symmetric under permutations of the components of each vector $\boldsymbol{j}^a$, $\boldsymbol{j}^b$ and $\boldsymbol{j}^c$, so that for any permutation $(\sigma_1, \ldots, \sigma_a)$ of $(1, \ldots, a)$,

$$F^{(a,b,c)}\left(\boldsymbol{j}_{\sigma_1}^a, \ldots, \boldsymbol{j}_{\sigma_a}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t\right) = F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t),$$

with similar relations holding for permutations in the components of $\boldsymbol{j}^b$ and $\boldsymbol{j}^c$. Using these definitions, the probability of being in any given state is then completely specified by the collection

$$\{F^{(a,b,c)}(\cdot, \cdot, \cdot, t) \,|\, a, b, \text{ and } c \text{ take all possible values}\}.$$

We now point out several relations that we will subsequently need. Consider an arbitrary state, $(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c})$, of the RDME and any corresponding set of molecule positions, $(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c)$ such that

$$a_{\boldsymbol{i}} = \left|\left\{\boldsymbol{j}_l^a \,\middle|\, \boldsymbol{j}_l^a = \boldsymbol{i}, l = 1 \ldots a\right\}\right|,$$

with similar relations holding for $b_{\boldsymbol{i}}$ and $c_{\boldsymbol{i}}$. Here $|\cdot|$ denotes the cardinality of a set. In what follows, we use this relation to treat $a_{\boldsymbol{i}}$ as a function of $\boldsymbol{j}^a$ within equations for the particle tracking model. Denote by $\tilde{\sigma}(\boldsymbol{j}^a)$ the set of all *distinct* vectors, $\tilde{\boldsymbol{j}}^a$, that are given by permutations of the components of $\boldsymbol{j}^a$. Note that $\tilde{\sigma}(\boldsymbol{j}^a) \subseteq \sigma(\boldsymbol{j}^a)$, and by identity appendix A.1 has cardinality

$$|\tilde{\sigma}(\boldsymbol{j}^a)| = a! \prod_{\boldsymbol{i} \in \mathbb{Z}^3} \frac{1}{a_{\boldsymbol{i}}!}. \tag{3}$$

With $\tilde{\sigma}(\boldsymbol{j}^b)$ and $\tilde{\sigma}(\boldsymbol{j}^c)$ defined similarly, let

$$\tilde{\sigma}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c) = \tilde{\sigma}(\boldsymbol{j}^a) \times \tilde{\sigma}(\boldsymbol{j}^b) \times \tilde{\sigma}(\boldsymbol{j}^c).$$

The cardinality of this set, $|\tilde{\sigma}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c)|$, gives the total number of distinct permutations of the components of $(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c)$ that correspond to the state $(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c})$, assuming $\boldsymbol{j}^a$ precedes $\boldsymbol{j}^b$, and $\boldsymbol{j}^b$ precedes $\boldsymbol{j}^c$. In terms of $\tilde{\sigma}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c)$ we define

$$C_{\boldsymbol{a},\boldsymbol{b},\boldsymbol{c}} = \frac{|\tilde{\sigma}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c)|}{a!b!c!} = \prod_{\boldsymbol{i} \in \mathbb{Z}^3} \frac{1}{a_{\boldsymbol{i}}!b_{\boldsymbol{i}}!c_{\boldsymbol{i}}!}.$$

Several identities involving $C_{\mathbf{a},\mathbf{b},\mathbf{c}}$ will subsequently be needed and are collected here:

$$a_i = (a_{i'} + 1)\,\frac{C_{\mathbf{a}+\mathbf{1}_{i'}-\mathbf{1}_i,\mathbf{b},\mathbf{c}}}{C_{\mathbf{a},\mathbf{b},\mathbf{c}}}, \tag{4}$$

$$c_i = (a_i + 1)\,(b_i + 1)\,\frac{C_{\mathbf{a}+\mathbf{1}_i,\mathbf{b}+\mathbf{1}_i,\mathbf{c}-\mathbf{1}_i}}{C_{\mathbf{a},\mathbf{b},\mathbf{c}}}, \tag{5}$$

$$a_i b_i = (c_i + 1)\,\frac{C_{\mathbf{a}-\mathbf{1}_i,\mathbf{b}-\mathbf{1}_i,\mathbf{c}+\mathbf{1}_i}}{C_{\mathbf{a},\mathbf{b},\mathbf{c}}}. \tag{6}$$

We now consider the normalization of $F^{(\mathbf{a},\mathbf{b},\mathbf{c})}$. Let $\Lambda(\mathbb{Z}^{3a}) = \{\boldsymbol{j}^a \in \mathbb{Z}^{3a} \mid \boldsymbol{j}^a_1 \leqslant \boldsymbol{j}^a_2 \leqslant \cdots \leqslant \boldsymbol{j}^a_a\}$, with $\Lambda(\mathbb{Z}^{3b})$ and $\Lambda(\mathbb{Z}^{3c})$ defined similarly. Assume that $f^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t)$ has the normalization,

$$\sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \sum_{\substack{\boldsymbol{j}^a \in \mathbb{Z}^{3a},\\ \boldsymbol{j}^b \in \mathbb{Z}^{3b},\\ \boldsymbol{j}^c \in \mathbb{Z}^{3c}}} f^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) = 1.$$

Then

$$\begin{aligned}
\sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \sum_{\substack{\boldsymbol{j}^a \in \mathbb{Z}^{3a},\\ \boldsymbol{j}^b \in \mathbb{Z}^{3b},\\ \boldsymbol{j}^c \in \mathbb{Z}^{3c}}} f^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) &= \sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \sum_{\substack{\boldsymbol{j}^a \in \Lambda(\mathbb{Z}^{3a}),\\ \boldsymbol{j}^b \in \Lambda(\mathbb{Z}^{3b}),\\ \boldsymbol{j}^c \in \Lambda(\mathbb{Z}^{3c})}} \sum_{\substack{\tilde{\boldsymbol{j}}^a \in \tilde{\sigma}(\boldsymbol{j}^a),\\ \tilde{\boldsymbol{j}}^b \in \tilde{\sigma}(\boldsymbol{j}^b),\\ \tilde{\boldsymbol{j}}^c \in \tilde{\sigma}(\boldsymbol{j}^c)}} f^{(a,b,c)}(\tilde{\boldsymbol{j}}^a, \tilde{\boldsymbol{j}}^b, \tilde{\boldsymbol{j}}^c, t), \\
&= \sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \sum_{\substack{\boldsymbol{j}^a \in \Lambda(\mathbb{Z}^{3a}),\\ \boldsymbol{j}^b \in \Lambda(\mathbb{Z}^{3b}),\\ \boldsymbol{j}^c \in \Lambda(\mathbb{Z}^{3c})}} C_{\mathbf{a},\mathbf{b},\mathbf{c}} \sum_{\substack{\tilde{\boldsymbol{j}}^a \in \sigma(\boldsymbol{j}^a),\\ \tilde{\boldsymbol{j}}^b \in \sigma(\boldsymbol{j}^b),\\ \tilde{\boldsymbol{j}}^c \in \sigma(\boldsymbol{j}^c)}} f^{(a,b,c)}(\tilde{\boldsymbol{j}}^a, \tilde{\boldsymbol{j}}^b, \tilde{\boldsymbol{j}}^c, t), \\
&= \sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \sum_{\substack{\boldsymbol{j}^a \in \Lambda(\mathbb{Z}^{3a}),\\ \boldsymbol{j}^b \in \Lambda(\mathbb{Z}^{3b}),\\ \boldsymbol{j}^c \in \Lambda(\mathbb{Z}^{3c})}} C_{\mathbf{a},\mathbf{b},\mathbf{c}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c),
\end{aligned}$$

where the second line follows by identity appendix A.2 and the third by (2). We thus conclude that

$$\sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \sum_{\substack{\boldsymbol{j}^a \in \Lambda(\mathbb{Z}^{3a}),\\ \boldsymbol{j}^b \in \Lambda(\mathbb{Z}^{3b}),\\ \boldsymbol{j}^c \in \Lambda(\mathbb{Z}^{3c})}} C_{\mathbf{a},\mathbf{b},\mathbf{c}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) = 1. \tag{7}$$

When $F^{(a,b,c)}$ is defined as in (2), the normalization factor $C_{\mathbf{a},\mathbf{b},\mathbf{c}}$ is needed. It accounts for the multiple inclusion within the sums of states where two or more molecules of the same species are located at the same location. In the spatially-continuous formulation of [4] this factor is not needed. There the sums over the lattice become spatial integrals, and the set of locations where two or more molecules of a given species are at the same position has measure zero. Note though, since this factor is left out pointwise results, such as ([4], equation (17)), are only valid almost everywhere. (In particular, they are incorrect at spatial locations where two or more molecules of the same species occupy the same point.) We subsequently restrict our state space to $\Lambda(\mathbb{Z}^{3a}) \times \Lambda(\mathbb{Z}^{3b}) \times \Lambda(\mathbb{Z}^{3c})$. Note the identity

$$\sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \sum_{\substack{\boldsymbol{j}^a \in \Lambda(\mathbb{Z}^{3a}),\\ \boldsymbol{j}^b \in \Lambda(\mathbb{Z}^{3b}),\\ \boldsymbol{j}^c \in \Lambda(\mathbb{Z}^{3c})}} C_{\boldsymbol{a},\boldsymbol{b},\boldsymbol{c}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) = \sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \frac{1}{a!b!c!} \sum_{\substack{\boldsymbol{j}^a \in \mathbb{Z}^{3a},\\ \boldsymbol{j}^b \in \mathbb{Z}^{3b},\\ \boldsymbol{j}^c \in \mathbb{Z}^{3c}}} C_{\boldsymbol{a},\boldsymbol{b},\boldsymbol{c}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t).$$

We now relate $F^{(a,b,c)}$ to the reaction–diffusion master equation. The probability of being in any state $(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c})$, $P(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t)$, is equivalent to the probability of being in any state, $(\tilde{\boldsymbol{j}}^a, \tilde{\boldsymbol{j}}^b, \tilde{\boldsymbol{j}}^c)$, within the set $\tilde{\sigma}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c)$. (Assuming $(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c)$ is one collection of molecule positions that are consistent with the state $(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c})$.) We therefore have that

$$\begin{aligned} P(\boldsymbol{a}, \boldsymbol{b}, \boldsymbol{c}, t) &= \sum_{(\tilde{\boldsymbol{j}}^a, \tilde{\boldsymbol{j}}^b, \tilde{\boldsymbol{j}}^c) \in \tilde{\sigma}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c)} f^{(a,b,c)}(\tilde{\boldsymbol{j}}^a, \tilde{\boldsymbol{j}}^b, \tilde{\boldsymbol{j}}^c, t), \\ &= C_{\boldsymbol{a},\boldsymbol{b},\boldsymbol{c}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t), \end{aligned}$$

Where the last line follows by identity appendix A.2 and the definition of $F^{(\boldsymbol{a},\boldsymbol{b},\boldsymbol{c})}$. Substituting this expression into equation (1) and dividing by $C_{\boldsymbol{a},\boldsymbol{b},\boldsymbol{c}}$, we obtain the equations of evolution satisfied by $F^{(a,b,c)}$,

$$\frac{\mathrm{d}F^{(a,b,c)}}{\mathrm{d}t}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) = (\tilde{L}_h F^{(a,b,c)} + \tilde{R}_h F^{(a,b,c)})(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t). \tag{8}$$

Before deriving $\tilde{L}_h$ and $\tilde{R}_h$, we must first introduce new notations for removing and adding elements to a position vector, $\boldsymbol{j}^a$. Let $\boldsymbol{j}^a \backslash \boldsymbol{j}_l^a$ denote $\boldsymbol{j}^a$ with the lth molecule removed, i.e.,

$$\boldsymbol{j}^a \backslash \boldsymbol{j}_l^a = \left(\boldsymbol{j}_1^a, \ldots, \boldsymbol{j}_{l-1}^a, \boldsymbol{j}_{l+1}^a, \ldots, \boldsymbol{j}_a^a\right).$$

Similarly, $\boldsymbol{j}^a \backslash \{\boldsymbol{i}\}$ will denote removing any one component of $\boldsymbol{j}^a$ that has the value $\boldsymbol{i}$. Note that since we are only considering a symmetrized density, it does not matter which component with the value $\boldsymbol{i}$ is removed. We use the convention that $F^{(a-1,b,c)}(\boldsymbol{j}^a \backslash \{\boldsymbol{i}\}, \boldsymbol{j}^b, \boldsymbol{j}^c, t)$ is zero if $\boldsymbol{i}$ is not equal to one of the components of $\boldsymbol{j}^a$ (with similar conventions for removing B or C molecules). Adding an additional molecule to $\boldsymbol{j}^a$ is denoted by $\boldsymbol{j}^a \cup \boldsymbol{j}_{a+1}^a$, i.e.,

$$\boldsymbol{j}^a \cup \boldsymbol{j}_{a+1}^a = \left(\boldsymbol{j}_1^a, \ldots, \boldsymbol{j}_a^a, \boldsymbol{j}_{a+1}^a\right).$$

To add the specific value $\boldsymbol{i}$ for the new molecule's position, the notation $\boldsymbol{j}^a \cup \{\boldsymbol{i}\}$ is used.

With the preceding definitions, and using identity (4), the diffusion operator, $\tilde{L}_h$, is

$$\begin{aligned} (\tilde{L}_h F^{(a,b,c)})(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) = \sum_{\boldsymbol{i} \in \mathbb{Z}^3} \sum_{\boldsymbol{i}' \in \mathbb{Z}^3} \\ \times \Big(\big[k_{\boldsymbol{i}\boldsymbol{i}'}^{\mathrm{A}} a_{\boldsymbol{i}} F^{a,b,c}(\boldsymbol{j}^a \backslash \{\boldsymbol{i}\} \cup \{\boldsymbol{i}'\}, \boldsymbol{j}^b, \boldsymbol{j}^c, t) - k_{\boldsymbol{i}'\boldsymbol{i}}^{\mathrm{A}} a_{\boldsymbol{i}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) \big] \\ + \big[k_{\boldsymbol{i}\boldsymbol{i}'}^{\mathrm{B}} b_{\boldsymbol{i}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b \backslash \{\boldsymbol{i}\} \cup \{\boldsymbol{i}'\}, \boldsymbol{j}^c, t) - k_{\boldsymbol{i}'\boldsymbol{i}}^{\mathrm{B}} b_{\boldsymbol{i}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) \big] \\ + \big[k_{\boldsymbol{i}\boldsymbol{i}'}^{\mathrm{C}} c_{\boldsymbol{i}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c \backslash \{\boldsymbol{i}\} \cup \{\boldsymbol{i}'\}, t) - k_{\boldsymbol{i}'\boldsymbol{i}}^{\mathrm{C}} c_{\boldsymbol{i}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) \big] \Big). \end{aligned} \tag{9}$$

Since $a_{\boldsymbol{i}}$ gives the number of molecule positions within $\boldsymbol{j}^a$ that have the value $\boldsymbol{i}$,

$$k_{\boldsymbol{i}'\boldsymbol{i}}^{\mathrm{A}} a_{\boldsymbol{i}} F^{(a,b,c)} = \sum_{l \in \{\tilde{l} \mid \boldsymbol{j}_{\tilde{l}}^a = \boldsymbol{i}\}} k_{\boldsymbol{i}'\boldsymbol{j}_l^a}^{\mathrm{A}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t). \tag{10}$$

Similarly,

$$\begin{aligned} k_{\boldsymbol{i}\boldsymbol{i}'}^{\mathrm{A}} a_{\boldsymbol{i}} F^{(a,b,c)}(\boldsymbol{j}^a \backslash \{\boldsymbol{i}\} \cup \{\boldsymbol{i}'\}, \boldsymbol{j}^b, \boldsymbol{j}^c, t) \\ = \sum_{l \in \{\tilde{l} \mid \boldsymbol{j}_{\tilde{l}}^a = \boldsymbol{i}\}} k_{\boldsymbol{j}_l^a \boldsymbol{i}'}^{\mathrm{A}} F^{(a,b,c)}\left(\boldsymbol{j}_1^a, \ldots, \boldsymbol{j}_{l-1}^a, \boldsymbol{i}', \boldsymbol{j}_{l+1}^a, \ldots, \boldsymbol{j}_a^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t\right). \end{aligned}$$

Finally, noting that for the previous two equations

$$\sum_{\boldsymbol{i}\in\mathbb{Z}^3}\sum_{l\in\{\tilde{l}\,|\,\boldsymbol{j}^a_{\tilde{l}}=\boldsymbol{i}\}}(\cdot)=\sum_{l=1}^{a}(\cdot), \tag{11}$$

we find that equation (9) simplifies to

$$\begin{aligned}(\tilde{L}_h F^{(a,b,c)})(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t) = \sum_{\boldsymbol{i}'\in I^3}\Bigg(&\sum_{l=1}^{a}\big[k^A_{\boldsymbol{j}^a_l\boldsymbol{i}'}F^{(a,b,c)}\big(\boldsymbol{j}^a_1,\ldots,\boldsymbol{j}^a_{l-1},\boldsymbol{i}',\boldsymbol{j}^a_{l+1},\ldots,\boldsymbol{j}^a_a,\boldsymbol{j}^b,\boldsymbol{j}^c,t\big)\\ &-k^A_{\boldsymbol{i}'\boldsymbol{j}^a_l}F^{(a,b,c)}\big(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t\big)\big]+\sum_{l=1}^{b}\\ \big[k^B_{\boldsymbol{j}^b_l\boldsymbol{i}'}F^{(a,b,c)}\big(\boldsymbol{j}^a,\boldsymbol{j}^b_1,\ldots,\boldsymbol{j}^b_{l-1},\boldsymbol{i}',\boldsymbol{j}^b_{l+1},\ldots,\boldsymbol{j}^b_b,\boldsymbol{j}^c,t\big)&-k^B_{\boldsymbol{i}'\boldsymbol{j}^b_l}F^{(a,b,c)}\big(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t\big)\big]\\ &+\sum_{l=1}^{c}\big[k^C_{\boldsymbol{j}^c_l\boldsymbol{i}'}F^{(a,b,c)}\big(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c_1,\ldots,\boldsymbol{j}^c_{l-1},\boldsymbol{i}',\boldsymbol{j}^c_{l+1},\ldots,\boldsymbol{j}^c_c,t\big)\\ &-k^C_{\boldsymbol{i}'\boldsymbol{j}^c_l}F^{(a,b,c)}\big(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t\big)\big]\Bigg).\end{aligned} \tag{12}$$

As we have shown in [11], the diffusive jump rates should be chosen so as to determine a discretization of the Laplacian. This ensures that for systems in which no chemical reactions may occur we correctly recover the diffusion of individual molecules in the continuum limit that the mesh spacing approaches zero. Recall we denote by h the mesh spacing of the Cartesian grid, so that h^3 is the volume of a single voxel. For $\Omega=\mathbb{R}^3$, the rates, $k^{\mathrm{A}}_{\boldsymbol{j}\boldsymbol{i}}$ are then

$$k^{\mathrm{A}}_{\boldsymbol{j}\boldsymbol{i}}=\begin{cases}D^{\mathrm{A}}/h^2, & \boldsymbol{j}\text{ a non-diagonal neighbor of }\boldsymbol{i},\\ 0, & \text{else,}\end{cases}$$

with $k^{\mathrm{B}}_{\boldsymbol{j}\boldsymbol{i}}$ and $k^{\mathrm{C}}_{\boldsymbol{j}\boldsymbol{i}}$ defined similarly. For appropriate jump rates in bounded domains with geometrically complex boundaries, see [11]. With these definitions, we denote by $(\Delta_h)^a_l$ the discrete Laplacian acting on the $\boldsymbol{j}^a_l$ coordinates,

$$\begin{aligned}(\Delta_h)^a_l F^{(a,b,c)}&(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t)\\ &=\sum_{d=1}^{3}\sum_{\pm}\frac{1}{h^2}\big[F^{(a,b,c)}\big(\boldsymbol{j}^a_1,\ldots,\boldsymbol{j}^a_{l-1},\boldsymbol{j}^a_l\pm\boldsymbol{e}_d,\boldsymbol{j}^a_{l+1},\ldots,\boldsymbol{j}^a_a,\boldsymbol{j}^b,\boldsymbol{j}^c,t\big)\\ &\quad-F^{(a,b,c)}(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t)\big].\end{aligned}$$

Here $\boldsymbol{e}_d$ denotes the unit vector along the dth coordinate axis of $\mathbb{R}^3$. The total Laplacian acting on all of the $\boldsymbol{j}^a$ coordinates is then defined to be

$$\Delta^a_h=\sum_{l=1}^{a}(\Delta_h)^a_l.$$

With Δ^b_h and Δ^c_h defined similarly, equation (12) can be simplified to

$$(\tilde{L}_h F^{(a,b,c)})\big(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t\big)=\big(D^{\mathrm{A}}\Delta^a_h+D^{\mathrm{B}}\Delta^b_h+D^{\mathrm{C}}\Delta^c_h\big)\,F^{(a,b,c)}\big(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t\big). \tag{13}$$

Note, for chemical systems in which the molecules simply diffuse and cannot react, this equation implies that we correctly recover the independent Brownian motion of each molecule as $h\to 0$.

Using equations (5) and (6), the reaction operator, $\tilde{R}_h$, is

$$\begin{aligned}
&(\tilde{R}_h F^{(a,b,c)})(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) \\
&\quad = \frac{k_+}{h^3} \sum_{\boldsymbol{i} \in \mathbb{Z}^3} \Big[c_{\boldsymbol{i}} F^{(a+1,b+1,c-1)}\big(\boldsymbol{j}^a \cup \{\boldsymbol{i}\}, \boldsymbol{j}^b \cup \{\boldsymbol{i}\}, \boldsymbol{j}^c \backslash \{\boldsymbol{i}\}, t\big) \\
&\qquad - a_{\boldsymbol{i}} b_{\boldsymbol{i}} F^{(a,b,c)}\big(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t\big)\Big] \\
&\qquad + k_- \sum_{\boldsymbol{i} \in \mathbb{Z}^3} \Big[a_{\boldsymbol{i}} b_{\boldsymbol{i}} F^{(a-1,b-1,c+1)}\big(\boldsymbol{j}^a \backslash \{\boldsymbol{i}\}, \boldsymbol{j}^b \backslash \{\boldsymbol{i}\}, \boldsymbol{j}^c \cup \{\boldsymbol{i}\}, t\big) \\
&\qquad - c_{\boldsymbol{i}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t)\Big].
\end{aligned} \tag{14}$$

Defining the Kronecker delta

$$\delta_{\boldsymbol{i}\boldsymbol{j}} = \begin{cases} 1, & \boldsymbol{i} = \boldsymbol{j}, \\ 0, & \text{else}, \end{cases}$$

we find

$$a_{\boldsymbol{i}} b_{\boldsymbol{i}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) = \sum_{l \in \{l' \mid \boldsymbol{j}^a_{l'} = \boldsymbol{i}\}} \sum_{\tilde{l}=1}^{b} \delta_{\boldsymbol{j}^a_l \boldsymbol{j}^b_{\tilde{l}}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t). \tag{15}$$

Similarly,

$$\begin{aligned}
&a_{\boldsymbol{i}} b_{\boldsymbol{i}} F^{(a-1,b-1,c+1)}(\boldsymbol{j}^a \backslash \{\boldsymbol{i}\}, \boldsymbol{j}^b \backslash \{\boldsymbol{i}\}, \boldsymbol{j}^c \cup \{\boldsymbol{i}\}, t) \\
&\quad = \sum_{l \in \{l' \mid \boldsymbol{j}^a_{l'} = \boldsymbol{i}\}} \sum_{\tilde{l}=1}^{b} \delta_{\boldsymbol{j}^a_l \boldsymbol{j}^b_{\tilde{l}}} F^{(a-1,b-1,c+1)}\big(\boldsymbol{j}^a \backslash \boldsymbol{j}^a_l, \boldsymbol{j}^b \backslash \boldsymbol{j}^b_{\tilde{l}}, \boldsymbol{j}^c \cup \boldsymbol{j}^a_l, t\big).
\end{aligned} \tag{16}$$

We now expand each term in (14) into a sum over molecule indexes using equations (10), (15), and (16). Reusing equation (11), we obtain the final expression for the reaction operator,

$$\begin{aligned}
&(\tilde{R}_h F^{(a,b,c)})(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) \\
&\quad = \frac{k_+}{h^3} \left[\sum_{l=1}^{c} F^{(a+1,b+1,c-1)}\big(\boldsymbol{j}^a \cup \boldsymbol{j}^c_l, \boldsymbol{j}^b \cup \boldsymbol{j}^c_l, \boldsymbol{j}^c \backslash \boldsymbol{j}^c_l, t\big) \right. \\
&\qquad \left. - \sum_{l=1}^{a} \sum_{\tilde{l}=1}^{b} \delta_{\boldsymbol{j}^a_l \boldsymbol{j}^b_{\tilde{l}}} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) \right] \\
&\qquad + k_- \left[\sum_{l=1}^{a} \sum_{\tilde{l}=1}^{b} \delta_{\boldsymbol{j}^a_l \boldsymbol{j}^b_{\tilde{l}}} F^{(a-1,b-1,c+1)}\big(\boldsymbol{j}^a \backslash \boldsymbol{j}^a_l, \boldsymbol{j}^b \backslash \boldsymbol{j}^b_{\tilde{l}}, \boldsymbol{j}^c \cup \boldsymbol{j}^a_l, t\big) \right. \\
&\qquad \left. - \sum_{l=1}^{c} F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) \right].
\end{aligned} \tag{17}$$

The reformulated model, equation (8) with the operators (13) and (17), corresponds to a discrete version of the 'probability distribution function' model of Doi ([4], see sections 2 and 5). Note in (17) that all bimolecular interaction terms simply depend on the separation vector, $\boldsymbol{j}^a_l - \boldsymbol{j}^b_{\tilde{l}}$, between pairs of A and B molecules. Letting $\delta_h\big(\boldsymbol{j}^a_l - \boldsymbol{j}^b_{\tilde{l}}\big) = h^{-3}\delta_{\boldsymbol{j}^a_l \boldsymbol{j}^b_{\tilde{l}}}$, the discrete bimolecular reaction rate between molecules $\boldsymbol{j}^a_l$ and $\boldsymbol{j}^b_{\tilde{l}}$ is then

$$k_+ \delta_h\big(\boldsymbol{j}^a_l - \boldsymbol{j}^b_{\tilde{l}}\big). \tag{18}$$

3. Relation to quantum field theory

We now show the equivalence of the new representation of the reaction–diffusion master equation, equation (8), to a discrete-space second quantization Fock space model. Just as (8) corresponds to a discrete version of the probability distribution function model of [4], the Fock space model we now give corresponds to a discrete version of the spatially-continuous second quantization Fock space model of [4]. Our discussion parallels that of [4].

Discrete-space second quantization representations of the reaction–diffusion master equation go back to the work of [15]. Our Fock space representation is related to that of [15] in the same way that (1) is related to (8) (i.e. we change state variables from the number of molecules of a given species in a given voxel to the total number of each species in the system and the locations of all molecules of each species).

Following [4], we define creation and annihilation operators for species A, $\mathcal{A}^{\dagger}(\boldsymbol{i})$ and $\mathcal{A}(\boldsymbol{i})$, by the commutation relations

$$[\mathcal{A}(\boldsymbol{i}), \mathcal{A}^{\dagger}(\boldsymbol{i}')] = \delta_{\boldsymbol{i}\boldsymbol{i}'}, \qquad [\mathcal{A}(\boldsymbol{i}), \mathcal{A}(\boldsymbol{i}')] = [\mathcal{A}^{\dagger}(\boldsymbol{i}), \mathcal{A}^{\dagger}(\boldsymbol{i}')] = 0, \tag{19}$$

with similar relations for the species B and C operators (denoted by $\mathcal{B}(\boldsymbol{i})$, $\mathcal{B}^{\dagger}(\boldsymbol{i})$, $\mathcal{C}(\boldsymbol{i})$ and $\mathcal{C}^{\dagger}(\boldsymbol{i})$). Note that any two operators for different species will commute. To completely specify the creation and annihilation operators we also need to define their action on the vacuum (no molecule) state, denoted by $|0\rangle$,

$$\mathcal{A}(\boldsymbol{i})|0\rangle = 0, \qquad \langle 0|\mathcal{A}^{\dagger}(\boldsymbol{i}) = 0,$$

again, with similar relations for the B and C operators. We let $|\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c\rangle$ represent the 'quantum' state corresponding to the chemical state $(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c)$ of the last section, defined as

$$\begin{aligned} |\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c\rangle &= \left[\prod_{l=1}^{a}\prod_{m=1}^{b}\prod_{n=1}^{c} \mathcal{A}^{\dagger}(\boldsymbol{j}^a_l)\mathcal{B}^{\dagger}(\boldsymbol{j}^b_m)\mathcal{C}^{\dagger}(\boldsymbol{j}^c_n)\right]|0\rangle, \\ \langle \boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c| &= \langle 0|\left[\prod_{l=1}^{a}\prod_{m=1}^{b}\prod_{n=1}^{c} \mathcal{A}(\boldsymbol{j}^a_l)\mathcal{B}(\boldsymbol{j}^b_m)\mathcal{C}(\boldsymbol{j}^c_n)\right]. \end{aligned}$$

With these definitions we find

$$\begin{aligned} \mathcal{A}(\boldsymbol{i})|\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c\rangle &= a_{\boldsymbol{i}}|\boldsymbol{j}^a\backslash\{\boldsymbol{i}\}, \boldsymbol{j}^b, \boldsymbol{j}^c\rangle, \\ \mathcal{A}^{\dagger}(\boldsymbol{i})|\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c\rangle &= \ |\boldsymbol{j}^a \cup \{\boldsymbol{i}\}, \boldsymbol{j}^b, \boldsymbol{j}^c\rangle, \end{aligned}$$

with similar relations for the B and C operators. As in section 2, $a_{\boldsymbol{i}}$ denotes the number of molecules in the $\boldsymbol{i}$th voxel when in the state $|\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c\rangle$. With these definitions, $\mathcal{N}(\boldsymbol{i}) = \mathcal{A}^{\dagger}(\boldsymbol{i})\mathcal{A}(\boldsymbol{i})$ then gives the number operator for species A within the $\boldsymbol{i}$th voxel.

Denote by $\mathbf{1}_{\sigma(\boldsymbol{j}^a)}(\tilde{\boldsymbol{j}}^{\tilde{a}})$ the indicator function on the set of permutations of $\boldsymbol{j}^a, \sigma(\boldsymbol{j}^a)$, evaluated at $\tilde{\boldsymbol{j}}^{\tilde{a}}$. The commutation properties (19) imply that

$$\langle \boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c|\tilde{\boldsymbol{j}}^{\tilde{a}}, \tilde{\boldsymbol{j}}^{\tilde{b}}, \tilde{\boldsymbol{j}}^{\tilde{c}}\rangle = \frac{\delta_{a\tilde{a}}\delta_{b\tilde{b}}\delta_{c\tilde{c}}}{C_{\boldsymbol{a},\boldsymbol{b},\boldsymbol{c}}}\mathbf{1}_{\sigma(\boldsymbol{j}^a)}(\tilde{\boldsymbol{j}}^{\tilde{a}})\mathbf{1}_{\sigma(\boldsymbol{j}^b)}(\tilde{\boldsymbol{j}}^{\tilde{b}})\mathbf{1}_{\sigma(\boldsymbol{j}^c)}(\tilde{\boldsymbol{j}}^{\tilde{c}}).$$

We define the 'quantum state' of our stochastic reaction–diffusion field theory, $|F(t)\rangle$, as

$$|F(t)\rangle = \sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty}\ \sum_{\substack{\boldsymbol{j}^a\in\Lambda(\mathbb{Z}^{3a}),\\ \boldsymbol{j}^b\in\Lambda(\mathbb{Z}^{3b}),\\ \boldsymbol{j}^c\in\Lambda(\mathbb{Z}^{3c})}} C_{\boldsymbol{a},\boldsymbol{b},\boldsymbol{c}}F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t)|\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c\rangle.$$

Note, we may recover $F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t)$ as

$$F^{(a,b,c)}(\boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c, t) = \langle \boldsymbol{j}^a, \boldsymbol{j}^b, \boldsymbol{j}^c|F(t)\rangle,$$

so that there is a one-to-one correspondence between the collection $\{F^{(a,b,c)}(\cdot,\cdot,\cdot,t)\}_{(a,b,c)}$ and $|F(t)\rangle$. By (7) we have the normalization

$$\sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \sum_{\substack{\boldsymbol{j}^a\in\Lambda(\mathbb{Z}^{3a}),\\ \boldsymbol{j}^b\in\Lambda(\mathbb{Z}^{3b}),\\ \boldsymbol{j}^c\in\Lambda(\mathbb{Z}^{3c})}} C_{a,b,c}\langle \boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c|F(t)\rangle = 1. \tag{20}$$

This may be written more compactly through the introduction of a projection state, $\langle|$ defined by

$$\langle| = \langle 0|\,\mathrm{e}^{\sum_{\boldsymbol{i}\in\mathbb{Z}^3}\mathcal{A}(\boldsymbol{i})+\mathcal{B}(\boldsymbol{i})+\mathcal{C}(\boldsymbol{i})}.$$

Taylor series expanding the exponential and using the commutation properties of the annihilation and creation operators we recover (20), so that

$$\langle|F(t)\rangle = 1.$$

With these definitions, we may now write the evolution equation for the state $|F(t)\rangle$. Using (8) we find

$$\frac{\mathrm{d}}{\mathrm{d}t}|F(t)\rangle = -H|F(t)\rangle,$$

where H is the Hamiltonian-like operator

$$\begin{aligned} H = &-\sum_{\boldsymbol{i}\in\mathbb{Z}^3}\left[D^{\mathrm{A}}(\Delta_h\mathcal{A}^\dagger)(\boldsymbol{i})\mathcal{A}(\boldsymbol{i}) + D^{\mathrm{B}}(\Delta_h\mathcal{B}^\dagger)(\boldsymbol{i})\mathcal{B}(\boldsymbol{i}) + D^{\mathrm{C}}(\Delta_h\mathcal{C}^\dagger)(\boldsymbol{i})\mathcal{C}(\boldsymbol{i})\right] \\ &-\sum_{\boldsymbol{i}\in\mathbb{Z}^3}\left[\frac{k_+}{h^3}(\mathcal{A}(\boldsymbol{i})\mathcal{B}(\boldsymbol{i})\mathcal{C}^\dagger(\boldsymbol{i}) - \mathcal{A}^\dagger(\boldsymbol{i})\mathcal{A}(\boldsymbol{i})\mathcal{B}^\dagger(\boldsymbol{i})\mathcal{B}(\boldsymbol{i}))\right. \\ &\left.-k_-(\mathcal{A}^\dagger(\boldsymbol{i})\mathcal{B}^\dagger(\boldsymbol{i})\mathcal{C}(\boldsymbol{i}) - \mathcal{C}^\dagger(\boldsymbol{i})\mathcal{C}(\boldsymbol{i}))\right]. \end{aligned} \tag{21}$$

Here the discrete Laplacian of a creation operator is defined as

$$(\Delta_h\mathcal{A}^\dagger)(\boldsymbol{i}) = \frac{1}{h^2}\sum_{d=1}^{3}\sum_{\pm}(\mathcal{A}^\dagger(\boldsymbol{i}\pm\boldsymbol{e}_d) - \mathcal{A}^\dagger(\boldsymbol{i})),$$

where $\boldsymbol{e}_d$ denotes a unit vector along the dth coordinate axis of $\mathbb{R}^3$. Note that the form of H in (21) is the same we would obtain if $|F(t)\rangle$ and the creation and annihilation operators were instead defined in terms of the quantum 'occupation number' states $|\boldsymbol{a},\boldsymbol{b},\boldsymbol{c}\rangle$. This alternative, equivalent approach was introduced by Peliti [15], and corresponds to directly mapping the reaction–diffusion master equation (1) to a quantum field theory.

We now consider how to calculate expectations of functions of molecule number and positions. Denote by $A(t)$ the stochastic process for the number of molecules of species A at time t and by $\boldsymbol{J}^{A(t)}(t)$ the stochastic process for the positions of the A molecules. Define $B(t)$, $C(t)$, $\boldsymbol{J}^{B(t)}$ and $\boldsymbol{J}^{C(t)}$ similarly. The expected value of any symmetrized function, $g^{(A(t),B(t),C(t))}(\boldsymbol{J}^{A(t)},\boldsymbol{J}^{B(t)},\boldsymbol{J}^{C(t)})$, can then be found as

$$\begin{aligned} &\mathbb{E}[g^{(A(t),B(t),C(t))}(\boldsymbol{J}^{A(t)},\boldsymbol{J}^{B(t)},\boldsymbol{J}^{C(t)})] \\ &\quad= \sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \sum_{\substack{\boldsymbol{j}^a\in\Lambda(\mathbb{Z}^{3a}),\\ \boldsymbol{j}^b\in\Lambda(\mathbb{Z}^{3b}),\\ \boldsymbol{j}^c\in\Lambda(\mathbb{Z}^{3c})}} C_{a,b,c}\, g^{(a,b,c)}(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c) F^{(a,b,c)}(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t), \\ &\quad= \langle|\mathcal{G}|F(t)\rangle, \end{aligned}$$

where $\mathcal{G}$ is the quantum operator defined by

$$\mathcal{G}|F(t)\rangle = \sum_{\substack{a=0,\\ b=0,\\ c=0}}^{\infty} \sum_{\substack{\boldsymbol{j}^a\in\Lambda(\mathbb{Z}^{3a}),\\ \boldsymbol{j}^b\in\Lambda(\mathbb{Z}^{3b}),\\ \boldsymbol{j}^c\in\Lambda(\mathbb{Z}^{3c})}} C_{\boldsymbol{a},\boldsymbol{b},\boldsymbol{c}}\, g^{(a,b,c)}(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c) F^{(a,b,c)}(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t)|\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c\rangle.$$

As described in [4], one can also derive explicit representations of the operator $\mathcal{G}$ in terms of $g^{(a,b,c)}(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c)$ and creation/annihilation operators. With these definitions we can calculate, using the quantum field theory formalism, statistical averages for functions of the stochastic processes representing the state of a spatially distributed chemical system.

4. Formal continuum limit

In section 2 our calculations were exact and mathematically rigorous. We now consider the relation between the discrete reaction–diffusion master equation (1) and the continuum 'probability distribution function' formulation of Doi [4]. This is investigated by taking a formal continuum limit, $h \to 0$, in the equation of evolution for $F^{(a,b,c)}$ (8). We shall recover a final model of the same type as ([4], equation (51)). Note, however, that the subsequent analysis is *formal* and does not give the mathematically correct continuum limit. As we proved in [10], for the bimolecular chemical reaction $\mathrm{A}+\mathrm{B} \to \varnothing$ with one molecule of A and one molecule of B initially, in the continuum limit that the mesh spacing approaches zero the molecules just diffuse relative to each other, never reacting. While the convergence results of [10] are for a special case, we expect them to generalize to the bimolecular reaction $\mathrm{A}+\mathrm{B} \leftrightarrows \mathrm{C}$ with arbitrary initial numbers of substrate molecules.

What the analysis of this section does show is the connection between the reaction–diffusion master equation and the continuum probability distribution function model of [4], by utilizing the formal continuum limit of the particle tracking representation. Despite the loss of reaction in the continuum limit, this connection is important since, as we discussed in [10] for the simplified model mentioned above, the formal limiting equation may be rigorously defined and is an asymptotic approximation to a Smoluchowski diffusion-limited reaction model [17]. (By a diffusion-limited reaction model we mean a model where molecules undergo Brownian motion, with bimolecular reactions occurring instantaneously when reactants reach specified reaction radii). The RDME may therefore by interpreted as a non-convergent attempt to approximate the formal limiting equations of the particle tracking representation, which suggests investigating if the RDME is also an asymptotic approximation to the diffusion-limited reaction model. As we have proven in [10] that the RDME for the two molecule annihilation reaction is an asymptotic approximation to the corresponding diffusion-limited reaction model, we expect that the RDME for general biochemical systems is also such an approximation.

To derive the formal continuum limit of the particle tracking model of section 2, we begin by rescaling the probability $F^{(a,b,c)}(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t)$ to obtain a probability density, $\rho_h^{(a,b,c)}(\boldsymbol{q}^a,\boldsymbol{q}^b,\boldsymbol{q}^c,t)$. Here,$(\boldsymbol{q}^a,\boldsymbol{q}^b,\boldsymbol{q}^c)$ are taken to be spatial position vectors that correspond to the centroid of the voxel labeled by the components of $(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c)$. We define

$$\rho_h^{(a,b,c)}(\boldsymbol{q}^a,\boldsymbol{q}^b,\boldsymbol{q}^c,t) = \frac{1}{h^{3(a+b+c)}} F^{(a,b,c)}(\boldsymbol{j}^a,\boldsymbol{j}^b,\boldsymbol{j}^c,t). \tag{22}$$

With this definition, we are assuming that molecules within a mesh voxel are well mixed (i.e. uniformly distributed). Substituting this rescaling into equation (8), the equation of evolution for $\rho_h^{(a,b,c)}$ is then

$$\frac{\mathrm{d}\rho_h^{(a,b,c)}}{\mathrm{d}t}(\boldsymbol{q}^a,\boldsymbol{q}^b,\boldsymbol{q}^c,t) = \big(\tilde{L}_h\rho_h^{(a,b,c)} + \hat{R}_h\rho_h^{(a,b,c)}\big)(\boldsymbol{q}^a,\boldsymbol{q}^b,\boldsymbol{q}^c,t). \tag{23}$$

Note that the diffusion operator, $\tilde{L}_h$, is unchanged from equation (8). This is due to the linearity of the operator and the invariance of the total amounts of each species under the action of the operator. In contrast, the reaction operator is altered giving the new operator,

$$\begin{aligned}
&\left(\tilde{R}_h \rho_h^{(a,b,c)}\right)(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t) \\
&\quad = k_+\left[\sum_{l=1}^{c} \rho_h^{(a+1,b+1,c-1)}\left(\boldsymbol{q}^a \cup \boldsymbol{q}_l^c, \boldsymbol{q}^b \cup \boldsymbol{q}_l^c, \boldsymbol{q}^c \backslash \boldsymbol{q}_l^c, t\right)\right. \\
&\qquad \left. - \sum_{l=1}^{a}\sum_{\tilde{l}=1}^{b} \delta_h\left(\boldsymbol{q}_l^a - \boldsymbol{q}_{\tilde{l}}^b\right)\rho_h^{(a,b,c)}(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t)\right] \\
&\qquad + k_-\left[\sum_{l=1}^{a}\sum_{\tilde{l}=1}^{b} \delta_h\left(\boldsymbol{q}_l^a - \boldsymbol{q}_{\tilde{l}}^b\right)\rho_h^{(a-1,b-1,c+1)}\left(\boldsymbol{q}^a \backslash \boldsymbol{q}_l^a, \boldsymbol{q}^b \backslash \boldsymbol{q}_{\tilde{l}}^b, \boldsymbol{q}^c \cup \boldsymbol{q}_l^a, t\right)\right. \\
&\qquad \left. - \sum_{l=1}^{c} \rho_h^{(a,b,c)}\left(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t\right)\right]. \qquad (24)
\end{aligned}$$

We now consider the formal continuum limit of (23). The molecule position vectors, $(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c)$, now become arbitrary points within our domain, $\Omega = \mathbb{R}^3$. We *assume* that the discrete space density, $\rho_h^{(a,b,c)}$, converges to a continuum density, $\rho^{(a,b,c)}$. Denote by Δ_l^a the continuum three-dimensional Laplacian, acting on the lth molecule of species a. Letting

$$\Delta^a = \sum_{l=1}^{a} \Delta_l^a,$$

we find that the diffusion operator, $\tilde{L}_h$ goes over into the continuum diffusion operator

$$(\tilde{L}\rho^{(a,b,c)})(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t) = (D^{\mathrm{A}}\Delta^a + D^{\mathrm{B}}\Delta^b + D^{\mathrm{C}}\Delta^c)\rho^{(a,b,c)}(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t). \qquad (25)$$

The discrete delta function, $\delta_h\left(\boldsymbol{q}_l^a - \boldsymbol{q}_{\tilde{l}}^b\right)$, will converge to the continuum delta function, $\delta\left(\boldsymbol{q}_l^a - \boldsymbol{q}_{\tilde{l}}^b\right)$, though only in a distributional sense. We thus find that the reaction operator, $\tilde{R}_h$, converges to the continuum reaction operator

$$\begin{aligned}
&\left(\tilde{R}\rho^{(a,b,c)}\right)(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t) \\
&\quad = k_+\left[\sum_{l=1}^{c} \rho^{(a+1,b+1,c-1)}\left(\boldsymbol{q}^a \cup \boldsymbol{q}_l^c, \boldsymbol{q}^b \cup \boldsymbol{q}_l^c, \boldsymbol{q}^c \backslash \boldsymbol{q}_l^c, t\right)\right. \\
&\qquad \left. - \sum_{l=1}^{a}\sum_{\tilde{l}=1}^{b} \delta\left(\boldsymbol{q}_l^a - \boldsymbol{q}_{\tilde{l}}^b\right)\rho^{(a,b,c)}(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t)\right] \\
&\qquad + k_-\left[\sum_{l=1}^{a}\sum_{\tilde{l}=1}^{b} \delta\left(\boldsymbol{q}_l^a - \boldsymbol{q}_{\tilde{l}}^b\right)\rho^{(a-1,b-1,c+1)}\left(\boldsymbol{q}^a \backslash \boldsymbol{q}_l^a, \boldsymbol{q}^b \backslash \boldsymbol{q}_{\tilde{l}}^b, \boldsymbol{q}^c \cup \boldsymbol{q}_l^a, t\right)\right. \\
&\qquad \left. - \sum_{l=1}^{c} \rho^{(a,b,c)}\left(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t\right)\right]. \qquad (26)
\end{aligned}$$

This definition can be rewritten in the form of the reaction operator from [4, 5] by defining the reaction rate terms

$$\begin{aligned}
\alpha_+\left(\boldsymbol{q}_l^a, \boldsymbol{q}_{l'}^b, \boldsymbol{q}_{\tilde{l}}^c\right) &= k_+\delta\left(\boldsymbol{q}_l^a - \boldsymbol{q}_{l'}^b\right)\delta\left(\boldsymbol{q}_l^a - \boldsymbol{q}_{\tilde{l}}^c\right), \\
\alpha_-\left(\boldsymbol{q}_l^a, \boldsymbol{q}_{l'}^b, \boldsymbol{q}_{\tilde{l}}^c\right) &= k_-\delta\left(\boldsymbol{q}_l^a - \boldsymbol{q}_{l'}^b\right)\delta\left(\boldsymbol{q}_l^a - \boldsymbol{q}_{\tilde{l}}^c\right).
\end{aligned}$$

Equation (26) then becomes

$$
\begin{aligned}
(\tilde{R}\rho^{(a,b,c)})(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t)
&= \Bigg[\sum_{l=1}^{c} \left(\int_\Omega \int_\Omega \alpha_+\big(\boldsymbol{q}_1, \boldsymbol{q}_2, \boldsymbol{q}_l^c\big)\rho^{(a+1,b+1,c-1)}\big(\boldsymbol{q}^a \cup \boldsymbol{q}_1, \boldsymbol{q}^b \cup \boldsymbol{q}_2, \boldsymbol{q}^c \backslash \boldsymbol{q}_l^c, t\big)\, \mathrm{d}\boldsymbol{q}_1\, \mathrm{d}\boldsymbol{q}_2 \right) \\
&\quad - \sum_{l=1}^{a} \sum_{\tilde{l}=1}^{b} \int_\Omega \alpha_+\big(\boldsymbol{q}_l^a, \boldsymbol{q}_{\tilde{l}}^b, \boldsymbol{q}_3\big)\rho^{(a,b,c)}\big(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t\big)\, \mathrm{d}\boldsymbol{q}_3 \Bigg] \\
&\quad + \Bigg[\sum_{l=1}^{a} \sum_{\tilde{l}=1}^{b} \left(\int_\Omega \alpha_-\big(\boldsymbol{q}_l^a, \boldsymbol{q}_{\tilde{l}}^b, \boldsymbol{q}_3\big)\rho^{(a-1,b-1,c+1)}\big(\boldsymbol{q}^a \backslash \boldsymbol{q}_l^a, \boldsymbol{q}^b \backslash \boldsymbol{q}_{\tilde{l}}^b, \boldsymbol{q}^c \cup \boldsymbol{q}_3, t\big)\, \mathrm{d}\boldsymbol{q}_3 \right) \\
&\quad - \sum_{l=1}^{c} \int_\Omega \int_\Omega \alpha_-\big(\boldsymbol{q}_1, \boldsymbol{q}_2, \boldsymbol{q}_l^c\big)\rho^{(a,b,c)}\big(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t\big)\, \mathrm{d}\boldsymbol{q}_1\, \mathrm{d}\boldsymbol{q}_2 \Bigg]. \qquad (27)
\end{aligned}
$$

The equation of evolution, equation (23), now becomes

$$
\frac{\mathrm{d}\rho^{(a,b,c)}}{\mathrm{d}t}(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t) = (\tilde{L}\rho^{(a,b,c)} + \tilde{R}\rho^{(a,b,c)})(\boldsymbol{q}^a, \boldsymbol{q}^b, \boldsymbol{q}^c, t). \qquad (28)
$$

A key point about the preceding analysis is that the formulation given by the operators (25) and (27) with equation (28) provides a possible *initial* model of the chemical reaction A + B $\leftrightarrows$ C, for many different possible choices of α_+ and α_-. We are formally using point reactions to represent binding interactions, but there is no reason that α_+ could not allow binding within a certain binding radius as is done in [5]. Likewise, there is no reason that unbinding might not produce two molecules a fixed separation apart. In fact, such interaction models are commonly used in spatially-continuous stochastic reaction–diffusion formulations that track individual particles [2]. While the preceding analysis is not rigorous, it does provide a mechanism to start with a more microscopic molecular interaction model and then, through an appropriate discretization mechanism, try to obtain a reaction–diffusion master equation model. (By specifying the reaction interaction terms, and then applying the analysis of this section and section 2 in the reverse order.)

With regards to the specific molecular interactions derived above, α_+ and α_-, we note that the critical steps in the derivation are the assumption that the discrete delta functions go over into continuum delta functions, and that the solutions to the discrete equations approach well-defined solutions to the continuum equations. Unfortunately, just giving a rigorous mathematical meaning to the continuum equations is difficult because of the delta function coefficients. The definition of solutions to PDEs with delta function coefficients has been previously considered, but only in certain special cases has been made mathematically rigorous (see for example [1]). It can be shown rigorously, see [10] for a discussion, that the formal continuum limit of the simplified model in [10] is an asymptotic approximation to a diffusion-limited reaction model. Assuming one can also interpret (28) as an asymptotic approximation to a multi-particle diffusion-limited reaction model, this suggests, as we proved for the simplified model in [10], that the multi-particle RDME for a bimolecular reaction may also be interpreted as an asymptotic approximation to a diffusion limited reaction.

5. Conclusions

We have shown how to convert from the RDME, a model tracking the numbers of molecules of each chemical species in each mesh voxel, to an ‘individual particle’ model tracking the total population of each chemical species and the locations of all molecules. This alternative representation of the RDME is of the same form as the spatially continuous stochastic reaction–diffusion model of [4]. We have also shown how to map the particle tracking model to a field theory, complementing the known procedures for mapping the RDME to a field theory [15] and mapping the spatially-continuous model of [4] to a field theory [4]. The form of the Hamiltonian operator (21) we derive is the same that would be obtained when directly mapping the RDME to a field theory.

We have shown that the formal, incorrect, continuum limit of the RDME is equivalent to a coupled system of PDEs that have the form of the 'probability distribution function' stochastic reaction diffusion model of [4]. In our formal limiting equations, bimolecular reactions give rise to singular coefficients in the PDEs representing point interactions between reactants. We expect these formal limiting equations to be asymptotic approximations to a Smoluchowski diffusion-limited reaction model, suggesting the RDME is also such an approximation. Our rigorous results for the two molecule annihilation reaction in [10] bolster this hypothesis.

The analysis of section 2 also provides a possible mechanism for deriving master equation type models from the spatially-continuous stochastic reaction–diffusion model of [4]. This could be achieved by developing appropriate discretizations of the spatially-continuous model, and then applying the analysis of sections 2 and 4 in reverse.

As has been pointed out by one of the referees, it should be straightforward to extend the results of this work to arbitrary dimensions. Note, in one dimension we expect the discrete-space particle tracking representation of the RDME to the converge to the spatially-continuous particle tracking model.

Finally, as one of the referees has brought to our attention, there is an alternative Fermion second quantization representation for discrete-space master equation models with site restrictions [9, 16]. An example of such a master equation is when only one molecule is allowed to occupy a given lattice site. Master equations with site restrictions can also be rewritten in a particle tracking type representation. Since they make use of different bimolecular reaction mechanisms, we would not expect to obtain the same equations as in section 4 when taking the formal continuum limit. What the formal continuum equations for these models are, and what they rigorously approximate, remain interesting questions to explore.

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Appendix. Basic combinatorics results

Consider the vector of objects, $\boldsymbol{m} = (m_1, \dots, m_M)$, where M gives the number of components of $\boldsymbol{m}$. Suppose $\boldsymbol{m}$ contains N distinct objects, and assume that the number of each of the N distinct objects is given by $(n_1, \dots, n_N)$. Therefore,

$$M = \sum_{i=1}^{N} n_i.$$

Denote by $\tilde{\sigma}\,(\boldsymbol{m})$ the set of all distinct vectors generated by permutations of the components of $\boldsymbol{m}$. Then, *Identity A.1 The number of elements in* $\tilde{\sigma}\,(\boldsymbol{m})$ *is*

$$M!\prod_{i=1}^{N}\frac{1}{n_i!}.$$

Let $\sigma\,(\boldsymbol{m})$ denote the set of all vectors, including multiple copies, generated by permutations of the components of $\boldsymbol{m}$. $\sigma\,(\boldsymbol{m})$ contains $M!$ elements. Then,

Identity A.2 For any function $f\,(\boldsymbol{m})$,

$$\sum_{\tilde{\boldsymbol{m}}\in\tilde{\sigma}(\boldsymbol{m})} f\,(\tilde{\boldsymbol{m}}) = \left(\prod_{i=1}^{N}\frac{1}{n_i!}\right)\sum_{\tilde{\boldsymbol{m}}\in\sigma(\boldsymbol{m})} f\,(\tilde{\boldsymbol{m}})\,.$$

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