

## Stochastic phase-space description for reactions that change particle numbers

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**Abstract** A stochastic phase-space description is derived for a particle-based system whose total number of particles can change in time due to chemical reactions. Transition rates are specified explicitly for the Selkov reaction mechanism and incorporate local reactions, local collisions and free-streaming of particles. The collision mechanism corresponds to a numerically efficient multi-particle collision model that conserves mass, momentum and energy during the collision process. Through an appropriate averaging procedure, the stochastic description is shown to lead to the correct macroscopic rate law in a well-stirred homogeneous system, and simulations from the corresponding numerical method are shown to confirm these results in large three-dimensional systems. Simulations for smaller systems were performed to demonstrate the effects of spatial fluctuations on the system. Our results indicate that the phase-space description, whose transition rates correspond to a particular numerical method, provides a suitable framework from which the non-equilibrium nature of chemically reacting media can be explored. The methods are well-suited to investigate the breakdown of continuum models in spatially extended chemical systems for which the total number of particles changes in time. The novel stochastic phase-space description derived here has not been considered elsewhere. Coupled to the numerical method, our approach allows exploration of far-from-equilibrium conditions, and a means to connect the numerical results to a theoretical model. The methods provide a powerful tool that can be used in various applications including biochemical networks and fluid flow of chemical media.

**Keywords** Phase-space description · Chemical reactions · Multi-particle collision dynamics · Spatial fluctuations

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## 1 Introduction

It is fairly well known that small-scale fluctuations can give rise to complex large-scale behaviour that can be difficult or impossible to model using a mean-field approach. The addition of stochastic noise to mean-field equations has been successful at capturing some of these effects, but these methods can only be used if the fluctuations in the system are small compared to the time evolution of the quantities of interest. In some chemical systems for which low concentrations of some or all of its chemical constituents is possible, such as in biochemical networks for gene expression, this may not be the case, and to adequately incorporate the effects of noise arising from spatial fluctuations in such systems, more sophisticated approaches are necessary [1]. In chemical systems that are far from equilibrium, near bifurcation points, or in the chaotic regime, fluctuations can also play an important role leading to complex behaviour that cannot be captured using mean-field dynamics alone [2].

A number of techniques have been developed that correctly recover the mean-field dynamics in appropriate limits, and that have the potential to explore some of the rich dynamics that can arise due to spatial fluctuations in the system. Cellular automaton models are one such example, and these have been quite popular as they incorporate particle motion and interaction using simple rules that are computationally easy to carry out. Such approaches have been successfully used to study various phenomena arising in physics [3–6], biology [1, 7] and chemistry [4, 5, 8–20]. An extensive review of the different probabilistic cellular automaton models used to study spatially extended systems is given in [21, 22]. One key disadvantage of such approaches is that the particles are generally restricted to sites on a lattice, and particle interaction is not physically realistic.

More realistic particle-based methods that are still computationally feasible but do not require the particle dynamics to be restricted to sites on a lattice have recently been introduced [23–25]. Using appropriate arguments, it has been shown that the corresponding stochastic phase-space description has an H theorem, and the Navier–Stokes equations can be derived by means of a Chapman–Enskog expansion. Correct velocity profiles have been recovered in several classical hydrodynamic flow problems [23, 26, 27], and proper Green–Kubo relations have also been obtained, connecting transport coefficients to moments of the stochastic description [23, 28–33]. Recently, the methods have been extended to incorporate reactions that conserve particle numbers [34, 35], and used as an alternative to simulate fluid flows in various applications [26, 27]. It is this numerical method that has been extended here to allow for the total number of particles to fluctuate in the system and an appropriate stochastic phase-space description has been connected to it.

The outline of the paper is as follows. In Sect. 2 we derive a generalized Master equation that will be appropriately interpreted in Sect. 3 to provide the evolution equation for a phase-space description corresponding to a particle-based system. The particle dynamics includes local reactions and collisions, as well as free-streaming of the individual particles. Section 4 follows with a specific application to the Selkov model, where we also derive the corresponding macroscopic rate law using appropriate equilibrium assumptions together with an appropriate averaging procedure. Our numerical results for the Selkov model are presented in Sect. 5 where both large and

small systems are considered so as to capture the effects of spatial fluctuations on the system. Important discussions of our results and conclusions form the final section of this paper.

### 2 Derivation of a generalized Master equation

In this section we derive a Master equation for the conditional probability density of a Markov process for a random variable whose total number of components may change in time. The derivation generalizes the traditional small-time expansion of the Chapman–Kolmogorov equation [36], but requires proper extension to allow for the gain and loss of the number of components of the random variable in time.

Suppose a sample space  $S$  is made up of mutually exclusive sets  $S_i, i \in \{0, \mathbb{Z}^+\}$  so that the realization of the random variable  $X$  at time  $t$  satisfies  $X(t) = \xi \in S_i$ . Let  $P_i(\xi, t)$  be the probability that the random variable  $X$  has the realization  $\xi \in S_i$  at time  $t$ , and let  $P_{i|j}(\xi, t_1|\xi_0, t_0)$  be the conditional probability that the random variable  $X$  has the realization  $\xi \in S_i$  at time  $t_1$  given that it had the realization  $\xi_0 \in S_j$  at time  $t_0$ .

Then normalization over the sample space  $S$  means

$$\sum_{i=0}^{\infty} \int_{S_i} P_i(\xi, t) d\xi = 1,$$

and if the process is assumed to be Markovian, then  $P_{i|j}$  satisfies the Chapman–Kolmogorov equation

$$P_{i|j}(\xi, t_1|\xi_0, t_0) = \sum_{k=0}^{\infty} \int_{S_k} P_{i|k}(\xi, t_1|\xi', t') P_{k|j}(\xi', t'|\xi_0, t_0) d\xi', \quad \forall i, j \in \{0, \mathbb{Z}^+\} \tag{1}$$

Assuming further that the process is homogeneous in time, and that  $t_1 > t' > t_0$  without loss of generality, we make the small time expansions

$$P_{\beta|\beta}(\xi, t + \Delta t|\xi', t) = [1 - \Delta t a_{\beta}(\xi')] \delta(\xi - \xi') + \Delta t W_{\beta|\beta}(\xi|\xi') + o(\Delta t), \text{ for } \beta \in \{0, \mathbb{Z}^+\} \tag{2a}$$

$$P_{\alpha|\beta}(\xi, t + \Delta t|\xi', t) = \Delta t W_{\alpha|\beta}(\xi|\xi') + o(\Delta t), \text{ for } \alpha, \beta \in \{0, \mathbb{Z}^+\}, \alpha \neq \beta, \tag{2b}$$

where

$$a_{\beta}(\xi') = \sum_{\alpha=0}^{\infty} \int_{S_{\alpha}} W_{\alpha|\beta}(\xi|\xi') d\xi, \tag{3}$$

to satisfy normalization up to  $o(\Delta t)$  (see Appendix A).

Picking  $t_1 = t + \Delta t$ ,  $t' = t$  and  $t_0 = 0$  in (1), and using the small time expansions (2a) and (2b) thus leaves

$$\begin{aligned}
 P_{i|j}(\xi, t + \Delta t | \xi_0, 0) &= \sum_{k=0}^{\infty} \int_{S_k} P_{i|k}(\xi, t + \Delta t | \xi', t) P_{k|j}(\xi', t | \xi_0, 0) d\xi', \quad \forall i, j \in \{0, \mathbb{Z}^+\} \\
 &= \sum_{\substack{k=0 \\ k \neq i}}^{\infty} \int_{S_k} [\Delta t W_{i|k}(\xi | \xi') + o(\Delta t)] P_{k|j}(\xi', t | \xi_0, 0) d\xi' \\
 &\quad + \int_{S_i} \{ [1 - \Delta t a_i(\xi')] \delta(\xi - \xi') + \Delta t W_{i|i}(\xi | \xi') + o(\Delta t) \} \\
 &\quad \times P_{i|j}(\xi', t | \xi_0, 0) d\xi',
 \end{aligned}$$

which, subject to the usual procedure of rearranging and letting  $\Delta t \rightarrow 0$ , leads to the generalized Master equation

$$\begin{aligned}
 \frac{\partial}{\partial t} P_{i|j}(\xi, t | \xi_0, 0) &= \sum_{k=0}^{\infty} \int_{S_k} [W_{i|k}(\xi | \xi') P_{k|j}(\xi', t | \xi_0, 0) \\
 &\quad - W_{k|i}(\xi' | \xi) P_{i|j}(\xi, t | \xi_0, 0)] d\xi', \quad (4)
 \end{aligned}$$

for all  $i, j \in \{0, \mathbb{Z}^+\}$ . As usual, if some or all of the components of  $\xi$  are discrete, the integrals over those components should be replaced by appropriate summations.

Note that if  $W_{i|k} = 0$  for all  $i \neq k$ , one recovers a system of uncoupled Master equations that are of the standard forms used in [36]. The novelty of our approach is the introduction and subsequent interpretation of these non-vanishing transition rates.

### 3 Evolution equation for a particle-based system

In part 1 of this section we describe the particle dynamics governed by the numerical method, and part 2 follows with an appropriate interpretation of the stochastic variable in (4), that corresponds to the stochastic description for the same particle-based system.

#### 3.1 Particle dynamics

We now describe the particle dynamics that has been incorporated in both the numerical model, as well as in the stochastic description. We consider a finite volume  $V$  containing  $N$  particles initially that can free-stream, react and collide. The description describes the evolution of *all* particles in the system, and reactions and collisions are treated locally.

To incorporate local events, the system volume is divided into  $L$  cells [23,34] that are distinguished by use of the subscript  $\mu$ . Given a system comprised of  $s$  different

species of particles labeled  $X_j$ ,  $j = 1, \dots, s$ , we define the number of particles of species type  $X_j$  in a given cell  $\mu$  as [34]

$$n_\mu^{X_j} = \sum_{i | \mathbf{x}_i \in V_\mu} \delta_{\alpha_i, X_j}, \text{ for } j = 1, \dots, s,$$

where  $\alpha_i$  is the species type of particle  $i$ ,  $\mathbf{x}_i$  is its position, and  $\delta_{\alpha_i, X_j}$  is the usual Kronecker delta function for which

$$\delta_{\alpha_i, X_j} = \begin{cases} 1, & \text{if } \alpha_i = X_j \\ 0, & \text{if } \alpha_i \neq X_j. \end{cases}$$

The total number of all particles in cell  $\mu$  is then given by

$$n_\mu = \sum_{j=1}^s n_\mu^{X_j}.$$

One can also define the center of mass velocity  $\mathbf{V}_\mu^{X_j}$  of particles of species type  $X_j$  in cell  $\mu$  as

$$\mathbf{V}_\mu^{X_j} = \frac{1}{n_\mu^{X_j}} \sum_{i | \mathbf{x}_i \in V_\mu} \delta_{\alpha_i, X_j} \mathbf{v}_i,$$

and the center of mass velocity of all particles in a cell as

$$\mathbf{V}_\mu = \frac{\sum_{j=1}^s n_\mu^{X_j} m_{X_j} \mathbf{V}_\mu^{X_j}}{\sum_{j=1}^s n_\mu^{X_j} m_{X_j}},$$

where  $m_{X_j}$  is the mass of a particle of species type  $X_j$ .

Using a numerically efficient mass, momentum and energy-conserving mechanism introduced in [34], local collisions will change velocities of particles according to

$$\mathbf{v}_i = \mathbf{V}'_\mu + \hat{\omega}_\mu (\mathbf{V}'_\mu^{\alpha_i} - \mathbf{V}'_\mu) + \hat{\omega}_\mu^{\alpha_i} \hat{\omega}_\mu (\mathbf{v}'_i - \mathbf{V}'_\mu^{\alpha_i}) \tag{5}$$

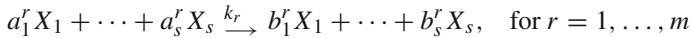
where primes denote velocities of particles before the collision. Also,  $\hat{\omega}_\mu$  and  $\hat{\omega}_\mu^{X_j}$  are rotation operators randomly chosen from a set of rotation operators  $\Omega = \{\hat{\omega}_1, \hat{\omega}_2, \dots, \hat{\omega}_n\}$  at each time step, that vary from cell to cell, and—in the case of a superscript—from one species to another. Thus, (5) corresponds to a local “all-species collision”—a collision involving all particles in a given cell—followed by a “single-species collision” involving collisions between particles of the same species type in the cell.

Free-streaming of particles during a time interval  $\Delta t$  updates positions according to

$$\mathbf{x}_i = \mathbf{x}'_i + \mathbf{v}_i \Delta t$$

where  $\mathbf{v}_i$  is the velocity of the particle after the collision step, and  $\mathbf{x}'_i$  the position of the particle before collision.

Reaction mechanisms of the type



either change the species type of existing particles in cell  $\mu$ , or add or remove particles from a cell, depending on the stoichiometric coefficients  $a_i^r$  and  $b_i^r$ , and on the reaction rates  $k_r$  for the  $r = 1, \dots, m$  possible reactions.

### 3.2 Evolution equation

The generalized Master equation derived in Sect. 2 can be used to describe the evolution of a phase-space description for a particle based system for which the number of particles may change in time due to chemical reactions. With this application in mind, the random variable  $\xi \in S_i$  takes the form

$$\xi = (\alpha_{(i)}, \mathbf{x}_{(i)}, \mathbf{v}_{(i)}) = (\alpha_1, \dots, \alpha_i, \mathbf{x}_1, \mathbf{v}_1, \dots, \mathbf{x}_i, \mathbf{v}_i), \quad (6)$$

incorporating all species types  $\alpha_1, \dots, \alpha_i$ , and all phase-space coordinates  $\mathbf{x}_1, \mathbf{v}_1, \dots, \mathbf{x}_i, \mathbf{v}_i$  for the  $i$  particles in the system at the given time. The corresponding Master Eq. 4 for the probability density  $P_i(\xi, t)$  now takes the form

$$\frac{\partial}{\partial t} P_i(\xi, t) = \sum_{k=0}^{\infty} \int [W_{i|k}(\xi|\xi') P_k(\xi', t) - W_{k|i}(\xi'|\xi) P_i(\xi, t)] d\xi', \quad (7)$$

where the subscript for  $P$  is used to denote the dimension of  $\xi$  at time  $t$ , and all conditionals have been dropped for brevity. We will treat species types as discrete, and positions and velocities as continuous so that the first term on the right hand side of (7) takes the explicit form

$$\begin{aligned} & \int W_{i|k}(\xi|\xi') P_k(\xi', t) d\xi' \\ &= \sum_{\alpha'_{(k)}} \int \int W_{i|k}(\alpha_{(i)}, \mathbf{x}_{(i)}, \mathbf{v}_{(i)} | \alpha'_{(k)}, \mathbf{x}'_{(k)}, \mathbf{v}'_{(k)}) P_k(\alpha'_{(k)}, \mathbf{x}'_{(k)}, \mathbf{v}'_{(k)}, t) d\mathbf{x}'_{(k)} d\mathbf{v}'_{(k)}. \end{aligned}$$

To incorporate particle collisions, reactions and free-streaming, the transition rates will be assumed to have the form

$$W_{i|k} = \mathcal{F}_i \delta_{i,k} + \mathcal{R}_{i|k}$$

where  $\mathcal{F}_i$  represents free-streaming of particles for which the total number of particles remains unchanged, and  $\mathcal{R}_{i|k}$  incorporates local particle collisions as well as the reactive events that change the number of particles in the system from  $k$  to  $i$ .

If we assume that the free-streaming operator takes the form

$$\mathcal{F}_i(\xi|\xi') = \prod_{k=1}^i \delta(\mathbf{x}_k - \mathbf{x}'_k - \mathbf{v}'_k \Delta t) \delta(\mathbf{v}'_k - \mathbf{v}_k) \delta_{\alpha'_k, \alpha_k},$$

then the free-streaming portion of the right-hand-side of (7) becomes

$$\begin{aligned} & P_i(\alpha_{(i)}, \mathbf{x}_{(i)}, \mathbf{v}_{(i)}, t) - P_i(\alpha_{(i)}, \mathbf{x}_{(i)} - \mathbf{v}_{(i)} \Delta t, \mathbf{v}_{(i)}, t) \\ & \approx \mathbf{v}_{(i)} \cdot \frac{\partial}{\partial \mathbf{x}_{(i)}} P_i(\alpha_{(i)}, \mathbf{x}_{(i)}, \mathbf{v}_{(i)}, t) \\ & = \sum_{k=1}^i \mathbf{v}_k \cdot \frac{\partial}{\partial \mathbf{x}_k} P_i(\alpha_{(i)}, \mathbf{x}_{(i)}, \mathbf{v}_{(i)}, t) \end{aligned}$$

for  $\Delta t$  sufficiently small.

Thus, the generalized evolution equation is

$$\begin{aligned} & \frac{\partial}{\partial t} P_i(\xi, t) + \mathcal{L}_0 P_i(\xi, t) \\ & = \sum_{k=0}^{\infty} \int \left[ \tilde{W}_{i|k}(\xi|\xi') P_k(\xi', t) - \tilde{W}_{k|i}(\xi'|\xi) P_i(\xi, t) \right] d\xi', \end{aligned} \tag{8}$$

where  $\mathcal{L}_0 = \sum_{k=1}^i \mathbf{v}_k \cdot \frac{\partial}{\partial \mathbf{x}_k}$  is the standard Liouville operator and  $\tilde{W}_{i|k} = \mathcal{R}_{i|k}$  incorporates local reactions and collisions.

Interpretation of  $\xi \in S_i$  as in (6) to correspond to a particle-based system comprised of  $i$  particles coupled to a Markov process (7,8) for which the number of particles can change in time represents the novelty of our approach. Phase-space descriptions for which  $i$  is constant (e.g.  $\tilde{W}_{i|k} = 0$  for  $i \neq k$ ) have already been used for some time, but true *phase-space* descriptions that allow changes in the number of particles in the system is new.

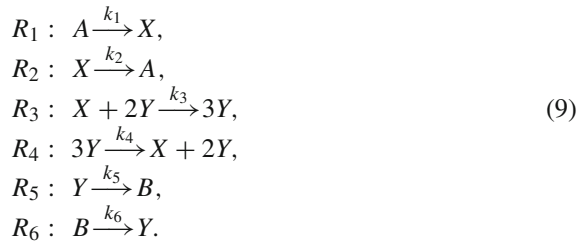
Note that if the particle dynamics occurs at discrete times  $m\tau$ , then the transition rates can be written as

$$\tilde{W}_{i|k} = \sum_{m=0}^{\infty} \delta(t - m\tau) (\mathcal{R}_{i|k} - 1),$$

so that integration of (8) over a time interval  $m\tau - \epsilon$  to  $(m + 1)\tau - \epsilon$  gives a corresponding discrete time equation for the system.

#### 4 Example—the Selkov model

To demonstrate the ability of our model to adequately account for gains and losses of particles in a spatially extended system, we now consider an open chemical system whose reaction dynamics is governed by the Selkov model [37]



Here  $R_1, \dots, R_6$  represent the six possible reactions with rates denoted by  $k_1, \dots, k_6$  respectively.

To adequately test our stochastic description, concentrations of  $A$  and  $B$  particles will be kept constant through external controls, and the stochastic description keeps track of  $X$  and  $Y$  particles only ( $s = 2$  chemical species with  $X_1 = X$  and  $X_2 = Y$ ), whose numbers thus fluctuate if reactions  $R_1, R_2, R_5$  or  $R_6$  have occurred. We will assume that there is an equal probability that a given  $X$ -particle will be considered for reaction  $R_3$  to become a  $Y$  particle with probability  $k_3 n_\mu^Y (n_\mu^Y - 1)$ , as it is for reaction  $R_2$  where it is removed from the system with probability  $k_2$ . Likewise, a  $Y$ -particle is as likely to become an  $X$ -particle at rate  $k_4 (n_\mu^Y - 1)(n_\mu^Y - 2)$ , as it is to be removed from the system at rate  $k_5$ . Addition of particles due to  $R_1$  or  $R_6$  will lead to  $X$  or  $Y$  particles placed at random locations in a cell with velocities randomly chosen from a Maxwellian velocity distribution.

Using  $s, t$  to denote the number of particles added to the system due to  $R_1$  and  $R_6$  reactions respectively, and  $m, n$  for the number of particles lost due to  $R_2$  and  $R_5$ , the non-vanishing transition rates for the Selkov reaction mechanism (9) can be written as

$$\begin{aligned}
 \tilde{W}_{i|i+m+n-s-t}(\xi|\xi') &= \mathcal{R}_{i|i+m+n-s-t}(\xi|\xi') \\
 \tilde{W}_{i-m-n+s+t|i}(\xi'|\xi) &= \mathcal{R}_{i-m-n+s+t|i}(\xi'|\xi),
 \end{aligned} \tag{10}$$

where  $\mathcal{R}_{i|i+m+n-s-t}(\xi|\xi')$  incorporates all possible reactions taking the system from state  $\xi'$  with  $i + m + n - s - t$  particles to one with  $i$  particles in state  $\xi$ . Comparing to (8), non-vanishing transition rates thus correspond to  $k = i + m + n - s - t$  or  $i - m - n + s + t$ , and

$$\sum_{k=0}^{\infty} = \sum_{s=0}^L \sum_{t=0}^L \sum_{m=0}^{N_{max}} \sum_{n=0}^{N_{max}}.$$

Here  $L$  is still the number of cells in the (entire) volume, and  $N_{max}$  is the possibly infinite, maximum number of particles allowed in the system.



### 4.1 Derivation of the macroscopic rate law

If we assume that reactions occur independently in a cell, and that the time step is small enough so that only one reaction occurs in a cell during a time step, then one can write a Master equation in the form (8) for each cell. In this case, transition rates (10) can be replaced by *local* transition rates  $\tilde{W}_{k|i}^\mu$ , and the number of particles corresponds to the number of particles in a cell rather than in the system.

Under these assumptions, non-vanishing transition rates exist only for  $m + n + s + t = 0$  or 1, and

$$\begin{aligned} \tilde{W}_{i|i+m+n-s-t}^\mu(\xi|\xi') &= \left[ \mathcal{A}_{i|i-1}^{R_1}(\xi|\xi')\delta_{s,1}\delta_{t,0} + \mathcal{A}_{i|i-1}^{R_6}(\xi|\xi')\delta_{t,1}\delta_{s,0} \right] \delta_{m+n,0} \\ &+ \left[ \mathcal{U}_{i|i}^{R_3}(\xi|\xi') + \mathcal{U}_{i|i}^{R_4}(\xi|\xi') \right] \delta_{m+n+s+t,0} \\ &+ \left[ \mathcal{D}_{i|i+1}^{R_2}(\xi|\xi')\delta_{m,1}\delta_{n,0} + \mathcal{D}_{i|i+1}^{R_5}(\xi|\xi')\delta_{m,0}\delta_{n,1} \right] \delta_{s+t,0}, \end{aligned}$$

with corresponding

$$\begin{aligned} \tilde{W}_{i|-m-n+s+t|i}^\mu(\xi'|\xi) &= \left[ \mathcal{A}_{i+1|i}^{R_1}(\xi'|\xi)\delta_{s,1}\delta_{t,0} + \mathcal{A}_{i+1|i}^{R_6}(\xi'|\xi)\delta_{s,0}\delta_{t,1} \right] \delta_{m+n,0} \\ &+ \left[ \mathcal{U}_{i|i}^{R_3}(\xi'|\xi) + \mathcal{U}_{i|i}^{R_4}(\xi'|\xi) \right] \delta_{m+n+s+t,0} \\ &+ \left[ \mathcal{D}_{i-1|i}^{R_2}(\xi'|\xi)\delta_{m,1}\delta_{n,0} + \mathcal{D}_{i-1|i}^{R_5}(\xi'|\xi)\delta_{m,0}\delta_{n,0} \right] \delta_{s+t,0}, \end{aligned}$$

where  $\mathcal{A}$  and  $\mathcal{D}$  are used to indicate that a particle has been added or deleted from the cell, and  $\mathcal{U}$  to denote that the number of particles remained unchanged by the reaction mechanism indicated by the superscripts.

The Master equation for the cell, now takes the form

$$\begin{aligned} \frac{\partial}{\partial t} P_i(\xi, t) &= \int \left[ \mathcal{A}_{i|i-1}^{R_1}(\xi|\xi') + \mathcal{A}_{i|i-1}^{R_6}(\xi|\xi') \right] P_{i-1}(\xi', t) d\xi' \\ &- \int \left[ \mathcal{A}_{i+1|i}^{R_1}(\xi'|\xi) + \mathcal{A}_{i+1|i}^{R_6}(\xi'|\xi) \right] P_i(\xi, t) d\xi' \\ &+ \int \left[ \mathcal{U}_{i|i}^{R_3}(\xi|\xi') + \mathcal{U}_{i|i}^{R_4}(\xi|\xi') \right] P_i(\xi', t) d\xi' \\ &- \int \left[ \mathcal{U}_{i|i}^{R_3}(\xi'|\xi) + \mathcal{U}_{i|i}^{R_4}(\xi'|\xi) \right] P_i(\xi, t) d\xi' \\ &+ \int \left[ \mathcal{D}_{i|i+1}^{R_2}(\xi|\xi') + \mathcal{D}_{i|i+1}^{R_5}(\xi|\xi') \right] P_{i+1}(\xi', t) d\xi' \\ &- \int \left[ \mathcal{D}_{i-1|i}^{R_2}(\xi'|\xi) + \mathcal{D}_{i-1|i}^{R_5}(\xi'|\xi) \right] P_i(\xi, t) d\xi'. \end{aligned}$$

All  $\mu$  superscripts have been dropped for brevity.

In this context, integration over the subspace  $S_i$  of the sample space  $S$  for any function  $f(\alpha_{(i)}, \mathbf{X}_{(i)}, \mathbf{V}_{(i)})$  will mean

$$\int_{S_i} f d\xi = \sum_{\alpha^{(i)}} \int \int f d\mathbf{x}_{(i)} d\mathbf{v}_{(i)}.$$

By construction, if  $\xi \in S_i$ , the cell contains  $i$  particles.

The average number of particles of species type  $X$  can be computed from

$$\bar{n}_X(t) = \sum_{i=0}^{\infty} \int_{S_i} \sum_{k=1}^i \delta_{\alpha_k, X} P_i(\alpha_{(i)}, \mathbf{X}_{(i)}, \mathbf{V}_{(i)}) d\xi,$$

and likewise for  $\bar{n}_Y$ , while the average number of particles in the cell at time  $t$  corresponds to

$$\bar{N}(t) = \sum_{i=0}^{\infty} \int_{S_i} i P_i(\alpha_{(i)}, \mathbf{X}_{(i)}, \mathbf{V}_{(i)}) d\xi.$$

Note that  $\bar{n}_Y(t) = \bar{N}(t) - \bar{n}_X(t)$ .

Based on our numerical method,

$$\begin{aligned} \mathcal{A}_{j|j-1}^{R_1}(\xi|\xi') &= \frac{1}{\|\Omega\|} \sum_{\Omega} \frac{k_1}{j} \sum_{l=1}^j \delta_{\alpha_l, X} \frac{1}{V} \left( \frac{1}{2\pi k_B T} \right)^{3/2} e^{-\|\mathbf{v}_l\|^2/2k_B T} \\ &\times \prod_{r=1}^{l-1} \delta_{\alpha_r, \alpha'_r} \delta(\mathbf{x}_r - \mathbf{x}'_r) \delta(\mathbf{v}_r - \mathbf{V}' - \hat{\omega}(\mathbf{V}'^{\alpha'_r} - \mathbf{V}')) \\ &- \hat{\omega}^{\alpha_r} \hat{\omega}(\mathbf{v}'_r - \mathbf{V}'^{\alpha'_r})) \\ &\times \prod_{s=l}^{j-1} \delta_{\alpha_{s+1}, \alpha'_s} \delta(\mathbf{x}_{s+1} - \mathbf{x}'_s) \delta(\mathbf{v}_{s+1} - \mathbf{V}' - \hat{\omega}(\mathbf{V}'^{\alpha'_s} - \mathbf{V}')) \\ &- \hat{\omega}^{\alpha'_s} \hat{\omega}(\mathbf{v}'_s - \mathbf{V}'^{\alpha'_s})), \end{aligned}$$

$$\begin{aligned} \mathcal{D}_{j|j+1}^{R_2}(\xi|\xi') &= \frac{1}{\|\Omega\|} \sum_{\Omega} k_2 \sum_{l=1}^{j+1} \delta_{\alpha'_l, X} \\ &\times \prod_{r=1}^{l-1} \delta_{\alpha_r, \alpha'_r} \delta(\mathbf{x}_r - \mathbf{x}'_r) \delta(\mathbf{v}_r - \mathbf{V}' - \hat{\omega}(\mathbf{V}'^{\alpha'_r} - \mathbf{V}')) \\ &- \hat{\omega}^{\alpha'_r} \hat{\omega}(\mathbf{v}'_r - \mathbf{V}'^{\alpha'_r})) \end{aligned}$$

$$\begin{aligned} &\times \prod_{s=l}^j \delta_{\alpha_s, \alpha'_{s+1}} \delta(\mathbf{x}_s - \mathbf{x}'_{s+1}) \delta(\mathbf{v}_s - \mathbf{V}' - \hat{\omega}(\mathbf{V}'(\alpha'_{s+1}) - \mathbf{V}')) \\ &- \hat{\omega}^{\alpha'_{s+1}} \hat{\omega}(\mathbf{v}'_{s+1} - \mathbf{V}'(\alpha'_{s+1}))), \end{aligned}$$

$$\begin{aligned} \mathcal{U}_{j|j}^{R_3}(\xi|\xi') &= \frac{1}{\|\Omega\|} \sum_{\Omega} \sum_{l=1}^j k_3 n'_Y (n'_Y - 1) \delta_{\alpha'_l, X} \delta_{\alpha_l, Y} \prod_{\substack{s=1, \\ s \neq l}}^j \delta_{\alpha_s, \alpha'_s} \\ &\times \prod_{r=1}^j \delta(\mathbf{x}_r - \mathbf{x}'_r) \delta(\mathbf{v}_r - \mathbf{V}' - \hat{\omega}(\mathbf{V}'(\alpha'_r) - \mathbf{V}')) - \hat{\omega}^{\alpha'_r} \hat{\omega}(\mathbf{v}'_r - \mathbf{V}'(\alpha'_r)) \end{aligned}$$

$$\begin{aligned} \mathcal{U}_{j|j}^{R_4}(\xi|\xi') &= \frac{1}{\|\Omega\|} \sum_{\Omega} \sum_{l=1}^j k_4 (n'_Y - 1) (n'_Y - 2) \delta_{\alpha'_l, Y} \delta_{\alpha_l, X} \prod_{\substack{s=1, \\ s \neq l}}^j \delta_{\alpha_s, \alpha'_s} \\ &\times \prod_{r=1}^j \delta(\mathbf{x}_r - \mathbf{x}'_r) \delta(\mathbf{v}_r - \mathbf{V}' - \hat{\omega}(\mathbf{V}'(\alpha'_r) - \mathbf{V}')) - \hat{\omega}^{\alpha'_r} \hat{\omega}(\mathbf{v}'_r - \mathbf{V}'(\alpha'_r)) \end{aligned}$$

$$\begin{aligned} \mathcal{D}_{j|j+1}^{R_5}(\xi|\xi') &= \frac{1}{\|\Omega\|} \sum_{\Omega} k_5 \sum_{l=1}^{j+1} \delta_{\alpha'_l, Y} \\ &\times \prod_{r=1}^{l-1} \delta_{\alpha_r, \alpha'_r} \delta(\mathbf{x}_r - \mathbf{x}'_r) \delta(\mathbf{v}_r - \mathbf{V}' - \hat{\omega}(\mathbf{V}'(\alpha'_r) - \mathbf{V}')) \\ &- \hat{\omega}^{\alpha'_r} \hat{\omega}(\mathbf{v}'_r - \mathbf{V}'(\alpha'_r)) \\ &\times \prod_{s=l}^j \delta_{\alpha_s, \alpha'_{s+1}} \delta(\mathbf{x}_s - \mathbf{x}'_{s+1}) \delta(\mathbf{v}_s - \mathbf{V}' - \hat{\omega}(\mathbf{V}'(\alpha'_{s+1}) - \mathbf{V}')) \\ &- \hat{\omega}^{\alpha'_{s+1}} \hat{\omega}(\mathbf{v}'_{s+1} - \mathbf{V}'(\alpha'_{s+1}))), \end{aligned}$$

and

$$\begin{aligned} \mathcal{A}_{j|j-1}^{R_6}(\xi|\xi') &= \frac{1}{\|\Omega\|} \sum_{\Omega} k_6 \sum_{l=1}^j \delta_{\alpha_l, Y} \frac{1}{V} \left( \frac{1}{2\pi k_B T} \right)^{3/2} e^{-\|\mathbf{v}_l\|^2/2k_B T} \\ &\times \prod_{r=1}^{l-1} \delta_{\alpha_r, \alpha'_r} \delta(\mathbf{x}_r - \mathbf{x}'_r) \delta(\mathbf{v}_r - \mathbf{V}' - \hat{\omega}(\mathbf{V}'(\alpha'_r) - \mathbf{V}')) \\ &- \hat{\omega}^{\alpha_r} \hat{\omega}(\mathbf{v}'_r - \mathbf{V}'(\alpha'_r)) \end{aligned}$$

$$\begin{aligned} &\times \prod_{s=l}^{j-1} \delta_{\alpha_{s+1}, \alpha'_s} \delta(\mathbf{x}_{s+1} - \mathbf{x}'_s) \delta(\mathbf{v}_{s+1} - \mathbf{V}' - \hat{\omega}(\mathbf{V}'(\alpha'_s) - \mathbf{V}')) \\ &- \hat{\omega}^{\alpha'_s} \hat{\omega}(\mathbf{v}'_s - \mathbf{V}'(\alpha'_s)), \end{aligned}$$

where  $V$  is the volume of a cell.

To explain a bit further, the second and third lines of each of the rates represent the collision process of (5) as outlined in Sect. 3.1, ensuring that species types of these particles is unchanged in the collision step. Two lines are required since addition or removal of a particle essentially requires renumbering of the particles in the system. For example, adding a particle in the  $l$ -th position requires all particles labeled  $l$  or higher, to increase their particle number by one, while removing a particle in the  $l$ th position, requires all particles labeled  $l + 1$  or higher to decrease their particle number by one. The first line of each term specifies the details of how the  $l$ th particle is added or removed from the system, or the change in its species type due to a reaction.

If we assume that the non-reactive events are sufficiently fast to ensure a local Maxwellian velocity distribution, and that the locations of particles within the cell are uniformly distributed, then

$$P_i(\boldsymbol{\xi}) = \frac{1}{V^i} \frac{1}{(2\pi k_B T)^{3i/2}} e^{-\sum_{k=1}^i \|v_k\|^2 / 2k_B T} P_i(\alpha_{(i)}).$$

Conservation of energy in the collision process can then be used to replace primed velocities with unprimed velocities after integrating over the primed velocities (with appropriately renumbering the corresponding particles in the case of adding/removing particles from the system). Furthermore, integrating the resulting equation with respect to  $\mathbf{x}_{(i)}$  and  $\mathbf{v}_{(i)}$  then eliminates all positions and velocities from the equation leaving, in simplified form,

$$\begin{aligned} \frac{\partial}{\partial t} P_i(\boldsymbol{\alpha}_{(i)}, t) &= \sum_{l=1}^i \left( \frac{k_1}{i} \delta_{\alpha_l, X} + \frac{k_6}{i} \delta_{\alpha_l, Y} \right) P_{i-1}(\alpha_1, \dots, \alpha_{l-1}, \alpha_{l+1}, \dots, \alpha_i) \\ &- (k_1 + k_6) P_i(\boldsymbol{\alpha}_{(i)}) \\ &+ k_2 \sum_{l=1}^{i+1} P_{i+1}(\alpha_1, \dots, \alpha_{l-1}, \alpha'_l = X, \alpha_l, \alpha_{l+1}, \dots, \alpha_i) \\ &- k_2 \sum_{l=1}^i \delta_{\alpha_l, X} P_i(\boldsymbol{\alpha}_{(i)}) \\ &+ k_3 \sum_{l=1}^i \delta_{\alpha_l, Y} (n_Y - 1)(n_Y - 2) P_i(\alpha_1, \dots, \alpha'_l = X, \dots, \alpha_i) \\ &- k_3 \sum_{l=1}^i \delta_{\alpha_l, X} n_Y (n_Y - 1) P_i(\boldsymbol{\alpha}_{(i)}) \end{aligned} \tag{11}$$

$$\begin{aligned}
 &+ k_4 \sum_{l=1}^i \delta_{\alpha_l, X} n_Y (n_Y - 1) P_i(\alpha_1, \dots, \alpha'_l = Y, \dots, \alpha_i) \\
 &- k_4 \sum_{l=1}^i \delta_{\alpha_l, Y} (n_Y - 1)(n_Y - 2) P_i(\alpha_{(i)}) \\
 &+ k_5 \sum_{l=1}^{i+1} P_{i+1}(\alpha_1, \dots, \alpha_{l-1}, \alpha'_l = Y, \alpha_l, \alpha_{l+1}, \dots, \alpha_i) \\
 &- k_5 \sum_{l=1}^i \delta_{\alpha_l, Y} P_i(\alpha_{(i)}).
 \end{aligned}$$

Assuming that the probability is the same irrespective of the ordering of the particles by number, we consider the ordered state  $\alpha_{(i)} = (\alpha_1 = X, \dots, \alpha_{n_X} = X; \alpha_{n_X+1} = Y, \dots, \alpha_i = Y)$ , and let  $P_i(\alpha_1 = X, \dots, \alpha_{n_X} = X; \alpha_{n_X+1} = Y, \dots, \alpha_i = Y) = P_i(n_X, n_Y)$  where  $n_X + n_Y = i$ . This step connects our Master equation to the traditional “keeping track of numbers” approach used in standard stochastic descriptions for chemical reactive media [36,38]. Then Eq. 11 simplifies to

$$\begin{aligned}
 \frac{\partial}{\partial t} P_i(n_X, n_Y, t) &= \frac{k_1}{i} \sum_{l=1}^{n_X} P_{i-1}(n_X - 1, n_Y) + \frac{k_6}{i} \sum_{l=1}^{n_Y} P_{i-1}(n_X, n_Y - 1) \\
 &- (k_1 + k_6) P_i(n_X, n_Y, t) \\
 &+ k_2(i + 1) P_{i+1}(n_X + 1, n_Y) - k_2 \sum_{i=1}^{n_X} P_i(n_X, n_Y) \\
 &+ k_3 \sum_{l=n_X+1}^i (n_Y - 1)(n_Y - 2) P_i(n_X + 1, n_Y - 1) \\
 &- k_3 \sum_{l=1}^{n_X} n_Y (n_Y - 1) P_i(n_X, n_Y) \\
 &+ k_4 \sum_{l=1}^{n_X} n_Y (n_Y - 1) P_{i+1}(n_X, n_Y + 1) \\
 &- k_4 \sum_{l=n_X+1}^i (n_Y - 1)(n_Y - 2) P_i(n_X, n_Y) \\
 &+ k_5(i + 1) P_{i+1}(n_X, n_Y + 1) - k_5 \sum_{l=1}^{n_Y} P_i(n_X, n_Y)
 \end{aligned}$$

or rather,

$$\begin{aligned}
 \frac{\partial}{\partial t} P_i(n_X, n_Y, t) &= \frac{k_1}{i} n_X P_{i-1}(n_X - 1, n_Y) + \frac{k_6}{i} n_Y P_{i-1}(n_X, n_Y - 1) \\
 &- (k_1 + k_6) P_i(n_X, n_Y, t)
 \end{aligned}$$

$$\begin{aligned}
& + k_2(i+1)P_{i+1}(n_X+1, n_Y) - k_2n_X P_i(n_X, n_Y) \\
& + k_3(i-n_X)(i-n_X-1)(i-n_X-2)P_i(n_X+1, n_Y-1) \\
& - k_3n_X(i-n_X)(i-n_X-1)P_i(n_X, n_Y) \\
& + k_4n_X(i-n_X)(i-n_X-1)P_{i+1}(n_X, n_Y+1) \\
& - k_4(i-n_X)(i-n_X-1)(i-n_X-2)P_i(n_X, n_Y) \\
& + k_5(i+1)P_{i+1}(n_X, n_Y+1) - k_5n_Y P_i(n_X, n_Y)
\end{aligned} \tag{12}$$

Assuming a local Poissonian number distribution

$$P_i(n_X, n_Y) = \frac{e^{-\bar{N}}}{i!} \bar{n}_X^{n_X} \bar{n}_Y^{n_Y}$$

and realizing that the normalization condition under these assumptions means

$$\sum_{i=0}^{\infty} \sum_{n_X=0}^i \binom{i}{n_X} P_i(n_X, n_Y) = 1$$

we multiply (12) by  $\binom{i}{n_X} n_X$  and sum over  $n_X$ , and  $i$ , to get the macroscopic rate law for  $\bar{n}_X$

$$\frac{d}{dt} \bar{n}_X = k_1 - k_2 \bar{n}_X - k_3 \bar{n}_X \bar{n}_Y^2 + k_4 \bar{n}_Y^3.$$

Similarly, multiplying (12) by  $\binom{i}{n_X} (i-n_X)$ , where  $n_Y = i-n_X$  and appropriate summation gives the rate law for  $\bar{n}_Y$  as

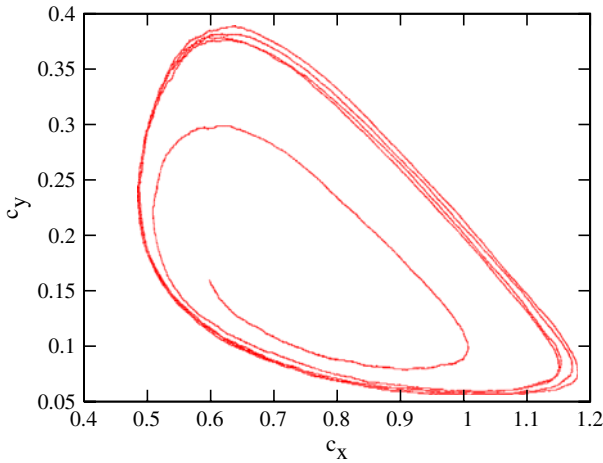
$$\begin{aligned}
\frac{d}{dt} \bar{n}_Y &= \frac{d}{dt} (\bar{N} - \bar{n}_X) \\
&= k_6 - k_5 \bar{n}_Y - k_4 \bar{n}_Y^3 + k_3 \bar{n}_X \bar{n}_Y^2,
\end{aligned}$$

likewise corresponding to the macroscopic rate law. (Note that  $V = 1$  in our case.)

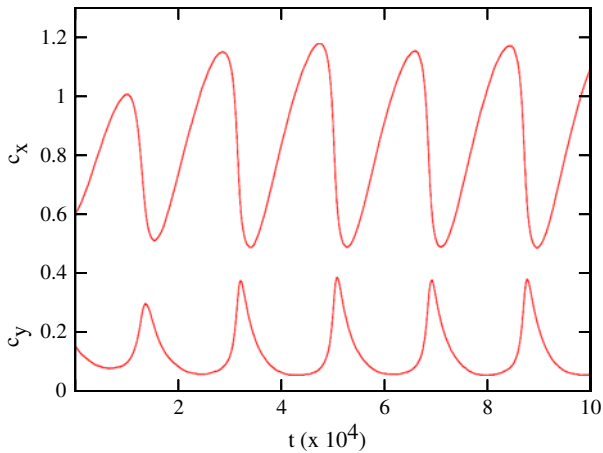
## 5 Numerical results

Simulations were performed on a 3-d cubic domain with  $L = 50^3$  cells of unit volume. The Selkov reaction mechanism was simulated in the oscillatory domain with  $k_1 = 0.0001897$ ,  $k_2 = 0.01$ ,  $k_3 = 0.001$ ,  $k_4 = 0.0001$ ,  $k_5 = 0.01$  and  $k_6 = 0.0000253$ , so as to appropriately test our methods in far-from-equilibrium situations. Preliminary simulations were conducted to ensure that the particle dynamics was sufficiently effective to relax quickly to equilibrium in the absence of reactions.

In Fig. 1 we show the phase portrait for average  $X$  and  $Y$  concentrations ( $c_X = \bar{n}_X/V = \bar{n}_X$ ) starting from initial concentrations of 0.6 and 0.16 particles per unit



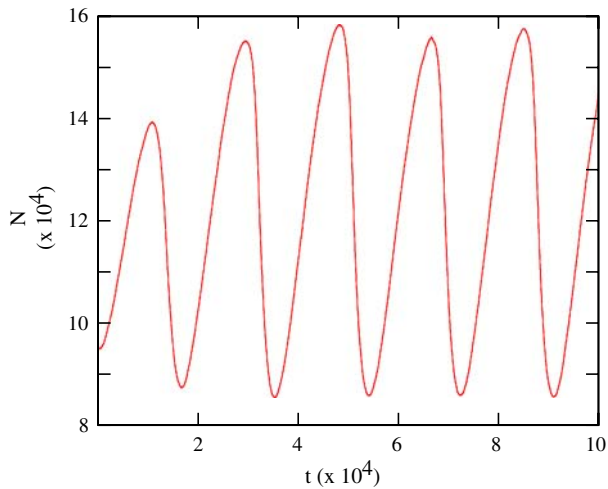
**Fig. 1** Phase portrait for the Selkov model for  $0 \leq t \leq 100,000$  with  $L = 50^3$



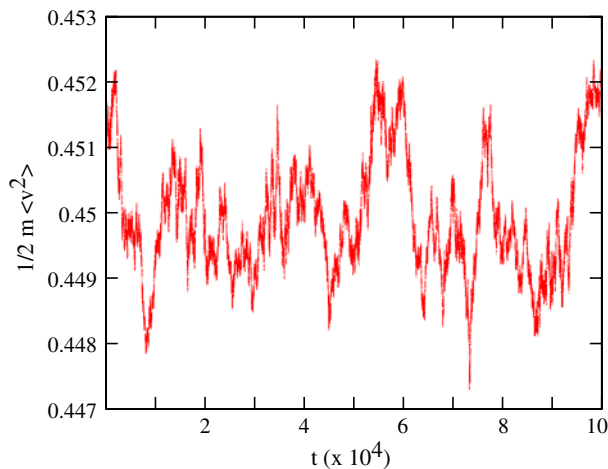
**Fig. 2** Time evolution of  $c_x, c_y$  versus  $t$  for  $L = 50^3$

volume respectively. The system evolves to the oscillatory steady-state, and agrees well with simulations of the corresponding macroscopic rate law. The temporal evolution of the two individual concentrations over the same time interval ( $0 < t < 100,000$ ) can be seen in Fig. 2. Again, the temporal evolution of the concentrations compares well with simulations of the macroscopic rate equations. In Fig. 3 we show that the total number of particles in the system undergoes large oscillations in time, demonstrating that our methods correctly capture the dynamics in a far-from-equilibrium system.

The addition and removal of particles leads to fluctuations in momentum and energy in the system. The temporal evolution of the average kinetic energy ( $\frac{m}{2} \langle V^2 \rangle = \frac{m}{2} (\langle u^2 \rangle + \langle v^2 \rangle + \langle w^2 \rangle)$ ), as well as the  $x$ -,  $y$ - and  $z$ -momenta with  $k_B T = 0.3$  are shown in Figs. 4 and 5. The fluctuations are clearly visible in the Figures, and one can also see that the addition and removal of particles leads to *minor* fluctuations in temperature



**Fig. 3** Time evolution of the total number of particles  $N$  in the system. Note that the system undergoes large fluctuations in the number of particles in time



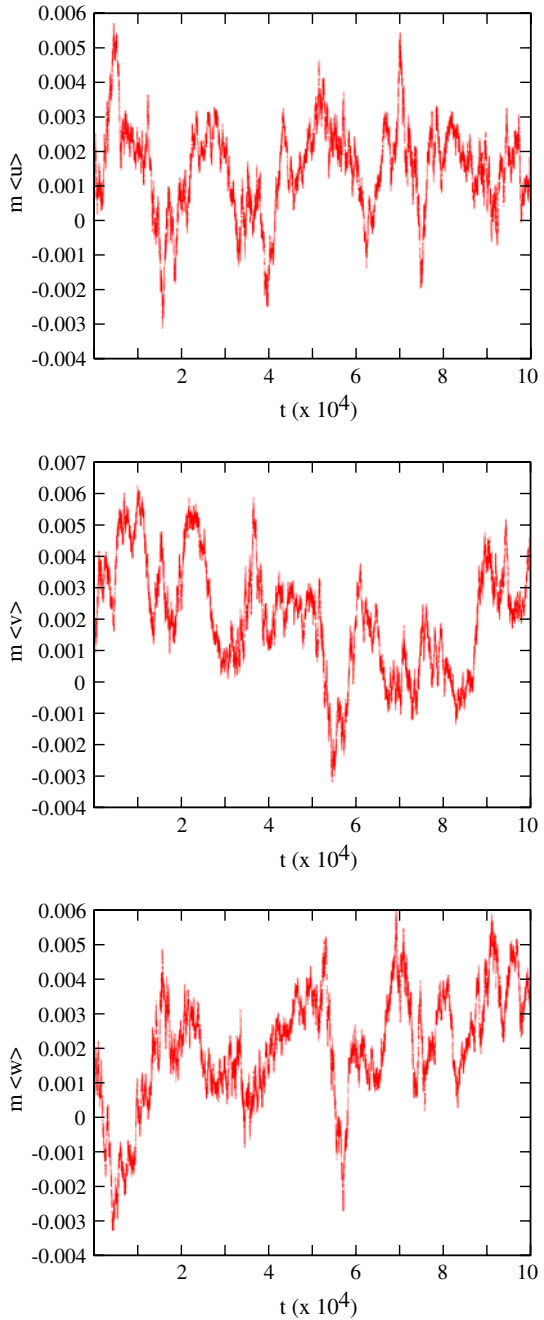
**Fig. 4** Plot of average kinetic energy of the system ( $1/2m\langle V^2 \rangle$ ,  $m = 1$ ) as a function of time. Note that the temperature of the system stays very close to the equilibrium value of  $k_B T = 0.3$  even though the total number of particles changes significantly over time

and momenta in the system even though the system undergoes large fluctuations in particle numbers, as seen in Fig. 3 by the oscillatory nature of  $N$ .

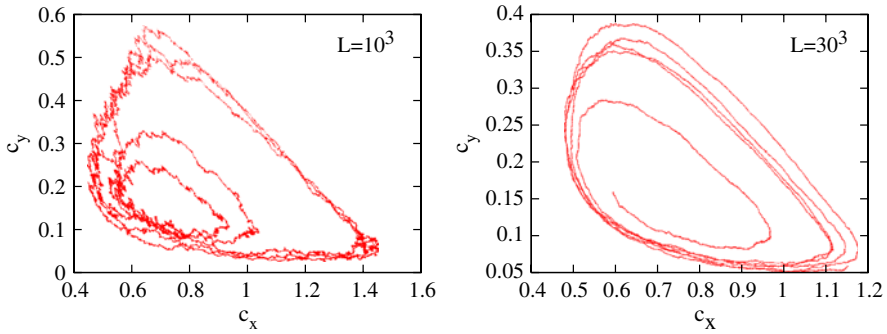
In Fig. 6 we show simulation results for the temporal evolution of average  $X$  and  $Y$  concentrations for smaller systems ( $L = 10^3$  on the left,  $L = 30^3$  on the right of the figure). The effect of spatial fluctuations in these smaller systems is evidenced by the deviations from the macroscopic rate law, which is more pronounced in the smallest system considered. We also observed more pronounced fluctuations in the energy and



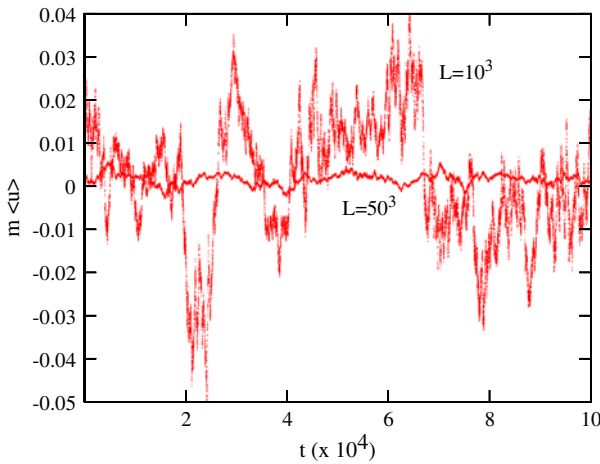
**Fig. 5** Plot of  $x$ ,  $y$ , and  $z$ -momenta ( $m\langle u \rangle$ ,  $m\langle v \rangle$ ,  $m\langle w \rangle$  respectively) versus time. Note that the addition and removal of particles leads to negligible fluctuations in momenta



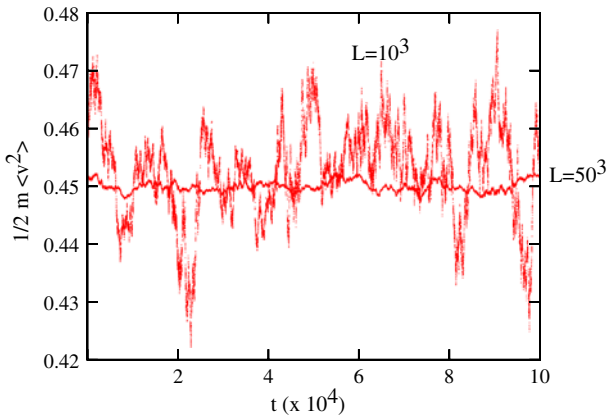
momenta in the smaller systems. We show this in Figs. 7 and 8, where the fluctuations in the smaller system ( $L = 10^3$ ) are significantly more pronounced than for  $L = 50^3$ .



**Fig. 6** Phase portrait for smaller systems of size  $L = 10^3$  and  $L = 20^3$ . Here spatial fluctuations lead to deviations from the macroscopic rate law



**Fig. 7** Temporal evolution of  $x$  momentum ( $m\langle u \rangle$ ) for systems of different size. Note that as the system size increases, the fluctuations become negligible, but can be significant for smaller systems



**Fig. 8** Comparison of average kinetic energy as a function of system size. As the system size increases, the fluctuations become negligible

### 6 Discussion and conclusions

In this paper, we have derived a generalized master equation from the Chapman–Kolmogorov equation so as to provide a theoretical framework for a system in which the number of components of the random variable can change in time. As an application of the theory, we chose a particle-based system for which the random variable incorporates the species types, and phase-space coordinates of the particles in the system at a given time. To appropriately test the model, we chose a Selkov reaction mechanism driven out of equilibrium through addition/removal of two of the chemical species, so that the total number of particles in the system changes in time. Transition rates were specified explicitly to account for local particle collisions, free-streaming of particles, and local reactions according to the Selkov model. To check the validity of our approach, we derived the macroscopic rate law from the Master equation using appropriate equilibrium assumptions and by defining an appropriate averaging procedure for the stochastic model. We also verified that in large systems, the corresponding numerical method agrees with the solutions of the macroscopic rate law. Furthermore, our simulations for smaller systems showed that spatial fluctuations can affect the system, demonstrating the ability of our methods to incorporate such effects. Having successfully derived a stochastic phase-space description that—coupled to a numerical model—has been shown to lead to correct macroscopic behaviour, we have provided a framework in which the effects of spatial fluctuations can be assessed numerically as well as theoretically. Application for which these methods are important include biochemical networks and reactive fluid flows.

### Appendix A:

In this appendix, we show that the small time expansions (2a) and (2b) subject to (3), are consistent with the normalization condition up to  $o(\Delta t)$ .

For every  $\beta \in \{0, \mathbb{Z}^+\}$ , consider  $\xi' \in S_\beta$ , where  $S = \cup_{i=0}^\infty S_i$  from Sect. 2. Then,

$$\begin{aligned} \int_S P(\xi, t + \Delta t | \xi', t) d\xi &= \sum_{\alpha=0}^\infty \int_{S_\alpha} P_{\alpha|\beta}(\xi, t + \Delta t | \xi', t) d\xi \\ &= \sum_{\substack{\alpha=0 \\ \alpha \neq \beta}}^\infty \int_{S_\alpha} P_{\alpha|\beta}(\xi, t + \Delta t | \xi', t) d\xi + \int_{S_\beta} P_{\beta|\beta}(\xi, t + \Delta t | \xi', t) d\xi \\ &= \sum_{\substack{\alpha=0 \\ \alpha \neq \beta}}^\infty \int_{S_\alpha} [\Delta t W_{\alpha|\beta}(\xi | \xi') + o(\Delta t)] d\xi + \int_{S_\beta} \{ [1 - \Delta t a_\beta(\xi')] \delta(\xi - \xi') \\ &\quad + \Delta t W_{\beta|\beta}(\xi | \xi') + o(\Delta t) \} d\xi \\ &\text{(using (2a) and (2b))} \end{aligned}$$

$$= 1 - \Delta t a_{\beta}(\xi') + \Delta t \sum_{\alpha=0}^{\infty} \int_{S_{\alpha}} W_{\alpha|\beta}(\xi, \xi') d\xi + o(\Delta t)$$

$$= 1 + o(\Delta t),$$

using (3).

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