Physica A 395 (2014) 236–246

Contents lists available at ScienceDirect

Physica A

journal homepage: www.elsevier.com/locate/physa

Distinguishing between mean-field, moment dynamics and stochastic descriptions of birth–death–movement processes

Matthew J. Simpson [a,b,*], Jesse A. Sharp [a], Ruth E. Baker [c]

[a] Mathematical Sciences, Queensland University of Technology, GPO Box 2434, Brisbane, Queensland 4001, Australia

[b] Tissue Repair and Regeneration Program, Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia

[c] Mathematical Institute, University of Oxford, Radcliffe Observatory Quarter, Woodstock Road, Oxford, OX2 6GG, UK

HIGHLIGHTS

- Discrete model of birth–death–movement processes is analyzed.
- Mean-field and moment dynamics descriptions are derived.
- The mean-field and moment dynamics descriptions are not always valid.
- Standard calibration procedures are misleading.
- Propose an indirect measure of patchiness to indicate when each description is valid.

ARTICLE INFO

Article history:
Received 10 July 2013
Received in revised form 7 September 2013
Available online 23 October 2013

Keywords:
Birth–death process
Continuum model
Moment dynamics model
Patchiness
Clustering

ABSTRACT

Mathematical descriptions of birth–death–movement processes are often calibrated to measurements from cell biology experiments to quantify tissue growth rates. Here we describe and analyze a discrete model of a birth–death–movement process applied to a typical two-dimensional cell biology experiment. We present three different descriptions of the system: (i) a standard mean-field description which neglects correlation effects and clustering; (ii) a moment dynamics description which approximately incorporates correlation and clustering effects; and (iii) averaged data from repeated discrete simulations which directly incorporates correlation and clustering effects. Comparing these three descriptions indicates that the mean-field and moment dynamics approaches are valid only for certain parameter regimes, and that both these descriptions fail to make accurate predictions of the system for sufficiently fast birth and death rates where the effects of spatial correlations and clustering are sufficiently strong. Without any method to distinguish between the parameter regimes where these three descriptions are valid, it is possible that either the mean-field or moment dynamics model could be calibrated to experimental data under inappropriate conditions, leading to errors in parameter estimation. In this work we demonstrate that a simple measurement of agent clustering and correlation, based on coordination number data, provides an indirect measure of agent correlation and clustering effects, and can therefore be used to make a distinction between the validity of the different descriptions of the birth–death–movement process.

* Corresponding author at: Mathematical Sciences, Queensland University of Technology, GPO Box 2434, Brisbane, Queensland 4001, Australia. Tel.: +61 7 31385241.
E-mail address: matthew.simpson@qut.edu.au (M.J. Simpson).

0378-4371/$ – see front matter
http://dx.doi.org/10.1016/j.physa.2013.10.026

1. Introduction

Mathematical models describing birth–death–movement processes are often used to interpret cell biology experiments such as the growth to confluence experiments shown in Fig. 1(a) [1–3]. In these experiments a population of cells is initially distributed, approximately uniformly, at low density on a two-dimensional substrate. The individual cells undergo motility, birth and death events which leads to changes in the density of the cells on the substrate. Such experiments play an important role in informing our understanding of wound healing and tissue engineering [1–3]. Typical approaches to modeling this kind of experiment involve applying standard continuum descriptions, such as the logistic model, without necessarily examining the underlying assumptions [3,4].

In this work we consider a discrete, lattice-based model of a birth–death–movement process and apply this model to replicate a growth to confluence experiment [5]. We show that the standard mean-field description of this discrete model gives accurate predictions for relatively slow agent proliferation and death rates [6]. A more sophisticated description, based on a moment dynamics approach which accounts for the density of agents and density of pairs of agents [7–15], provides an accurate description of averaged data from the discrete model for moderate proliferation and death rates [16,17]. For rapid proliferation and death rates both the mean-field and moment dynamics descriptions fail to predict the averaged discrete behavior and we must rely on using repeated, computationally intensive and time consuming, discrete simulations.

Since we have several potential mathematical descriptions of the same birth–death–movement process, two of which become inaccurate for sufficiently large birth and death rates, it is relevant for us to develop an understanding of the different parameter regimes where each description is valid. Without such information it is conceivable that a particular model, such as the standard mean-field logistic model, could be calibrated to match experimental data without any explicit consideration of whether that description is appropriate [3,16]. Such an oversight could lead to incorrect parameter estimation as an inaccurate model is calibrated to the observed data [3,16]. We will demonstrate this problem explicitly in Section 5.

In summary, we present a through parameter investigation of a birth–death–movement model that is applied to replicate a growth to confluence experiment from the cell biology literature [1–3]. We show that both the standard mean-field description and a more sophisticated moment dynamics description of the system can fail to produce accurate predictions of the averaged discrete data depending on the movement, birth and death rates in the discrete model, and the degree to which the distribution of agents is spatially correlated. Using simulation data we show that it is possible to distinguish between the applicability of different descriptions of the system using a relatively straightforward estimation of the agent coordination number [18] which provides a measure of the degree to which the distribution of agents is spatially correlated.

2. Discrete model

We consider a discrete model of biological cell motility, proliferation and death processes which has been described previously [16]. In brief, the discrete model consists of a two-dimensional square lattice with lattice spacing Δ, in which each lattice compartment can be occupied by, at most, a single agent. Each agent has a transition rate P_m per unit time describing the motion of agents to a nearest neighbor site, a proliferation rate P_p per unit time describing the production of new agents and a death rate P_d per unit time. We suppose that motility events are unbiased so that an agent at (x, y) attempts to step to $(x \pm \Delta, y)$ or $(x, y \pm \Delta)$ such that each target site is chosen with equal probability. Proliferation events are also unbiased so that a proliferative agent at (x, y) attempts to deposit a daughter agent at $(x \pm \Delta, y)$ or $(x, y \pm \Delta)$ with each target site chosen with equal probability. A dying agent at site (x, y) is simply removed from the system. The model is an exclusion process [19] since potential motility and proliferation events can only take place if the target site is vacant [20]. To be consistent with the experimental images in Fig. 1(a), we consider the initial distribution of agents to be spatially uniform [3] and we denote the number of agents on the lattice at time t by $Q(t)$. Discrete simulations of this process are performed using the Gillespie algorithm with periodic boundary conditions [16,21].

Typical snapshots of the discrete process are shown in Fig. 1(b)–(d) where each simulation was randomly initiated by occupying each site with probability 5%. Snapshots are presented at later times T_1 and T_2, with $0 \leq T_1 \leq T_2$, and we see that the growing population exhibits different spatial patterns depending on the parameters in the simulation. The simulation in Fig. 1(b) illustrates a situation where the distribution of agents remains uniformly distributed with time whereas the simulations in Fig. 1(c)–(d) illustrate significant pattern development that is associated with agent clustering. Both uniform and clustered population growth processes have been observed previously in the experimental literature [3] and it is relevant for us to develop mathematical descriptions of these processes in order to interpret such experimental observations.

3. Continuum models

We use k-point distribution functions [3], $\rho^{(k)}$ ($k = 1, 2, 3, \ldots$), to describe the evolution of the average properties of the discrete model. The $\rho^{(k)}$ functions are multivariate probability distribution functions describing the occupancy of k-tuplets of sites. We use l, m and n to denote various lattice sites, and $\sigma_l \in \{0, A\}$ to be the lattice variable describing the state of site l. With $k = 1$ we have

$$\rho^{(1)}(A_l) = c_l, \qquad \rho^{(1)}(0_l) = 1 - c_l, \tag{1}$$

where c_l is the density of agents at site l. Since we consider a translationally invariant system, c_l represents the density of agents at any site l and we now drop the subscript for notational convenience. For our initial condition the distribution