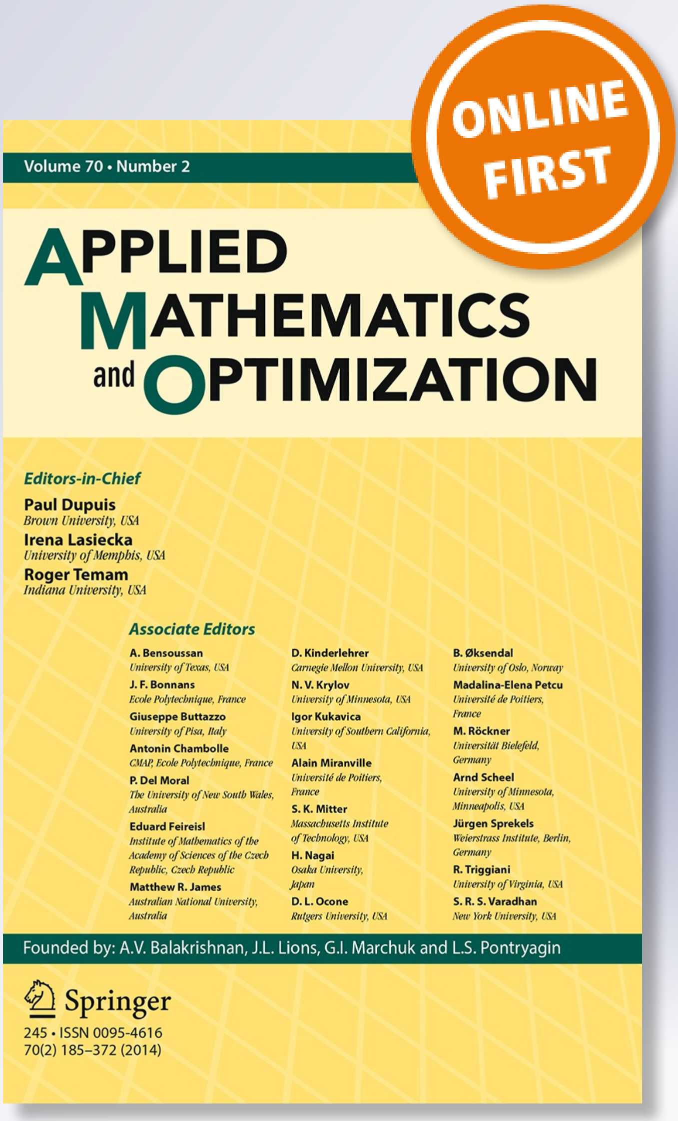
Weak Convergence of a Mass-Structured Individual-Based Model

Fabien Campillo & Coralie Fritsch

Applied Mathematics & Optimization

ISSN 0095-4616

Appl Math Optim
DOI 10.1007/s00245-014-9271-3



ONLINE FIRST

Volume 70 • Number 2

APPLIED MATHEMATICS and OPTIMIZATION

Editors-in-Chief

Paul Dupuis
Brown University, USA
Irena Lasiecka
University of Memphis, USA
Roger Temam
Indiana University, USA

Associate Editors

A. Bensoussan
University of Texas, USA
J. F. Bonnans
Ecole Polytechnique, France
Giuseppe Buttazzo
University of Pisa, Italy
Antonin Chambolle
CMAP, Ecole Polytechnique, France
P. Del Moral
The University of New South Wales, Australia
Eduard Feireisl
Institute of Mathematics of the Academy of Sciences of the Czech Republic, Czech Republic
Matthew R. James
Australian National University, Australia
D. Kinderlehrer
Carnegie Mellon University, USA
N. V. Krylov
University of Minnesota, USA
Igor Kukavica
University of Southern California, USA
Alain Miranville
Université de Poitiers, France
S. K. Mitter
Massachusetts Institute of Technology, USA
H. Nagai
Osaka University, Japan
D. L. Ocone
Rutgers University, USA
B. Øksendal
University of Oslo, Norway
Madalina-Elena Petcu
Université de Poitiers, France
M. Röckner
Universität Bielefeld, Germany
Arnd Scheel
University of Minnesota, Minneapolis, USA
Jürgen Sprekels
Weierstrass Institute, Berlin, Germany
R. Triggiani
University of Virginia, USA
S. R. S. Varadhan
New York University, USA

Founded by: A.V. Balakrishnan, J.L. Lions, G.I. Marchuk and L.S. Pontryagin

Springer
245 • ISSN 0095-4616
70(2) 185–372 (2014)

Springer

Appl Math Optim
DOI 10.1007/s00245-014-9271-3

Weak Convergence of a Mass-Structured Individual-Based Model

Fabien Campillo · Coralie Fritsch

Abstract We propose a model of chemostat where the bacterial population is individually-based, each bacterium is explicitly represented and has a mass evolving continuously over time. The substrate concentration is represented as a conventional ordinary differential equation. These two components are coupled with the bacterial consumption. Mechanisms acting on the bacteria are explicitly described (growth, division and washout). Bacteria interact via consumption. We set the exact Monte Carlo simulation algorithm of this model and its mathematical representation as a stochastic process. We prove the convergence of this process to the solution of an integro-differential equation when the population size tends to infinity. Finally, we propose several numerical simulations.

Keywords Individually-based model · Integro-differential equation · Weak convergence of Markov processes · Mass-structured chemostat model · Monte Carlo

Mathematics Subject Classification Primary 60J80 · 60J85 · Secondary 37N25 · 92D25

Fabien Campillo and Coralie Fritsch are members of the MODEMIC joint INRA and INRIA project-team.

F. Campillo (✉)
INRIA, Montpellier, France
e-mail: Fabien.Campillo@inria.fr

C. Fritsch
Montpellier 2 University and INRA/MIA, Montpellier, France
e-mail: Coralie.Fritsch@supagro.inra.fr

F. Campillo · C. Fritsch
MODEMIC Project-Team, INRA/INRIA, UMR MISTEA, 2 Place Pierre Viala,
34060 Montpellier Cedex 01, France

1 Introduction

Individual-based models (IBM) are in constant development for a couple of decades in the field of ecology and biology [10]. Proposed as alternatives to conventional continuous models based on differential or integro-differential equations (IDE), they are even sometimes presented in opposition to these models: the former being described in terms of discrete variables usually with a stochastic dynamic as the latter are described in terms of continuous variables usually with a deterministic dynamic. Moreover, commonly IBM's are described as computer models while the IDE's are described as mathematical models.

This apparent antagonism is only formal as these approaches are complementary. Many IDE's models are actually continuous/deterministic macroscopic representations of discrete/stochastic microscopic models. So it is particularly relevant to demonstrate that the latter models are approximations, in large population, of the former ones; that is to prove a functional law of large numbers. The IDE models will be valid in large population while the IBM's apply to all population sizes but in practice can only be simulated for relatively small population sizes.

Many IBM's, like the one we will present here, can be expressed as Markov processes with values in a space of punctual measures and we can rely on the theory of weak convergence of Markov processes [12] to prove that this process converges in law, after renormalization, to the solution of a deterministic IDE. This approach has been developed in a series of papers: for a simple model of position [14], for the evolution of trait structured population [5], which is then extended to take into account the age of individuals [29,30]. Finkelshtein et al. [13] proposed also an equivalent approach.

In Sect. 2 we introduce an IBM for a chemostat model where each individual in the bacterial population is explicitly represented by its mass. In Sect. 3 we introduce some notation, then in Sect. 4 we construct the stochastic process associated with the IBM as a Markov process with values in the space of finite measures over the state-space of masses and we derive its infinitesimal generator. In Sect. 5 we prove the convergence, in large population limit, of the IBM towards an integro-differential equation of the population-balance equation type [15,24,25] coupled with an equation for the dynamics of the substrate. Finally in Sect. 6 we present several numerical simulations.

2 A Model of Chemostat Structured in Mass

The chemostat is a biotechnological process of continuous culture developed in the 50s [22,23] and which is at the heart of several industrial applications as well as laboratory devices [28]. Bioreactors operating under this mode are maintained under perfect mixing conditions and usually at large bacterial population sizes.

These features allow such processes to be modeled by ordinary (deterministic) differential systems since, in large populations and under certain conditions, demographic randomness can be neglected. Moreover, perfect mixing conditions permit us to neglect the spatial distribution and express these models in terms of mean concentration in the chemostat. In its simplest version, the chemostat model is expressed as a system of two coupled ordinary differential equations respectively for biomass and substrate concentrations [28]. This approach extends to the case of several bacterial species and several substrates. The simplicity of such models makes possible the development of efficient tools for automatic control and the improvement of the associated biotechnological processes. However, it is increasingly necessary to develop models beyond the standard assumption of perfect mixing with a bacterial population possessing uniform characteristics. For this purpose, several paths are available which take into account the different sources of randomness or the structuring of the bacterial population and its discrete nature. All these aspects have been somewhat neglected in previous models.

Beyond classic models based on systems of (deterministic) ordinary differential equations (ODE) which neglect any structuring of the bacterial populations, have also appeared in the 60s and 70s bacterial growth models structured in size or mass based on IDE [15,24], see also the monograph [25] on these so-called population balance equations for growth-fragmentation models.

Also various research papers have been devoted to the stochastic modeling of the chemostat (see references in [4]). In recent years, many models for the evolution in chemostats have been proposed either using integro-differential equations (IDEs) [11,20,21] or IBM [6]. In the latter model the dynamics of the substrate is described by deterministic differential equations. Indeed, the difference in scale between a bacterial cell and a substrate molecule guaranties that, at the scale of the bacterial population, the dynamics of the substrate can be correctly represented by the fluid limit model, while the dynamics of the bacterial population is discrete and random.

We describe the phenomenon which the model will take into account at a microscopic scale: individual cell growth, cell division, washout (substrate and bacteria are constantly withdrawn from the chemostat vessel), as well as the individual consumption described as a coupling with the ordinary differential equation which models the dynamics of the substrate. Then we describe the associated Monte Carlo algorithm, noting that this algorithm is asynchronous in time, i.e. different events occur at random instants which are not predetermined.

2.1 Description of the Dynamics

We consider an *individual-based model (IBM) structured in mass* where the bacterial population is represented as individuals growing in a perfectly mixed vessel of volume V (l). Each individual is solely characterized by its mass $x \in \mathcal{X} \stackrel{\text{def}}{=} [0, m_{\max}]$, this model does not take into account spatialization. At time t the system is characterized by the pair:

$$(S_t, \nu_t),$$

where

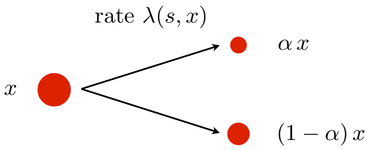
(i) S_t is the *substrate concentration* ($\mathrm{mg\,l^{-1}}$) which is assumed to be uniform in the vessel;

(ii) ν_t is the *bacterial population*, that is N_t individuals and the mass of the individual number i will be denoted x_t^i (mg) for $i = 1, \dots, N_t$. It will be convenient to represent the population $\{x_t^i\}_{i=1,\dots,N_t}$ at time t as the following punctual measure:

$$\nu_t(\mathrm{d}x) = \sum_{i=1}^{N_t} \delta_{x_t^i}(\mathrm{d}x). \tag{1}$$

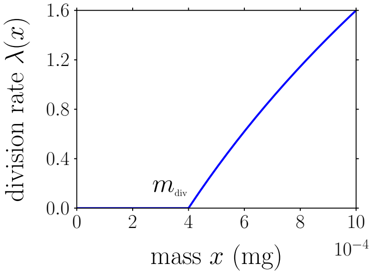
The dynamics of the chemostat combines *discrete evolutions*, cell division and bacterial washout, as well as *continuous evolutions*, the growth of each individual and the dynamics of the substrate. We now describe the four components of the dynamics, first the discrete ones and then the continuous ones which occur between the discrete ones.

(i) *Cell division* Each individual of mass x divides at rate $\lambda(s, x)$ into two individuals of respective masses $\alpha\, x$ *and* $(1-\alpha)\, x$:



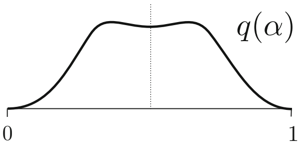
where α is distributed according to a given probability distribution $Q(\mathrm{d}\alpha)$ *on* $[0, 1]$, and s is the substrate concentration.

For instance, the function $\lambda(s, x)$ does not depend on the substrate concentration s and could be of the following form which will be used in the simulation presented in Sect. 6:



Thus, below a certain mass m_{div} it is assumed that the cell cannot divide. There are models where the rate also depends on the concentration s, see for example [8,16].

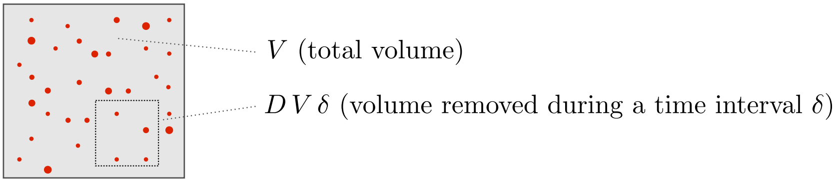
We suppose that the distribution $Q(\mathrm{d}\alpha)$ is symmetric with respect to $\frac{1}{2}$, i.e. $Q(\mathrm{d}\alpha) = Q(1-\mathrm{d}\alpha)$. It also may admit a density $Q(\mathrm{d}\alpha) = q(\alpha)\,\mathrm{d}\alpha$ with the same symmetry:



Thus, the division kernel of an individual of mass x is $K(x, \mathrm{d}y) = Q(\frac{1}{x}\,\mathrm{d}y)$ with support $[0, x]$. In the case of perfect mitosis, an individual of mass x is divided into two individuals of masses $\frac{x}{2}$ and then $Q(\mathrm{d}\alpha) = \delta_{1/2}(\mathrm{d}\alpha)$.

It is therefore assumed that, relative to their mass, the division kernel is the same for all individuals. This allows us to reduce the model to a single division kernel. More complex scenarios can also be investigated.

(ii) *Washout* Each individual is withdrawn from the chemostat at rate D. One places oneself in the framework of a *perfect mixing* hypothesis, where individuals are uniformly distributed in the volume V independently from their mass. During a time step δ, a total volume of $D\,V\,\delta$ is withdrawn from the chemostat:



Therefore, if we assume that all individuals have a negligible volume, each individual has a probability $D\,\delta$ to be withdrawn from the chemostat during the time interval δ, where D is the dilution rate.

Under a non-perfect mixing hypothesis, one could imagine a more complex model where the washout rate of the cells from the chemostat depends on their mass, in this case the rate no longer coincides with the dilution rate. The results presented here generalize without difficulty to the latter case provided that the washout rate is bounded and regular.

When the division of an individual occurs, the size of the population instantaneously jumps from N_t to $N_t + 1$; when an individual is withdrawn from the vessel, the size of the population jumps instantaneously from N_t to $N_t - 1$; between each discrete event the size N_t remains constant and the chemostat evolves according to the following two continuous mechanisms:

(iii) *Growth of each individual* Each individual of mass x growths at speed $\rho_{\mathrm{g}}(S_t, x)$:

$$\dot{x}_t^i = \rho_{\mathrm{g}}(S_t, x_t^i) \quad i = 1, \ldots, N_t, \tag{2}$$

where $\rho_{\mathrm{g}} : \mathbb{R}_+^2 \mapsto \mathbb{R}_+$ is given. For the simulation we will consider the following Gompertz model:

$$\rho_{\mathrm{g}}(s, x) \stackrel{\mathrm{def}}{=} r(s)\, \log\left(\frac{m_{\max}}{x}\right) x,$$

where the growth rate $r(s)$ depends on the substrate concentration according to the Monod kinetics:

$$r(s) = r_{\max}\, \frac{s}{k_r + s}$$

here $m_{\max}$ is the maximum weight that an individual can reach. In Sect. 5.2 we also present an example of a function $\rho_{\mathrm{g}}(s,x)$ linear in x which will lead to the classic model of chemostat.

(iv) *Dynamic of the substrate concentration* The substrate concentration evolves according to the ordinary differential equation:

$$\dot{S}_t = \rho_{\mathrm{s}}(S_t, \nu_t), \tag{3}$$

where

$$\begin{aligned}
\rho_{\mathrm{s}}(s,\nu) &\stackrel{\mathrm{def}}{=} D(\mathbf{s}_{\mathrm{in}} - s) - k\,\mu(s,\nu)\,,\\
\mu(s,\nu) &\stackrel{\mathrm{def}}{=} \frac{1}{V}\int_{\mathcal{X}} \rho_{\mathrm{g}}(s,x)\,\nu(\mathrm{d}x) = \frac{1}{V}\sum_{i=1}^{N} \rho_{\mathrm{g}}(s,x^i)
\end{aligned}$$

with $\nu = \sum_{i=1}^{N} \delta_{x^i}$; D is the dilution rate (1/h), $\mathbf{s}_{\mathrm{in}}$ is the input concentration (mg l^{-1}), k is the stoichiometric coefficient (inverse of the yield coefficient), and V is the representative volume (l). Mass balance leads to Equation (3) and the initial condition S_0 may be random.

To ensure the existence and uniqueness of solutions of the ordinary differential Eqs. (2) and (3), we assume that application $\rho_{\mathrm{g}}(s,x)$ is Lipschitz continuous w.r.t. s uniformly in x:

$$\left|\rho_{\mathrm{g}}(s_1,x) - \rho_{\mathrm{g}}(s_2,x)\right| \leq k_g\,|s_1 - s_2| \tag{4}$$

for all $s_1,\ s_2 \geq 0$ and all $x \in \mathcal{X}$. It is further assumed that $0 \leq \rho_{\mathrm{g}}(s,x) \leq \bar{g}$ for all $(s,x) \in \mathbb{R}_+ \times \mathcal{X}$, and that in the absence of substrate the bacteria do not grow, i.e. $\rho_{\mathrm{g}}(0,x) = 0$ for all $x \in \mathcal{X}$. To ensure that the mass of a bacterium stays between 0 and $m_{\max}$, it is finally assumed that $\rho_{\mathrm{g}}(s, m_{\max}) = 0$ for any $s \geq 0$.

We also assume that $\lambda(s,x)$ is Lipschitz continous w.r.t. s uniformly in x:

$$\left|\lambda(s_1,x) - \lambda(s_2,x)\right| \leq k_\lambda\,|s_1 - s_2| \tag{5}$$

for all $s_1,\ s_2 \geq 0$ and all $x \in \mathcal{X}$. This hypothesis as well as Hypothesis (4) will be used to demonstrate the convergence of IBM, see Theorem 5.2.

2.2 Algorithm

The law of the Markov process which we have presented is characterized by its infinitesimal generator which we will introduce further on in the paper. This characterization is relatively abstract, so we subsequently propose now an exact Monte Carlo algorithm that simulates a trajectory of the Markov process that provides an empirical representation of this law. The method is exact as, up to the pseudo-random numbers generator approximation and the numerical integration of the coupled ODEs (2) and (3), it generates a trajectory of a process which has the same law as the considered process. Moreover it will permit us to propose an explicit representation of the process in Sect. 4.

```
$t \leftarrow 0$
sample $(S_0, \nu_0 = \sum_{i=1}^{N_0} \delta_{x_t^i})$
while $t \le t_{\max}$ do
   $N \leftarrow \langle \nu_t, 1\rangle$
   $\tau \leftarrow (\bar\lambda + D)\, N$
   $\Delta t \sim \mathrm{Exp}(\tau)$
   integrate the equations for the mass (2) and the substrate (3) over $[t, t+\Delta t]$
   $t \leftarrow t + \Delta t$
   draw $x$ uniformly in $\{x_t^i\,;\, i = 1, \dots, N_t\}$
   $u \sim U[0,1]$
   if $u \le \lambda(S_t, x)/(\bar\lambda + D)$ then
      $\alpha \sim Q$
      $\nu_t \leftarrow \nu_t - \delta_x + \delta_{\alpha\, x} + \delta_{(1-\alpha)\, x}$ % division
   else if $u \le (\lambda(S_t, x) + D)/(\bar\lambda + D)$ then
      $\nu_t \leftarrow \nu_t - \delta_x$ % washout
   end if
end while
```

Algorithm 1: *"Exact" Monte Carlo simulation of the individual-based model: approximations only lie in the numerical integration of the ODEs and in the pseudo-random numbers generators.*

In the model described above, the division rate $\lambda(s, x)$ depends on the concentration of substrate s and on the mass x of each individual which continuously evolves according to the system of coupled ordinary differential Eqs. (2) and (3), so to simulate the division of the cell we make use of a rejection sampling technique. It is assumed that there exists $\bar\lambda < \infty$ such that:

$$\lambda(s, x) \le \bar\lambda$$

hence an upper bound for the rate of event, division and washout combined, at the population level is given by:

$$\tau \overset{\text{def}}{=} (\bar\lambda + D)\, N.$$

At time $t + \Delta t$ with $\Delta t \sim \mathrm{Exp}(\tau)$, we determine if an event has occurred and what is its type by acceptance/rejection. To this end, the masses of the N individuals and the substrate concentration evolve according to the coupled ODEs (2) and (3). Then we chose uniformly at random an individual within the population $\nu_{(t+\Delta t)^-}$, that is the population at time $t + \Delta t$ before any possible event, let $x_{(t+\Delta t)^-}$ denotes its mass, then:

(i) With probability: $\frac{\bar\lambda}{(\bar\lambda + D)}$ we determine if there has been division by acceptance/rejection:

- division occurs, that is:

$$\nu_{t+\Delta t} = \nu_{(t+\Delta t)^-} - \delta_{x_{(t+\Delta t)^-}} + \delta_{\alpha\, x_{(t+\Delta t)^-}} + \delta_{(1-\alpha)\, x_{(t+\Delta t)^-}} \quad \text{with } \alpha \sim Q \tag{6}$$

  with probability $\lambda(S_t, x_{(t+\Delta t)^-})/\bar{\lambda}$;
- no event occurs with probability $1 - \lambda(S_t, x_{(t+\Delta t)^-})/\bar{\lambda}$.

In conclusion, the event (6) occurs with probability:

$$\frac{\lambda\big(S_t, x_{(t+\Delta t)^-}\big)}{\bar{\lambda}}\,\frac{\bar{\lambda}}{(\bar{\lambda}+D)} = \frac{\lambda\big(S_t, x_{(t+\Delta t)^-}\big)}{(\bar{\lambda}+D)}.$$

(ii) With probability: $\frac{D}{(\bar{\lambda}+D)} = 1 - \frac{\bar{\lambda}}{(\bar{\lambda}+D)}$ the individual is withdrawn, that is:

$$\nu_{t+\Delta t} = \nu_{(t+\Delta t)^-} - \delta_{x_{(t+\Delta t)^-}} \tag{7}$$

Finally, the events and the associated probabilities are:

- division (6) with probability $\lambda(S_t, x_{(t+\Delta t)^-})/(\bar{\lambda}+D)$,
- washout (7) with probability $D/(\bar{\lambda}+D)$

and no event (rejection) with the remaining probability. The details are given in Algorithm 1.

Technically, the numbering of individuals is as follows: at the initial time individuals are numbered from 1 to N, in case division the daughter cell $\alpha\, x$ keeps the index of the parent cell and the daughter cell $(1-\alpha)\, x$ takes the index $N+1$; in case of the washout, the individual N acquires the index of the withdrawn cell.

3 Notations

Before proposing an explicit mathematical description of the process $(\nu_t)_{t\geq 0}$ we introduce some notations.

3.1 Punctual Measures

Notation (1) designating the bacterial population seems somewhat abstract but it will bridge the gap between the "discrete"—counting punctual measures—and the "continuous" – continuous measures of the population densities— in the context of the asymptotic large population analysis. Indeed for any measure $\nu(\mathrm{d}x)$ defined on $\mathbb{R}_+$ and any function $\varphi : \mathbb{R}_+ \mapsto \mathbb{R}$, we define:

$$\langle \nu, \varphi\rangle \stackrel{\text{def}}{=} \int_{\mathbb{R}_+} \varphi(x)\, \nu(\mathrm{d}x).$$

This notation is valid for continuous measures as well as for punctual measures $\nu_t(\mathrm{d}x)$ defined by (1), in the latter case $\langle \nu_t, \varphi \rangle = \sum_{i=1}^{N_t} \varphi(x_t^i)$.

Practically, this notation allows us to link to macroscopic quantities, e.g. at time t the *population size* is:

$$N_t = \langle \nu_t, 1 \rangle$$

and the *total biomass* is:

$$X_t \overset{\text{def}}{=} \langle \nu_t, I \rangle = \sum_{i=1}^{N_t} x_t^i,$$

where $1(x) \equiv 1$ and $I(x) \equiv x$. Finally:

$$x \in \nu_t = \sum_{i=1}^{N_t} \delta_{x_t^i}(\mathrm{d}x)$$

will denote any individual among $\{x_t^1, \ldots, x_t^{N_t}\}$.

The set of finite and positive measures on $\mathcal{X}$ is denoted $\mathcal{M}_F(\mathcal{X})$, and $\mathcal{M}(\mathcal{X})$ is the subset of punctual finite measures on $\mathcal{X}$:

$$\mathbb{M}(\mathcal{X}) \overset{\text{def}}{=} \left\{ \sum_{i=1}^{N} \delta_{x^i} \quad N \in \mathbb{N},\ x^i \in \mathcal{X} \right\},$$

where by convention $\sum_{i=1}^{0} \delta_{x^i}$ is the null measure. The space $\mathcal{M}_F(\mathcal{X})$ is equipped with the topology of the weak convergence (metrized by the Prokhorov metric).

3.2 Growth Flow

Let:

$$\begin{aligned} A_t : \mathbb{R}_+ \times \mathcal{M}(\mathcal{X}) &\longrightarrow \mathbb{R}_+ \times \mathcal{M}(\mathcal{X}) \\ (s, \nu) &\longrightarrow A_t(s, \nu) \end{aligned}$$

be the differential flow associated with the couple system of ODEs (3)–(2) apart from any event (division or washout), i.e.:

$$A_t(s, \nu) = \left(A_t^0(s, \nu)\ ,\ \sum_{i=1}^{N} \delta_{A_t^i(s,\nu)} \right) \ \text{ with } \nu = \sum_{i=1}^{N} \delta_{x^i},$$

where $A_t^0(s, \nu)$ and $(A_t^i(s, \nu) \quad i = 1, \ldots, N)$ are the coupled solutions of (3)–(2) taken at time t from the initial condition (s, ν), that is:

$$
\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}A_t^0(s,\nu) &= \rho_{\mathrm{s}}\Big(A_t^0(s,\nu),\sum_{i=1}^{N}\delta_{A_t^i(s,\nu)}\Big)\\
&= D\,(\mathbf{s}_{\mathrm{in}} - A_t^0(s,\nu)) - \frac{k}{V}\sum_{i=1}^{N}\rho_{\mathrm{g}}(A_t^0(s,\nu),A_t^i(s,\nu)) \quad A_0^0(s,\nu)=s\,,\\
\frac{\mathrm{d}}{\mathrm{d}t}A_t^i(s,\nu) &= \rho_{\mathrm{g}}(A_t^0(s,\nu),A_t^i(s,\nu)) \quad A_0^i(s,\nu)=x^i
\end{aligned}
$$

for $i=1,\dots,N$. Hence the flow $A_t(s,\nu)$ depends implicitly on the size $N=\langle\nu,1\rangle$ of the population ν.

The stochastic process $(\nu_t)_{t\geq 0}$ features a jump dynamics (division and washout) and follows the dynamics of the flow A_t between the jumps. We can therefore generalize a well-known formula for the pure jump process:

$$
\Phi(S_t,\nu_t) = \Phi(A_t(S_0,\nu_0)) + \sum_{u\leq t}\big[\Phi(A_{t-u}(S_u,\nu_u)) - \Phi(A_{t-u}(S_u,\nu_{u^-}))\big] \quad t\geq 0 \tag{8}
$$

for any function Φ defined on $\mathbb{R}\times\mathcal{M}(\mathcal{X})$.

The sum $\sum_{u\leq t}$ contains only a finite number of terms as the process $(\nu_t)_{t\geq 0}$ admits only a finite number of jumps over any finite time interval. Indeed, the number of jumps in the process $(\nu_t)_{t\geq 0}$ is bounded by a linear birth and death process with *per capita* birth rate $\bar{\lambda}$ and *per capita* death rate D [1].

4 Representation of the Process and of the Infinitesimal Generator

First we derive an explicit representation of a function of the process together with its semimartingale decomposition for a particular class of functions. Second we deduce the representation of the infinitesimal generator on that class.

4.1 Representation of the Process

Let (S_0,ν_0) denote the initial condition of the process, it is a random variable with values in $\mathbb{R}_+\times\mathcal{M}(\mathcal{X})$.

The Eq. (8) includes information on the flow, i.e. the dynamics between the jumps, but no information on the jumps themselves. To obtain an explicit equation for $(S_t,\nu_t)_{t\geq 0}$ we introduce Poisson random measures which manage the incoming of new individuals by cell division on the one hand, and the withdrawal of individuals by washout on the other. To this end we consider two punctual Poisson random measures $N_1(\mathrm{d}u,\mathrm{d}j,\mathrm{d}\alpha,\mathrm{d}\theta)$ and $N_2(\mathrm{d}u,\mathrm{d}j)$ respectively defined on $\mathbb{R}_+\times\mathbb{N}^*\times[0,1]\times[0,1]$ and $\mathbb{R}_+\times\mathbb{N}^*$ with respective intensity measures:

$$
\begin{aligned}
n_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}\alpha, \mathrm{d}\theta) &\overset{\text{def}}{=} \bar{\lambda}\, \mathrm{d}u \Big(\sum_{k \geq 1} \delta_k(\mathrm{d}j) \Big)\, Q(\mathrm{d}\alpha)\, \mathrm{d}\theta\,, \\
n_2(\mathrm{d}u, \mathrm{d}j) &\overset{\text{def}}{=} D\, \mathrm{d}u \Big(\sum_{k \geq 1} \delta_k(\mathrm{d}j) \Big).
\end{aligned}
$$

Suppose that N_1, N_2, S_0 and ν_0 are mutually independent. Let $(\mathcal{F}_t)_{t \geq 0}$ be the canonical filtration generated by (S_0, ν_0), N_1 and N_2. Consider the compensated Poisson random measures associated with N_1 and N_2:

$$
\begin{aligned}
\tilde{N}_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}y, \mathrm{d}\theta) &\overset{\text{def}}{=} N_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}y, \mathrm{d}\theta) - n_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}y, \mathrm{d}\theta)\,, \\
\tilde{N}_2(\mathrm{d}u, \mathrm{d}j) &\overset{\text{def}}{=} N_2(\mathrm{d}u, \mathrm{d}j) - n_2(\mathrm{d}u, \mathrm{d}j).
\end{aligned}
$$

According to (8), for any function Φ defined on $\mathbb{R} \times \mathcal{M}(\mathcal{X})$:

$$
\begin{aligned}
\Phi(S_t, \nu_t) = \Phi(A_t(S_0, \nu_0)) + &\iiiint_{[0,t] \times \mathbb{N}^* \times [0,1]^2} 1_{\{j \leq N_{u^-}\}}\, 1_{\{0 \leq \theta \leq \lambda(S_u, x^j_{u^-})/\bar{\lambda}\}} \\
&\times \Big[\Phi(A_{t-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}} + \delta_{\alpha\, x^j_{u^-}} + \delta_{(1-\alpha)\, x^j_{u^-}})) \\
&- \Phi(A_{t-u}(S_u, \nu_{u^-})) \Big]\, N_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}\alpha, \mathrm{d}\theta) \\
&+ \iint_{[0,t] \times \mathbb{N}^*} 1_{\{j \leq N_{u^-}\}} \Big[\Phi(A_{t-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}})) \\
&- \Phi(A_{t-u}(S_u, \nu_{u^-})) \Big]\, N_2(\mathrm{d}u, \mathrm{d}j). \qquad (9)
\end{aligned}
$$

In particular, we obtain the following explicit representation of the process (S_t, ν_t):

$$
\begin{aligned}
(S_t, \nu_t) = A_t(S_0, \nu_0) + &\iiiint_{[0,t] \times \mathbb{N}^* \times [0,1]^2} 1_{\{j \leq N_{u^-}\}}\, 1_{\{0 \leq \theta \leq \lambda(S_u, x^j_{u^-})/\bar{\lambda}\}} \\
&\times \Big[A_{t-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}} + \delta_{\alpha\, x^j_{u^-}} + \delta_{(1-\alpha)\, x^j_{u^-}}) \\
&- A_{t-u}(S_u, \nu_{u^-}) \Big]\, N_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}\alpha, \mathrm{d}\theta) \\
&+ \iint_{[0,t] \times \mathbb{N}^*} 1_{\{j \leq N_{u^-}\}} \Big[A_{t-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}}) - A_{t-u}(S_u, \nu_{u^-}) \Big]\, N_2(\mathrm{d}u, \mathrm{d}j). \\
&\qquad (10)
\end{aligned}
$$

From now on, we consider test functions Φ of the form:

$$
\Phi(s, \nu) = F(s, \langle \nu, f \rangle)
$$

with $F \in C^{1,1}(\mathbb{R}^+ \times \mathbb{R})$ and $f \in C^1(\mathcal{X})$.

Proposition 4.1 *For any $t > 0$:*

$$
\begin{aligned}
F(S_t, \langle \nu_t, f\rangle) &= F(S_0, \langle \nu_0, f\rangle) \\
&\quad + \int_0^t \big[\rho_{\rm s}(S_u, \nu_u)\, \partial_s F\,(S_u,\ \langle \nu_u, f\rangle) + \langle \nu_u,\ \rho_{\rm g}(S_u, .)\, f'\rangle\, \partial_x F\,(S_u,\ \langle \nu_u, f\rangle)\big]\, \mathrm{d}u \\
&\quad + \int_0^t \int_{\mathcal{X}} \lambda(S_u, x) \int_0^1 \Big[F\big(S_u\,,\ \langle \nu_u - \delta_x + \delta_{\alpha\, x} + \delta_{(1-\alpha)\, x}, f\rangle\big) \\
&\quad - F\big(S_u, \langle \nu_u, f\rangle\big)\Big]\, Q(\mathrm{d}\alpha)\, \nu_u(\mathrm{d}x)\, \mathrm{d}u \\
&\quad + D \int_0^t \int_{\mathcal{X}} \Big[F\big(S_u,\ \langle \nu_u - \delta_x, f\rangle\big) - F\big(S_u,\ \langle \nu_u, f\rangle\big)\Big]\, \nu_u(\mathrm{d}x)\, \mathrm{d}u + Z_t, \qquad (11)
\end{aligned}
$$

where $Z_t = M_t^{1,F,f} + M_t^{2,F,f}$, with:

$$
\begin{aligned}
M_t^{1,F,f} &\overset{def}{=} \iiiint\limits_{[0,t]\times\mathbb{N}^*\times[0,1]^2} 1_{\{j \le N_{u-}\}}\, 1_{\{0 \le \theta \le \lambda(S_u, x^j_{u-})/\bar{\lambda}\}} \\
&\qquad \times \Big[F\Big(S_u, \langle \nu_{u^-} - \delta_{x^j_{u-}} + \delta_{\alpha\, x^j_{u-}} + \delta_{(1-\alpha)\, x^j_{u-}}, f\rangle\Big) - F\,(S_u,\ \langle \nu_{u^-}, f\rangle)\Big] \\
&\qquad \times \tilde{N}_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}\alpha, \mathrm{d}\theta)\,, \\
M_t^{2,F,f} &\overset{def}{=} \iint\limits_{[0,t]\times\mathbb{N}^*} 1_{\{j \le N_{u-}\}} \Big[F\Big(S_u, \langle \nu_{u^-} - \delta_{x^j_{u-}}, f\rangle\Big) - F\,(S_u,\ \langle \nu_{u^-}, f\rangle)\Big]\, \tilde{N}_2(\mathrm{d}u, \mathrm{d}j).
\end{aligned}
$$

Proof From (9):

$$
\begin{aligned}
\langle \nu_t, f\rangle &= \sum_{i=1}^{N_0} f(A^i_t(S_0, \nu_0)) + \iiiint\limits_{[0,t]\times\mathbb{N}^*\times[0,1]^2} 1_{\{j \le N_{u-}\}}\, 1_{\{0 \le \theta \le \lambda(S_u, x^j_{u-})/\bar{\lambda}\}} \\
&\qquad \times \Big[\sum_{i=1}^{N_{u-}+1} f(A^i_{t-u}(S_u, \nu_{u^-} - \delta_{x^j_{u-}} + \delta_{\alpha\, x^j_{u-}} + \delta_{(1-\alpha)\, x^j_{u-}})) \\
&\qquad - \sum_{i=1}^{N_{u-}} f(A^i_{t-u}(S_u, \nu_{u^-}))\Big]\, N_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}\alpha, \mathrm{d}\theta) + \iint\limits_{[0,t]\times\mathbb{N}^*} 1_{\{j \le N_{u-}\}} \\
&\qquad \times \Big[\sum_{i=1}^{N_{u-}-1} f(A^i_{t-u}(S_u, \nu_{u^-} - \delta_{x^j_{u-}})) - \sum_{i=1}^{N_{u-}} f(A^i_{t-u}(S_u, \nu_{u^-}))\Big] N_2(\mathrm{d}u, \mathrm{d}j).
\end{aligned}
$$

According to the chain rule formula, for any $\nu = \sum_{i=1}^{N} \delta_{x^i}$:

$$
\begin{aligned}
f(A^i_{t-u}(s,\nu)) &= f(x^i) + \int_u^t \rho_{\mathrm{g}}(A^0_{\tau-u}(s,\nu),\, A^i_{\tau-u}(s,\nu))\, f'(A^i_{\tau-u}(s,\nu))\,\mathrm{d}\tau \\
&= f(x^i) + \int_u^t \varphi(A^0_{\tau-u}(s,\nu),\, A^i_{\tau-u}(s,\nu))\,\mathrm{d}\tau
\end{aligned}
$$

for $i \le N$, with $\varphi(s,x) \stackrel{\mathrm{def}}{=} \rho_{\mathrm{g}}(s,x)\, f'(x)$. Hence:

$$
\begin{aligned}
\langle \nu_t, f\rangle = \langle \nu_0, f\rangle &+ \iiiint\limits_{[0,t]\times\mathbb{N}^*\times[0,1]^2} 1_{\{j\le N_{u^-}\}}\, 1_{\{0\le\theta\le\lambda(S_u, x^j_{u^-})/\bar{\lambda}\}} \\
&\times \Big[f(\alpha\, x^j_{u^-}) + f((1-\alpha)\, x^j_{u^-}) - f(x^j_{u^-}) \Big]\, N_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}\alpha, \mathrm{d}\theta) \\
&- \iint\limits_{[0,t]\times\mathbb{N}^*} 1_{\{j\le N_{u^-}\}}\, f(x^j_{u^-})\ N_2(\mathrm{d}u, \mathrm{d}j) + T_0 + T_1 + T_2,
\end{aligned}
$$

where:

$$
\begin{aligned}
T_0 &\stackrel{\mathrm{def}}{=} \sum_{i=1}^{N_0} \int_0^t \varphi(A^0_\tau(S_0, \nu_0),\, A^i_\tau(S_0, \nu_0))\,\mathrm{d}\tau \\
T_1 &\stackrel{\mathrm{def}}{=} \iiiint\limits_{[0,t]\times\mathbb{N}^*\times[0,1]^2} 1_{\{j\le N_{u^-}\}}\, 1_{\{0\le\theta\le\lambda(S_u, x^j_{u^-})/\bar{\lambda}\}} \\
&\quad \times \int_u^t \Big[\sum_{i=1}^{N_{u^-}+1} \varphi(A^0_{\tau-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}} + \delta_{\alpha\, x^j_{u^-}} + \delta_{(1-\alpha)\, x^j_{u^-}}), \\
&\quad A^i_{\tau-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}} + \delta_{\alpha\, x^j_{u^-}} + \delta_{(1-\alpha)\, x^j_{u^-}})) \\
&\quad - \sum_{i=1}^{N_{u^-}} \varphi(A^0_{\tau-u}(S_u, \nu_{u^-}),\, A^i_{\tau-u}(S_u, \nu_{u^-})) \Big]\,\mathrm{d}\tau \\
&\quad \times N_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}\alpha, \mathrm{d}\theta) \\
T_2 &\stackrel{\mathrm{def}}{=} \iint\limits_{[0,t]\times\mathbb{N}^*} 1_{\{j\le N_{u^-}\}} \int_u^t \left[\sum_{i=1}^{N_{u^-}-1} \varphi(A^0_{\tau-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}}),\, A^i_{\tau-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}})) \right. \\
&\quad \left. - \sum_{i=1}^{N_{u^-}} \varphi(A^0_{\tau-u}(S_u, \nu_{u^-}),\, A^i_{\tau-u}(S_u, \nu_{u^-})) \right] \mathrm{d}\tau\ N_2(\mathrm{d}u, \mathrm{d}j).
\end{aligned}
$$

Fubini's theorem applied to T_1 and T_2 leads to:

$$
\begin{aligned}
T_1 = \int_0^t & \iiiint\limits_{[0,\tau]\times\mathbb{N}^*\times[0,1]^2} 1_{\{j\le N_{u^-}\}} \times 1_{\{0\le\theta\le\lambda(S_u,x^j_{u^-})/\bar{\lambda}\}} \\
& \times \Bigg[\sum_{i=1}^{N_{u^-}+1} \varphi(A^0_{\tau-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}} + \delta_{\alpha\, x^j_{u^-}} + \delta_{(1-\alpha)\, x^j_{u^-}}), \\
& \quad A^i_{\tau-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}} + \delta_{\alpha\, x^j_{u^-}} + \delta_{(1-\alpha)\, x^j_{u^-}})) \\
& - \sum_{i=1}^{N_{u^-}} \varphi(A^0_{\tau-u}(S_u, \nu_{u^-}), A^i_{\tau-u}(S_u, \nu_{u^-})) \Bigg] \\
& \times N_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}\alpha, \mathrm{d}\theta)\, \mathrm{d}\tau \\
T_2 \overset{\text{def}}{=} \int_0^t & \iint\limits_{[0,\tau]\times\mathbb{N}^*} 1_{\{j\le N_{u^-}\}} \Bigg[\sum_{i=1}^{N_{u^-}-1} \varphi(A^0_{\tau-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}}), A^i_{\tau-u}(S_u, \nu_{u^-} - \delta_{x^j_{u^-}})) \\
& - \sum_{i=1}^{N_{u^-}} \varphi(A^0_{\tau-u}(S_u, \nu_{u^-}), A^i_{\tau-u}(S_u, \nu_{u^-})) \Bigg] N_2(\mathrm{d}u, \mathrm{d}j)\, \mathrm{d}\tau
\end{aligned}
$$

so, according to (9):

$$
T_0 + T_1 + T_2 = \int_0^t \langle \nu_\tau, \varphi(S_\tau, .)\rangle\, \mathrm{d}\tau.
$$

Finally,

$$
\begin{aligned}
\langle \nu_t, f\rangle = & \langle \nu_0, f\rangle + \int_0^t \langle \nu_u, \rho_{\mathrm{g}}(S_u, .)\, f'\rangle\, \mathrm{d}u + \iiiint\limits_{[0,t]\times\mathbb{N}^*\times[0,1]^2} 1_{\{j\le N_{u^-}\}}\, 1_{\{0\le\theta\le\lambda(S_u,x^j_{u^-})/\bar{\lambda}\}}, \\
& \times \big[f(\alpha\, x^j_{u^-}) + f((1-\alpha)\, x^j_{u^-}) - f(x^j_{u^-}) \big] N_1(\mathrm{d}u, \mathrm{d}j, \mathrm{d}\alpha, \mathrm{d}\theta) \\
& - \iint\limits_{[0,t]\times\mathbb{N}^*} 1_{\{j\le N_{u^-}\}}\, f(x^j_{u^-})\ N_2(\mathrm{d}u, \mathrm{d}j).
\end{aligned}
$$

Since f and f' are continuous and bounded (bounded as defined on a compact set), we can conclude this proof by using the Itô formula for stochastic integrals with respect to Poisson random measures [27] to develop the differential of $F(S_t, \langle \nu_t, f\rangle)$ using Eq. (3) and the previous equation. □

As the integrands in the Poissonian integrals of (11) are predictable, one can make use of the result of Ikeda and Watanabe [17, p. 62]:

Proposition 4.2 *We have the following properties of martingales:*

(i) *If for any* $t \geq 0$*:*

$$\mathbb{E}\bigg(\int_0^t \int_{\mathcal{X}} \lambda(S_u, x) \int_0^1 \big|F(S_u, \langle \nu_u - \delta_x + \delta_{\alpha\, x} + \delta_{(1-\alpha)\, x}, f\rangle) - F(S_u, \langle \nu_u, f\rangle)\big|\, Q(\mathrm{d}\alpha)\, \nu_u(\mathrm{d}x)\, \mathrm{d}u\bigg) < +\infty$$

then $(M_t^{1,F,f})_{t\geq 0}$ *is a martingale. If moreover, for any* $t \geq 0$*:*

$$\mathbb{E}\bigg(\int_0^t \int_{\mathcal{X}} \lambda(S_u, x) \int_0^1 \big|F(S_u, \langle \nu_u - \delta_x + \delta_{\alpha\, x} + \delta_{(1-\alpha)\, x}, f\rangle) - F(S_u, \langle \nu_u, f\rangle)\big|^2\, Q(\mathrm{d}\alpha)\, \nu_u(\mathrm{d}x)\, \mathrm{d}u\bigg) < +\infty$$

then $(M_t^{1,F,f})_{t\geq 0}$ *is a square integrable martingale and predictable quadratic variation:*

$$\langle M^{1,F,f}\rangle_t \overset{def}{=} \int_0^t \int_{\mathcal{X}} \lambda(S_u, x) \int_0^1 \big[F(S_u, \langle \nu_u - \delta_x + \delta_{\alpha\, x} + \delta_{(1-\alpha)\, x}, f\rangle) - F(S_u, \langle \nu_u, f\rangle)\big]^2\, Q(\mathrm{d}\alpha)\, \nu_u(\mathrm{d}x)\, \mathrm{d}u;$$

(ii) *If for any* $t \geq 0$

$$\mathbb{E}\bigg(\int_0^t \int_{\mathcal{X}} \big|F(S_u, \langle \nu_u - \delta_x, f\rangle) - F(S_u, \langle \nu_u, f\rangle)\big|\, \nu_u(\mathrm{d}x)\, \mathrm{d}u\bigg) < +\infty$$

then $(M_t^{2,F,f})_{t\geq 0}$ *is a martingale. If moreover, for any* $t \geq 0$*:*

$$\mathbb{E}\bigg(\int_0^t \int_{\mathcal{X}} |F(S_u, \langle \nu_u - \delta_x, f\rangle) - F(S_u, \langle \nu_u, f\rangle)|^2\, \nu_u(\mathrm{d}x)\, \mathrm{d}u\bigg) < +\infty$$

then $(M_t^{2,F,f})_{t\geq 0}$ *is a square integrable martingale and predictable quadratic variation:*

$$\langle M^{2,F,f}\rangle_t \overset{def}{=} D \int_0^t \int_{\mathcal{X}} [F(S_u, \langle \nu_u - \delta_x, f\rangle) - F(S_u, \langle \nu_u, f\rangle)]^2\, \nu_u(\mathrm{d}x)\, \mathrm{d}u.$$

Hence under these hypotheses, Eq. (11) *is the semimartingale decomposition of the process* $F(S_t, \langle \nu_t, f\rangle)$.

Corollary 4.3 (Control of the population size) *Let* $T > 0$, *if there exists* $p \geq 1$ *such that* $\mathbb{E}(\langle \nu_0, 1\rangle^p) < \infty$, *then:*

$$\mathbb{E}\left(\sup_{t\in[0,T]}\langle\nu_t,1\rangle^p\right)\leq C_{p,T},$$

where $C_{p,T}<\infty$ *depends only on* p *and* T.

Proof For any $n\in\mathbb{N}$, define the following stopping time:

$$\tau_n\overset{\text{def}}{=}\inf\{t\geq 0,\ N_t\geq n\}.$$

Proposition 4.1 applied to $F(s,x)=x^p$ and $f(x)=1$ leads to:

$$\sup_{u\in[0,t\wedge\tau_n]}\langle\nu_u,1\rangle^p\leq\langle\nu_0,1\rangle^p+\int_0^t\int_{\mathcal{X}}\lambda(S_u,x)\left[(\langle\nu_{u^-},1\rangle+1)^p-\langle\nu_{u^-},1\rangle^p\right]\\ \times\nu_u(\mathrm{d}x)\,\mathrm{d}u+M_t^{1,F,f}$$

From inequality $(1+y)^p-y^p\leq C_p\,(1+y^{p-1})$ we get:

$$\sup_{u\in[0,t\wedge\tau_n]}\langle\nu_u,1\rangle^p\leq\langle\nu_0,1\rangle^p+C_p\int_0^t\int_{\mathcal{X}}\lambda(S_u,x)\left[(1+\langle\nu_{u^-},1\rangle^{p-1}\right]\\ \times\nu_u(\mathrm{d}x)\,\mathrm{d}u+M_t^{1,F,f}$$

Proposition 4.2, together with the inequality $(1+y^{p-1})\,y\leq 2\,(1+y^p)$ give:

$$\mathbb{E}\left(\sup_{u\in[0,t\wedge\tau_n]}\langle\nu_u,1\rangle^p\right)\leq\mathbb{E}(\langle\nu_0,1\rangle^p)+2\,\bar{\lambda}\,C_p\,\mathbb{E}\int_0^t\left(1+\langle\nu_{u\wedge\tau_n},1\rangle^p\right)\mathrm{d}u.$$

Fubini's theorem and Gronwall's inequality allow us to conclude that for any $T<\infty$:

$$\mathbb{E}\left(\sup_{t\in[0,T\wedge\tau_n]}\langle\nu_t,1\rangle^p\right)\leq\left(\mathbb{E}\left(\langle\nu_0,1\rangle^p\right)+2\,\bar{\lambda}\,C_p\,T\right)\exp(2\,\bar{\lambda}\,C_p\,T)\leq C_{p,T},$$

where $C_{p,T}<\infty$ as $\mathbb{E}(\langle\nu_0,1\rangle^p)<\infty$.

In addition, the sequence of stopping times τ_n tends to infinity, otherwise there would exist $T_0<\infty$ such that $\mathbb{P}(\sup_n\tau_n<T_0)=\varepsilon_{T_0}>0$ hence $\mathbb{E}(\sup_{t\in[0,T_0\wedge\tau_n]}\langle\nu_t,1\rangle^p)\geq\varepsilon_{T_0}\,n^p$ which contradicts the above inequality. Finally, Fatou's lemma gives:

$$\mathbb{E}\left(\sup_{t\in[0,T]}\langle\nu_t,1\rangle^p\right)=\mathbb{E}\left(\liminf_{n\to\infty}\sup_{t\in[0,T\wedge\tau_n]}\langle\nu_t,1\rangle^p\right)\\ \leq\liminf_{n\to\infty}\mathbb{E}\left(\sup_{t\in[0,T\wedge\tau_n]}\langle\nu_t,1\rangle^p\right)\leq C_{p,T}.$$

□

Remark 4.4 In particular, if $\mathbb{E}\langle \nu_0, 1\rangle < \infty$ and if the function F is bounded, then by Corollary 4.3 and Proposition 4.2, $(M_t^{1,F,f})_{t\geq 0}$ and $(M_t^{2,F,f})_{t\geq 0}$ are martingales.

Corollary 4.5 *If* $\mathbb{E}\langle \nu_0, 1\rangle + \mathbb{E}(S_0) < \infty$ *then:*

$$\mathbb{E}\left(\int_0^t |\rho_{\mathrm{s}}(S_u, \nu_u)|\,\mathrm{d}u\right) \leq D\,t\,\mathbb{E}(S_0 \vee \mathbf{s}_{\mathrm{in}}) + \frac{k}{V}\,\bar{g}\,\mathbb{E}\left(\int_0^t \langle \nu_u, 1\rangle\,\mathrm{d}u\right) < \infty.$$

Proof As $S_u \geq 0$ and ρ_{g} is a non negative function,

$$\rho_{\mathrm{s}}(S_u, \nu_u) \leq D\,\mathbf{s}_{\mathrm{in}}.$$

Furthermore, for any $(s, x) \in \mathbb{R}_+ \times \mathcal{X}$, $\rho_{\mathrm{g}}(s, x) \leq \bar{g}$, and $S_u \leq S_0 \vee \mathbf{s}_{\mathrm{in}}$ so:

$$\rho_{\mathrm{s}}(S_u, \nu_u) \geq -D\,(S_0 \vee \mathbf{s}_{\mathrm{in}}) - \frac{k}{V}\,\bar{g}\,\langle \nu_u, 1\rangle.$$

We therefore deduce that:

$$\int_0^t |\rho_{\mathrm{s}}(S_u, \nu_u)|\,\mathrm{d}u \leq D\,t\,(S_0 \vee \mathbf{s}_{\mathrm{in}}) + \frac{k}{V}\,\bar{g}\int_0^t \langle \nu_u, 1\rangle\,\mathrm{d}u.$$

According to Corollary 4.3, the last term is integrable which concludes the proof. □

4.2 The Infinitesimal Generator

Proposition 4.6 *The process* $(S_t, \nu_t)_{t\geq 0}$ *is Markovian with values in* $\mathbb{R}_+ \times \mathcal{M}(\mathcal{X})$. *On the space* $\mathcal{H}$ *of functions* $\Phi(s, \nu) = F(s, \langle \nu, f\rangle)$ *with* $F \in C_b^{1,1}(\mathbb{R}^+ \times \mathbb{R})$ *and* $f \in C^1(\mathcal{X})$, *the infinitesimal generator of the process is:*

$$\begin{aligned}\mathcal{L}\Phi(s, \nu) \overset{def}{=}& \big(D(\mathbf{s}_{\mathrm{in}} - s) - k\,\mu(s, \nu)\big)\,\partial_s F(s, \langle \nu, f\rangle) + \langle \nu, \rho_{\mathrm{g}}(s, .)\,f'\rangle\,\partial_x F(s, \langle \nu, f\rangle)\\ &+ \int_{\mathcal{X}} \lambda(s, x)\int_0^1 \big[F(s, \langle \nu - \delta_x + \delta_{\alpha\,x} + \delta_{(1-\alpha)\,x}, f\rangle)\\ &- F(s, \langle \nu, f\rangle)\big]\,Q(\mathrm{d}\alpha)\,\nu(\mathrm{d}x)\\ &+ D\int_{\mathcal{X}} \big[F(s, \langle \nu - \delta_x, f\rangle) - F(s, \langle \nu, f\rangle)\big]\,\nu(\mathrm{d}x). \end{aligned} \tag{12}$$

for any $s \in \mathbb{R}_+$ *and* $\nu \in \mathcal{M}_F(\mathcal{X})$. *Thereafter* $\mathcal{L}\Phi(s, \nu)$ *is denoted* $\mathcal{L}F(s, \langle \nu, f\rangle)$.

We restrict ourselves to the special class $\mathcal{H}$ of functions where the expression of the generator is explicit, this is sufficient as this class is separating and more specifically convergence determining (see definition in [12, p. 112]). Indeed, it is straightforward to extend the Theorem 3.2.6 of [9], given for measures only, to the case of the product of s by a measure. Hence the expression of the generator on $\mathcal{H}$ determines the distribution of the process.

Proof Consider a deterministic initial condition: $S_0 = s \in \mathbb{R}_+$ and $\nu_0 = \nu \in \mathcal{M}_F(\mathcal{X})$. First we suppose that $\nu \in \mathcal{M}(\mathcal{X})$. According to Proposition 4.1, to the fact that functions F, $\partial_s F$, $\partial_x F$, f' and ρ_{g} are bounded, to Corollaries 4.3 and 4.5 and Proposition 4.2:

$$\mathbb{E}\left(F\left(S_t, \langle \nu_t, f\rangle\right)\right) = F(s, \langle \nu, f\rangle) + \mathbb{E}(\Psi(t)),$$

where:

$$\begin{aligned}\Psi(t) \overset{\text{def}}{=} &\int_0^t \rho_{\text{s}}(S_u, \nu_u)\, \partial_s F(S_u, \langle \nu_u, f\rangle)\, \mathrm{d}u \\ &+ \int_0^t \langle \nu_u, \rho_{\text{g}}(S_u, .)\, f'\rangle\, \partial_x F(S_u, \langle \nu_u, f\rangle)\, \mathrm{d}u \\ &+ \int_0^t \int_{\mathcal{X}} \int_0^1 \lambda(S_u, x)\, \left[F\left(S_u, \langle \nu_u - \delta_x + \delta_{\alpha\, x} + \delta_{(1-\alpha)\, x}\,,\, f\rangle\right)\right. \\ &\left. - F(S_u, \langle \nu_u, f\rangle)\right]\, Q(\mathrm{d}\alpha)\, \nu_u(\mathrm{d}x)\, \mathrm{d}u \\ &+ D \int_0^t \int_{\mathcal{X}} \Big[F(S_u, \langle \nu_u - \delta_x, f\rangle) - F(S_u, \langle \nu_u, f\rangle)\Big]\, \nu_u(\mathrm{d}x)\, \mathrm{d}u.\end{aligned}$$

Also:

$$\begin{aligned}\frac{\partial}{\partial t}\Psi(t)\Big|_{t=0} &= \big(D(\mathbf{s}_{\text{in}} - s) - k\,\mu(s, \nu)\big)\, \partial_s F(s, \langle \nu, f\rangle) + \langle \nu, \rho_{\text{g}}(s, .)\, f'\rangle\, \partial_x F(s, \langle \nu, f\rangle) \\ &+ \int_{\mathcal{X}} \int_0^1 \lambda(s, x) \Big[F\left(s, \langle \nu - \delta_x + \delta_{\alpha\, x} + \delta_{(1-\alpha)\, x}, f\rangle\right) - F(s, \langle \nu, f\rangle)\Big]\, Q(\mathrm{d}\alpha)\, \nu(\mathrm{d}x) \\ &+ D \int_{\mathcal{X}} \Big[F(s, \langle \nu - \delta_x, f\rangle) - F(s, \langle \nu, f\rangle)\Big]\, \nu(\mathrm{d}x),\end{aligned}$$

hence:

$$\begin{aligned}\left|\frac{\partial}{\partial t}\Psi(t)\Big|_{t=0}\right| &\le D\,(\mathbf{s}_{\text{in}} + s) \\ &+ \left(\frac{k}{V}\, \bar{g}\, \|\partial_s F\|_\infty + \bar{g}\, \left\|f'\right\|_\infty\, \|\partial_x F\|_\infty + 2\,(\bar{\lambda} + D)\, \|F\|_\infty\right) \langle \nu, 1\rangle.\end{aligned}$$

The right side of the last equation is finite. One may apply the theorem of differentiation under the integral sign, hence the application $t \mapsto \mathbb{E}(F(S_t, \langle \nu_t, f\rangle))$ is differentiable at $t = 0$ with derivative $\mathcal{L}F(s, \langle \nu, f\rangle)$ defined by (12).

Suppose now that $\nu \in \mathcal{M}_F(\mathcal{X})$, then there exists a sequence $\{\nu^n\} \subset \mathcal{M}(\mathcal{X})$ that converges toward ν in $\mathcal{M}_F(\mathcal{X})$ and by continuity of $\nu \to \mathcal{L}F(s, \langle \nu, f\rangle)$ we obtain the result. □

Remark 4.7 We define the total washout time as the stopping time:

$$\tau_{\text{w}} \overset{\text{def}}{=} \inf\{t \ge 0 \quad N_t = \langle \nu_t, 1\rangle = 0\}$$

with the convention $\inf \emptyset = +\infty$. Before τ_{w} the infinitesimal generator is given by (12), after this time ν_t is the null measure, i.e. the chemostat does not contain any bacteria, and the infinitesimal generator is simply reduced to the generator associated with the ordinary differential equation $\dot{S}_t = D\,(\mathbf{s}_{\mathrm{in}} - S_t)$ coupled with the null measure given by $\langle \nu_t, f \rangle = 0$ for all f.

5 Convergence in Distribution of the Individual-Based Model

5.1 Renormalization

In this section we will prove that the coupled process of the substrate concentration and the bacterial population converges in distribution to a deterministic process in the space:

$$\mathcal{C}([0,T],\mathbb{R}_+) \times \mathcal{D}([0,T],\mathcal{M}_F(\mathcal{X}))$$

equipped with the product metric: (*i*) the uniform norm on $\mathcal{C}([0,T],\mathbb{R}_+)$; (*ii*) the Skorohod metric on $\mathcal{D}([0,T],\mathcal{M}_F(\mathcal{X}))$ where $\mathcal{M}_F(\mathcal{X})$ is equipped with the topology of the weak convergence of measures (see Appendix).

Renormalization must have the effect that the density of the bacterial population must grow to infinity. To this end, we first consider a growing volume, i.e. in the previous model the volume is replaced by:

$$V_n = n\,V$$

and $(S^n_t, \nu^n_t)_{t\geq 0}$ will denote the process (10) where V is replaced by V_n and $x^{n,1}_t, \dots, x^{n,N^n_t}_t$ the N^n_t individuals of ν^n_t; second we introduce the rescaled process:

$$\bar{\nu}^n_t \overset{\mathrm{def}}{=} \frac{1}{n}\,\nu^n_t\,, \quad t \geq 0 \tag{13}$$

and we suppose that:

$$\bar{\nu}^n_0 = \frac{1}{n}\,\nu^n_0 \xrightarrow[n\to\infty]{} \xi_0 \text{ in distribution in } \mathcal{M}_F(\mathcal{X}).$$

ξ_0 is the limit measure after renormalization of the population density at the initial time, we suppose that ξ_0 is deterministic and that $\langle \xi_0, 1 \rangle > 0$. We also suppose that $S^n_0 = S_0$ for all n where S_0 is deterministic.

Therefore, this asymptotic consists in simultaneously letting the volume of chemostat and the size of the initial population tend to infinity.

As the substrate concentration is maintained at the same value, it implies that the population tends to infinity. We will show that the rescaled process $(S^n_t, \bar{\nu}^n_t)_{t\geq 0}$ defined by (13) converges in distribution to the solution $(S_t, \xi_t)_{t\geq 0}$ of a deterministic system of equations.

The process $(S^n_t, \nu^n_t)_{t\geq 0}$ is defined by:

$$\begin{aligned}
\dot{S}^n_t &= D\,(\mathbf{s}_{\text{in}} - S^n_t) - \frac{k}{V_n}\int_X \rho_{\text{g}}(S^n_t, x)\,\nu^n_t(\mathrm{d}x) \\
&= D(\mathbf{s}_{\text{in}} - S^n_t) - \frac{k}{V}\int_X \rho_{\text{g}}(S^n_t, x)\,\bar{\nu}^n_t(\mathrm{d}x) = \rho_{\text{s}}(S^n_t, \bar{\nu}^n_t)
\end{aligned}$$

and

$$\begin{aligned}
\bar{\nu}^n_t &= \frac{1}{n}\sum_{j=1}^{n} \delta_{A^j_t(S^n_0, \nu^n_0)} \\
&+ \frac{1}{n}\iiiint\limits_{[0,t]\times\mathbb{N}^*\times[0,1]^2} 1_{\{i\leq N^n_{u-}\}}\,1_{\{0\leq\theta\leq\lambda(S^n_u, x^{n,i}_{u-})/\bar{\lambda}\}} \Bigg[-\sum_{j=1}^{N^n_{u-}} \delta_{A^j_{t-u}(S^n_u, \nu^n_{u-})} \\
&+ \sum_{j=1}^{N^n_{u-}+1} \delta_{A^j_{t-u}(S^n_u\,,\,\nu^n_{u-} - \delta_{x^{n,i}_{u-}} + \delta_{\alpha x^{n,i}_{u-}} + \delta_{(1-\alpha)x^{n,i}_{u-}})}\Bigg] N_1(\mathrm{d}u, \mathrm{d}i, \mathrm{d}\alpha, \mathrm{d}\theta) \\
&+ \frac{1}{n}\iint\limits_{[0,t]\times\mathbb{N}^*} 1_{\{i\leq N^n_{u-}\}} \Bigg[-\sum_{j=1}^{N^n_{u-}} \delta_{A^j_{t-u}(S^n_u, \nu^n_{u-})} + \sum_{j=1}^{N^n_{u-}-1} \delta_{A^j_{t-u}(S^n_u, \nu^n_{u-} - \delta_{x^{n,i}_{u-}})}\Bigg] N_2(\mathrm{d}u, \mathrm{d}i)
\end{aligned}$$

Remark 5.1 Due to the structure of the previous system and specifically the above equation, it will be sufficient to prove the convergence in distribution of the component $\bar{\nu}^n_t$ to deduce also the convergence of the component S^n_t.

We can now state the main result of this work:

Theorem 5.2 (Convergence of the IBM towards the IDE) *Suppose that the assumptions of Sect. 2 are fulfilled and that* $\mathbb{E}(\langle\bar{\nu}^n_0, 1\rangle^2) < \infty$ *for all n, then the process* $(S^n_t, \bar{\nu}^n_t)_{t\geq 0}$ *converges in distribution in the product space* $\mathcal{C}([0,T], \mathbb{R}_+) \times \mathcal{D}([0,T], \mathcal{M}_F(\mathcal{X}))$ *towards the solution* $(S_t, \xi_t)_{t\geq 0}$ *of the deterministic system of equations:*

$$S_t = S_0 + \int_0^t \left[D\,(\mathbf{s}_{\text{in}} - S_u) - \frac{k}{V}\int_{\mathcal{X}} \rho_{\text{g}}(S_u, x)\,\xi_u(\mathrm{d}x)\right]\mathrm{d}u\,, \tag{14}$$

$$\begin{aligned}
\langle\xi_t, f\rangle = \langle\xi_0, f\rangle + \int_0^t \Bigg[&\int_{\mathcal{X}} \rho_{\text{g}}(S_u, x)\, f'(x)\,\xi_u(\mathrm{d}x) \\
&+ \int_{\mathcal{X}}\int_0^1 \lambda(S_u, x)\Big[f(\alpha\,x) + f((1-\alpha)\,x) - f(x)\Big]\,Q(\mathrm{d}\alpha)\,\xi_u(\mathrm{d}x) \\
&- D\int_{\mathcal{X}} f(x)\,\xi_u(\mathrm{d}x)\Bigg]\mathrm{d}u\,,
\end{aligned} \tag{15}$$

for any $f \in C^1(\mathcal{X})$.

Sections 5.3 and 5.4 will be dedicated to the proof of this theorem, the link with the classic deterministic model is presented in the next subsection.

5.2 Link with the Classic Deterministic Model

Equation (15) is actually a weak version of an IDE that can be easily identified. Indeed suppose that the solution ξ_t of Eq. (15) admits a density $p_t(x)\,\mathrm{d}x = \xi_t(\mathrm{d}x)$, and that $Q(\mathrm{d}\alpha) = q(\alpha)\,\mathrm{d}\alpha$, then the system of Eqs. (14), (15) is a weak version of the following system:

$$\frac{\mathrm{d}}{\mathrm{d}t} S_t = D\,(\mathbf{s}_{\text{in}} - S_t) - \frac{k}{V}\int_{\mathcal{X}} \rho_{\text{g}}(S_t, x)\, p_t(x)\,\mathrm{d}x, \tag{16}$$

$$\begin{aligned}&\frac{\partial}{\partial t} p_t(x) + \frac{\partial}{\partial x}\big(\rho_{\text{g}}(S_t, x)\, p_t(x)\big) + \big(\lambda(S_t, x) + D\big)\, p_t(x)\\ &\quad = 2\int_{\mathcal{X}} \frac{\lambda(S_t, z)}{z}\, q\left(\frac{x}{z}\right)\, p_t(z)\,\mathrm{d}z.\end{aligned} \tag{17}$$

In fact, this is the population balance equation introduced by Fredrickson and co-authors [15,24] for growth-fragmentation models.

It is easy to link the model (16), (17) to the classic chemostat model. Indeed suppose that the growth function $x \mapsto \rho_{\text{g}}(s, x)$ is proportional to x, i.e.:

$$\rho_{\text{g}}(s, x) = \tilde{\mu}(s)\, x.$$

The results presented now are formal insofar as a linear growth function does not verify the assumptions made in this article. We introduce the bacterial concentration:

$$Y_t \overset{\text{def}}{=} \frac{1}{V}\int_{\mathcal{X}} x\, p_t(x)\,\mathrm{d}x.$$

As $\sup_{0\le t\le T}\langle p_t, 1\rangle < \infty$, from (17):

$$\begin{aligned}&\frac{\mathrm{d}}{\mathrm{d}t} Y_t - \frac{1}{V}\int_{\mathcal{X}} x\,\frac{\partial}{\partial x}\big(\rho_{\text{g}}(S_t, x)\, p_t(x)\big)\,\mathrm{d}x + \frac{1}{V}\int_{\mathcal{X}} x\,\lambda(S_t, x)\, p_t(x)\,\mathrm{d}x + D\,Y_t\\ &\quad = \frac{2}{V}\int_{\mathcal{X}} x\int_{\mathcal{X}} \frac{\lambda(S_t, z)}{z}\, q(x/z)\, p_t(z)\,\mathrm{d}z\,\mathrm{d}x\,,\end{aligned}$$

but

$$\begin{aligned}&\int_{\mathcal{X}} x\int_{\mathcal{X}} \frac{\lambda(S_t, z)}{z}\, q(x/z)\, p_t(z)\,\mathrm{d}z\,\mathrm{d}x\\ &\quad = \int_{\mathcal{X}}\int_0^1 z\,\lambda(S_t, z)\,\alpha\, q\,(\alpha)\;\; p_t(z)\,\mathrm{d}\alpha\,\mathrm{d}z\\ &\quad = \int_{\mathcal{X}}\int_0^1 z\,\lambda(S_t, z)\,\alpha\, q\,(1-\alpha)\;\; p_t(z)\,\mathrm{d}\alpha\,\mathrm{d}z \quad \text{(by symmetry of } q\text{)}\end{aligned}$$

$$
\begin{aligned}
&= \int_{\mathcal{X}} \int_0^1 z\, \lambda(S_t, z)\, (1-\alpha)\, q\,(\alpha)\;\; p_t(z)\, \mathrm{d}\alpha\, \mathrm{d}z \\
&= - \int_{\mathcal{X}} \int_0^1 z\, \lambda(S_t, z)\, \alpha\, q\,(\alpha)\;\; p_t(z)\, \mathrm{d}\alpha\, \mathrm{d}z + \int_{\mathcal{X}} z\, \lambda(S_t, z)\, p_t(z)\, \mathrm{d}z
\end{aligned}
$$

thus:

$$
2 \int_{\mathcal{X}} x \int_{\mathcal{X}} \frac{\lambda(S_t, z)}{z}\, q(x/z)\, p_t(z)\, \mathrm{d}z\, \mathrm{d}x = \int_{\mathcal{X}} z\, \lambda(S_t, z)\, p_t(z)\, \mathrm{d}z.
$$

The function $x \mapsto p_t(x)$ is the population density at time t. On the one hand $p_0(x)$ has compact support. On the other hand the growth of each bacterium is defined by a differential equation whose right-hand side is bounded by a linear function in x, uniformly in s. Hence for all $t \leq T$, we can uniformly bound the mass of all the bacteria and $p_t(x)$ has a compact support, i.e. there exists $m_{\max}$ such that the support of $p_t(x)$ is included in $[0, m_{\max}]$ with $p_t(m_{\max}) = 0$, so we choose $\mathcal{X} = [0, m_{\max}]$. Moreover $\rho_{\mathrm{g}}(S_t, 0) = 0$ hence:

$$
\int_{\mathcal{X}} x\, \frac{\partial}{\partial x}\big(\rho_{\mathrm{g}}(S_t, x)\, p_t(x)\big)\, \mathrm{d}x = - \int_{\mathcal{X}} \rho_{\mathrm{g}}(S_t, x)\, p_t(x)\, \mathrm{d}x.
$$

Finally:

$$
\frac{\mathrm{d}}{\mathrm{d}t} Y_t = \frac{1}{V} \int_{\mathcal{X}} \rho_{\mathrm{g}}(S_t, x)\, p_t(x)\, \mathrm{d}x - D\, Y_t = \tilde{\mu}(S_t)\, Y_t - D\, Y_t.
$$

We deduce that the concentrations $(Y_t, S_t)_{t \geq 0}$ of biomass and substrate are the solution of the following closed system of ordinary differential equations:

$$
\begin{aligned}
\dot{Y}_t &= \big(\tilde{\mu}(S_t) - D\big)\, Y_t\,, \\
\dot{S}_t &= D\,(\mathbf{s}_{\mathrm{in}} - S_t) - k\, \tilde{\mu}(S_t)\, Y_t
\end{aligned}
$$

which is none other than the classic chemostat equation [28].

5.3 Preliminary Results

Lemma 5.3 *For all $t > 0$,*

$$
\begin{aligned}
F(S^n_t, \langle \bar{\nu}^n_t, f\rangle) &= F(S^n_0, \langle \bar{\nu}^n_0, f\rangle) \\
&\quad + \int_0^t \Big(D\,(\mathbf{s}_{\mathrm{in}} - S^n_u) - \tfrac{k}{V} \int_X \rho_{\mathrm{g}}(S^n_u, x)\, \bar{\nu}^n_u(\mathrm{d}x)\Big)\, \partial_s F(S^n_u,\ \langle \bar{\nu}^n_u, f\rangle)\, \mathrm{d}u \\
&\quad + \int_0^t \langle \bar{\nu}^n_u, \rho_{\mathrm{g}}(S^n_u, .)\, f'\rangle\, \partial_x F(S^n_u,\ \langle \bar{\nu}^n_u, f\rangle)\, \mathrm{d}u \\
&\quad + n \int_0^t \int_{\mathcal{X}} \lambda(S^n_u, x) \int_0^1 \Big[F\big(S^n_u\,,\ \langle \bar{\nu}^n_u, f\rangle + \tfrac{1}{n} f(\alpha\, x) + \tfrac{1}{n} f((1-\alpha)\, x) - \tfrac{1}{n} f(x)\big)
\end{aligned}
$$

$$
\begin{aligned}
&- F\big(S_u^n, \langle \bar{\nu}_u^n, f\rangle\big)\Big]\, Q(\mathrm{d}\alpha)\, \bar{\nu}_u^n(\mathrm{d}x)\, \mathrm{d}u \\
&+ D\, n \int_0^t \int_{\mathcal{X}} \Big[F\big(S_u^n,\, \langle \bar{\nu}_u^n, f\rangle - \tfrac{1}{n} f(x)\big) - F\big(S_u^n,\, \langle \bar{\nu}_u^n, f\rangle\big)\Big]\, \bar{\nu}_u^n(\mathrm{d}x)\, \mathrm{d}u + Z_t^{F,f,n},
\end{aligned}
$$

where $Z_t^{F,f,n} = M_t^{1,F,f,n} + M_t^{2,F,f,n}$ *with:*

$$
\begin{aligned}
M_t^{1,F,f,n} &\overset{\mathit{def}}{=} \iiiint\limits_{[0,t]\times\mathbb{N}^*\times[0,1]^2} 1_{\{i\le N_{u-}^n\}}\, 1_{\{0\le\theta\le\lambda(S_u^n, x_{u-}^{n,i})/\bar{\lambda}\}} \\
&\qquad \Big[F\big(S_u^n,\, \langle \bar{\nu}_{u-}^n, f\rangle + \tfrac{1}{n} f(\alpha\, x_{u-}^{n,i}) + \tfrac{1}{n} f((1-\alpha)\, x_{u-}^{n,i}) - \tfrac{1}{n} f(x_{u-}^{n,i})\big) \\
&\qquad - F\big(S_u^n, \langle \bar{\nu}_{u-}^n, f\rangle\big)\Big]\, \tilde{N}_1(\mathrm{d}u, \mathrm{d}i, \mathrm{d}\alpha, \mathrm{d}\theta) \\
M_t^{2,F,f,n} &\overset{\mathit{def}}{=} \iint\limits_{[0,t]\times\mathbb{N}^*} 1_{\{i\le N_{u-}^n\}} \Big[F\big(S_u^n, \langle \bar{\nu}_{u-}^n, f\rangle - \tfrac{1}{n} f(x_{u-}^{n,i})\big) \\
&\qquad - F\big(S_u^n, \langle \bar{\nu}_{u-}^n, f\rangle\big)\Big]\, \tilde{N}_2(\mathrm{d}u, \mathrm{d}i)
\end{aligned}
$$

Proof It is sufficient to note that $F(S_t^n, \langle \bar{\nu}_t^n, f\rangle) = F(S_t^n, \langle \nu_t^n, \frac{1}{n} f\rangle)$ and to apply Proposition 4.1. ☐

Lemma 5.4 *If* $\sup_{n\in\mathbb{N}^*} \mathbb{E}(\langle \bar{\nu}_0^n, 1\rangle^p) < \infty$ *for some* $p \ge 1$, *then:*

$$
\sup_{n\in\mathbb{N}^*} \mathbb{E}\bigg(\sup_{u\in[0,t]} \langle \bar{\nu}_u^n, 1\rangle^p\bigg) < C_{t,p},
$$

where $C_{t,p}$ *depends only on* t *and* p.

This lemma will be used for $p = 1$.

Proof Define the stopping time:

$$
\tau_N^n \overset{\text{def}}{=} \inf\{t \ge 0,\, \langle \bar{\nu}_t^n, 1\rangle \ge N\}.
$$

According to Lemma 5.3 applied with $F(s, x) = x^p$ and $f(x) = 1$:

$$
\begin{aligned}
&\sup_{u\in[0,t\wedge\tau_N^n]} \langle \bar{\nu}_u^n, 1\rangle^p \le \langle \bar{\nu}_0^n, 1\rangle^p \\
&\quad + n \int_0^{t\wedge\tau_N^n} \int_{\mathcal{X}} \lambda(S_u^n, x)\, \Big[\big(\langle \bar{\nu}_u^n, 1\rangle + \tfrac{1}{n}\big)^p - \langle \bar{\nu}_u^n, 1\rangle^p\Big]\, \bar{\nu}_u(\mathrm{d}x)\, \mathrm{d}u + M_t^{1,F,f,n}
\end{aligned}
$$

From the inequality $(1+y)^p - y^p \le C_p\,(1+y^{p-1})$, one can easily check that $(\frac{1}{n}+y)^p - y^p \le \frac{C_p}{n}\,(1+y^{p-1})$. Taking expectation in the previous inequality and applying Proposition 4.2 (in the rescale conditions) lead to:

$$\begin{aligned}
&\mathbb{E}\left(\sup_{u\in[0,t\wedge\tau_N^n]}\langle\bar{\nu}_u^n,1\rangle^p\right)\\
&\leq \mathbb{E}\big(\langle\bar{\nu}_0^n,1\rangle^p\big)+\mathbb{E}\int_0^{t\wedge\tau_N^n} C_p\left(1+\langle\bar{\nu}_u^n,1\rangle^{p-1}\right)\int_{\mathcal{X}}\lambda(S_u^n,x)\,\bar{\nu}_u^n(\mathrm{d}x)\,\mathrm{d}u\\
&\leq \mathbb{E}\big(\langle\bar{\nu}_0^n,1\rangle^p\big)+\bar{\lambda}\,C_p\int_0^t\mathbb{E}\left(\langle\bar{\nu}_{u\wedge\tau_N^n}^n,1\rangle+\langle\bar{\nu}_{u\wedge\tau_N^n}^n,1\rangle^p\right)\mathrm{d}u.
\end{aligned}$$

As:

$$\langle\bar{\nu}_{u\wedge\tau_N^n}^n,1\rangle+\langle\bar{\nu}_{u\wedge\tau_N^n}^n,1\rangle^p\leq 2\left(1+\langle\bar{\nu}_{u\wedge\tau_N^n}^n,1\rangle^p\right),$$

we get:

$$\begin{aligned}
\mathbb{E}\left(\sup_{u\in[0,t\wedge\tau_N^n]}\langle\bar{\nu}_u^n,1\rangle^p\right)\leq&\,\mathbb{E}\left(\langle\bar{\nu}_0^n,1\rangle^p\right)+2\,\bar{\lambda}\,C_p\,t+2\,\bar{\lambda}\,C_p\\
&\times\int_0^t\mathbb{E}\left(\sup_{u\in[0,u\wedge\tau_N^n]}\langle\bar{\nu}_u^n,1\rangle^p\right)\mathrm{d}u
\end{aligned}$$

and from Gronwall's inequality we obtain:

$$\mathbb{E}\left(\sup_{u\in[0,t\wedge\tau_N^n]}\langle\bar{\nu}_u^n,1\rangle^p\right)\leq\left(\mathbb{E}(\langle\bar{\nu}_0^n,1\rangle^p)+2\,\bar{\lambda}\,C_p\,t\right)\exp(2\,\bar{\lambda}\,C_p\,t).$$

The sequence of stopping times τ_N^n tends to infinity as N tends to infinity for the same reasons as those set in the proof of Corollary 4.3. From Fatou's lemma we deduce:

$$\begin{aligned}
\mathbb{E}\left(\sup_{u\in[0,t]}\langle\bar{\nu}_u^n,1\rangle^p\right)&=\mathbb{E}\left(\liminf_{N\to\infty}\sup_{u\in[0,t\wedge\tau_N^n]}\langle\bar{\nu}_u^n,1\rangle^p\right)\\
&\leq\liminf_{N\to\infty}\mathbb{E}\left(\sup_{u\in[0,t\wedge\tau_N^n]}\langle\bar{\nu}_u^n,1\rangle^p\right)\\
&\leq\left(\mathbb{E}\left(\langle\bar{\nu}_0^n,1\rangle^p\right)+2\,\bar{\lambda}\,C_p\,t\right)\exp(2\,\bar{\lambda}\,C_p\,t)
\end{aligned}$$

and as $\sup_n\mathbb{E}\left(\langle\bar{\nu}_0^n,1\rangle^p\right)<\infty$, we deduce the proof of the lemma. □

Corollary 5.5 *Let $f \in C^1(\mathcal{X})$, suppose that $\mathbb{E}(\langle \bar\nu_0^n, 1\rangle^2) < \infty$, then for all $t > 0$:*

$$\begin{aligned}
\langle \bar\nu_t^n, f\rangle = \langle \bar\nu_0^n, f\rangle + \int_0^t \langle \bar\nu_u^n,\ \rho_{\mathrm{g}}(S_u^n, .)\, f'\rangle\,\mathrm{d}u \\
+ \int_0^t \int_{\mathcal{X}} \lambda(S_u^n, x) \int_0^1 \big[f(\alpha\, x) + f((1-\alpha)\, x) - f(x)\big]\, Q(\mathrm{d}\alpha)\, \bar\nu_u^n(\mathrm{d}x)\,\mathrm{d}u \\
- D \int_0^t \int_{\mathcal{X}} f(x)\, \bar\nu_u^n(\mathrm{d}x)\,\mathrm{d}u + Z_t^{F_0, f, n},
\end{aligned} \tag{18}$$

where $Z_t^{F_0,f,n} = Z_t^{F,f,n}$ with $F_0(s,x) = x$, that is:

$$\begin{aligned}
Z_t^{F_0,f,n} \overset{\mathit{def}}{=} \frac{1}{n} \iiiint\limits_{[0,t]\times\mathbb{N}^*\times[0,1]^2} 1_{\{i\le N_{u-}^n\}}\, 1_{\{0\le\theta\le\lambda(S_u^n, x_{u-}^{i,n})/\bar\lambda\}} \\
\times \Big[f(\alpha\, x_{u-}^{i,n}) + f((1-\alpha)\, x_{u-}^{i,n}) - f(x_{u-}^{i,n})\Big]\, \tilde N_1(\mathrm{d}u, \mathrm{d}i, \mathrm{d}\alpha, \mathrm{d}\theta) \\
- \frac{1}{n} \iint\limits_{[0,t]\times\mathbb{N}^*} 1_{\{i\le N_{u-}^n\}}\, f(x_{u-}^{i,n})\, \tilde N_2(\mathrm{d}u, \mathrm{d}i)
\end{aligned} \tag{19}$$

is a martingale with the following predictable quadratic variation:

$$\begin{aligned}
\langle Z^{F_0,f,n}\rangle_t = \frac{1}{n}\int_0^t \int_{\mathcal{X}} \lambda(S_u^n, x) \int_0^1 [f(\alpha\, x) + f((1-\alpha)\, x) - f(x)]^2 \\
\times\, Q(\mathrm{d}\alpha)\, \bar\nu_u^n(\mathrm{d}x)\,\mathrm{d}u + \frac{1}{n} D \int_0^t \int_{\mathcal{X}} f(x)^2\, \bar\nu_u^n(\mathrm{d}x)\,\mathrm{d}u.
\end{aligned} \tag{20}$$

Proof Equation (18) is obtained by applying Lemma 5.3 with $F = F_0$. Moreover as the random measures $\tilde N_1$ and $\tilde N_2$ are independent, we have:

$$\langle Z^{F_0,f,n}\rangle_t = \langle M^{1,F_0,f,n}\rangle_t + \langle M^{2,F_0,f,n}\rangle_t.$$

From Proposition 4.2 and Corollary 4.3 we deduce the proof of the corollary. □

Remark 5.6 The infinitesimal generator of the renormalized process $(S_t^n, \bar\nu_t^n)_{t\ge0}$ is:

$$\begin{aligned}
\mathcal{L}^n \Phi(s,\nu) \overset{\mathrm{def}}{=} \big(D(\mathbf{s}_{\mathrm{in}} - s) - k\,\mu(s,\nu)\big)\, \partial_s F(s, \langle\nu, f\rangle) + \langle \nu, \rho_{\mathrm{g}}(s, .)\, f'\rangle\, \partial_x F(s, \langle\nu, f\rangle) \\
+ n \int_{\mathcal{X}} \lambda(s,x) \int_0^1 \Big[F\big(s, \langle \nu - \tfrac{1}{n}\delta_x + \tfrac{1}{n}\delta_{\alpha\, x} + \tfrac{1}{n}\delta_{(1-\alpha)\, x}\,,\ f\rangle\big) - F(s, \langle\nu, f\rangle)\Big] \\
\times Q(\mathrm{d}\alpha)\, \nu(\mathrm{d}x) + n\, D \int_{\mathcal{X}} \Big[F\big(s, \langle \nu - \tfrac{1}{n}\delta_x\,,\ f\rangle\big) - F(s, \langle\nu, f\rangle)\Big]\, \nu(\mathrm{d}x)
\end{aligned}$$

for any $\Phi(s,\nu) = F(s, \langle\nu, f\rangle)$ with $F \in C_b^{1,1}(\mathbb{R}^+ \times \mathbb{R})$ and $f \in C^1(\mathcal{X})$. Note that this generator has the same "substrat" part than that of the initial generator (12) which again justifies the Remark 5.1.

5.4 Proof of Theorem 5.2

The proof is in three steps[1]: first the uniqueness of the solution of the limit Eqs. (14), (15), second the tightness (of the sequence of distribution) of $\bar\nu^n$ and lastly the convergence in distribution of the sequence.

Step 1: Uniqueness of the Solution of (14), (15)

Let $(S_t, \xi_t)_{t\geq 0}$ be a solution of (14), (15). We first show that $(\xi_t)_t$ is of finite mass for all $t \geq 0$:

$$\begin{aligned}\langle \xi_t, 1\rangle &= \langle \xi_0, 1\rangle + \int_0^t \int_{\mathcal{X}} \int_0^1 \lambda(S_u, x)\, Q(\mathrm{d}\alpha)\, \xi_u(\mathrm{d}x)\, \mathrm{d}u - D \int_0^t \int_{\mathcal{X}} \xi_u(\mathrm{d}x)\, \mathrm{d}u \\ &\leq \langle \xi_0, 1\rangle + (\bar\lambda - D) \int_0^t \langle \xi_u, 1\rangle\, \mathrm{d}u\end{aligned}$$

and according to Gronwall's inequality: $\langle \xi_t, 1\rangle \leq \langle \xi_0, 1\rangle\, e^{(\bar\lambda - D)\,t} < \infty$.

We introduce the following norm on $\mathcal{M}_F(\mathcal{X})$:

$$|||\bar\nu||| \overset{\text{def}}{=} \sup\Big\{ |\langle \bar\nu, f\rangle| \quad f \in C^1(\mathcal{X}),\ \|f\|_\infty \leq 1,\ \big\|f'\big\|_\infty \leq 1 \Big\}$$

and consider two solutions $(S^1_t, \xi^1_t)_{t\geq 0}$ and $(S^2_t, \xi^2_t)_{t\geq 0}$ of (14), (15).

It was previously shown that ξ^1_t and ξ^2_t are of finite mass on $\mathbb{R}_+$, so we can define:

$$C_t \overset{\text{def}}{=} \sup_{0\leq u\leq t} \langle \xi^1_u + \xi^2_u, 1\rangle.$$

According to (15), for any $f \in C^1(\mathcal{X})$ such that $\|f\|_\infty \leq 1$ and $\big\|f'\big\|_\infty \leq 1$ we have:

$$\begin{aligned}|\langle \xi^1_t - \xi^2_t, f\rangle| \leq &\int_0^t \bigg| \int_{\mathcal{X}} f'(x) \Big[\rho_{\mathrm{g}}(S^1_u, x)\, [\xi^1_u(\mathrm{d}x) - \xi^2_u(\mathrm{d}x)] \\ &- [\rho_{\mathrm{g}}(S^2_u, x) - \rho_{\mathrm{g}}(S^1_u, x)]\, \xi^2_u(\mathrm{d}x) \Big] \bigg|\, \mathrm{d}u \\ &+ \int_0^t \bigg| \int_{\mathcal{X}} \int_0^1 [f(\alpha\, x) + f((1-\alpha)\, x) - f(x)]\ Q(\mathrm{d}\alpha) \\ &\times \Big[\lambda(S^1_u, x)\, [\xi^1_u(\mathrm{d}x) - \xi^2_u(\mathrm{d}x)] - [\lambda(S^2_u, x) - \lambda(S^1_u, x)]\, \xi^2_u(\mathrm{d}x) \Big] \bigg|\, \mathrm{d}u\end{aligned}$$

---

[1] Note that our situation is simpler than that studied by Roelly-Coppoletta [26] and Mard and Roelly[19] since in our case $\mathcal{X}$ is compact: in fact in our case the weak topology—the smallest topology which makes the applications $\nu \to \langle \nu, f\rangle$ continuous for any f continuous and bounded—and the vague topology—the smallest topology which makes the applications $\nu \to \langle \nu, f\rangle$ continuous for all f continuous with compact support—are identical.

$$
\begin{aligned}
&+ D \int_0^t \left| \int_{\mathcal{X}} f(x)\,(\xi_u^1(\mathrm{d}x) - \xi_u^2(\mathrm{d}x)) \right| \mathrm{d}u \\
&\leq (\bar{g} + 3\,\bar{\lambda} + D) \int_0^t |||\xi_u^1 - \xi_u^2|||\,\mathrm{d}u + C_t\,(k_g + 3\,k_\lambda) \int_0^t |S_u^1 - S_u^2|\,\mathrm{d}u.
\end{aligned}
$$

Taking the supremum over the functions f, we obtain:

$$
|||\xi_t^1 - \xi_t^2||| \leq (\bar{g} + 3\,\bar{\lambda} + D) \int_0^t |||\xi_u^1 - \xi_u^2|||\,\mathrm{d}u + C_t\,(k_g + 3\,k_\lambda) \int_0^t |S_u^1 - S_u^2|\,\mathrm{d}u.
$$

Moreover, from (14) we get:

$$
\begin{aligned}
|S_t^1 - S_t^2| &\leq D \int_0^t |S_u^1 - S_u^2|\,\mathrm{d}u + \frac{k}{V} \int_0^t \left| \int_{\mathcal{X}} \Big(\rho_{\mathrm{g}}(S_u^1, x)\,[\xi_u^1(\mathrm{d}x) - \xi_u^2(\mathrm{d}x)] \right. \\
&\qquad \left. - [\rho_{\mathrm{g}}(S_u^2, x) - \rho_{\mathrm{g}}(S_u^1, x)]\,\xi_u^2(\mathrm{d}x) \Big) \right| \mathrm{d}u \\
&\leq \Big(D + \frac{k}{V}\,C_t\,k_g \Big) \int_0^t |S_u^1 - S_u^2|\,\mathrm{d}u + \frac{k}{V}\,\bar{g} \int_0^t |||\xi_u^1 - \xi_u^2|||\,\mathrm{d}u.
\end{aligned}
$$

We define:

$$
M_t \overset{\text{def}}{=} \max \left\{ \bar{g} + 3\,\bar{\lambda} + D + \frac{k}{V}\,\bar{g}\,,\; C_t\,(k_g + 3\,k_\lambda) + D + \frac{k}{V}\,C_t\,k_g \right\}
$$

hence:

$$
|||\xi_t^1 - \xi_t^2||| + |S_t^1 - S_t^2| \leq M_t \int_0^t \Big(|||\xi_u^1 - \xi_u^2||| + |S_u^1 - S_u^2| \Big)\,\mathrm{d}u
$$

Finally from Gronwall's inequality we get $|||\xi_t^1 - \xi_t^2||| + |S_t^1 - S_t^2| = 0$ for all $t \geq 0$, hence $\xi_t^1 = \xi_t^2$ and $S_t^1 = S_t^2$.

Step 2: Tightness of $(\bar{\nu}^n)_{n\in\mathbb{N}^*}$

The tightness of $\bar{\nu}^n$ is equivalent to the fact that from any subsequence one can extract a subsequence that converges in distribution in the space $\mathcal{D}([0, T], \mathcal{M}_F(\mathcal{X}))$. According to [26, Theorem 2.1] this amounts to proving the tightness of $\langle \bar{\nu}^n, f \rangle$ in $\mathcal{D}([0, T], \mathbb{R})$ for all f in a set dense in $\mathcal{C}(\mathcal{X})$, here we will consider $f \in \mathcal{C}^1(\mathcal{X})$. To prove the latter result, it is sufficient to check the following Aldous-Rebolledo criteria [18, Corollary 2.3.3]:

(i) The sequence $(\langle \bar{\nu}_t^n, f \rangle)_{n\in\mathbb{N}^*}$ is tight for any $t \geq 0$.
(ii) Consider the following semimartingale decomposition:

$$
\langle \bar{\nu}_t^n, f \rangle = \langle \bar{\nu}_0^n, f \rangle + A_t^n + Z_t^n,
$$

where Z_t^n is a short notation for the martingale $Z_t^{F_0,f,n}$ defined in (19) and A_t^n is of finite variation. For all $t>0$, $\epsilon>0$, $\eta>0$ there exists n_0 such that for any sequence τ_n of stopping times with $\tau_n\leq t$ we have:

$$\sup_{n\geq n_0}\sup_{\theta\in[0,\delta]}\mathbb{P}\Big(\big|A^n_{\tau_n+\theta}-A^n_{\tau_n}\big|\geq\eta\Big)\leq\epsilon\,,$$

$$\sup_{n\geq n_0}\sup_{\theta\in[0,\delta]}\mathbb{P}\Big(\big|\langle Z^n\rangle_{\tau_n+\theta}-\langle Z^n\rangle_{\tau_n}\big|\geq\eta\Big)\leq\epsilon.$$

Proof of (i)

For any $K>0$,

$$\mathbb{P}\big(|\langle\bar\nu_t^n,f\rangle|\geq K\big)\leq\frac{1}{K}\,\|f\|_\infty\sup_{n\in\mathbb{N}^*}\mathbb{E}\big(\langle\bar\nu_t^n,1\rangle\big)$$

and using Lemma 5.4, we deduce (i).

Proof of (ii)

$$\begin{aligned}A_t^n&=\int_0^t\langle\bar\nu_u^n,\rho_{\rm g}(S_u^n,.)\,f'\rangle\,{\rm d}u\\&\quad+\int_0^t\int_{\mathcal{X}}\int_0^1\lambda(S_u^n,x)\big[f(\alpha\,x)+f((1-\alpha)\,x)-f(x)\big]\,Q({\rm d}\alpha)\,\bar\nu_u^n({\rm d}x)\,{\rm d}u\\&\quad-D\int_0^t\int_{\mathcal{X}}f(x)\,\bar\nu_u^n({\rm d}x)\,{\rm d}u\end{aligned}$$

hence, according to Lemma 5.4:

$$\mathbb{E}|A^n_{\tau_n+\theta}-A^n_{\tau_n}|\leq(\big\|f'\big\|_\infty\,\bar g+3\,\|f\|_\infty\,\bar\lambda+D\,\|f\|_\infty)\,C_{t+\theta,1}\,\theta.$$

Using (20), we also have:

$$\mathbb{E}|\langle Z^n\rangle_{\tau_n+\theta}-\langle Z^n\rangle_{\tau_n}|\leq\frac{1}{n}\,\big(9\,\bar\lambda+D\big)\,\|f\|_\infty^2\,C_{t+\theta,1}\,\theta.$$

Hence $\mathbb{E}|A^n_{\tau_n+\theta}-A^n_{\tau_n}|+\mathbb{E}|\langle Z^n\rangle_{\tau_n+\theta}-\langle Z^n\rangle_{\tau_n}|\leq C\,\theta$ and we obtain (ii) from the Markov inequality.

In conclusion, from the Aldous-Rebolledo criteria, the sequence $(\bar\nu^n)_{n\in\mathbb{N}^*}$ is tight.

Step 3: Convergence of the Sequence $(\bar\nu^n)_{n\in\mathbb{N}^*}$

To conclude the proof of the theorem it is suffice to show that the sequence $(\bar\nu^n)_{n\in\mathbb{N}^*}$ has a unique accumulation point and that this point is equal to ξ described in Step 1. In order to characterize ξ, the solution of (15), we introduce, for any given $f \in C^1(\mathcal{X})$, the following function defined for all $\zeta \in \mathcal{D}([0,T], \mathbb{M}_F(\mathcal{X}))$:

$$\begin{aligned}\Psi_t(\zeta) \overset{\text{def}}{=} \langle \zeta_t, f\rangle - \langle \zeta_0, f\rangle - \int_0^t \bigg[\int_{\mathcal{X}} \rho_{\text{g}}(S^\zeta_u, x)\, f'(x)\, \zeta_u(\mathrm{d}x) \\ + \int_{\mathcal{X}} \int_0^1 \lambda(S^\zeta_u, x) \big[f(\alpha\, x) + f((1-\alpha)\, x) - f(x)\big]\, Q(\mathrm{d}\alpha)\, \zeta_u(\mathrm{d}x) \\ - D \int_{\mathcal{X}} f(x)\, \zeta_u(\mathrm{d}x)\bigg]\, \mathrm{d}u,\end{aligned} \tag{21}$$

where S^ζ_t is defined by:

$$S^\zeta_t \overset{\text{def}}{=} S_0 + \int_0^t \Big(D\,(\mathbf{s}_{\text{in}} - S^\zeta_u) - \frac{k}{V} \int_{\mathcal{X}} \rho_{\text{g}}(S^\zeta_u, x)\, \zeta_u(\mathrm{d}x)\Big)\, \mathrm{d}u. \tag{22}$$

Hence, if $\Psi_t(\zeta) = 0$ for all $t \geq 0$ and all $f \in C^1(\mathcal{X})$ then $(S^\zeta, \zeta) = (S, \xi)$ where (S, ξ) is the unique solution of (14), (15).

We consider a subsequence $\bar{\nu}^{n'}$ of $\bar{\nu}^n$ which converges in distribution in the space $\mathcal{D}([0,T], \mathbb{M}_F(\mathcal{X}))$ and $\tilde{\nu}$ its limit.

Sub-step 3.1: A.s. Continuity of the limit $\tilde{\nu}$.

Lemma 5.7 $\tilde{\nu}(\omega) \in \mathcal{C}([0,T], \mathbb{M}_F(\mathcal{X}))$ *for all* $\omega \in \Omega$ *a.s.*

Proof For any $f \in \mathcal{C}(\mathcal{X})$ such that $\|f\|_\infty \leq 1$:

$$\big|\langle \bar{\nu}^{n'}_t, f\rangle - \langle \bar{\nu}^{n'}_{t-}, f\rangle\big| \leq \frac{1}{n'}\,\big|\langle \nu^{n'}_t, 1\rangle - \langle \nu^{n'}_{t-}, 1\rangle\big|.$$

But $|\langle \nu^{n'}_t, 1\rangle - \langle \nu^{n'}_{t-}, 1\rangle|$ represents the difference between the number of individuals in $\nu^{n'}_t$ and in $\nu^{n'}_{t-}$, which is at most 1. Hence:

$$\sup_{t\in[0,T]} \|\bar{\nu}^{n'}_t - \bar{\nu}^{n'}_{t-}\|_{\text{TV}} \leq \frac{1}{n'}$$

which proves that the limit process $\tilde{\nu}$ is a.s. continuous [12, Theorem 10.2 p. 148] as the Prokhorov metric is dominated by the total variation metric. □

Sub-step 3.2: Continuity of $\zeta \to \Psi_t(\zeta)$ in any ζ continuous.

Lemma 5.8 *For any given* $t \in [0,T]$ *and* $f \in C^1(\mathcal{X})$*, the function* Ψ_t *defined by* (21) *is continuous from* $\mathcal{D}([0,T], \mathcal{M}_F(\mathcal{X}))$ *with values in* $\mathbb{R}$ *in any point* $\zeta \in \mathcal{C}([0,T], \mathcal{M}_F(\mathcal{X}))$.

Proof Consider a sequence $(\zeta^n)_{n\in\mathbb{N}}$ which converges towards ζ in $\mathcal{D}([0,T],\mathcal{M}_F(\mathcal{X}))$ with respect to the Skorohod topology. As the limit ζ is continuous we have that ζ^n converges to ζ with the uniform topology:

$$\sup_{0\le t\le T} d_{\text{PR}}(\zeta_t^n,\zeta_t)\underset{n\to\infty}{\to}0,$$

where d_{PR} is the Prokhorov metric (see Appendix).

The functions $\lambda(s,x)$ and $\rho_{\text{g}}(s,x)$ are Lipschitz continuous functions w.r.t. s uniformly in x and also bounded, see (5) and (4), so from (22) we can easily check that:

$$\begin{aligned}|S_t^{\zeta^n}-S_t^{\zeta}| &\le C\int_0^t\Big(|S_u^{\zeta^n}-S_u^{\zeta}|+\Big|\int_{\mathcal{X}}\rho_{\text{g}}(S_u^{\zeta^n},x)\,[\zeta_u^n(\mathrm{d}x)-\zeta_u(\mathrm{d}x)]\\&\quad-\int_{\mathcal{X}}[\rho_{\text{g}}(S_u^{\zeta},x)-\rho_{\text{g}}(S_u^{\zeta^n},x)]\,\zeta_u(\mathrm{d}x)\Big|\Big)\,\mathrm{d}u\\&\le C\int_0^t\Big(|S_u^{\zeta^n}-S_u^{\zeta}|+|\langle\zeta_u^n-\zeta_u,1\rangle|\Big)\,\mathrm{d}u\end{aligned}$$

and the Gronwall's inequality leads to:

$$|S_t^{\zeta^n}-S_t^{\zeta}|\le C\int_0^t|\langle\zeta_u^n-\zeta_u,1\rangle|\,\mathrm{d}u.$$

Here and in the rest of the proof the constant C will depend only on T, f and on the parameters of the models. Hence, from (21):

$$\begin{aligned}|\Psi_t(\zeta^n)-\Psi_t(\zeta)| &\le C\Big[|\langle\zeta_t^n-\zeta_t,1\rangle|+|\langle\zeta_0^n-\zeta_0,1\rangle|\\&\quad+\int_0^t|S_u^{\zeta^n}-S_u^{\zeta}|\,\mathrm{d}u+\int_0^t|\langle\zeta_u^n-\zeta_u,1\rangle|\,\mathrm{d}u\Big]\\&\le C\sup_{0\le t\le T}|\langle\zeta_t^n-\zeta_t,1\rangle|.\end{aligned}$$

Let $\delta_t=d_{\text{PR}}(\zeta_t^n,\zeta_t)$, by definition of the Prokhorov metric:

$$\zeta_t^n(\mathcal{X})-\zeta_t(\mathcal{X}^{\delta_t})\le\delta_t,\quad\zeta_t(\mathcal{X})-\zeta_t^n(\mathcal{X}^{\delta_t})\le\delta_t,$$

but $\mathcal{X}^{\delta_t}=\mathcal{X}$ hence $|\zeta_t^n(\mathcal{X})-\zeta_t(\mathcal{X})|\le\delta_t$. Note finally that $|\zeta_t^n(\mathcal{X})-\zeta_t(\mathcal{X})|=|\langle\zeta_t^n-\zeta_t,1\rangle|$, so we get:

$$|\Psi_t(\zeta^n)-\Psi_t(\zeta)|\le C\sup_{0\le t\le T}d_{\text{PR}}(\zeta_t^n,\zeta_t)$$

which tends to zero. □

Sub-step 3.3: Convergence in Distribution of $\Psi_t(\bar{\nu}^{n'})$ *to* $\Psi_t(\tilde{\nu})$.

The sequence $\bar{\nu}^{n'}$ converges in distribution to $\tilde{\nu}$ and $\tilde{\nu}(\omega) \in \mathcal{C}([0,T],\mathcal{M}_F(\mathcal{X}))$; moreover the application Ψ_t is continuous in any point of $\mathcal{C}([0,T],\mathcal{M}_F(\mathcal{X}))$, thus according to the continuous mapping theorem [2, Theorem 2.7 p. 21] we get:

$$\Psi_t(\bar{\nu}^{n'}) \xrightarrow[n\to\infty]{\text{loi}} \Psi_t(\tilde{\nu}). \tag{23}$$

Sub-step 3.4: $\tilde{\nu} = \xi$ *a.s.*

From (18), for any $n \in \mathbb{N}^*$ we have:

$$\Psi_t(\bar{\nu}^n) = Z_t^n.$$

Also, (20) gives:

$$\mathbb{E}(|Z_t^n|^2) = \mathbb{E}\langle Z^n\rangle_t \leq \frac{1}{n}\,(9\,\bar{\lambda} + D)\;\|f\|_\infty^2\; C_{t,1}\,t.$$

Hence $\Psi_t(\bar{\nu}^n)$ converges to 0 in L^2 but also in L^1. Furthermore, we easily show that:

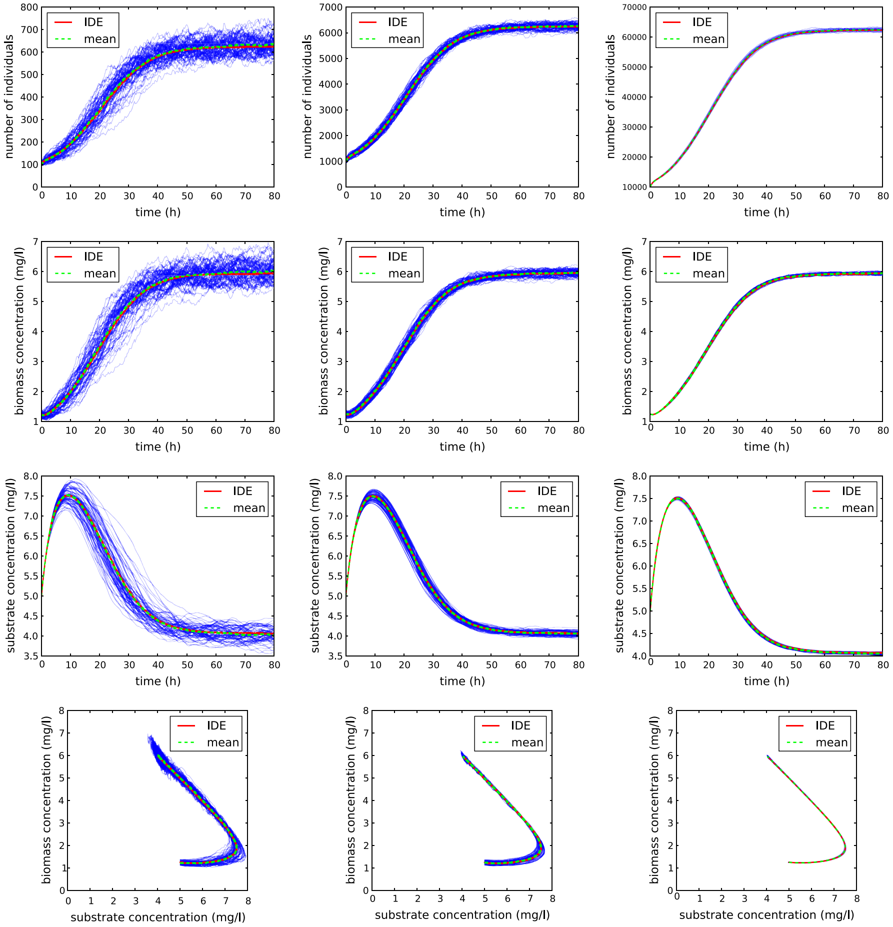
$$|\Psi_t(\zeta)| \leq C_{f,t} \sup_{0\leq u\leq t} \langle \zeta_u, 1\rangle$$

moreover, from Lemma 5.4, $(\Psi_t(\bar{\nu}^{n'}))_{n'}$ is uniformly integrable. The dominated convergence theorem and (23) imply:

$$0 = \lim_{n'\to\infty} \mathbb{E}|\Psi_t(\bar{\nu}^{n'})| = \mathbb{E}|\Psi_t(\tilde{\nu})|.$$

Table 1 Simulation parameters

Parameters	Values
D	$0.2\,\mathrm{h}^{-1}$
S_0	$5\,\mathrm{mg\,l}^{-1}$
$\mathbf{s}_{\mathrm{in}}$	$10\,\mathrm{mg\,l}^{-1}$
$m_{\max}$	0.001 mg
m_{div}	0.0004 mg
$\bar{\lambda}$	$1\,\mathrm{h}^{-1}$
p_λ	1,000
p_β	7
$r_{\max}$	$1\,\mathrm{h}^{-1}$
k_r	$10\,\mathrm{mg\,l}^{-1}$
k	1



small population size
$V = 0.05$ l, $N_0 = 100$

medium population size
$V = 0.5$ l, $N_0 = 1000$

large population size
$V = 5$ l, $N_0 = 10000$

Fig. 1 From *top to bottom* time evolutions of the population size, the biomass concentration, the concentration substrate and the concentrations phase portrait for the three levels of population sizes (small, medium and large). The *blue curves* represent the trajectories of 60 independent runs of IBM. The *green curve* represents the mean value of these runs. The *red curve* represents the solution of the IDE (Color figure online)

So $\Psi_t(\tilde{\nu}) = 0$ a.s. and $\tilde{\nu}$ is a.s. equal to ξ where (S, ξ) is the unique solution of (14)-(15).

This last step concludes the proof of Theorem 5.2.

6 Simulations

In this section we compare the behavior of the IBM and the IDE model (16), (17). The resolution of the IDE was made following classic finite difference schemes [3].

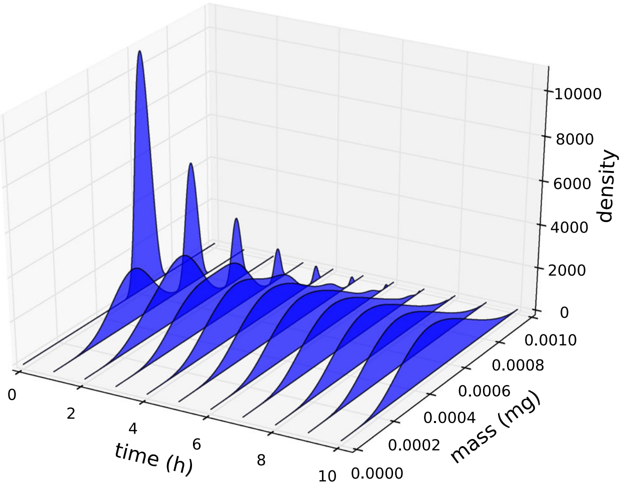


Fig. 2 Time evolution of the normalized mass distribution for the IDE (17): we represent the simulation until time $T = 10$ (h) only to illustrate the transient phenomenon due to the choice of the initial distribution (24). After a few iterations in time this distribution is bimodal, the upped mode growths in mass and disappears before $T = 10$ (h)

In the simulations proposed in this section, the division rate of an individual is given by the following function:

$$\lambda(s, x) = \frac{\bar{\lambda}}{\log\big((m_{\max} - m_{\text{div}})\, p_\lambda + 1\big)}\, \log\big((x - m_{\text{div}})\, p_\lambda + 1\big)\, 1_{\{x \geq m_{\text{div}}\}}$$

which does not depend on the substrate concentration.

The division kernel $Q(\mathrm{d}\alpha) = q(\alpha)\,\mathrm{d}\alpha$ is given by a symmetric beta distribution:

$$q(\alpha) = \frac{1}{B(p_\beta)}\, \big(\alpha\,(1-\alpha)\big)^{p_\beta - 1},$$

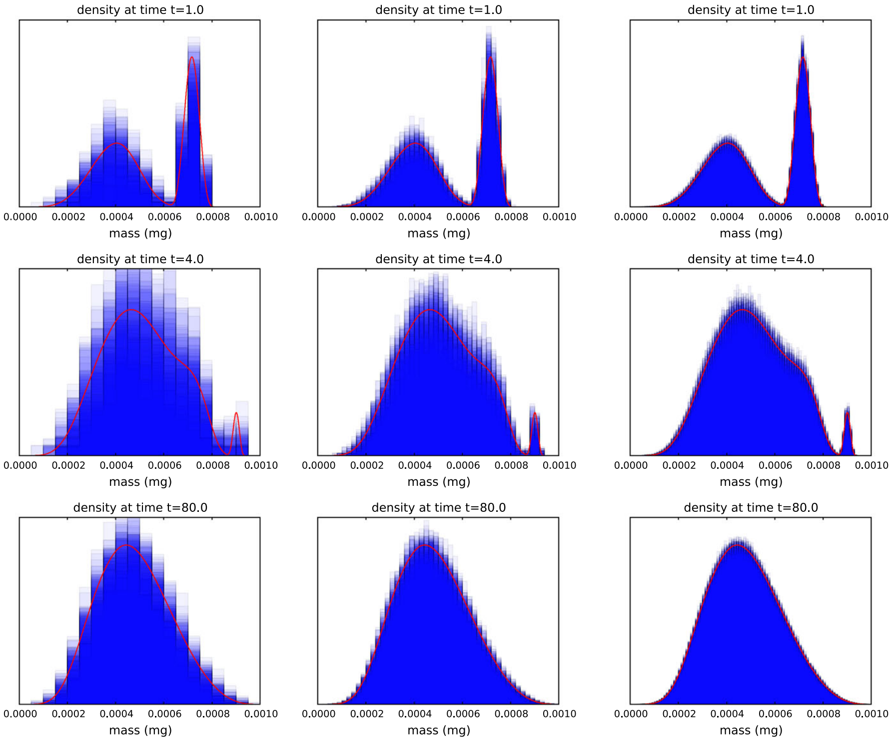
where $B(p_\beta) = \int_0^1 \big(\alpha\,(1-\alpha)\big)^{p_\beta-1}\,\mathrm{d}\alpha$ is a normalizing constant.

Individual growth follows a Gompertz model, with a growth rate depending on the substrate concentration:

$$g(s, x) = r_{\max}\, \frac{s}{k_r + s}\, \log\left(\frac{m_{\max}}{x}\right) x.$$

The masses of individuals at the initial time are sampled according to the following probability density function:

$$d(x) = \text{cst} \times \left(\frac{x - 0.0005}{0.00025}\left(1 - \frac{x - 0.0005}{0.00025}\right)\right)^5 1_{\{0.0005 < x < 0.00075\}}. \qquad (24)$$



small population size $V = 0.05$ l, $N_0 = 100$

medium population size $V = 0.5$ l, $N_0 = 1000$

large population size $V = 5$ l, $N_0 = 10000$

Fig. 3 Mass distribution for the time $t = 1$ (*above*), $t = 4$ (*middle*) and $t = 80$ (*bottom*) in small (*left*), medium (*middle*) and large (*right*) population size. For each graph, the *blue* histograms represent the empirical mass distributions of individuals for the 60 independent runs of IBM. In order to plot the histogram we have adapted the number of bins according to the population size. The *red curve* represents the mass distribution given by the IDE. Again the convergence of the IBM solution to the IDE in large population limit is observed (Color figure online)

The simulations were performed using the parameters in Table 1. The parameters V and N_0 will be specified for each simulation.

To illustrate the convergence in large population asymptotic of the IBM to the IDE, we performed simulations at different levels of population size. To this end we vary the volume of the chemostat and the number of individuals at the initial time. We considered three cases:

(i) small size: $V = 0.05$ l and $N_0 = 100$,
(ii) medium size: $V = 0.5$ l and $N_0 = 1{,}000$,
(iii) large size: $V = 5$ l and $N_0 = 10{,}000$.

In each of these three cases, and with the same initial biomass concentration distribution, we simulate: 60 independent runs of the IBM and the numerical approximation of (16), (17) using the finite difference schemes detailed in [3].

The convergence of IBM to EID is clearly illustrated in Fig. 1 where the evolutions of the population size, of the biomass concentration, and of the substrate concentration are represented.

In Fig. 2 the time evolution of the normalized mass distribution is depicted, i.e. the normalized solution of the IDE (17). We have represented the simulation until time $T = 10$ (h) to illustrate the transient phenomenon due to the choice of the initial distribution (24): after a few time iterations this distribution is bimodal; the upper mode (large mass) grows in mass and disappears before time $T = 10$ (h). The lower mode (small mass) corresponds to the mass of the bacteria resulting from the division; the upper mode corresponds to the mass of the bacteria from the initial bacteria before their division. Thus, the upper mode is set to disappear quickly by division or by washout. The IBM realizes this phenomenon, see Fig. 3.

Figure 3 presents this normalized mass distribution at three different instants, $t = 1,\ 4,\ 80$ (h), and the simulation of the IDE is compared to 60 independent runs of the IBM, again for the three levels of population sizes described above. Depending on whether the population is large, medium or small, we needed to adapt the number of bins of the histograms so that the resulting graphics are clear. The convergence of the IBM solution to the IDE in large population limit can be observed.

In conclusion, the IBM converges in large population limit to the IDE and variability "around" the asymptotic model is relatively large in small or medium population size; note that there is no reason why the IDE represents the mean value of the IBM.

Acknowledgments The authors are grateful to Jme Harmand and Claude Lobry for discussions on the model, to Pierre Pudlo and Pascal Neveu for their help concerning the programming of the IBM. This work is partially supported by the project "Modles Numriques pour les cosystmes Microbiens" of the French National Network of Complex Systems (RNSC call 2012). The work of Coralie Fritsch is partially supported by the Meta-omics of Microbial Ecosystems (MEM) metaprogram of INRA.

Appendix: Skorohod Topology

The space of finite measures $\mathcal{M}_F(\mathcal{X})$ on $\mathcal{X}$ is equipped with the topology of the weak convergence, that is the smallest topology for which the applications $\zeta \to \langle \zeta, f\rangle = \int_{\mathcal{X}} f(x)\,\zeta(\mathrm{d}x)$ are continuous for any $f \in \mathcal{C}(\mathcal{X})$. This topology is metrized by the Prokhorov metric:

$$d_{\text{PR}}(\zeta,\zeta') \overset{\text{def}}{=} \inf\Big\{\epsilon > 0 \quad \zeta(F) \le \zeta'(F^\epsilon) + \epsilon \\ \zeta'(F) \le \zeta(F^\epsilon) + \epsilon\,, \quad \text{for all closed } F \subset \mathcal{X}\Big\},$$

where $F^\epsilon \overset{\text{def}}{=} \{x \in \mathcal{X};\, \inf_{y\in F}|x-y| < \epsilon\}$ (see [7, Appendix A2.5]). The Prokhorov distance is bounded by the distance of the total variation $d_{\text{TV}}(\zeta,\zeta') = \|\zeta - \zeta'\|_{\text{TV}}$ associated with the norm defined by:

$$\|\zeta\|_{\text{TV}} \overset{\text{def}}{=} \sup_{A\in\mathcal{B}(\mathcal{X})} |\zeta(A) + \zeta(A^c)| = \zeta_+(\mathcal{X}) + \zeta_-(\mathcal{X}) = \sup_{\substack{f \text{ continuous} \\ \|f\|_\infty \le 1}} |\langle \zeta, f\rangle|$$

for any finite and signed measure ζ where $\zeta = \zeta_+ - \zeta_-$ is the Hahn–Jordan decomposition of ζ.

The space $\mathcal{D}([0,T], \mathcal{M}_F(\mathcal{X}))$ is equipped with the Skorohod metric $d_{\rm S}$. Instead of giving the definition of this metric [12, Eq. (5.2) p. 117] we recall a characterization of the convergence for this metric given in [12, Proposition 5.3, p. 119].

A sequence $(\zeta^n)_{n\in\mathbb{N}}$ converges to ζ in $\mathcal{D}([0,T], \mathcal{M}_F(\mathcal{X}))$, i.e. $d_{\rm S}(\zeta^n, \zeta) \to 0$, if and only if there exists a sequence $\lambda_n(t)$ of time change functions (i.e. strictly increasing bijective functions on $[0,T]$, with $\lambda_n(0) = 0$ and $\lambda_n(T) = T$) satisfying:

$$\sup_{0\le t\le T} d_{\rm PR}(\zeta_t^n, \zeta_{\lambda_n(t)}) \xrightarrow[n\to\infty]{} 0 \tag{25}$$

and

$$\sup_{0\le t\le T} |\lambda_n(t) - t| \to 0. \tag{26}$$

If $(\zeta^n)_{n\in\mathbb{N}}$ converges to ζ in $\mathcal{D}([0,T], \mathcal{M}_F(\mathcal{X}))$ and if $\zeta \in \mathcal{C}([0,T], \mathcal{M}_F(\mathcal{X}))$ then in:

$$\sup_{0\le t\le T} d_{\rm PR}(\zeta_t^n, \zeta_t) \le \sup_{0\le t\le T} d_{\rm PR}(\zeta_t^n, \zeta_{\lambda_n(t)}) + \sup_{0\le t\le T} d_{\rm PR}(\zeta_{\lambda_n(t)}, \zeta_t)$$

the first term of the right-hand side tends to 0 because of (25); the second one tends to 0 because of (26) and the uniform continuity of ζ in $[0,T]$. This proves that ζ^n converges to ζ in $\mathcal{D}([0,T], \mathcal{M}_F(\mathcal{X}))$ also for the uniform metric.

References

1. Allen, L.J.: An Introduction to Stochastic Processes with Biology Applications. Prentice Hall, Upper Saddle River (2003)
2. Billingsley, P.: Convergence of Probability Measures. John Wiley & Sons, New York (1968)
3. Campillo, F., Fritsch, C.: A mass-structured individual-based model of the chemostat: convergence and simulation. ArXiv Mathematics e-prints. arXiv:1308.2411 [math.ST] (2013)
4. Campillo, F., Joannides, M., Larramendy-Valverde, I.: Stochastic modeling of the chemostat. Ecol. Model. **222**(15), 2676–2689 (2011)
5. Champagnat, N.: A microscopic interpretation for adaptive dynamics trait substitution sequence models. Stoch. Process. Appl. **116**(8), 1127–1160 (2006)
6. Champagnat, N., Jabin, P.-E., Méléard, S.: Adaptation in a stochastic multi-resources chemostat model. J. Math. Pure. Appl. **101**(6), 755–788 (2014)
7. Daley, D., Vere-Jones, D.: An Introduction to the Theory of Point Processes: Volume I: Elementary Theory and Methods, 2nd edn. Springer, New York (2003)
8. Daoutidis, P., Henson, M.A.: Dynamics and control of cell populations in continuous bioreactors. AIChE Symp. Ser. **326**, 274–289 (2002)
9. Donald, A.: Dawson. Measure-valued markov processes. In: Hennequin, P.-L. (ed.) École d'Été de Probabilités de Saint-Flour XXI–1991. Lecture Notes in Mathematics, vol. 1541, pp. 1–250. Springer-Verlag, Berlin (1993)
10. DeAngelis, Donald L., Gross, Louis J. (eds.): Individual-based models and approaches in ecology: populations, communities and ecosystems. Chapman and Hall, New York (1992)
11. Diekmann, O., Jabin, P.-E., Mischler, S., Perthame, B.: The dynamics of adaptation: an illuminating example and a Hamilton–Jacobi approach. Theor. Popul. Biol. **67**(4), 257–271 (2005)

12. Ethier, S.N., Kurtz, T.G.: Markov Processes: Characterization and Convergence. John Wiley & Sons, New York (1986)
13. Finkelshtein, D., Kondratiev, Y., Kutoviy, O.: Kutoviy. Individual based model with competition in spatial ecology. SIAM J. Math. Anal. **41**, 297–317 (2009)
14. Fournier, N., Méléard, S.: A microscopic probabilistic description of a locally regulated population and macroscopic approximations. Ann. Appl. Probab. **14**(4), 1880–1919 (2004)
15. Fredrickson, A.G., Ramkrishna, D., Tsuchiya, H.M.: Statistics and dynamics of procaryotic cell populations. Math. Biosci. **1**(3), 327–374 (1967)
16. Henson, M.A.: Dynamic modeling and control of yeast cell populations in continuous biochemical reactors. Comput. Chem. Eng. **27**(8–9), 1185–1199 (2003)
17. Ikeda, N., Watanabe, S.: Stochastic Differential Equations and Diffusion Processes. North-Holland/Kodansha, Tokyo (1981)
18. Joffe, A., Métivier, M.: Weak convergence of sequences of semimartingales with applications to multitype branching processes. Adv. Appl. Probab. **18**, 20–65 (1986)
19. Méléard, S., Roelly, S.: Sur les convergences étroite ou vague de processus à valeurs mesures. C. R. Acad. Sci. Paris Sér. **1**(317), 785–788 (1993)
20. Mirrahimi, S., Perthame, B., Wakano, J.Y.: Direct competition results from strong competition for limited resource. J. Math. Biol. **68**(4), 931–949 (2014)
21. Mirrahimi, S., Perthame, B., Wakano, J.Y.: Evolution of species trait through resource competition. J. Math. Biol. **64**(7), 1189–1223 (2012)
22. Monod, J.: La technique de culture continue, théorie et applications. Ann. Inst. Pasteur **79**(4), 390–410 (1950)
23. Novick, A., Szilard, L.: Description of the chemostat. Science **112**(2920), 715–716 (1950)
24. Ramkrishna, D.: Statistical Models of Cell Populations. Advances in Biochemical Engineering, vol. 11, pp. 1–47. Springer, Berlin (1979)
25. Ramkrishna, D.: Population Balances: Theory and Applications to Particulate Systems in Engineering. Elsevier Science, San Diego (2000)
26. Roelly-Coppoletta, S.: A criterion of convergence of measure-valued processes: application to measure branching processes. Stochastics **17**(1–2), 43–65 (1986)
27. Rüdiger, B., Ziglio, G.: Itô formula for stochastic integrals w.r.t. compensated Poisson random measures on separable Banach spaces. Stoch. Int. J. Probab. Stoch. Process. **78**(6), 377–410 (2006)
28. Smith, H.L., Waltman, P.E.: The Theory of the Chemostat: Dynamics of Microbial Competition. Cambridge University Press, Cambridge (1995)
29. Tran, V.C.: Modèles particulaires stochastiques pour des problèmes d'évolution adaptative et pour l'approximation de solutions statistiques. PhD thesis, Université de Nanterre - Paris X (2006)
30. Tran, V.C.: Large population limit and time behaviour of a stochastic particle model describing an age-structured population. ESAIM **12**, 345–386 (2008)