A host-parasite multilevel interacting process and continuous approximations

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Abstract

We are interested in modeling some two-level population dynamics, resulting from the interplay of ecological interactions and phenotypic variation of individuals (or hosts) and the evolution of cells (or parasites) of two types living in these individuals. The ecological parameters of the individual dynamics depend on the number of cells of each type contained by the individual and the cell dynamics depends on the trait of the invaded individual.

Our models are rooted in the microscopic description of a random (discrete) population of individuals characterized by one or several adaptive traits and cells characterized by their type. The population is modeled as a stochastic point process whose generator captures the probabilistic dynamics over continuous time of birth, mutation and death for individuals and birth and death for cells. The interaction between individuals (resp. between cells) is described by a competition between individual traits (resp. between cell types). We look for tractable large population approximations. By combining various scalings on population size, birth and death rates and mutation step, the single microscopic model is shown to lead to contrasting nonlinear macroscopic limits of different nature: deterministic approximations, in the form of ordinary, integro- or partial differential equations, or probabilistic ones, like stochastic partial differential equations or superprocesses. The study of the long time behavior of these processes seems very hard and we only develop some simple cases enlightening the difficulties involved.

Key-words: two-level interacting processes, birth-death-mutation-competition point process, host-parasite stochastic particle system, nonlinear integro-differential equations, nonlinear partial differential equations, superprocesses.

1 Introduction

In this paper, we are interested in describing the adaptive effects in a host-parasite system. We model two-level population dynamics resulting from the interplay of ecological interactions and phenotypic variation of individuals (or hosts) and the evolution of cells (or

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parasites) of two types living in these individuals. In one hand, the ecological parameters of the individual dynamics depend on its number of cells of each type. In another hand, the cells develop their own birth and death dynamics and their ecological parameters depend on the trait of the invaded individual.

We consider more precisely the following two-level population. The first level is composed of individuals governed by a mutation-birth and death process. Moreover each individual is a collection of cells of two types (types 1 and 2) which have their own dynamics and compose the second level. The model can easily be generalized to cells with a finite number of different types. We denote by n_1^i (resp. by n_2^i) the number of cells of type 1 (resp. of type 2) living in the individual i. This individual is moreover characterized by a continuous quantitative phenotypic trait x^i. The individual i can be removed or copied according a birth-and-death process depending on x^i, n_1^i, n_2^i. An offspring usually inherits the trait values of her progenitor except when a mutation occurs during the reproduction mechanism. In this case the offspring makes an instantaneous mutation step at birth to new trait value. The death of an individual can be natural or can be due to the competition exerted by the other individuals, for example sharing food. This competition between individuals through their traits will induce a nonlinear convolution term. The cells in the individual i also reproduce and remove according to another birth-and-death process, depending on x^i, n_1^i, n_2^i. At this second level, cell competition occurs and its pressure depends on the invaded individual trait.

Our model generalizes some approach firstly developed in Dawson and Hochberg [3] and in Wu [11], [12]. In these papers, a two-level system is studied: individuals and cells follow a branching dynamics but there is no interaction between individuals and between cells. Thus all the specific techniques these authors use - as Laplace transforms - are no more available for our model.

In this paper, we firstly rigorously construct the underlying mathematical model and prove its existence. Thus we obtain moment and martingale properties which are the key point to deduce approximations for large individual and cell populations. By combining various scalings on population size, birth and death rates and mutation step, the single microscopic model is shown to lead to contrasting macroscopic limits of different nature: deterministic approximations, in the form of ordinary, integro- or partial differential equations, or probabilistic ones, like stochastic partial differential equations or superprocesses. The study of the long time behavior of these processes seems very hard and we only develop some simple cases enlightening the difficulties involved.

2 Population point process

2.1 The model

We model the evolving population by a stochastic interacting individual system, where each individual i is characterized by a vector phenotypic trait value x^i and by the number of its cells of type 1, n_1^i, and of type 2, n_2^i. The trait space $\mathcal{X}$ is assumed to be a compact subset of $\mathbb{R}^d$, for some $d \geq 1$. We denote by $M_F = M_F(\mathcal{X} \times \mathbb{N} \times \mathbb{N})$ the set of finite non-negative measures on $\mathcal{X} \times \mathbb{N} \times \mathbb{N}$, endowed with the weak topology. Let also $\mathcal{M}$ be the subset of M_F consisting of all finite point measures:

$$\mathcal{M} = \left\{ \sum_{i=1}^{I} \delta_{(x^i, n_1^i, n_2^i)},\ x^i \in \mathcal{X}, (n_1^i, n_2^i) \in \mathbb{N} \times \mathbb{N},\ 1 \leq i \leq I,\ I \in \mathbb{N} \right\}.$$

Here and below $\delta_{(x,n_1,n_2)}$ denotes the Dirac mass at (x, n_1, n_2). In case where $I = 0$, the measure is the null measure.
Therefore, for a population modelled by $\nu = \sum_{i=1}^{I} \delta_{(x^i,n_1^i,n_2^i)}$, the total number of its individuals is $\langle \nu, 1 \rangle = I$ and, if we denote by $n := n_1 + n_2$ the number of cells of an individual (irrespective of type), then $\langle \nu, n \rangle = \sum_{i=1}^{I} (n_1^i + n_2^i)$ is the total number of cells in the population ν.

Let us now describe the two-level dynamics. Any individual of the population with trait x and cell state (n_1, n_2) follows a mutation-selection-birth-and-death dynamics with

- birth (or reproduction) rate $B(x, n_1, n_2)$,
- the reproduction is clonal with probability $1 - p(x)$ (the offspring inherits the trait x),
- a mutation occurs with probability $p(x)$,
- the mutant trait $x + z$ is distributed according the mutation kernel $M(x, z)\, dz$ which only weights z such that $x + z \in \mathcal{X}$,
- death rate $D(x, n_1, n_2) + \alpha(x, n_1, n_2) \sum_{j=1}^{I} U(x - x^j)$.

Thus the interaction between individuals is modeled by a comparison between their respective trait values described by the competition kernel U. By simplicity, the mutations parameters p and M are assumed to be only influenced by the trait x. They could also depend on the cell composition (n_1, n_2) without inducing any additional technical difficulty.

Any cell of type 1 (resp. of type 2) inside an individual with trait x and cell state (n_1, n_2) follows a birth-and-death dynamics with

- birth rate $b_1(x)$, (resp. $b_2(x)$),
- death rate $d_1(x) + \beta_1(x)(n_1\lambda_{11} + n_2\lambda_{12})$, (resp. $d_2(x) + \beta_2(x)(n_1\lambda_{21} + n_2\lambda_{22})$).

The nonnegative parameters λ_{11}, λ_{22}, λ_{12}, λ_{21} quantify the cell interactions. The rate functions b_1, b_2, d_1, d_2, β_1, β_2 are assumed to be continuous (and thus bounded on the compact set $\mathcal{X}$).

The population dynamics can be described by its possible transitions from a state ν to the following other states:

1 - Individual dynamics due to an individual with trait x and cell state (n_1, n_2):

$$
\begin{aligned}
\nu &\mapsto \nu + \delta_{(x,n_1,n_2)} \text{ with rate } B(x,n_1,n_2)(1-p(x)) \ ; \\
\nu &\mapsto \nu - \delta_{(x,n_1,n_2)} \text{ with rate } D(x,n_1,n_2) + \alpha(x,n_1,n_2)\sum_{j=1}^{I} U(x-x^j) \ ; \\
\nu &\mapsto \nu + \delta_{(x+z,n_1,n_2)} \text{ with rate } B(x,n_1,n_2)\, p(x), \text{ where } z \text{ is distributed following } M(x,z)\,dz.
\end{aligned}
$$

2 - Cell dynamics:

$$
\begin{aligned}
\nu &\mapsto \nu + \delta_{(x,n_1+1,n_2)} - \delta_{(x,n_1,n_2)} \text{ with rate } b_1(x) \ ; \\
\nu &\mapsto \nu + \delta_{(x,n_1,n_2+1)} - \delta_{(x,n_1,n_2)} \text{ with rate } b_2(x) \ ; \\
\nu &\mapsto \nu + \delta_{(x,n_1-1,n_2)} - \delta_{(x,n_1,n_2)} \text{ with rate } d_1(x) + \beta_1(x)(\lambda_{11}n_1 + \lambda_{12}n_2) \ ; \\
\nu &\mapsto \nu + \delta_{(x,n_1,n_2-1)} - \delta_{(x,n_1,n_2)} \text{ with rate } d_2(x) + \beta_2(x)(\lambda_{21}n_1 + \lambda_{22}n_2).
\end{aligned}
$$

Let us now prove the existence of a càdlàg Markov process $(\nu_t)_{t\geq 0}$ belonging to $\mathbb{D}(\mathbb{R}_+, \mathcal{M})$ modeling the dynamics of such a discrete population. More precisely, we consider

$$
\nu_t = \sum_{i=1}^{I(t)} \delta_{(X^i(t), N_1^i(t), N_2^i(t))} \tag{2.1}
$$

where $I(t) \in \mathbb{N}$ stands for the number of individuals alive at time t, $X^1(t), ..., X^{I(t)}(t) \in \mathcal{X}$ describes the traits of these individuals at time t and $N_1^1(t), ..., N_1^{I(t)}(t)$ (resp. $N_2^1(t), ..., N_2^{I(t)}(t)$) are the numbers of cells of type 1 (resp. of type 2) for the individuals alive at time t.
To write down the infinitesimal generator of ν, we need an appropriate class of test functions. For bounded measurable functions ϕ, f, g_1, g_2 defined respectively on $\mathbb{R}$, $\mathbb{R}^d$, $\mathbb{N}$ and $\mathbb{N}$, $\phi_{fg_1g_2}$ is given by

$$
\begin{aligned}
\phi_{fg_1g_2}(\nu) &:= \phi(<\nu, fg_1g_2>) = \phi\left(\int_{\mathcal{X}\times\mathbb{N}^2} f(x)g_1(n_1)g_2(n_2)\nu(dx,dn_1,dn_2)\right) \\
&= \phi\left(\sum_{n_1,n_2\in\mathbb{N}^2} \int_{\mathcal{X}} f(x)g_1(n_1)g_2(n_2)\nu(n_1,n_2,dx)\right).
\end{aligned} \tag{2.2}
$$

The infinitesimal generator L of the Markov process $(\nu_t, t \geq 0)$ applied to such function $\phi_{fg_1g_2}$ is given by:

$$
\begin{aligned}
&L\phi_{fg_1g_2}(\nu) = \\
&\sum_{i=1}^{I}(\phi(\langle\nu, fg_1g_2\rangle + f(x^i)g_1(n_1^i)g_2(n_2^i)) - \phi(\langle\nu, fg_1g_2\rangle))B(x^i, n_1^i, n_2^i)(1 - p(x^i)) \\
&+ \sum_{i=1}^{I}\int(\phi(\langle\nu, fg_1g_2\rangle + f(x^i + z)g_1(n_1^i)g_2(n_2^i)) - \phi(\langle\nu, fg_1g_2\rangle))B(x^i, n_1^i, n_2^i)\, p(x^i)M(x^i, z)dz \\
&+ \sum_{i=1}^{I}(\phi(\langle\nu, fg_1g_2\rangle - f(x^i)g_1(n_1^i)g_2(n_2^i)) - \phi(\langle\nu, fg_1g_2\rangle))(D(x^i, n_1^i, n_2^i) + \alpha(x^i, n_1^i, n_2^i)U * \nu(x^i, n_1^i, n_2^i)) \\
&+ \sum_{i=1}^{I}(\phi(\langle\nu, fg_1g_2\rangle + f(x^i)(g_1(n_1^i + 1) - g_1(n_1^i))g_2(n_2^i)) - \phi(\langle\nu, fg_1g_2\rangle))b_1(x^i)n_1^i \\
&+ \sum_{i=1}^{I}(\phi(\langle\nu, fg_1g_2\rangle + f(x^i)g_1(n_1^i)(g_2(n_2^i + 1) - g_2(n_2^i))) - \phi(\langle\nu, fg_1g_2\rangle))b_2(x^i)n_2^i \\
&+ \sum_{i=1}^{I}(\phi(\langle\nu, fg_1g_2\rangle + f(x^i)(g_1(n_1^i - 1) - g_1(n_1^i))g_2(n_2^i)) - \phi(\langle\nu, fg_1g_2\rangle)) \\
&\qquad\qquad (d_1(x^i) + \beta_1(x^i)(\lambda_{11}n_1^i + \lambda_{12}n_2^i))n_1^i \\
&+ \sum_{i=1}^{I}(\phi(\langle\nu, fg_1g_2\rangle + f(x^i)g_1(n_1^i)(g_2(n_2^i - 1) - g_2(n_2^i))) - \phi(\langle\nu, fg_1g_2\rangle)) \\
&\qquad\qquad (d_2(x^i) + \beta_2(x^i)(\lambda_{21}n_1^i + \lambda_{22}n_2^i))n_2^i. \qquad (2.3)
\end{aligned}
$$

The three first terms of (2.3) capture the effects of births and deaths of individuals of the population and the for last terms that of the cells. The competition makes the death terms nonlinear.

2.2 Process construction

Let us give a pathwise construction of a Markov process admitting L as infinitesimal generator.

Assumptions (H1):

There exist constants $\bar{B}$, $\bar{D}$, $\bar{G}$ $\bar{\alpha}$, $\bar{U}$ and $\bar{C}$ and a probability density function $\bar{M}$ on $\mathbb{R}^d$ such that for $x, z \in \mathcal{X}$, $n_1, n_2 \in \mathbb{R}_+$,

$$
\begin{aligned}
&B(x, n_1, n_2) \leq \bar{B}\ ; \\
&D(x, n_1, n_2) \leq \bar{D}\,(n_1 + n_2) = \bar{D}\,n\ ; \\
&\alpha(x, n_1, n_2) \leq \bar{\alpha}\,(n_1 + n_2) = \bar{\alpha}\,n\ ; \\
&U(x) \leq \bar{U},\ \ M(x, z) \leq \bar{C}\bar{M}(z).
\end{aligned}
$$

Remark that the jump rate of an individual with n cells in the population ν is then upper-bounded by a constant times n $(1 + \langle\nu, 1\rangle)$ and that the cell jump rate of such individual is upper-bounded by a constant times $n(1+n)$. Thus the model presents a double nonlinearity since the population jump rates may depend on the product of the size of the population times the number of cells and quadratically on the number of cells.

Let us now give a pathwise description of the population process $(\nu_t)_{t\geq 0}$.

Notation 2.1 *We associate to any population state* $\nu = \sum_{i=1}^{I} \delta_{(x^i,n_1^i,n_2^i)} \in \mathcal{M}$ *the triplet* $H^i(\nu) = (X^i(\nu), N_1^i(\nu), N_2^i(\nu))$ *as the trait and state of the ith-individual, obtained by ordering all triplets with respect to some arbitrary order on* $\mathbb{R}^d \times \mathbb{N} \times \mathbb{N}$ *(for example the lexicographic order).*

We now introduce the probabilistic objects we will need.

Definition 2.2 *Let* $(\Omega, \mathcal{F}, P)$ *be a probability space on which we consider the following independent random elements:*

(i) *a* $\mathcal{M}$*-valued random variable* ν_0 *(the initial distribution),*

(ii) *A Poisson point measure* $Q(ds, di, dz, d\theta)$ *on* $\mathbb{R}_+ \times \mathbb{N}^* \times \mathcal{X} \times \mathbb{R}_+$ *with intensity measure* $ds \left(\sum_{k\geq 1} \delta_k(di)\right) \bar{M}(z) dz d\theta$ *.*

Let us denote by $(\mathcal{F}_t)_{t\geq 0}$ *the canonical filtration generated by* ν_0 *and* Q*.*

Let us finally define the quantities $\theta_1^i(s)$, $\theta_2^i(s)$, $\theta_3^i(s)$, $\theta_4^i(s)$, $\theta_5^i(s)$, $\theta_6^i(s)$, $\theta_7^i(s)$ *related to the different jump rates at time* s *as:*

$$
\begin{aligned}
\theta_1^i(s) &= B(H^i(\nu_{s-}))(1 - p(X^i(\nu_{s-})));\\
\theta_2^i(s) - \theta_1^i(s) &= B(H^i(\nu_{s-}))p(X^i(\nu_{s-}))\frac{M(X^i(\nu_{s-}), z)}{\bar{M}(z)};\\
\theta_3^i(s) - \theta_2^i(s) &= D(H^i(\nu_{s-})) + \alpha(H^i(\nu_{s-}))\ U * \nu_{s-}(X^i(\nu_{s-}));\\
\theta_4^i(s) - \theta_3^i(s) &= b_1(X^i(\nu_{s-}))\ N_1^i(\nu_{s-});\\
\theta_5^i(s) - \theta_4^i(s) &= b_2(X^i(\nu_{s-}))\ N_2^i(\nu_{s-});\\
\theta_6^i(s) - \theta_5^i(s) &= d_1(X^i(\nu_{s-})) + \beta_1(X^i(\nu_{s-}))(N_1^i(\nu_{s-})\lambda_{11} + N_2^i(\nu_{s-})\lambda_{12})\ N_1^i(\nu_{s-});\\
\theta_7^i(s) - \theta_6^i(s) &= d_2(X^i(\nu_{s-})) + \beta_2(X^i(\nu_{s-}))(N_1^i(\nu_{s-})\lambda_{21} + N_2^i(\nu_{s-})\lambda_{22})\ N_2^i(\nu_{s-}).
\end{aligned}
\tag{2.4}
$$

We finally define the population process in terms of these stochastic objects.

Definition 2.3 *Assume* $(H1)$*. A* $(\mathcal{F}_t)_{t\geq 0}$*-adapted stochastic process* $\nu = (\nu_t)_{t\geq 0}$ *is called a population process if a.s., for all* $t \geq 0$*,*

$$
\begin{aligned}
\nu_t = \nu_0 + \int_{(0,t]\times\mathbb{N}^*\times\mathcal{X}\times\mathbb{R}_+} \Big\{ & \delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-}),N_2^i(\nu_{s-}))} \mathbf{1}_{\{i\le\langle\nu_{s-},1\rangle\}} \mathbf{1}_{\{\theta\le\theta_1^i(s)\}} \\
& + \delta_{(X^i(\nu_{s-})+z,N_1^i(\nu_{s-}),N_2^i(\nu_{s-}))} \mathbf{1}_{\{i\le\langle\nu_{s-},1\rangle\}} \mathbf{1}_{\{\theta_1^i(s)\le\theta\le\theta_2^i(s)\}} \\
& - \delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-}),N_2^i(\nu_{s-}))} \mathbf{1}_{\{i\le\langle\nu_{s-},1\rangle\}} \mathbf{1}_{\{\theta_2^i(s)\le\theta\le\theta_3^i(s)\}} \\
& + \Big(\delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-})+1,N_2^i(\nu_{s-}))} - \delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-}),N_2^i(\nu_{s-}))}\Big) \mathbf{1}_{\{i\le\langle\nu_{s-},1\rangle\}} \mathbf{1}_{\{\theta_3^i(s)\le\theta\le\theta_4^i(s)\}} \\
& + \Big(\delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-}),N_2^i(\nu_{s-})+1)} - \delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-}),N_2^i(\nu_{s-}))}\Big) \mathbf{1}_{\{i\le\langle\nu_{s-},1\rangle\}} \mathbf{1}_{\{\theta_4^i(s)\le\theta\le\theta_5^i(s)\}} \\
& + \Big(\delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-})-1,N_2^i(\nu_{s-}))} - \delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-}),N_2^i(\nu_{s-}))}\Big) \mathbf{1}_{\{i\le\langle\nu_{s-},1\rangle\}} \mathbf{1}_{\{\theta_5^i(s)\le\theta\le\theta_6^i(s)\}} \\
& + \Big(\delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-}),N_2^i(\nu_{s-})-1)} - \delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-}),N_2^i(\nu_{s-}))}\Big) \mathbf{1}_{\{i\le\langle\nu_{s-},1\rangle\}} \mathbf{1}_{\{\theta_6^i(s)\le\theta\le\theta_7^i(s)\}} \Big\} \\
& \qquad Q(ds,di,dz,d\theta)
\end{aligned} \tag{2.5}
$$

Let us now show that if ν solves (2.5), then ν follows the Markovian dynamics we are interested in.

Proposition 2.4 *Assume $(H1)$ and consider a process $(\nu_t)_{t\ge0}$ defined by (2.5) such that for all $T>0$, $\mathbb{E}(\sup_{t\le T}\langle\nu_t,1\rangle^3)<+\infty$ and $\mathbb{E}(\sup_{t\le T}\langle\nu_t,n^2\rangle)<+\infty$. Then $(\nu_t)_{t\le0}$ is a Markov process. Its infinitesimal generator L applied to any bounded and measurable maps $\phi_{fg_1g_2}:\mathcal{M}\mapsto\mathbb{R}$ and $\nu\in\mathcal{M}$ satisfies (2.3). In particular, the law of $(\nu_t)_{t\ge0}$ does not depend on the chosen order in Notation 2.1.*

Proof The fact that $(\nu_t)_{t\ge0}$ is a Markov process is immediate. Let us now consider a function $\phi_{fg_1g_2}$ as in the statement. Using the decomposition (2.5) of the measure ν_t and the fact that

$$
\phi_{fg_1g_2}(\nu_t) = \phi_{fg_1g_2}(\nu_0) + \sum_{s\le t}(\phi_{fg_1g_2}(\nu_{s-}+(\nu_s-\nu_{s-})) - \phi_{fg_1g_2}(\nu_{s-})) \quad \text{a.s.,} \tag{2.6}
$$

we get a decomposition of $\phi_{fg_1g_2}(\nu_t)$.
Thanks to the moment assumptions, $\phi_{fg_1g_2}(\nu_t)$ is integrable. Let us check it for the non-linear individual death term (which is the more delicate to deal with):

$$
\begin{aligned}
&\mathbb{E}\Big(\int_{(0,t]\times\mathbb{N}^*\times\mathcal{X}\times\mathbb{R}_+} (\phi(\langle\nu_{s-}-\delta_{(X^i(\nu_{s-}),N_1^i(\nu_{s-}),N_2^i(\nu_{s-}))},fg_1g_2\rangle - \phi(\langle\nu_{s-},fg_1g_2\rangle)\mathbf{1}_{\{i\le\langle\nu_{s-},1\rangle\}} \\
&\qquad\qquad \mathbf{1}_{\{\theta_2^i(s)\le\theta\le\theta_3^i(s)\}} Q(ds,di,dz,d\theta)\Big) \\
&= \\
&\mathbb{E}\Big(\int_0^t \langle\nu_s,(\phi(\langle\nu_s,fg_1g_2\rangle - f(x)g_1(n_1)g_2(n_2)) - \phi(\langle\nu_s,fg_1g_2\rangle)(D(x,n_1,n_2)+\alpha(x,n_1,n_2)\,U*\nu_s(x))\rangle ds\Big).
\end{aligned}
$$

Since ϕ is bounded and thanks to Assumption $(H1)$, the right hand side term will be finite as soon as

$$\mathbb{E}\left(\sup_{t\leq T}(\langle \nu_t, n\rangle + \langle \nu_t, n\rangle\langle \nu_t, 1\rangle)\right) < \infty.$$

Remark firstly that $\langle \nu, n\rangle \leq \langle \nu, n^2\rangle$. Moreover we get $n\langle \nu, 1\rangle \leq 1/2(n^2 + \langle \nu, 1\rangle^2)$ and thus

$$\langle \nu, n\rangle\,\langle \nu, 1\rangle \leq 1/2(\langle \nu, n^2 + \langle \nu, 1\rangle^2\rangle) = 1/2(\langle \nu, n^2\rangle + \langle \nu, 1\rangle^3).$$

The moment assumptions allow us to conclude and to show that the expectation is differentiable in time at $t = 0$. It leads to (2.3). □

Let us show existence and moment properties for the population process.

Theorem 2.5 *Assume (H1).*

(i) If $\mathbb{E}\left(\langle \nu_0, 1\rangle\right) < +\infty$, *then the process* $(\nu_t)_t$ *introduced in Definition 2.3 is well defined on* $\mathbb{R}_+$.

(ii) Furthermore, if for some $p \geq 1$, $\mathbb{E}\left(\langle \nu_0, 1\rangle^p\right) < +\infty$, *then for any* $T < \infty$,

$$\mathbb{E}(\sup_{t\in[0,T]} \langle \nu_t, 1\rangle^p) < +\infty. \tag{2.7}$$

(iii) If moreover $\mathbb{E}\left(\left\langle \nu_0, n^2\right\rangle\right) < +\infty$, *then for any* $T < \infty$,

$$\mathbb{E}(\sup_{t\in[0,T]} \left\langle \nu_t, n^2\right\rangle) < +\infty. \tag{2.8}$$

Proof We compute $\phi(<\nu_t, 1>)$ using (2.5) and (2.6) for $f \equiv g_1 \equiv g_2 \equiv 1$: we get

$$\begin{aligned}\phi(<\nu_t, 1>) = \phi(<\nu_0, 1>) + \int_{(0,t]\times\mathbb{N}^*\times\mathcal{X}\times\mathbb{R}_+} \Big\{ &(\phi(<\nu_{s-}, 1> +1) - \phi(<\nu_{s-}, 1>))\,\mathbf{1}_{\{\theta\leq\theta_2^i(s)\}} \\ &+ (\phi(<\nu_{s-}, 1> -1) - \phi(<\nu_{s-}, 1>))\,\mathbf{1}_{\{\theta_2^i(s)\leq\theta\leq\theta_3^i(s)\}}\Big\}\mathbf{1}_{\{i\leq\langle\nu_{s-},1\rangle\}}Q(ds, di, dz, d\theta)\end{aligned} \tag{2.9}$$

and for $g_1(n_1) = n_1$,

$$\begin{aligned}<\nu_t, n_1> = <\nu_0, n_1> + \int_{(0,t]\times\mathbb{N}^*\times\mathcal{X}\times\mathbb{R}_+} \Big\{ &N_1^i(\nu_{s-})\Big(\mathbf{1}_{\{\theta\leq\theta_2^i(s)\}} - \mathbf{1}_{\{\theta_2^i(s)\leq\theta\leq\theta_3^i(s)\}}\Big) \\ &+ \mathbf{1}_{\{\theta_3^i(s)\leq\theta\leq\theta_4^i(s)\}} - \mathbf{1}_{\{\theta_5^i(s)\leq\theta\leq\theta_6^i(s)\}}\Big\}\mathbf{1}_{\{i\leq\langle\nu_{s-},1\rangle\}}Q(ds, di, dz, d\theta).\end{aligned} \tag{2.10}$$

A similar decomposition holds for $<\nu_t, n_2>$.
The proof of (i) and (ii) is standard and can easily be adapted from [7]: we introduce for each integer k the stopping time $\tau_k = \inf\{t \geq 0,\ \langle \nu_t, 1\rangle \geq k\}$ and show that the sequence$(\tau_k)_k$ tends a.s. to infinity, using that

$$\sup_{s\in[0,t\wedge\tau_k]} \langle \nu_s, 1\rangle \leq \langle \nu_0, 1\rangle + \int_{(0,t\wedge\tau_k]\times\mathbb{N}^*\times\mathcal{X}\times\mathbb{R}^+} \mathbf{1}_{\{i\leq\langle\nu_{s-},1\rangle\}}\ \mathbf{1}_{\{\theta\leq\theta_2^i(s)\}}Q(ds, di, dz, d\theta),$$

and the estimates of moments up to time τ_k deduced from the latter and Assumption $(H1)$ and Gronwall's lemma.
Further, one may build the solution $(\nu_t)_{t\geq 0}$ step by step. One only has to check that the sequence of jump instants (T_k) goes a.s. to infinity as k tends to infinity, which follows from the previous result.

The proof of (iii) follows a similar argument with $\tau_k^1 := \inf\left\{t \geq 0,\ \left\langle \nu_t, n_1^2\right\rangle \geq k\right\}$. From

$$\sup_{s\in[0,t\wedge\tau_k^1]} \left\langle \nu_s, n_1^2\right\rangle \leq \left\langle \nu_0, n_1^2\right\rangle + \int_{(0,t\wedge\tau_k^1]\times\mathbb{N}^*\times\mathcal{X}\times\mathbb{R}^+} \mathbf{1}_{\{i\leq\langle\nu_{s-},1\rangle\}}$$
$$\left\{(N_1^i(\nu_{s-}))^2\,\mathbf{1}_{\left\{\theta\leq\theta_2^i(s)\right\}} + (2\,N_1^i(\nu_{s-})+1)\,\mathbf{1}_{\left\{\theta_3^i(s)\theta\leq\theta_4^i(s)\right\}}\right\}Q(ds,di,dz,d\theta),$$

and $\mathbb{E}\left(\left\langle \nu_0, n^2\right\rangle\right) < +\infty$ and (ii) since $2n_1+1 \leq n_1^2+2$, we firstly get, using Assumption $(H1)$ and Gronwall's lemma, that

$$\mathbb{E}(\sup_{t\in[0,T\wedge\tau_k^1]} \left\langle \nu_t, n_1^2\right\rangle) \leq C_T.$$

Then we deduce that τ_k^1 tends to infinity a.s. and that $\mathbb{E}(\sup_{t\in[0,T]}\left\langle \nu_t, n_1^2\right\rangle) < +\infty$. The same is true replacing n_1 by n_2. □

2.3 Martingale Properties

We finally give some martingale properties of the process $(\nu_t)_{t\geq 0}$, which are the key point of our approach. For measurable functions f, g_1, g_2, let us denote by F_{fg} the function defined on M_F by

$$F_{fg}(\nu) :=< \nu, fg_1g_2 > .$$

Theorem 2.6 *Assume $(H1)$ together with $\mathbb{E}\left(\langle\nu_0,1\rangle^3\right) < +\infty$ and $\mathbb{E}\left(\left\langle \nu_0, n^2\right\rangle\right) < +\infty$.*
(i) For all measurable functions ϕ, f, g_1, g_2 such that
$|\phi_{fg_1g_2}(\nu)| + |L\phi_{fg_1g_2}(\nu)| \leq C(1+\langle\nu,1\rangle^3+\langle\nu,n^2\rangle)$, the process

$$\phi_{fg_1g_2}(\nu_t) - \phi_{fg_1g_2}(\nu_0) - \int_0^t L\phi_{fg_1g_2}(\nu_s)ds \tag{2.11}$$

is a càdlàg $(\mathcal{F}_t)_{t\geq 0}$-martingale starting from 0, where $L\phi_{fg_1g_2}$ has been defined in (2.3).

(ii) For all measurable bounded functions f, g_1, g_2, the process

$$M_t^{fg} = \langle\nu_t, fg_1g_2\rangle - \langle\nu_0, fg_1g_2\rangle - \int_0^t LF_{fg}(\nu_s)ds \tag{2.12}$$

is a càdlàg square integrable $(\mathcal{F}_t)_{t\geq 0}$*-martingale starting from* 0*, where*

$$
\begin{aligned}
LF_{fg}(\nu) = \int_{\mathcal{X}\times\mathbb{N}^2} \Bigg\{ \Big(& B(x,n_1,n_2)(1-p(x,n_1,n_2)) - (D(x,n_1,n_2) + \alpha(x,n_1,n_2)U * \nu(x)) \Big) \\
& f(x)g_1(n_1)g_2(n_2) \\
& + p(x,n_1,n_2)B(x,n_1,n_2) \int f(x+z)g_1(n_1)g_2(n_2)M(x,n_1,n_2,z)dz \\
& + f(x)\big(g_1(n_1+1) - g_1(n_1)\big)g_2(n_2)b_1(x)n_1 + f(x)g_1(n_1)\big(g_2(n_2+1) - g_2(n_2)\big)b_2(x)n_2 \\
& + f(x)\big(g_1(n_1-1) - g_1(n_1)\big)g_2(n_2)\big(d_1(x) + \beta_1(x)(\lambda_{11}n_1 + \lambda_{12}n_2)\big)n_1 \\
& + f(x)g_1(n_1)\big(g_2(n_1-1) - g_2(n_2)\big)\big(d_2(x) + \beta_2(x)(\lambda_{21}n_1 + \lambda_{22}n_2)\big)n_2 \Bigg\} \nu(dx,dn_1,dn_2).
\end{aligned}
\tag{2.13}
$$

Its quadratic variation is given by

$$
\begin{aligned}
\langle M^{fg}\rangle_t = \int_0^t \int_{\mathcal{X}\times\mathbb{N}^2} \Bigg\{ \Big(& (1-p(x,n_1,n_2))B(x,n_1,n_2) + (D(x,n_1,n_2) + \alpha(x,n_1,n_2)U * \nu_s(x)) \Big) \\
& f^2(x)g_1^2(n_1)g_2^2(n_2) \\
& + p(x,n_1,n_2)B(x,n_1,n_2) \int f^2(x+z)g_1^2(n_1)g_2^2(n_2)M(x,n_1,n_2,z)dz \\
& + f^2(x)\big(g_1(n_1+1) - g_1(n_1)\big)^2 g_2^2(n_2)b_1(x)n_1 \\
& + f^2(x)g_1^2(n_1)\big(g_2(n_2+1) - g_2(n_2)\big)^2 b_2(x)n_2 \\
& + f^2(x)\big(g_1(n_1-1) - g_1(n_1)\big)^2 g_2^2(n_2)\big(d_1(x) + \beta_1(x)(\lambda_{11}n_1 + \lambda_{12}n_2)\big)n_1 \\
& + f^2(x)g_1^2(n_1)\big(g_2(n_1-1) - g_2(n_2)\big)^2\big(d_2(x) + \beta_2(x)(\lambda_{21}n_1 + \lambda_{22}n_2)\big)n_2 \Bigg\} \nu_s(dx,dn_1,dn_2)ds.
\end{aligned}
\tag{2.14}
$$

Proof The martingale property is immediate by Proposition 2.4 and Theorem 2.5. Let us justify the form of the quadratic variation process. Using a localization argument as in Theorem 2.5, we may compare two different expressions of $\langle \nu_t, fg_1g_2\rangle^2$. The first one is obtained by applying (2.11) with $\phi(\nu) := \langle \nu, fg_1g_2\rangle^2$. The second one is obtained by applying Itô's formula to compute $\langle \nu_t, fg_1g_2\rangle^2$ from (2.12). Comparing these expressions leads to (2.14). We may let go the localization stopping time sequence to infinity since $E\big(\langle \nu_0, 1\rangle^3\big) < +\infty$ and $E\left(\langle \nu_0, n^2\rangle\right) < +\infty$. Indeed, in this case, $E(\langle M^{fg}\rangle_t) < +\infty$ thanks to Theorem 2.5 and to the proof of Proposition 2.4. □

3 Deterministic large population approximations

We are interested in studying large population approximations of our individual-based system. We rescale the size of individual population by K and the size of the cell populations by K_1 respectively K_2. With $\kappa = (K, K_1, K_2)$, the process of interest is now the Markov process $(Y_t^\kappa)_{t\geq 0}$ defined as

$$
Y_t^\kappa = \frac{1}{K} \sum_{i=1}^{I_\kappa(t)} \delta_{\left(X_\kappa^i(t), \frac{N_{1,\kappa}^i(t)}{K_1}, \frac{N_{2,\kappa}^i(t)}{K_2}\right)} \in M_F(\mathcal{X}\times\mathbb{R}_+\times\mathbb{R}_+)
$$

in which cells of type 1 (resp. of type 2) have been weighted by $\frac{1}{K_1}$ (resp. by $\frac{1}{K_2}$) and individuals by $\frac{1}{K}$. The dynamics of the process $(X^i_\kappa(t), N^i_{1,\kappa}(t), N^i_{2,\kappa}(t))$ is the one described in Section 2 except some coefficients are depending on the scaling κ as described below. The individual dynamics depends on B_κ, p_κ, M_κ, D_κ, α_κ, U_κ which are assumed to satisfy the assumptions (H_1) of the section 2 for any fixed κ.

Notation: We say that $\kappa \to \infty$ when the three parameters K, K_1, K_2 tend to infinity.

Assumptions (H2):
1) There exist continuous functions B, D and α on $\mathcal{X} \times \mathbb{R}_+ \times \mathbb{R}_+$ such that

$$\lim_{\kappa\to\infty} \sup_{x,y_1,y_2} |B_\kappa(x, K_1y_1, K_2y_2) - B(x, y_1, y_2)| + |D_\kappa(x, K_1y_1, K_2y_2) - D(x, y_1, y_2)| = 0,$$
$$\lim_{\kappa\to\infty} \sup_{x,y_1,y_2} |\alpha_\kappa(x, K_1y_1, K_2y_2) - \alpha(x, y_1, y_2)| = 0. \tag{3.15}$$

We assume that the functions B, D and α satisfy Assumption $(H1)$.

2) The competition kernel U_κ satisfies

$$U_\kappa(x) = \frac{U(x)}{K}, \tag{3.16}$$

where U is a continuous function.

3) The others parameters $p_\kappa = p$ and $M_\kappa = M$ stay unchanged, as also the cell ecological parameters: $b_{1,\kappa} = b_1$, $b_{2,\kappa} = b_2$, $d_{1,\kappa} = d_1$,$d_{2,\kappa} = d_2$, $\beta_{1,\kappa} = \beta_1$, $\beta_{2,\kappa} = \beta_2$. The functions p and M are assumed to be continuous and the functions b_i, d_i and β_i are of class C^1. We assume

$$r_i = b_i - d_i > 0\ , \quad i \in \{1, 2\}.$$

4) Similarly to (3.16), the interaction rates between cells satisfy

$$\lambda^\kappa_{ij} = \frac{\lambda_{ij}}{K_j}, \qquad i, j \in \{1, 2\}. \tag{3.17}$$

Remark that Assumption (H2) 1) means that at a large scale K, the individuals are influenced in their ecological behavior by the cells if the number of the latter is of order K_1 for cells of type 1, resp. of order K_2 for cells of type 2. On the other side the hypothesis (H2) 2) may be a consequence of a fixed amount of available resources to be partitioned among all the individuals. Larger systems are made up of smaller interacting individuals whose biomass is scaled by $1/K$, which implies that the interaction effect of the global population on a focal individual is of order 1.

Examples

(i) If $K_1 = K_2$ and if the individual rates $B_\kappa, D_\kappa, \alpha_\kappa$ only depend on x, n_1, n_2 by the proportion of cells of type 1, then (3.15) is satisfied.

(ii) Assume that $K_1 = K_2 = K$ and that the functions $B_\kappa, D_\kappa, \alpha_\kappa$ only depend on the weighted total number of cells $\frac{1}{K}(n_1 + n_2)$.

3.1 A convergence theorem

We assume that the sequence of random initial conditions Y_0^κ converges in law to some finite measure $v_0 \in M_F(\mathcal{X} \times \mathbb{R}_+ \times \mathbb{R}_+)$ when $\kappa \to \infty$. Our aim is to study the limiting behavior of the processes $Y_\cdot^\kappa$ as $\kappa \to \infty$.
The generator L^κ of $(Y_t^\kappa)_{t\geq 0}$ is easily obtained by computing, for any measurable function ϕ from $M_F(\mathcal{X} \times \mathbb{R}_+ \times \mathbb{R}_+)$ into $\mathbb{R}$ and any $\mu \in M_F(\mathcal{X} \times \mathbb{R}_+ \times \mathbb{R}_+)$,

$$L^\kappa \phi(\mu) = \partial_t \mathbb{E}_\mu(\phi(Y_t^\kappa))_{t=0}.$$

In particular, similarly as in Theorem 2.6, we may summarize the moment and martingale properties of Y^κ.

Proposition 3.1 *Assume that for some $p \geq 3$, $\mathbb{E}(\langle Y_0^\kappa, 1\rangle^p + \langle Y_0^\kappa, y_1^2 + y_2^2\rangle) < +\infty$. Then*

(1) *For any $T > 0$, $\mathbb{E}\left(\sup_{t\in[0,T]}\langle Y_t^\kappa, 1\rangle^p + \sup_{t\in[0,T]}\langle Y_t^\kappa, y_1^2 + y_2^2\rangle\right) < +\infty$.*

(2) *For any measurable bounded functions f, g_1, g_2, the process*

$$\begin{aligned}
\tilde{M}_t^{\kappa,fg} = \langle Y_t^\kappa, fg_1g_2\rangle - \langle Y_0^\kappa, fg_1g_2\rangle - \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big\{ &\Big(B_\kappa(x, K_1y_1, K_2y_2)(1 - p(x)) \\
&- \big(D_\kappa(x, K_1y_1, K_2y_2) + \alpha_\kappa(x, K_1y_1, K_2y_2)\ U * Y_s^\kappa(x, y_1, y_2)\big)\Big) f(x)g_1(y_1)g_2(y_2) \\
&+ p(x)B_\kappa(x, K_1y_1, K_2y_2) \int f(x+z)g_1(y_1)g_2(y_2)M(x,z)dz \\
&+ f(x)\big(g_1(y_1 + \frac{1}{K_1}) - g_1(y_1)\big)g_2(y_2)\ b_1(x)\ K_1y_1 \\
&+ f(x)g_1(y_1)\big(g_2(y_2 + \frac{1}{K_2}) - g_2(y_2)\big)\ b_2(x)\ K_2y_2 \\
&+ f(x)\big(g_1(y_1 - \frac{1}{K_1}) - g_1(y_1)\big)g_2(y_2)\Big(d_1(x) + \beta_1(x)(\lambda_{11}y_1 + \lambda_{12}y_2)\Big)K_1y_1 \\
&+ f(x)g_1(y_1)\big(g_2(y_1 - \frac{1}{K_2}) - g_2(y_2)\big)\Big(d_2(x) + \beta_2(x)(\lambda_{21}y_1 + \lambda_{22}y_2)\Big)K_2y_2\Big\} \\
&Y_s^\kappa(dx, dy_1, dy_2)\ ds \qquad (3.18)
\end{aligned}$$

is a càdlàg square integrable martingale starting from 0 with quadratic variation

$$\langle \tilde{M}^{\kappa,fg}\rangle_t = \frac{1}{K}\int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big\{ \Big(B_\kappa(x,K_1y_1,K_2y_2)(1-p(x)) + \big(D_\kappa(x,K_1y_1,K_2y_2) + \alpha_\kappa(x,K_1y_1,K_2y_2)\; U * Y_s^\kappa(x,y_1,y_2)\big)\Big) f^2(x) g_1^2(y_1) g_2^2(y_2)$$
$$+ p(x)B_\kappa(x,K_1y_1,K_2y_2) \int f^2(x+z) g_1^2(y_1)g_2^2(y_2) M(x,z)dz$$
$$+ f^2(x)\; \big(g_1(y_1+\frac{1}{K_1}) - g_1(y_1)\big)^2\; g_2^2(y_2)\; b_1(x)\; K_1y_1$$
$$+ f^2(x)\; g_1^2(y_1)\; \big(g_2(y_2+\frac{1}{K_2}) - g_2(y_2)\big)^2\; b_2(x)\; K_2y_2$$
$$+ f^2(x)\; \big(g_1(y_1-\frac{1}{K_1}) - g_1(y_1)\big)^2\; g_2^2(y_2)\; \Big(d_1(x)+\beta_1(x)(\lambda_{11}y_1+\lambda_{12}y_2)\Big)K_1y_1$$
$$+ f^2(x)\; g_1^2(y_1)\; \big(g_2(y_2-\frac{1}{K_2}) - g_2(y_2)\big)^2\; \Big(d_2(x)+\beta_2(x)(\lambda_{21}y_1+\lambda_{22}y_2)\Big)K_2y_2 \Big\}$$
$$Y_s^\kappa(dx,dy_1,dy_2)\; ds. \quad (3.19)$$

We can now state our convergence result.

Theorem 3.2 *Assume (H2). Assume moreover that the sequence of initial conditions $Y_0^\kappa \in M_F(\mathcal{X}\times\mathbb{R}_+^2)$ satisfies $\sup_\kappa \mathbb{E}(\langle Y_0^\kappa, 1\rangle^3) < +\infty$ and $\sup_\kappa \mathbb{E}(\langle Y_0^\kappa, y_1^2+y_2^2\rangle) < +\infty$. If Y_0^κ converges in law, as κ tends to infinity, to a finite deterministic measure v_0, then the sequence of processes $(Y_t^\kappa)_{0\le t\le T}$ converges in law in the Skorohod space $\mathbb{D}([0,T], M_F(\mathcal{X}\times\mathbb{R}_+^2))$, as κ goes to infinity, to the unique (deterministic) measure-valued flow $v \in C([0,T], M_F(\mathcal{X}\times\mathbb{R}_+^2))$ satisfying for any bounded and continuous function f and any bounded functions g_1, g_2 of class C_b^1,*

$$\langle v_t, fg_1g_2\rangle = \langle v_0, fg_1g_2\rangle + \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big\{ \Big(B(x,y_1,y_2)(1-p(x)) - \big(D(x,y_1,y_2) + \alpha(x,y_1,y_2)\; U * v_s(x,y_1,y_2)\big)\Big) f(x)g_1(y_1)g_2(y_2)$$
$$+ p(x)B(x,y_1,y_2) \int f(x+z)M(x,z)dz\; g_1(y_1)g_2(y_2)$$
$$+ f(x)\Big[g_1'(y_1)g_2(y_2)b_1(x)\; y_1 + g_1(y_1)g_2'(y_2)b_2(x)\; y_2$$
$$- g_1'(y_1)g_2(y_2)\Big(d_1(x)+\beta_1(x)(\lambda_{11}y_1+\lambda_{12}y_2)\Big)y_1$$
$$- g_1(y_1)g_2'(y_2)\Big(d_2(x)+\beta_2(x)(\lambda_{21}y_1+\lambda_{22}y_2)\Big)y_2\Big]\Big\} v_s(dx,dy_1,dy_2)\; ds. \quad (3.20)$$

Note that for this dynamics, a transport term appears at the level of cells.

Remark 3.3 • A solution of (3.20) is a measure-valued solution of the nonlinear integro-differential equation

$$\frac{\partial}{\partial t} v_t = \Big(B(1-p) - \big(D + \alpha\; U * v_t\big)\Big) v_t + (B\, p\, v_t) * M - \nabla_y \cdot (c v_t) \quad (3.21)$$

with

$$\begin{aligned} c_1(x,y) &:= y_1\left(r_1(x) - \beta_1(x)\big(\lambda_{11}y_1 + \lambda_{12}y_2\big)\right) \\ c_2(x,y) &:= y_2\left(r_2(x) - \beta_2(x)\big(\lambda_{21}y_1 + \lambda_{22}y_2\big)\right). \end{aligned} \tag{3.22}$$

Thus, the existence of a weak solution for Equation (3.21) is obtained as corollary of Theorem 3.2.

- We deduce from (3.20) the limiting dynamics of the total number of individuals:

$$\langle v_t, 1\rangle = \langle v_0, 1\rangle + \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big(B(x,y_1,y_2) - D(x,y_1,y_2) \\ - \alpha(x,y_1,y_2)\; U * v_s(x,y_1,y_2)\Big) v_s(dx,dy_1,dy_2)\; ds, \tag{3.23}$$

while the total number $\langle v_t, y_i\rangle$ of cells of type i at time t is obtained by taking $f\equiv 1, g_i(y) = y, g_j \equiv 1$ $(i\neq j)$ in (3.20) :

$$\begin{aligned} &\langle v_t, y_i\rangle = \langle v_0, y_i\rangle \\ &+ \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big(B(x,y_1,y_2) - D(x,y_1,y_2) - \alpha(x,y_1,y_2)\; U * v_s(x,y_1,y_2)\Big) y_i\; v_s(dx,dy_1,dy_2) ds \\ &+ \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big((b_i(x) - d_i(x))y_i - \beta_i(x)(\lambda_{ii}y_i + \lambda_{ij}y_j)y_i\Big) v_s(dx,dy_1,dy_2)\; ds. \end{aligned} \tag{3.24}$$

Proof The proof of the theorem is obtained by a standard compactness-uniqueness result (see e.g. [4]). The compactness is a consequence, using Prokhorov's Theorem, of the uniform tightness of the sequence of laws of $(Y_t^\kappa, t\geq 0)$. This uniform tightness derives from uniform moment estimates. Their proof is standard and we refer for details to [10], [7] Theorem 5.3 or to [2]. To identify the limit, we first remark using (3.19) that the quadratic variation tends to 0 when K tends to infinity. Thus the limiting values are deterministic and it remains to prove the convergence of the drift term in (3.18) to the one in (3.20). The drift term in (3.18) has the form $\int_0^t \langle Y_s^\kappa, A^\kappa(Y_s^\kappa)(fg_1g_2)\rangle ds$ and the limiting term in (3.20) has the form $\int_0^t \langle v_s, A(v_s)(fg_1g_2)\rangle ds$. (The exact values of A^κ and A are immediately given by (3.18) and (3.20)).
Thus, let us show that if Y^κ is a sequence of random measure-valued processes weakly converging to a measure-valued flow Y and satisfying the moment assumptions

$$\sup_\kappa \mathbb{E}(\sup_{t\leq T}\langle Y_t^\kappa, 1\rangle^3) + \sup_\kappa \mathbb{E}(\sup_{t\leq T}\langle Y_t^\kappa, y^2\rangle) < +\infty, \tag{3.25}$$

then $\langle Y_t^\kappa, A^\kappa(Y_t^\kappa)(fg_1g_2)\rangle$ converges in L^1 to $\langle Y_t, A(Y_t)(fg_1g_2)\rangle$ uniformly in time $t\in[0,T]$. We write

$$\begin{aligned} &\langle Y_t^\kappa, A^\kappa(Y_t^\kappa)(fg_1g_2)\rangle - \langle Y_t, A(Y_t)(fg_1g_2)\rangle \\ &= \langle Y_t^\kappa, A^\kappa(Y_t^\kappa)(fg_1g_2) - A(Y_t^\kappa)(fg_1g_2)\rangle + \langle Y_t^\kappa, A(Y_t^\kappa)(fg_1g_2) - A(Y_t)(fg_1g_2)\rangle \\ &\quad + \langle Y_t^\kappa - Y_t, A(Y_t)(fg_1g_2)\rangle. \end{aligned} \tag{3.26}$$

The convergence of the first term to zero follows from Assumptions $(H2)$ and (3.25) and from the following remark, that for C_b^1-functions g_1 and g_2, the terms

$$K_i\Big(g_i(y_i - \frac{1}{K_i}) - g_i(y_i)\Big) + g_i'(y_i)$$

converge to 0 in a bounded pointwise sense, which allows us to apply the Lebesgue's theorem.
The convergence of the second term to 0 is immediately obtained by use of (3.25), since the functions α and U are continuous and bounded.
The convergence of the third term of (3.26) is due to the weak convergence of Y^κ to Y. We know that for all bounded and continuous functions ϕ, the quantity $\langle Y_t^\kappa - Y_t, \phi\rangle$ tends to 0. The function $A(Y_t)(fg_1g_2)$ is a continuous function which is not bounded because of linear terms in y and y^2. Thus we need to cutoff at a level M replacing y by $y \wedge M$. The remaining terms are proved to go to 0 using (3.25). Hence we have proved that each limiting value satisfies (3.20).

We have now to prove the uniqueness of the solutions $v \in C([0,T], M_F(\mathcal{X} \times \mathbb{R}_+^2))$ of (3.20). Our argument is based on properties of Lotka-Volterra's flows. Firstly we need the following comparison lemma.

Lemma 3.4 *If u_t is a non negative function with positive initial value and satisfying for some $a, b \in \mathbb{R}_+^*$ the inequality*

$$\begin{array}{rcl} \forall t > 0, \quad \dfrac{\partial}{\partial t} u_t & \leq & a u_t - b u_t^2, \\ \textit{then} \qquad 0 & \leq & \sup\limits_{t \geq 0} u_t =: \overline{u} < +\infty. \end{array}$$

Moreover 0 is an absorbing value: if $u_{t_0} = 0$ then for all $t \geq t_0, u_t \equiv 0$.

Proof of Lemma 3.4. Let us define U_t as solution of the associated logistic equation

$$\frac{\partial U_t}{\partial t} = aU_t - bU_t^2, \quad U_0 = u_0.$$

Then $\frac{\partial}{\partial t}(U_t - u_t) \geq a(U_t - u_t) - b(U_t^2 - u_t^2)$. With $\delta_t := U_t - u_t$ it holds

$$\frac{\partial}{\partial t}\delta_t \geq \Big(a - b(U_t + u_t)\Big)\delta_t, \quad \delta_0 = 0.$$

Let us show that $t \mapsto \delta_t$ increases, and therefore is positive. For $t = 0$, since $\delta_0 = 0$, $\frac{\partial \delta_t}{\partial t}|_{t=0} \geq 0$. Thus $\delta_t \geq 0$ in a neighborhood of 0.
Let define $t_0 := \sup\{t > 0 : \delta_t = 0\}$. If $t_0 = +\infty$ the problem is solved.
If not, $U_t \equiv u_t$ on $[0, t_0]$. Let us now define $t_1 := \inf\{t > t_0 : \delta_t < 0\}$. If $t_1 = +\infty$ the problem is solved. If $t_1 < +\infty$, by continuity $\delta_{t_1} = 0$ and then $\frac{\partial \delta_t}{\partial t}|_{t=t_1} \geq 0$. Thus, in a small time intervall after t_1, δ_t would increase and be positive, which is a contradiction with the definition of t_1. Therefore $t \mapsto \delta_t$ increases and stays positive, which implies that

$$0 \leq \overline{u} := \sup_{t \geq 0} u_t \leq \sup_{t \geq 0} U_t < +\infty.$$

□

Let us now recall some properties of the Lotka-Volterra's flow involved in the cell dynamics.

Lemma 3.5 *Let $t_0 \in [0,T]$, $x \in \mathcal{X}$ and $y = (y_1, y_2) \in \mathbb{R}_+^2$ be given. The differential equation*

$$\frac{\partial}{\partial t} y(t) = c(x, y(t)), \; t \in [t_0, T], \; \text{with } y(t_0) = y \tag{3.27}$$

where c defined in (3.22), admits in $\mathbb{R}_+^2$ a unique solution $t \mapsto \varphi_x^{t_0,y}(t) = (\varphi_{x,1}^{t_0,y}(t), \varphi_{x,2}^{t_0,y}(t))$. Moreover the mapping $(x,t,s,y) \mapsto \varphi_x^{s,y}(t)$ is C^0 in $x \in \mathcal{X}$ and C^∞ in $t, s, y \in [0,T]^2 \times \mathbb{R}_+^2$ and is a characteristic flow in the sense that for all s, t, u,

$$\varphi_x^{s,y}(t) = \varphi_x^{u,z}(t), \qquad \text{where } z = \varphi_x^{s,y}(u). \tag{3.28}$$

Proof of Lemma 3.5. Since the coefficients c_i are of class C^1 and thus locally bounded with locally bounded derivatives, the lemma is standard (cf [1]) as soon as the solution does not explode in finite time. The latter is obvious, since the quadratic terms are non positive. Indeed, the functions (y_1, y_2) are dominated by the solution (z_1, z_2) of the system

$$\frac{\partial}{\partial t} z_i(t) = r_i(x) z_i(t) - \beta_i(x)\lambda_{ii} z_i^2 \; ; \; z_i(0) = y_i, \quad i = 1, 2,$$

and we use Lemma 3.4.
The flow clearly satisfies

$$\begin{aligned}
\varphi_{x,1}^{t_0,y}(t) &= y_1 \exp\left(\int_{t_0}^t (r_1(x) - \beta_1(x)\big(\lambda_{11}\varphi_{x,1}^{t_0,y}(s) + \lambda_{12}\varphi_{x,2}^{t_0,y}(s)\big) ds \right), \\
\varphi_{x,2}^{t_0,y}(t) &= y_2 \exp\left(\int_{t_0}^t (r_2(x) - \beta_2(x)\big(\lambda_{21}\varphi_{x,1}^{t_0,y}(s) + \lambda_{22}\varphi_{x,2}^{t_0,y}(s)\big) ds \right).
\end{aligned}$$

□

The proof of uniqueness will be based on the mild equation satisfied by any solution of (3.20). Let us consider a function G defined on $\mathcal{X} \times \mathbb{R}_+^2$ of class C^1 on the two last variables and for any $x \in \mathcal{X}$, let us define the first-order differential operator

$$\mathcal{L}G(x,y) := c_1(x,y)\frac{\partial G}{\partial y_1}(x,y) + c_2(x,y)\frac{\partial G}{\partial y_2}(x,y) = c \cdot \nabla_y G\,(x,y), \tag{3.29}$$

where the notation $\cdot$ means the scalar product in $\mathbb{R}^2$.
Then the function $\tilde{G}(s,t,x,y) := G(x, \varphi_x^{s,y}(t))$ satisfies

$$\begin{aligned}
\frac{\partial}{\partial t}\tilde{G} &= \nabla_y G(x, \varphi_x^{s,y}(t)) \cdot \frac{\partial}{\partial t}\varphi_x^{t_0,y}(t) \\
&= c(x, \varphi_x^{t_0,y}(t)) \cdot \nabla_y G(x, \varphi_x^{s,y}(t)) \\
&= \mathcal{L}G(x, \varphi_x^{s,y}(t)) = \mathcal{L}\tilde{G}
\end{aligned} \tag{3.30}$$

Let us fix $t > 0$. We deduce from (3.30) and from the flow property (3.28) that $\tilde{G}$ satisfies the backward transport equation:

$$\frac{\partial}{\partial s}\tilde{G} + \mathcal{L}\tilde{G} = 0, \; \forall s \leq t \;\; \text{with} \quad \tilde{G}(t,t,x,y) = G(x,y). \tag{3.31}$$

We now write (3.20) applying the measure v_t to the time-dependent function $(s,x,y) \mapsto \tilde{G}(s,t,x,y)$ where $G(x,y) = f(x)g(y)$ and obtain the mild equation

$$\langle v_t, fg\rangle = \langle v_0, f\, g\circ \varphi_x^{0,y}(t)\rangle + \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big\{ \Big(B(x,y_1,y_2)(1-p(x)) \\ - \big(D(x,y_1,y_2) + \alpha(x,y_1,y_2)\, U * v_s(x,y_1,y_2)\big)\Big) f(x) g\circ\varphi_x^{s,y}(t) \\ + p(x)B(x,y_1,y_2) \int f(x+z) g\circ \varphi_{x+z}^{s,y}(t) M(x,z)dz \Big\} v_s(dx,dy_1,dy_2)\; ds. \tag{3.32}$$

(The last term involving the quantity $\frac{\partial}{\partial s} g\circ\varphi_x^{s,y}(t) + \mathcal{L}g(\varphi_x^{s,y}(t))$ vanishes by (3.31).)

Let us now consider two continuous functions v and $\bar{v}$ in $C([0,T], M_F(\mathcal{X}\times\mathbb{R}_+^2))$ solutions of (3.20) with the same initial condition v_0. Then the difference of both solutions satisfies

$$\langle v_t - \bar{v}_t, f g_1 g_2\rangle = \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big\{ \Big[\Big(B(x,y_1,y_2)(1-p(x)) - D(x,y_1,y_2)\Big) f(x) g\circ\varphi_x^{s,y}(t) \\ + p(x)B(x,y_1,y_2) \int f(x+z) g\circ\varphi_{x+z}^{s,y}(t) M(x,z)dz \Big] (v_s(dx,dy_1,dy_2) - \bar{v}_s(dx,dy_1,dy_2)) \\ - \alpha(x,y_1,y_2) f(x) g\circ\varphi_x^{s,y}(t) \Big(U * v_s(x,y_1,y_2) v_s(dx,dy_1,dy_2) - U*\bar{v}_s(x,y_1,y_2)\bar{v}_s(dx,dy_1,dy_2)\Big)\Big\} ds.$$

The finite variation norm of a measure v is defined as usual by

$$\|v\|_{FV} := \sup\{\langle v, h\rangle, h \text{ measurable and bounded by } 1\}.$$

Since all coefficients are bounded as well as the total masses of v_t and $\bar{v}_t$, it is easy to show that there exists a constant C_T such that

$$\|v_t - \bar{v}_t\|_{FV} \le C_T \int_0^t \|v_s - \bar{v}_s\|_{FV}\, ds,$$

which implies, by Gronwall's Lemma, that v and $\bar{v}$ are equal . □

Let us now prove that if the initial measure has a density with respect to Lebesgue measure, then there exists a unique function solution of (3.21). That gives a general existence and uniqueness result for such nontrivial equations with nonlinear reaction and transport terms, and a nonlocal term involved by the mutation kernel. The existence takes place in a very general set of L^1-functions.

Proposition 3.6 *Assume that the initial measure v_0 admits a density ϕ_0 with respect to the Lebesgue measure $dxdy_1dy_2$; then for each $t > 0$, the measure v_t solution of* (3.21) *also admits a density.*

Proof Let us come back to the equation (3.32) satisfied by v. Using basic results on linear parabolic equations, we construct by induction a sequence of functions $(\phi^n)_n$ satisfying in a weak sense the following semi-implicit scheme: $\phi_0^{n+1} \equiv \phi_0$ and

$$\langle \phi_t^{n+1}, fg\rangle = \langle \phi_0, f\, g\circ\varphi_x^{0,y}(t)\rangle + \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big[\Big\{\Big(B(x,y_1,y_2)(1-p(x))f(x)g\circ\varphi_x^{s,y}(t)$$
$$+ p(x)B(x,y_1,y_2)\int f(x+z)g\circ\varphi_{x+z}^{s,y}(t)M(x,z)dz\Big\}\phi_s^n(x,y_1,y_2)$$
$$- \big(D(x,y_1,y_2)+\alpha(x,y_1,y_2)\; U*\phi_s^n(x,y_1,y_2)\big)\Big)f(x)g\circ\varphi_x^{s,y}(t)\phi_s^{n+1}(x,y_1,y_2)\Big]dxdy_1dy_2ds. \quad (3.33)$$

Thanks to the nonnegativity of ϕ_0 and of the parameters B, p, $1-p$, and applying the maximum principle for transport equations (Cf. [1]), we can show that the functions ϕ^n are nonnegative. Taking $f=g=1$ and thanks to the nonnegativity of the functions ϕ^n and to the boundedness of the coefficients we get

$$\sup_{s\le t}\|\phi_s^{n+1}\|_1 \le \|\phi_0\|_1 + C_1\int_0^t \sup_{u\le s}\|\phi_u^n\|_1 du,$$

where the constant C_1 does not depend on n and can be chosen uniformly on [0,T]. By Gronwall's Lemma, we conclude that

$$\sup_n \sup_{t\le T}\|\phi_t^n\|_1 \le \|\phi_0\|_1\, e^{C_1 T}. \quad (3.34)$$

Let us now prove the convergence of the sequence ϕ^n in $L^\infty([0,T],L^1)$. A straightforward computation using (3.33), (3.34), the assumptions on the coefficients and similar arguments as above yields

$$\sup_{s\le t}\|\phi_s^{n+1}-\phi_s^n\|_1 \le C_2\int_0^t\Big(\sup_{u\le s}\|\phi_u^{n+1}-\phi_u^n\|_1 + \sup_{u\le s}\|\phi_u^n-\phi_u^{n-1}\|_1\Big)ds,$$

where C_2 is a positive constant independent of n and $t\in[0,T]$. It follows from Gronwall's Lemma that for each $t\le T$ and n,

$$\sup_{s\le t}\|\phi_s^{n+1}-\phi_s^n\|_1 \le C_3\int_0^t \sup_{u\le s}\|\phi_u^n-\phi_u^{n-1}\|_1\, ds.$$

We conclude that the series $\sum_n \sup_{t\in[0,T]}\|\phi_t^{n+1}-\phi_t^n\|_1$ converges for any $T>0$. Therefore the sequence of functions $(\phi^n)_n$ converges in $L^\infty([0,T],L^1)$ to a continuous function $t\mapsto\phi_t$ satisfying

$$\sup_{t\le T}\|\phi_t\|_1 \le \|\phi_0\|_1\, e^{C_1 T}.$$

Moreover, since the sequence converges in L^1, the limiting measure $\phi_t(x,y_1,y_2)dxdy_1dy_2$ is solution of (3.32) and then it is its unique solution. Hence, that implies that for all t,

$$v_t(dx,dy_1,dy_2) = \phi_t(x,y_1,y_2)\,dxdy_1dy_2.$$

□

We have thus proved that the nonlinear integro-differential equation (3.21) admits a unique weak function-valued solution as soon as the initial condition ϕ_0 is a L^1-function, without any additional regularity assumption.

3.2 Stationary states under a mean field assumption and without trait mutation

This part is a first step in the research of stationary states for the deterministic measure-valued process $(v_t, t \geq 0)$ defined above. We firstly remark that equation (3.23), which determines the evolution of the total number of individuals $t \mapsto \langle v_t, 1\rangle$, is not closed if the functions U, B, D or α are not constant, which makes the problem very hard. In this section we consider the simplest case where the individual ecological parameters B and D and the cell ecological parameters b_i and d_i are constant and where the mutation probability p vanishes. Moreover, we work under the mean field assumption, that is the competition/selection kernel U is a constant. We consider two different cases corresponding to different selection rates α.

3.2.1 Case with constant selection rate

Let us assume that the selection rate α is constant. In this case, the mass equation (3.23) is closed and reduces to the standard logistic equation

$$\langle v_t, 1\rangle = \langle v_0, 1\rangle + \int_0^t \langle v_s, 1\rangle\big((B-D) - \alpha U\langle v_s, 1\rangle\big)\, ds, \tag{3.35}$$

whose asymptotical behavior is well known: the mass of any stationary measure v_∞ satisfies

$$(B-D)\langle v_\infty, 1\rangle = \alpha U\langle v_\infty, 1\rangle^2.$$

Either $R := B - D \leq 0$ and there is extinction of the population, that is

$$\lim_{t\to+\infty}\langle v_t, 1\rangle = \langle v_\infty, 1\rangle = 0.$$

Or $R > 0$ and the mass of the population converges to a non degenerate value

$$\lim_{t\to+\infty}\langle v_t, 1\rangle = \langle v_\infty, 1\rangle = \frac{R}{\alpha U}. \tag{3.36}$$

Furthermore, the convergence of the mass holds exponentially fast: due to (3.35),

$$\frac{\partial}{\partial t}\langle v_t - v_\infty, 1\rangle = -\alpha U\langle v_t, 1\rangle\langle v_t - v_\infty, 1\rangle.$$

$$\text{Thus} \qquad \langle v_t - v_\infty, 1\rangle = \langle v_0 - v_\infty, 1\rangle\, e^{-\alpha U\int_0^t \langle v_s, 1\rangle\, ds} \tag{3.37}$$

which vanishes exponentially fast.

Assume $R > 0$ in such a way that the mass of the population does not vanish. In what follows we will need the following notations:

$$\overline{\langle v, 1\rangle} := \sup_t \langle v_t, 1\rangle < +\infty$$

and

$$\bar{\alpha} := \sup_t \alpha_t (< +\infty) \qquad \text{where} \qquad \alpha_t := R - \alpha U\langle v_t, 1\rangle = -\alpha U\langle v_t - v_\infty, 1\rangle.$$

Let us now consider the weak convergence of the measures v_t towards the stationary measure v_∞, which is concentrated on the equilibrium state of the Lotka-Volterra dynamics. Applying equation (3.20) to any bounded smooth fonction $g(y) = g_1(y_1)g_2(y_2)$,

$$\begin{aligned}\frac{\partial}{\partial t}\langle v_t, g\rangle &= \alpha_t\langle v_t, g\rangle + \langle v_t, r_1 y_1 \frac{\partial g}{\partial y_1} + r_2 y_2 \frac{\partial g}{\partial y_2}\rangle \\ &\quad -\langle v_t, \beta_1 \frac{\partial g}{\partial y_1}\big(\lambda_{11}y_1 + \lambda_{12}y_2\big)y_1 + \beta_2 \frac{\partial g}{\partial y_2}\big(\lambda_{21}y_1 + \lambda_{22}y_2\big)y_2\rangle \\ &= \alpha_t\langle v_t, g\rangle + \langle v_t, \mathcal{L}g\rangle \end{aligned} \tag{3.38}$$

where the differential first order operator $\mathcal{L} = c \cdot \nabla$ is the same as in (3.29) but without dependence on the trait x. Using the flow of Lotka-Volterra equation (see (3.27)), we represent the mild solution of (3.38) as

$$\langle v_t, g\rangle = \int_{\mathbb{R}_+^2} g \circ \varphi^{0,y}(t)\, v_0(dy) + \int_0^t \alpha_s \int_{\mathbb{R}_+^2} g \circ \varphi^{s,y}(t)\, v_s(dy)\, ds. \tag{3.39}$$

Let us firstly recall the long time behavior of the Lotka-Volterra system (3.27) in case where the coefficients c_i don't depend on x(see Istas [8]).

Lemma 3.7 *Any solution of*

$$\begin{aligned}\frac{\partial}{\partial t} y_1(t) &= y_1(t)\left(r_1 - \beta_1\big(\lambda_{11}y_1(t) + \lambda_{12}y_2(t)\big)\right) \\ \frac{\partial}{\partial t} y_2(t) &= y_2(t)\left(r_2 - \beta_2\big(\lambda_{21}y_1(t) + \lambda_{22}y_2(t)\big)\right)\end{aligned} \tag{3.40}$$

with non-zero initial condition in $\mathbb{R}_+^2$ converges for t large to a finite limit, called equilibrium and denoted by $\pi = (\pi_1, \pi_2) \in \mathbb{R}_+^2 \setminus \{(0,0)\}$. It takes the following values:

1. $\pi = (\frac{r_1}{\beta_1\lambda_{11}}, 0)$ *if* $r_2\lambda_{11} - r_1\lambda_{21} < 0$ *(resp.* $= 0$ *and* $r_1\lambda_{22} - r_2\lambda_{12} > 0$*).*
2. $\pi = (0, \frac{r_2}{\beta_2\lambda_{22}})$ *if* $r_1\lambda_{22} - r_2\lambda_{12} < 0$ *(resp.* $= 0$ *and* $r_2\lambda_{11} - r_1\lambda_{21} > 0$ *).*
3. *If* $r_2\lambda_{11} - r_1\lambda_{12} > 0$ *and* $r_1\lambda_{22} - r_2\lambda_{21} > 0$

$$\pi = \Big(\frac{\beta_1\lambda_{12}(b_2 - d_2) - \beta_2\lambda_{22}(b_1 - d_1)}{\beta_1\beta_2(\lambda_{12}\lambda_{21} - \lambda_{11}\lambda_{22})}, \frac{\beta_2\lambda_{21}(b_1 - d_1) - \beta_1\lambda_{11}(b_2 - d_2)}{\beta_1\beta_2(\lambda_{12}\lambda_{21} - \lambda_{11}\lambda_{22})}\Big). \tag{3.41}$$

Therefore we obtain the following convergence result.

Proposition 3.8 *The deterministic measure-valued process v_t converges for large time t - in the weak topology - towards the singular measure concentrated on the equilibrium state π of the associated Lotka-Volterra dynamics:*

$$\lim_{t\to+\infty} v_t = \frac{R}{\alpha U}\,\delta_{(\pi_1,\pi_2)},$$

where $\pi = (\pi_1, \pi_2)$ is defined in Lemma 3.7.

Proof First, the Lotka-Volterra flow $\varphi^{0,y}(t)$ converges for large t towards (π_1, π_2) given by Lemma 3.7. Since the test function g is continuous and bounded and v_0 has a finite mass, Lebesgue's dominated theorem implies that the first term in the right hand side of (3.39) converges:

$$\lim_t \int_{\mathbb{R}_+^2} g \circ \varphi^{0,y}(t)\, v_0(dy) = \int_{\mathbb{R}_+^2} \lim_t g \circ \varphi^{0,y}(t)\, v_0(dy) = g(\pi_1, \pi_2)\, \langle v_0, 1 \rangle.$$

Secondly, as already seen in (3.37), the mass $\langle v_t, 1 \rangle$ of the total population converges exponentially fast to its equilibrium size, that is α_t converges exponentially fast to 0:

$$\exists c > 0, \exists t_0, \quad \forall s > t_0 \quad \alpha_s \leq e^{-cs}.$$

Therefore the second term in the right hand side of (3.39) can be disintegrated, for t larger than t_0, in the sum of two integrals over $[0, t_0]$ and $[t_0, t]$. The control of the integral over $[t_0, t]$ is simple:

$$\left| \int_{t_0}^t \alpha_s \int_{\mathbb{R}_+^2} g \circ \varphi^{s,y}(t)\, v_s(dy)\, ds \right| \leq \langle \overline{v, 1} \rangle \sup_y |g(y)| \int_{t_0}^t e^{-cs} ds$$

which is as small as one wants, when t_0 is large enough.
On the compact time interval $[0, t_0]$ the following convergence holds:

$$\begin{aligned} \lim_t \int_0^{t_0} \alpha_s \int_{\mathbb{R}_+^2} g \circ \varphi^{s,y}(t)\, v_s(dy)\, ds &= \int_0^{t_0} \alpha_s \int_{\mathbb{R}_+^2} \lim_t g \circ \varphi^{s,y}(t)\, v_s(dy)\, ds \\ &= g(\pi_1, \pi_2) \int_0^{t_0} \alpha_s \int_{\mathbb{R}_+^2} v_s(dy)\, ds. \end{aligned}$$

Therefore for large time $t > t_0$, $\langle v_t, g \rangle$ is as close as one wants to

$$g(\pi_1, \pi_2)\, \langle v_0, 1 \rangle \; + g(\pi_1, \pi_2) \int_0^{t_0} \alpha_s \int_{\mathbb{R}_+^2} v_s(dy)\, ds = g(\pi_1, \pi_2)\, \langle v_{t_0}, 1 \rangle.$$

For t_0 large enough, this last quantity is close to $g(\pi_1, \pi_2)\, \langle v_\infty, 1 \rangle = \frac{R}{\alpha U} \langle \delta_{(\pi_1, \pi_2)}, g \rangle$.
This completes the proof of the weak convergence of the measures v_t. □

Remark 3.9 *The stationary state is a singular one even if the initial measure v_0 has a density: the absolute continuity property of the measure v_t is conserved for any finite time t, but it is lost in infinite time.*

Convergence of the number of cells
First we prove the boundedness of the number of cells of each type and the boundedness of its second moment. To this aim, we compare the multitype dynamics with a dynamics where the different types do not interact, which corresponds to two independent monotype systems.

Lemma 3.10 *If $\langle v_0, 1 \rangle + \langle v_0, y_i^2 \rangle < +\infty$ then $\sup_{t \geq 0} \langle v_t, y_i^2 \rangle < +\infty$.*

Proof Let us firstly prove that $\sup_{t\geq 0}\langle v_t, y_i\rangle < +\infty$.
At time $t=0$, $\langle v_0, y_i\rangle \leq \langle v_0, 1\rangle + \langle v_0, y_i^2\rangle < +\infty$. Moreover, equation (3.24) reads now

$$\begin{aligned}
\frac{\partial}{\partial t}\langle v_t, y_i\rangle &= \big(R-\alpha U\langle v_t,1\rangle\big)\langle v_t, y_i\rangle + (b_i-d_i)\langle v_t, y_i\rangle - \beta_i(\lambda_{ii}\langle v_t, y_i^2\rangle + \lambda_{ij}\langle v_t, y_i y_j\rangle) \\
&\leq (\alpha_t + b_i - d_i)\langle v_t, y_i\rangle - \beta_i\lambda_{ii}\langle v_t, y_i^2\rangle \\
&\leq (\alpha_t + b_i - d_i)\langle v_t, y_i\rangle - \frac{\beta_i\lambda_{ii}}{\langle v_t, 1\rangle}\langle v_t, y_i\rangle^2 \\
&\leq (\bar{\alpha} + r_i)\langle v_t, y_i\rangle - \frac{\beta_i\lambda_{ii}}{\overline{\langle v, 1\rangle}}\langle v_t, y_i\rangle^2. \qquad (3.42)
\end{aligned}$$

This inequality is a logistic one in the sense of Lemma 3.4. Therefore one deduces that the number of cells of type i is uniformly bounded in time:

$$\sup_{t\geq 0}\langle v_t, y_i\rangle < +\infty, \quad i=1,2.$$

By (3.20) applied with $f\equiv 1$, $g_1(y_1)=y_1^2$, $g_2\equiv 1$, one obtains

$$\begin{aligned}
\frac{\partial}{\partial t}\langle v_t, y_1^2\rangle &= \alpha_t\langle v_t, y_1^2\rangle + 2r_1\langle v_t, y_1^2\rangle - 2\beta_1\Big(\lambda_{11}\langle v_t, y_1^3\rangle + \lambda_{12}\langle v_t, y_1^2 y_2\rangle\Big) \\
&\leq (\alpha_t + 2r_1)\langle v_t, y_1^2\rangle - 2\beta_1\lambda_{11}\langle v_t, y_1^3\rangle \\
&\leq (\alpha_t + 2r_1)\langle v_t, y_1^2\rangle - 2\beta_1\lambda_{11}\frac{1}{\langle v_t, y_1\rangle}\langle v_t, y_1^2\rangle^2 \\
&\leq (\bar{\alpha} + 2r_1)\langle v_t, y_1^2\rangle - 2\beta_1\lambda_{11}\frac{1}{\overline{\langle v, y_1\rangle}}\langle v_t, y_1^2\rangle^2
\end{aligned}$$

since

$$\langle v_t, y_1^2\rangle^2 \leq \langle v_t, y_1^3\rangle\langle v_t, y_1\rangle.$$

This inequality on $\langle v_t, y_1^2\rangle$ is of logistic type as (3.42). Lemma 3.4 implies

$$\overline{\langle v, y_1^2\rangle} := \sup_{t\geq 0}\langle v_t, y_1^2\rangle < +\infty.$$

The same holds for $\overline{\langle v, y_2^2\rangle}$. □

Proposition 3.11 *If $\langle v_0, y_i\rangle < +\infty$ and $\langle v_0, y_i^2\rangle < +\infty$, then the total number of cells of each type per individual $\frac{\langle v_t, y_i\rangle}{\langle v_t, 1\rangle}$ stabilizes for t large:*

$$\lim_{t\to+\infty}\frac{\langle v_t, y_i\rangle}{\langle v_t, 1\rangle} = \pi_i.$$

Proof Due to Proposition 3.8, the family of measures $(v_t)_t$ converge weakly towards v_∞. Moreover, by Lemma 3.10, the second moments of v_t are uniformly bounded. Therefore y_i is uniformly integrable under the family of $(v_t)_t$ which leads to :

$$\lim_{t\to+\infty}\langle v_t, y_i\rangle = \langle \lim_{t\to+\infty} v_t, y_i\rangle = \langle v_\infty, y_i\rangle.$$

□

Let us underline the decorrelation at infinity between cell and individual dynamics.

3.2.2 Case with linear selection rate

Suppose now that the selection rate α does not depend on the trait x but is linear as function of the number of cells of each type :

$$\exists \alpha_1, \alpha_2 \in]0,1[, \quad \alpha(x, y_1, y_2) = \alpha_1 y_1 + \alpha_2 y_2 =: \alpha \cdot y.$$

With other words the selection increases linearly when the number of cells increases.
The new main difficulty comes from the fact that the mass equation is no more closed :

$$\langle v_t, 1\rangle = \langle v_0, 1\rangle + \int_0^t \langle v_s, 1\rangle \big(R - U\langle v_s, \alpha \cdot y\rangle\big)\, ds, \tag{3.43}$$

which has as (implicit) solution

$$\langle v_t, 1\rangle = \langle v_0, 1\rangle e^{-\int_0^t \left(U\langle v_s, \alpha\cdot y\rangle - R\right) ds}. \tag{3.44}$$

For this reason, unfortunately, we did not succeed in proving the convergence in time of $\langle v_t, 1\rangle$. Nevertheless, we can conjecture some limiting behavior of the process.

Conjecture : The deterministic measure-valued process v_t converges for large time t towards the following stationary value

$$\lim_{t\to+\infty} v_t = v_\infty := \frac{R}{U(\alpha_1\pi_1 + \alpha_2\pi_2)}\, \delta_{(\pi_1,\pi_2)}, \tag{3.45}$$

where $\pi = (\pi_1, \pi_2)$ is given in Lemma 3.7.

In this case too, the asymptotic proportions of the cells of different types per individual would become deterministic and independent.

Some partial answers

- Equation (3.43) implies that any stationary measure v_∞ should satisfy

  $$\langle v_\infty, 1\rangle \big(R - U\langle v_\infty, \alpha\cdot y\rangle\big) = 0.$$

  Then, either $\langle v_\infty, 1\rangle = 0$, that means the extinction of the individual population holds, or

  $$\langle v_\infty, \alpha \cdot y\rangle = \langle v_\infty, \alpha_1 y_1 + \alpha_2 y_2\rangle = \frac{B - D}{U} = \frac{R}{U} \tag{3.46}$$

  which describes a constraint between the limiting number of the different types of cells.

- *Boundedness of the number of cells.*

  Lemma 3.12

  $$\langle v_0, y_i\rangle < +\infty \quad \Longrightarrow \quad \sup_{t\geq 0} \langle v_t, y_i\rangle < +\infty.$$

Proof The number of cells of type i satisfies

$$\begin{aligned}\frac{\partial}{\partial t}\langle v_t, y_i\rangle &= \langle v_t, y_i\rangle\big(R+r_i\big) - U\langle v_t, y_i\alpha\cdot y\rangle\langle v_t,1\rangle - \beta_i\big(\lambda_{ii}\langle v_t, y_i^2\rangle + \lambda_{ij}\langle v_t, y_iy_j\rangle\big)\\ &\leq (R+r_i)\langle v_t, y_i\rangle - \alpha_i U\langle v_t, y_i\rangle^2 \qquad (3.47)\end{aligned}$$

which reduces to the monotype case solved in Lemma 3.4. □

- *Identification of a unique possible non trivial equilibrium.*

Applying Equation (3.20) to $f\equiv 1$, $g_i(y)=e^{-z_iy}$ and letting t tend to infinity, we remark that the Laplace transform $\mathbf{L}_\infty(z)$ of any non vanishing stationary state v_∞ should satisfy

$$\begin{aligned}&R\mathbf{L}_\infty(z) - U\langle v_\infty,1\rangle\langle v_\infty,(\alpha\cdot y)e^{-z\cdot y}\rangle\\ &-\sum_{i=1}^{2} z_i\Big(r_i\langle v_\infty, y_ie^{-z\cdot y}\rangle - \beta_i\big(\lambda_{ii}\langle v_\infty, y_i^2e^{-z\cdot y}\rangle + \lambda_{ij}\langle v_\infty, y_iy_je^{-z\cdot y}\rangle\big)\Big)=0\\ &\Rightarrow R\mathbf{L}_\infty + U\mathbf{L}_\infty(0)(\alpha_1\frac{\partial\mathbf{L}_\infty}{\partial z_1}+\alpha_2\frac{\partial\mathbf{L}_\infty}{\partial z_2})\\ &\quad+\sum_{i=1}^{2}\Big(z_ir_i\frac{\partial\mathbf{L}_\infty}{\partial z_i} + z_i\beta_i\big(\lambda_{ii}\frac{\partial^2\mathbf{L}_\infty}{\partial z_i^2}+\lambda_{ij}\frac{\partial^2\mathbf{L}_\infty}{\partial z_i\partial z_j})\Big)=0 \qquad (3.48)\end{aligned}$$

with usual boundary conditions

$$\mathbf{L}_\infty(0)=\langle v_\infty,1\rangle,\quad \frac{\partial\mathbf{L}_\infty}{\partial z_i}(0) = -\langle v_\infty, y_i\rangle.$$

The unique non trivial solution of this p.d.e. is

$$\mathbf{L}_\infty(z)=\langle v_\infty,1\rangle\, e^{-\tilde{\pi}\cdot z},$$

where $\langle v_\infty,1\rangle = \frac{U}{\alpha\cdot\tilde{\pi}}$ and where $\tilde{\pi}_i$, the equilibrium proportion of cells of type i in the global population, has to be equal to the equilibrium proportion given in Lemma 3.7: $\tilde{\pi}=\pi$.

- *Local stability of the non trivial equilibrium* $v_\infty := \frac{R}{U\alpha\cdot\pi}\,\delta_{(\pi_1,\pi_2)}$.

Although we cannot control the convergence of $\langle v_t,1\rangle$ to a positive number, we can analyze the stability of the nontrivial stationary state v_∞ in the following sense.

Stability of the mass around its positive stationary value $\frac{R}{U\alpha\cdot\pi}$
Let start with $v_0 = v_\infty + \varepsilon\delta_{(\zeta_1,\zeta_2)}$, where ε is small and $(\zeta_1,\zeta_2)\in\mathbb{R}_+^2$. From the mass equation (3.43) one obtains for t small :

$$\begin{aligned}\frac{\partial}{\partial t}\langle v_t,1\rangle &= \langle v_t,1\rangle\big(R-U\langle v_t,\alpha\cdot y\rangle\big)\\ &\simeq (\langle v_\infty,1\rangle+\varepsilon)\big(R-U\langle v_\infty,\alpha\cdot y\rangle - \varepsilon U\,\alpha\cdot\zeta\big)\\ &\simeq -\varepsilon\,\frac{\alpha\cdot\zeta}{\alpha\cdot\pi}+o(\varepsilon).\end{aligned}$$

This quantity is negative for small ε, which implies the stability of the mass around its positive stationary value.

Stability of the number of cells of each type around its limit value if $\max(r_1, r_2) < R$
We prove it only for the type 1. From (3.24) we get an expansion in ε of the variation of the global number of cells of type 1 for small time :

$$
\begin{aligned}
\frac{\partial}{\partial t}\langle v_t, y_1\rangle &= \langle v_t, y_1\rangle\big(R+r_1\big) - U\langle v_t, y_1\,\alpha\cdot y\rangle\langle v_t,1\rangle - \beta_1\big(\lambda_{11}\langle v_t, y_1^2\rangle + \lambda_{12}\langle v_t, y_1y_2\rangle\big)\\
&\simeq \big(\langle v_\infty, y_1\rangle + \varepsilon\zeta_1\big)\big(R+r_1\big) - U\big(\langle v_\infty, y_1\,\alpha\cdot y\rangle + \varepsilon\zeta_1\,\alpha\cdot\zeta\big)\big(\langle v_\infty,1\rangle+\varepsilon\big)\\
&\qquad -\beta_1\big(\lambda_{11}\langle v_\infty, y_1^2\rangle + \lambda_{12}\langle v_\infty, y_1y_2\rangle\big) - \varepsilon\beta_1(\lambda_{11}\zeta_1^2 + \lambda_{12}\zeta_1\zeta_2)\\
&= \varepsilon\Big((R+r_1)\zeta_1 - U\langle v_\infty, y_1\,\alpha\cdot y\rangle - U\zeta_1\,\alpha\cdot\zeta\langle v_\infty,1\rangle - \beta_1(\lambda_{11}\zeta_1^2 + \lambda_{12}\zeta_1\zeta_2)\Big) + o(\varepsilon)\\
&= \bar{P}_1(\zeta_1,\zeta_2) + o(\varepsilon)
\end{aligned}
$$

where $\bar{P}_1(y_1, y_2) \le P_1(y_1)$ for all $y_2 > 0$, with

$$P_1(X) := -\big(U\alpha_1\langle v_\infty, 1\rangle + \beta_1\lambda_{11}\big)X^2 + (R+r_1)X - U\alpha_1\pi_1^2\langle v_\infty,1\rangle.$$

As second degree polynomial P_1 is negative if its discriminant is non positive. This condition is fulfilled when

$$(R+r_1)^2 - 4U\alpha_1\pi_1^2\langle v_\infty,1\rangle\big(U\alpha_1\langle v_\infty,1\rangle + \beta_1\lambda_{11}\big) < 0.$$

It is true as soon as

$$(R+r_1)^2 - 4R^2 < 0 \Leftrightarrow r_1 < R.$$

Thus if $\max(r_1, r_2) < R$, the number of cells of each type is stable around its limiting value.

4 Diffusion and superprocess approximations

As in the above section we introduce the renormalization $\kappa = (K, K_1, K_2)$ both for individuals and for cells. Moreover we introduce an acceleration of individual births and deaths with a factor K^η (and a mutation kernel M_K with amplitude of order $K^{\eta/2}$) and an acceleration of cell births and deaths with a factor K_1 (resp. K_2).

We summarize below the assumptions we need on the model and which will be considered in all this section.

Assumptions (H3):
1) There exist continuous functions Γ, B, D, α *on* $\mathcal{X} \times \mathbb{R}_+ \times \mathbb{R}_+$ *such that*

$$\begin{aligned} B_\kappa(x, n_1, n_2) &= K^\eta\, \Gamma(x, \frac{n_1}{K_1}, \frac{n_2}{K_2}) + B(x, \frac{n_1}{K_1}, \frac{n_2}{K_2}); \\ D_\kappa(x, n_1, n_2) &= K^\eta\, \Gamma(x, \frac{n_1}{K_1}, \frac{n_2}{K_2}) + D(x, \frac{n_1}{K_1}, \frac{n_2}{K_2}); \\ \alpha_\kappa(x, n_1, n_2) &\equiv \alpha(x, \frac{n_1}{K_1}, \frac{n_2}{K_2}). \end{aligned} \tag{4.49}$$

The function Γ *is assumed to be bounded and* B, D, α *satisfy Assumptions (H1).*
2) As before, the competition kernel satisfies

$$U_\kappa(x) = \frac{U(x)}{K},$$

where U *is a continuous function which satisfies Assumption (H1).*
3) The mutation law $z \mapsto M_K(x, z)$ *is a centered probability density on* $\mathcal{X} - x$*. Its covariance matrix is* $\frac{\sigma(x)^2}{K^\eta} Id$*, where* σ *is a continuous function. We also assume that*

$$\lim_{K\to\infty} K^\eta \sup_x \int |z|^3 M_K(x, z) dz = 0.$$

The parameter p_κ *stays unchanged:* $p_\kappa(x) = p(x)$.
4) At the cell level, we introduce Lipschitz continuous functions b_i, d_i *on* $\mathcal{X}$ *and a continuous function* γ *such that*

$$\begin{aligned} b_{i,\kappa}(x) &= K_i\, \gamma(x) + b_i(x); \\ d_{i,\kappa}(x) &= K_i\, \gamma(x) + d_i(x), \quad i = 1, 2. \end{aligned} \tag{4.50}$$

The interaction between the cells is rescaled according on their type :

$$\lambda_{ij}^\kappa = \frac{\lambda_{ij}}{K_j}, \qquad i, j \in \{1, 2\}. \tag{4.51}$$

The other parameters stay unchanged: $\beta_{1,\kappa} = \beta_1$*,* $\beta_{2,\kappa} = \beta_2$*.*
5) **Ellipticity:** *The functions* p*,* σ*,* γ *and* Γ *are lower bounded by positive constants and* $\sigma\sqrt{p\,\Gamma}$ *and* $\sqrt{\gamma}$ *are Lipschitz continuous.*

As in the section 3, we define the measure-valued Markov process $(Z_t^\kappa)_{t\geq 0}$ as

$$Z_t^\kappa = \frac{1}{K} \sum_{i=1}^{I_\kappa(t)} \delta_{(X_\kappa^i(t), \frac{N_{1,\kappa}^i(t)}{K_1}, \frac{N_{2,\kappa}^i(t)}{K_2})}.$$

We may summarize as in Proposition 3.1 the moment and martingale properties of Z^κ.

Proposition 4.1 *Assume that for some $p \geq 3$, $\mathbb{E}(\langle Z_0^\kappa, 1\rangle^p + \langle Z_0^\kappa, y_1^2 + y_2^2\rangle) < +\infty$. Then*

(1) *For any $T > 0$, $\mathbb{E}\left(\sup_{t\in[0,T]}\langle Z_t^\kappa, 1\rangle^3 + \sup_{t\in[0,T]}\langle Z_t^\kappa, y_1^2 + y_2^2\rangle\right) < +\infty$.*

(2) *For any measurable bounded functions f, g_1, g_2, the process*

$$
\begin{aligned}
\bar{M}_t^{\kappa,fg} &= \langle Z_t^\kappa, fg_1g_2\rangle - \langle Z_0^\kappa, fg_1g_2\rangle \\
&- \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big\{ \Big(B(x,y_1,y_2) - D(x,y_1,y_2) - \alpha(x,y_1,y_2)\; U * Z_s^\kappa(x,y_1,y_2)\Big) f(x)g_1(y_1)g_2(y_2) \\
&\quad + p(x)\big(K^\eta\,\Gamma(x,y_1,y_2) + B(x,y_1,y_2)\big) \int \big(f(x+z) - f(x)\big)g_1(y_1)g_2(y_2)M_K(x,z)dz \\
&\quad + f(x)\big(g_1(y_1 + \frac{1}{K_1}) - g_1(y_1)\big)g_2(y_2)\; (K_1\gamma(x) + b_1(x))\; K_1y_1 \\
&\quad + f(x)g_1(y_1)\big(g_2(y_2 + \frac{1}{K_2}) - g_2(y_2)\big)\; (K_2\gamma(x) + b_2(x))\; K_2y_2 \\
&\quad + f(x)\big(g_1(y_1 - \frac{1}{K_1}) - g_1(y_1)\big)g_2(y_2)\,(K_1\gamma(x) + d_1(x) + \beta_1(x)(y_1\lambda_{11} + y_2\lambda_{12}))\,K_1y_1 \\
&\quad + f(x)g_1(y_1)\big(g_2(y_1 - \frac{1}{K_2}) - g_2(y_2)\big)\,(K_2\gamma(x) + d_2(x) + \beta_2(x)(y_1\lambda_{21} + y_2\lambda_{22}))\,K_2y_2\Big\} \\
&\qquad Z_s^\kappa(dx, dy_1, dy_2)\; ds \qquad (4.52)
\end{aligned}
$$

is a càdlàg square integrable $(\mathcal{F}_t)_{t\geq 0}$-martingale with quadratic variation

$$
\begin{aligned}
\langle \bar{M}^{\kappa,fg}\rangle_t &= \frac{1}{K}\int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big\{ \Big(2K^\eta\,\Gamma(x,y_1,y_2) + B(x,y_1,y_2) \\
&\qquad + D(x,y_1,y_2) + \alpha(x,y_1,y_2)\; U * Z_s^\kappa(x,y_1,y_2)\Big) f^2(x)g_1^2(y_1)g_2^2(y_2) \\
&+ p(x)\big(K^\eta\,\Gamma(x,y_1,y_2) + B(x,y_1,y_2)\big) \int \big(f(x+z) - f(x)\big)^2 M_K(x,z)dz\; g_1^2(y_1)g_2^2(y_2) \\
&+ f^2(x)\; \big(g_1(y_1 + \frac{1}{K_1}) - g_1(y_1)\big)^2\; g_2^2(y_2)\; (K_1\gamma(x) + b_1(x))\; K_1y_1 \\
&+ f^2(x)\; g_1^2(y_1)\; \big(g_2(y_2 + \frac{1}{K_2}) - g_2(y_2)\big)^2\; (K_2\gamma(x) + b_2(x))\; K_2y_2 \\
&+ f^2(x)\; \big(g_1(y_1 - \frac{1}{K_1}) - g_1(y_1)\big)^2\; g_2^2(y_2)\; \Big(K_1\gamma(x) + d_1(x) + \beta_1(x)(y_1\lambda_{11} + y_2\lambda_{12})\Big)K_1y_1 \\
&+ f^2(x)\; g_1^2(y_1)\; \big(g_2(y_2 - \frac{1}{K_2}) - g_2(y_2)\big)^2\; \Big(K_2\gamma(x) + d_2(x) + \beta_2(x)(y_1\lambda_{21} + y_2\lambda_{22})\Big)K_2y_2\Big\} \\
&\qquad Z_s^\kappa(dx, dy_1, dy_2)\; ds. \quad (4.53)
\end{aligned}
$$

We assume that the sequence of initial conditions Z_0^κ converges in law to some finite measure ζ_0. Let us study the limiting behavior of the processes Z^κ as κ tends to infinity. It depends on the value of η and leads to two different convergence results.
As before we denote by r_i the rate $b_i - d_i$.

Theorem 4.2 *Assume $(H3)$ and $\eta \in]0,1[$; suppose that the initial conditions $Z_0^\kappa \in M_F(\mathcal{X}\times \mathbb{R}_+^2)$ satisfies $\sup_\kappa E(\langle Z_0^\kappa, 1\rangle^3) < +\infty$. If further, the sequence of measures $(Z_0^\kappa)_\kappa$ converges in law to a finite deterministic measure w_0, then the sequence of processes $(Z_t^\kappa)_{0\le t\le T}$ converges in law in the Skorohod space $\mathbb{D}([0,T], M_F(\mathcal{X}\times\mathbb{R}_+^2))$, as κ goes to infinity, to the unique (deterministic) flow of functions $w \in C([0,T], \mathbb{L}^1(\mathcal{X}\times\mathbb{R}_+^2))$ weak solution of*

$$\frac{\partial}{\partial t} w_t = \Big(B - D - \alpha\ U * w_t\Big) w_t + \triangle_x\left(p\,\sigma^2\,\Gamma\, w_t\right) + \triangle_y(\gamma\, w_t) - \nabla_y\cdot(c w_t). \qquad (4.54)$$

Remark 4.3 *One obtains the existence and uniqueness of function-valued solutions of* (4.54) *even if the initial measure w_0 is a degenerate one without density.*

Proof The proof follows the same steps as the one of Theorem 3.2 except that the mutation term will lead to a Laplacian term in f since the mutation kernel is centered and the mutation steps converge to 0 in the appropriate scale. We first obtain the tightness of the sequence (Z^κ) and the fact that each subsequence converges to a measure-valued flow $w \in C([0,T], M_F(\mathcal{X}\times\mathbb{R}_+^2))$ satisfying for bounded C^2-functions f, g_1, g_2,

$$\begin{aligned}\langle w_t, f g_1 g_2\rangle = \langle w_0, f g_1 g_2\rangle + \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big\{ \Big(& B(x,y_1,y_2) \\ & - D(x,y_1,y_2) - \alpha(x,y_1,y_2)\ U * w_s(x,y_1,y_2)\Big) f(x) g_1(y_1) g_2(y_2) \\ & + p(x)\sigma^2(x)\Gamma(x,y_1,y_2) \triangle f(x)\, g_1(y_1) g_2(y_2) \\ & + f(x)\nabla g_1(y_1) g_2(y_2)\Big(r_1(x) - \beta_1(x)(y_1\lambda_{11} + y_2\lambda_{12})\Big)\ y_1 \\ & + f(x) g_1(y_1)\nabla g_2(y_2)\Big(r_2(x) - \beta_2(x)(y_1\lambda_{21} + y_2\lambda_{22})\Big)\ y_2 \\ & + f(x)\gamma(x)\left(\triangle g_1(y_1) g_2(y_2) + g_1(y_1)\triangle g_2(y_2)\right)\Big\} w_s(dx, dy_1, y_2)\, ds. \qquad (4.55)\end{aligned}$$

We can also apply w_t to smooth time-dependent test functions $h(t,x,y)$ defined on $\mathbb{R}_+\times\mathcal{X}\times\mathbb{R}_+^2$. That will add a term of the form $\langle \partial_s h, w_s\rangle$ in (4.55).
Let us now sketch the uniqueness argument. Thanks to the Lipschitz continuity and ellipticity assumption $(H3)$, the semigroup associated with the infinitesimal generator

$$\mathcal{A} := p\,\sigma^2\,\Gamma\,\triangle_x + \gamma\,\triangle_y + c\cdot\nabla_y$$

admits at each time $t > 0$ a smooth density denoted by $\psi^{x,y}(t,\cdot,\cdot)$ on $\mathcal{X}\times\mathbb{R}_+^2$. That is, for any bounded continuous function G on $\mathcal{X}\times\mathbb{R}_+^2$, the function

$$\check{G}(t,x,y) = \int \psi^{x,y}(t,x',y') G(x',y') dx' dy'$$

satisfies

$$\frac{\partial}{\partial t}\check{G} = \mathcal{A}\check{G}; \quad \check{G}(0,\cdot,\cdot) = G.$$

Thus (4.55) applied to the test function $(s,x,y) \mapsto \check{G}(t-s,x,y)$ leads to the mild equation: for any continuous and bounded function G,

$$\begin{aligned}
\langle w_t, G\rangle &= \langle w_0, \check{G}(t,\cdot)\rangle + \int_0^t \langle w_s, (B-D-\alpha U * w_s)\check{G}(t-s,\cdot)\rangle\, ds \\
&= \int_{\mathcal{X}\times\mathbb{R}_+^2} G(x',y') \int_{\mathcal{X}\times\mathbb{R}_+^2} \psi^{x,y}(t,x',y') w_0(dx,dy)\, dx'dy' \\
&+ \int G(x',y') \int_0^t \int \big(B-D-\alpha U * w_s\big)(x,y)\, \psi^{x,y}(t-s,x',y') w_s(dx,dy)\, ds\, dx'dy'.
\end{aligned} \tag{4.56}$$

It is simple to deduce from this representation the uniqueness of the measure-valued solutions of (4.55). Moreover, by Fubini's theorem and $(H3)$ and since $\sup_{t\leq T}\langle w_t, 1\rangle < +\infty$, one observes that

$$\langle w_t, G\rangle = \int_{\mathcal{X}\times\mathbb{R}_+^2} G(x',y') H_t(x',y') dx'dy',$$

with $H \in \mathbb{L}^\infty([0,T], \mathbb{L}^1(\mathcal{X}\times\mathbb{R}_+^2))$. Thus for any $t \leq T$, the finite measure w_t is absolutely continuous with respect to the Lebesgue's measure and the solution of (4.55) is indeed a function for any positive time. □

If $\eta = 1$ the limiting process of Z^κ is no more deterministic but is a random superprocess with values in $C([0,T], M_F(\mathcal{X}\times\mathbb{R}_+^2))$.

Theorem 4.4 *Assume $(H3)$ and $\eta = 1$. Assume moreover that the initial conditions $Z_0^\kappa \in M_F(\mathcal{X}\times\mathbb{R}_+^2)$ satisfy $\sup_\kappa E(\langle Z_0^\kappa, 1\rangle^3) < +\infty$. If they converge in law as κ tends to infinity to a finite deterministic measure ζ_0, then the sequence of processes $(Z_t^\kappa)_{0\leq t\leq T}$ converges in law in the Skorohod space $\mathbb{D}([0,T], M_F(\mathcal{X}\times\mathbb{R}_+^2))$, as κ goes to infinity, to the continuous measure-valued semimartingale $\zeta \in C([0,T], M_F(\mathcal{X}\times\mathbb{R}_+^2))$ satisfying for any bounded smooth functions f, g_1, g_2:*

$$\begin{aligned}
&M_t^{fg} := \langle \zeta_t, fg_1g_2\rangle - \langle \zeta_0, fg_1g_2\rangle \\
&- \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big\{ \Big(B(x,y_1,y_2) - D(x,y_1,y_2) - \alpha(x,y_1,y_2)\ U * \zeta_s(x,y_1,y_2)\Big) f(x)g_1(y_1)g_2(y_2) \\
&\quad + p(x)\sigma^2(x)\Gamma(x,y_1,y_2) \triangle f(x) g_1(y_1)g_2(y_2) \\
&\quad + f(x)\nabla g_1(y_1)g_2(y_2)\Big(r_1(x) - \beta_1(x)(y_1\lambda_{11} + y_2\lambda_{12})\Big)\ y_1 \\
&\quad + f(x)g_1(y_1)\nabla g_2(y_2)\Big(r_2(x) - \beta_2(x)(y_1\lambda_{21} + y_2\lambda_{22})\Big)\ y_2 \\
&\quad + f(x)\gamma(x)\left(\triangle g_1(y_1)g_2(y_2) + g_1(y_1) \triangle g_2(y_2)\right) \Big\} \zeta_s(dx,dy_1,dy_2)\ ds
\end{aligned} \tag{4.57}$$

is a continuous square integrable $(\mathcal{F}_t)_{t\geq 0}$-martingale with quadratic variation

$$\langle M^{fg}\rangle_t = \int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} 2\,\Gamma(x,y_1,y_2) f^2(x) g_1^2(y_1) g_2^2(y_2) \zeta_s(dx,dy_1,dy_2)\ ds. \tag{4.58}$$

Proof The convergence is obtained by a compactness-uniqueness argument. The uniform tightness of the laws and the identification of the limiting values can be adapted from [7] with some careful moment estimates and an additional drift term as in the proof of Theorem 3.2.
The uniqueness can be deduced from the one with $B = D = \alpha = 0$ by using the Dawson-Girsanov transform for measure-valued processes (cf. Theorem 2.3 in [5]), as soon as the ellipticity assumption for Γ is satisfied. Indeed,

$$\mathbb{E}\left(\int_0^t \int_{\mathcal{X}\times\mathbb{R}_+^2} \Big(B(x,y_1,y_2) - D(x,y_1,y_2) - \alpha(x,y_1,y_2)\; U * \zeta_s(x,y_1,y_2)\Big)^2 \zeta_s(dx,dy_1,dy_2)ds\right) < +\infty,$$

which allows us to use this transform.

In the case $B = D = \alpha = 0$ the proof of uniqueness can be adapted from the general results of Fitzsimmons, see [6] Corollary 2.23: the Laplace transform of the process is uniquely identified using the extension of the martingale problem (4.57) to test functions depending smoothly on the time like $(s,x,y_1,y_2) \mapsto \psi_{t-s} f(x,y_1,y_2)$ for bounded functions f (see [6] Proposition 2.13).

□

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