The mathematics of Darwinian evolution: from stochastic individual processes to adaptive dynamics

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Abstract

A distinctive signature of living systems is Darwinian evolution, that is, a propensity to generate as well as select individual diversity. To capture this intrinsic feature of life, new classes of mathematical models are emerging. These models are rooted in the "microscopic", stochastic description of a population of discrete individuals characterized by one or several adaptive traits. The population is modeled as a stochastic point process whose generator captures the probabilistic dynamics over continuous time of birth, mutation, and death, as influenced by each individual's trait values, and interactions between individuals. An offspring usually inherits the trait values of her progenitor, except when a "mutation" causes the offspring to take an instantaneous "mutation step" at birth to new trait values. Once this point process is in place, the quest for tractable approximations can follow different mathematical paths, which differ in the renormalizations they assume (taking limits, in appropriate order, on population size, mutation rate, mutation step, and rescaling time accordingly) and the nature of the corresponding approximation models (deterministic, in the form of ordinary, integro-, or partial differential equations, or probabilistic, like stochastic partial differential equations or superprocesses). Adaptive dynamics models form one class of such approximations; although their rigorous derivation from point processes remains incomplete, the analysis of adaptive dynamics models has already proved highly insightful from both mathematical and biological viewpoints. Ultimately, mathematical models of Darwinian evolution derived from individual stochastic processes should encompass wider mechanisms of variation and transmission (sexual reproduction, somatic mutations, plasticity, cultural innovation and inheritance) in fluctuating environment, population structure generated by organismal development (e.g. age or size structure), and trait spaces with more complex topologies.

Key-words: Darwinian evolution, birth and death process, local interactions, mutation – selection, point process, renormalization, fitness, adaptive dynamics, bifurcation analysis, adaptive reversal, evolutionary sliding, evolutionary branching.

1. Introduction

Evolutionary biology has long received the enlightment of mathematics. Population genetics is undoubtly one of the most "mathematized" area of biology. Not only classical mathematics have been heavily used to give population genetics the strong quantitative basis that data analysis required; population genetics is also one of few biological fields that led to the opening of entirely new avenues of prosperous research in mathematics. The coalescent provides a striking example.

A distinctive signature of living systems is Darwinian evolution, that is, a propensity to generate as well as select individual diversity. This is at odds with what we know of physical or chemical systems, and confront the mathematical approach with a major difficulty. Whereas physics and chemistry offer to mathematicians a fertile terrain to simplify the complexity of systems made up of many interacting components by "taking averages", the nature of biological systems in essence opposes that. All "individuals"—be they organic molecules, genes, genomes, cells or multicellular organisms—have a potential for being unique, and for generating even more uniqueness among themselves.

The emerging field of adaptive dynamics represents a serious attempt at designing a new class of mathematical models to capture this intrinsic feature of evolving life. Dieckmann and Law (1996) have offered appealing heuristics to scale the microscopic description of an evolving population as a "polymorphic stochastic" process, up to the macroscopic approximation given by a "deterministic monomorphic" model known as the "canonical equation of adaptive dynamics". From a biological point of view, this pathway from microscopic models to adaptive dynamics deserves a firm mathematical pavement for at least two reasons: to clarify the significance of biological assumptions which are used along the way, and to harvest the crop of new biological questions or applications that mathematics can suggest.

This paper aims at reviewing and consolidating the mathematical foundations of modeling adaptive evolution. Our presentation starts with the "microscopic" description of a population of discrete individuals characterized by one or several adaptive traits. The population is modeled as a stochastic point process whose generator captures the probabilistic dynamics over continuous time of birth, mutation and death, as influenced

by each individual's trait values. The adaptive nature of a trait implies that an offspring usually inherits the trait values of her progenitor, except when a "mutation" occurs—then the offspring makes an instantaneous "mutation step" at birth to new trait values. We will refer to the state space parametrized by adaptive traits as the "trait space", and will often (slightly abusively) call *trait* the actual trait *value*.

The mathematical construction of the population point process yields a "polymorphic stochastic" model of adaptive evolution, *sensu* Dieckmann and Law (1996). Once this point process is in place, the quest for tractable approximations can follow different mathematical paths, which depart from each other in the renormalizations they assume and the nature of the approximation models they are conducive to. Possible renormalizations involve taking limits on population size, mutation rate, mutation step, and rescaling time whenever appropriate; the approximation models can be deterministic (in the form of ordinary, integro-, or partial differential equations) or probabilistic (stochastic partial differential equations or superprocesses). By considering possible renormalizations in different, biologically relevant combinations, we can aim at the systematic construction of approximation models, in such a way that we gain a clear understanding of how the models relate to each other, and what their respective biological scope is.

The adaptive dynamics approach suggests to proceed from the stochastic polymorphic model by taking the following two steps (Fig. 1):

- First, two simultaneous renormalizations (large population and rare mutations) are assumed to lead to an approximation model qualifying as "monomorphic stochastic". This model is aimed to be a directed jump process over the trait space.

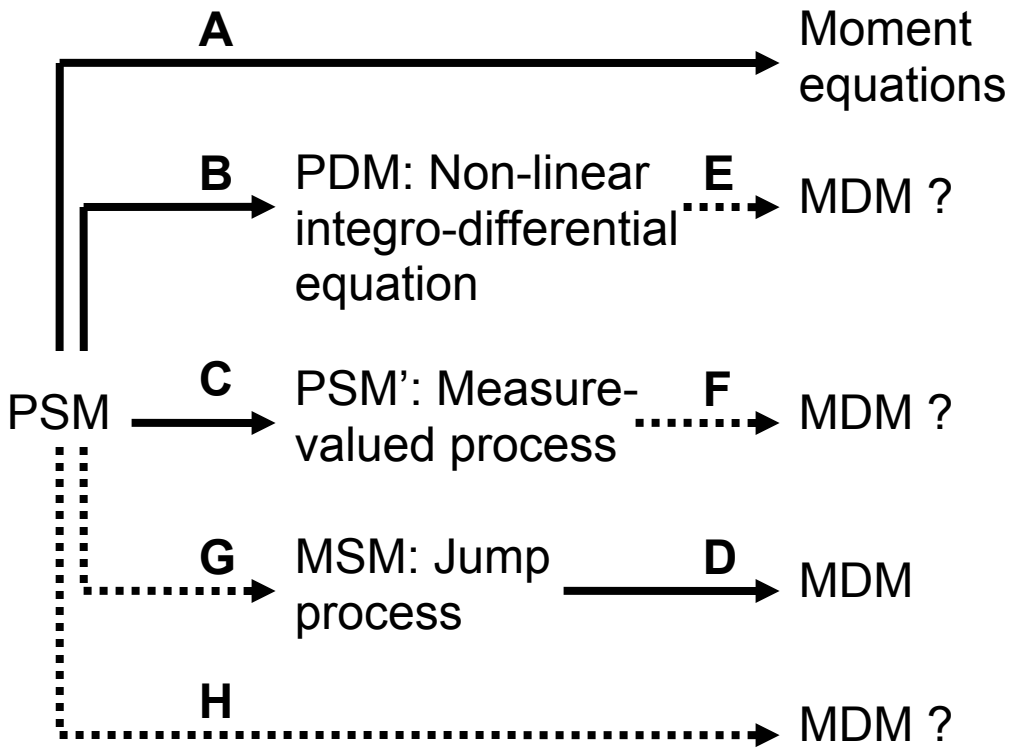

Fig. 1. Branching mathematical paths from the polymorphic stochastic model (PSM) to various possible deterministic approximations (moment equations, MDM: monomorphic deterministic models). Plain arrows (A-D) indicate established mathematical steps. (A) involves taking expectation on a large number of independent realizations (see section 2.2). (B) Large-population limit, rescaled interaction kernel (section 3.1). (C) Large-population limit, accelerated birth and death, infinitesimal mutation steps, rescaled interaction kernel (section 3.2). (D) Infinitesimal mutation steps, rescaled time (section 4.2). Dashed routes (E-H) have not received any firm mathematical pavement yet. Possible approximations: (G) Large-population and small-mutation rate limits. (H) Large-population and infinitesimal mutation step limits taken simultaneously.

- Then this jump process is approximated by a "monomorphic deterministic" model, derived through an infinitesimal-mutation renormalization taken along with rescaling time appropriately. This deterministic process over the state space appears to be driven by the so-called "canonical equation of adaptive dynamics" (Dieckmann and Law 1996).

At present, only the second step has received a full mathematical resolution (Champagnat et al. 2001, Champagnat 2003a, b). Simplifying the complexity of the stochastic polymorphic model *via* the derivation of a monomorphic stochastic approximation stands up as a mathematical challenge. Three alternative paths have been opened successfully, but it is not known yet how to continue them so as to recover models akin to the canonical equation:

- Considering the moment equations associated with the microscopic point process. These equations aim at describing the temporal dynamics of the moments of the distribution of individuals across the trait space.
- Taking the large-population limit alone to derive a "deterministic polymorphic" model in the form of a nonlinear integro-differential equation. This model generalizes the classical equation of mutation-selection balance studied in population genetics (e.g., Burger 2000).
- Applying simultaneously three renormalizations: large population, fast birth and death (hence fast mutation), infinitesimal mutation step. Depending on the acceleration of the birth and death process, this leads either to a deterministic reaction-diffusion equation, or to a continuous random measure-valued process which generalizes the superprocess introduced recently by Etheridge (2001) to model spatially structured population dynamics.

In section 2 we explain how to construct the microscopic point process, which provides a polymorphic stochastic model of the population; next we derive the corresponding moment equations. In section 3, we construct approximations of the polymorphic model based on a large-population limit. Section 4 aims at recovering the canonical equation of adaptive dynamics (and several extensions) by applying the infinitesimal mutation step renormalization on a postulated monomorphic approximation of the microscopic point process. Finally, section 5 presents the analysis of some recently developed examples of canonical equations. These two case studies suffice to unravel the richness of evolutionary dynamics and some of their unexpected features.

2. Population point process and moment equations

Evolution manifests itself as a change in the state of a population, while its basic mechanisms – mutation and selection – operate at the level of individuals. Here we derive a polymorphic stochastic model of an evolving population by constructing an "interacting individual system". The population is characterized by a counting measure, and evolves according to a Markov process on the path space $\mathbf{D}([0,\infty), M_F(\overline{\chi}))$ of càdlàg functions from $[0,\infty)$ to $M_F(\overline{\chi})$. $M_F(\overline{\chi})$ is the set of finite nonnegative measures on $\overline{\chi}$, where $\overline{\chi}$ denotes the trait space—the closure of a bounded connected open set of $\mathbf{R}^d$; $\overline{\chi}$ is defined in such a way that reproduction becomes impossible for individuals with traits located on the boundary of $\overline{\chi}$. The infinitesimal generator of the process captures the birth and death events that each individual experiences while interacting with other individuals.

2.1. Process construction

We consider a population in which individuals can give birth and die at rates that are influenced by the individual traits and by interactions with groups of individuals carrying the same or different traits. These events occur randomly, in continuous time. Reproduction is almost faithfull: there is some probability that a mutation causes an offspring's trait to differ from her progenitor's. Interactions translate into a dependence of the birth and death rates of any focal individual upon the number of individuals in the interacting groups.

Let ν_t denote the finite point measure describing the "distribution" of individuals over the trait space at time *t*. As we construct and analyse the infinitesimal generator *L* of the Markovian dynamics $(\nu_t)_{t\geq 0}$, we will be using the notation M_{FP} to denote the set of all finite point measures in $M_F(\overline{\chi})$, that is, $M_{FP} = \left\{ \sum_{i=1}^{I} \delta_{x^i}, I \in \mathbf{N}, x^1, \ldots x^I \in \overline{\chi} \right\}$, where δ_x is the Dirac measure at *x*. Also, for any $\nu = \sum_{i=1}^{I} \delta_{x^i} \in M_{FP}$ and for any measurable function φ on $\overline{\chi}$, we set $\langle \nu, \varphi \rangle = \int_{\overline{\chi}} \varphi \, d\nu = \sum_{i=1}^{I} \varphi(x^i)$.

The population is characterized at any time *t* by the finite point measure

(2.1) $\nu_t = \sum_{i=1}^{I(t)} \delta_{x_t^i}$.

$I(t) \in \mathbf{N}$ is the number of individuals alive at time *t*, and $x_t^1, \ldots x_t^{I(t)}$ denote the individuals' traits. The population dynamics are driven by a birth-mutation-death process defined as follows. For any trait $x \in \overline{\chi}$, individual mortality and reproduction are influenced by interactions between individuals. Let us set

- $d(x, U * \nu_t(x)) \in [0, \infty)$, the death rate of individuals with trait *x*,
- $b(x, V * \nu_t(x)) \in [0, \infty)$, the birth rate of individuals with trait *x*, with $b(x, \cdot) = 0$ for any *x* on the boundary of $\overline{\chi}$,

where

- $U(x) \in [0, \infty)$ is the interaction kernel affecting mortality,
- $V(x) \in [0, \infty)$ is the interaction kernel affecting reproduction.

Here * denotes the convolution operator, which means that the interaction effect of any individual with trait *y* on the death and birth rates of a focal individual with trait *x* is weighed by a function of the difference between the trait values, $x - y$.

Mutation-related parameters are expressed as functions of the individual trait values only (although there would be no formal predicament to include a dependency on the population state):

- $\mu(x) \in [0, 1]$ is the probability that an offspring produced by an individual with trait *x* carries a mutated trait,
- $M(x, dz)$ is the mutation step measure of the mutated offspring trait $x + z$ produced by individuals with trait *x*. *M* is assumed to satisfy $\int_{z \in \mathbf{R}^d,\, x+z \in \overline{\chi}} M(x, dz) = 1$ and $\int_{z \in \mathbf{R}^d,\, x+z \notin \overline{\chi}} M(x, dz) = 0$ for any $x \in \overline{\chi}$.

Thus, the individual processes that influence the population evolution can be described as follows:

- At $t = 0$ the population is characterized by a (possibly random) measure $\nu_0 \in M_{FP}$.
- Each individual has two independent exponential "clocks": a birth clock with parameter $b(x, V * \nu_t(x))$, and a death clock with parameter $d(x, U * \nu_t(x))$. Assuming

exponential distributions allows to reset both clocks to 0 every time one of them rings. At any time *t*:

- If the death clock of an individual rings, this individual dies and disappears.
- If the birth clock of an individual with trait *x* rings, this individual produces an offspring. With probability $1-\mu(x)$ the offspring carries the same trait *x*; with probability $\mu(x)$ the trait is mutated.
- If a mutation occurs, the mutated offspring instantly acquires a new trait $x+z$, picked randomly according to the mutation step measure $M(x,dz)$.

The natural candidate operator for being the infinitesimal generator of the process $(\nu_t)_{t\geq 0}$ is then

$$
\begin{aligned}
L\phi(\nu) &= \sum_{i=1}^{\langle \nu,1\rangle} [1-\mu(x_i)]\, b(x_i, V*\nu(x_i))\, [\phi(\nu+\delta_{x_i})-\phi(\nu)] \\
&+ \sum_{i=1}^{\langle \nu,1\rangle} \mu(x_i)\, b(x_i, V*\nu(x_i)) \int_{\mathbf{R}^d} [\phi(\nu+\delta_{x_i+z})-\phi(\nu)] M(x_i,dz) \\
&+ \sum_{i=1}^{\langle \nu,1\rangle} d(x_i, U*\nu(x_i))\, [\phi(\nu-\delta_{x_i})-\phi(\nu)]
\end{aligned}
\tag{2.2}
$$

where $\nu = \sum_{i=1}^{\langle \nu,1\rangle} \delta_{x_t^i}$ and $\phi : M_{FP} \to \mathbf{R}$. The first term of Eq. (2.2) captures the effect on the population of birth without mutation; the second term, that of birth with mutation; and the last term, that of death.

At this stage, the construction of the process is required to justify the existence of a Markov process admitting *L* as infinitesimal generator. Moreover, the explicit construction of $(\nu_t)_{t\geq 0}$ yields three side benefits: providing a rigorous and efficient algorithm for numerical simulations (given hereafter), laying the mathematical basis to derive the moment equations of the process (section 2.2), and establishing a general method that will be used to derive the canonical equation of adaptive dynamics from a monomorphic stochastic model (section 4). The construction method summarized here (and fully expanded in Fournier and Méléard 2003) utilizes Poisson point measures. We make the biologically natural assumptions that the trait dependence of all parameters is "bounded". That is, the interaction kernel *U* is upper bounded over $\overline{\chi}$ by a constant $\overline{U}$; there exist a constant $\overline{d}$ and a constant $\overline{b}$ such that $d(x,\zeta) \leq (1+|\zeta|)\,\overline{d}$ and $b(x,\zeta) \leq \overline{b}$; and there exist a constant *C* and a probability density $\overline{M}$ on $\mathbf{R}^d$ such that for any trait *x*,

$M(x,dz) = M(x,z)\,dz$ with $M(x,z) \le C\,\overline{M}(z)$. These assumptions ensure that there exists a constant $\overline{C}$ such that for any finite measure ν, the total event rate obtained as the sum of all event rates is bounded by $\overline{C}\,(\int_{\overline{\chi}} \nu(dx) + 1) \int_{\overline{\chi}} \nu(dx)$.

At time $t = 0$, the initial population state ν_0 contains $I(0) = K$ individuals. The vector of random variables $\mathbf{x}_0 = (x_0^i)_{1 \le i \le K}$ denotes the corresponding trait values. More generally the vector of traits of all individuals alive at time *t* is denoted by $\mathbf{x}_t$. We introduce the following sequences of independent random variables:

- $(W_k)_{k \in \mathbf{N}^*}$ with uniform law on $[0,1]$,
- $(z_k)_{k \in \mathbf{N}^*}$ with values in $\mathbf{R}^d$, with law $\overline{M}(z)dz$,
- $(\tau_k)_{k \in \mathbf{N}}$ with exponential law $\overline{C}e^{-\overline{C}t}\mathbf{1}_{t \ge 0}$ (hence $E(\tau_k) = 1/\overline{C}$).

We set $T_0 = 0$ and construct the process inductively for $k \ge 1$ as follows. Let $T_k = T_{k-1} + \dfrac{\tau_k}{I_{k-1}(I_{k-1}+1)}$. At time T_k, one chooses an individual $i_k = i$ uniformly at random among the I_{k-1} alive in the time interval $[T_{k-1}, T_k)$; this individual's trait is $x^i_{T_{k-1}}$. (If $I_{k-1} = 0$ then $\nu_t = 0$ for all $t \ge k-1$.)

- If $0 \le W_k \le \dfrac{d(x^i_{T_{k-1}}, \sum_{j=1}^{I_{k-1}} U(x^i_{T_{k-1}} - x^j_{T_{k-1}}))}{\overline{C}(I_{k-1}+1)} = W_1^i(\mathbf{x}_{T_{k-1}})$, then the chosen individual dies, and $I_k = I_{k-1} - 1$.
- If $W_1^i(\mathbf{x}_{T_{k-1}}) \le W_k \le W_1^i(\mathbf{x}_{T_{k-1}}) + \dfrac{[1-\mu(x^i_{T_{k-1}})]\,b(x^i_{T_{k-1}}, \sum_{j=1}^{I_{k-1}} V(x^i_{T_{k-1}} - x^j_{T_{k-1}}))}{\overline{C}(I_{k-1}+1)} = W_2^i(\mathbf{x}_{T_{k-1}})$, then the chosen individual gives birth to an offspring with the same trait, and $I_k = I_{k-1} + 1$.
- If

$$W_2^i(\mathbf{x}_{T_{k-1}}) \le W_k \le W_2^i(\mathbf{x}_{T_{k-1}}) + \frac{\mu(x^i_{T_{k-1}})\,b(x^i_{T_{k-1}}, \sum_{j=1}^{I_{k-1}} V(x^i_{T_{k-1}} - x^j_{T_{k-1}}))M(x^i_{T_{k-1}}, z_k)}{\overline{C}\;\overline{M}(z_k)\,(I_{k-1}+1)} = W_3^i(\mathbf{x}_{T_{k-1}}),$$

then the chosen individual gives birth to a mutant offspring with trait $x^i_{T_{k-1}} + z_k$, and $I_k = I_{k-1} + 1$.

- If $W_k \geq W_3^i(\mathbf{x}_{T_{k-1}})$, nothing happens, and $I_k = I_{k-1}$.

Notice that $\dfrac{\tau_k}{I_{k-1}(I_{k-1}+1)}$ represents the time between jumps for I_{k-1} particles, and $\overline{C}(I_{k-1}+1)$ gives an upper bound on the total event rate for each individual.

The number of individuals at any time $t \geq 0$ can then be defined as $I(t) = \sum_{k\geq 0} \mathbf{1}_{\{T_k \leq t < T_{k+1}\}} I_k$. By a standard coupling argument, one can show that the process $I(t)$ is stochastically upper-bounded by a Galton-Watson process with birth rate $\overline{b}(1+C)$ and birth times denoted by $(\beta_h)_{h\in\mathbf{N}}$. This process is of course well defined on the time interval $[0,+\infty)$, which means that $\lim_{h\to+\infty} \beta_h = +\infty$. Let us denote the *h*-th birth time of our population process by T_h^+, and the *h*-th death time by T_h^-. Obviously for $h \geq l$, $T_h^- \geq T_{h-l}^+$, and $T_h^+ \geq \beta_h$ in probability. We can therefore conclude that the polymorphic model is well defined on the time interval $[0,+\infty)$.

The polymorphic stochastic model can be expressed from the multivariate point measure $Q(dt,di,dw,dz) = \sum_{k\geq 1} \delta_{(T_k,i_k,W_k,z_k)}(dt,di,dw,dz)$ associated with the possible birth, mutation and death of individuals, defined on $\mathbf{R}_+ \times \mathbf{N} \times [0,1] \times \overline{\chi}$. The process $(\nu_\bullet)$ defined by Eq. (2.1) is càdlàg from M_{FP} into $\mathbf{R}_+$ and satisfies the explicit equation

$$\nu_t = \nu_0 + \int \ldots \int_{[0,t]\times\mathbf{N}\times[0,1]\times\overline{\chi}} \Big(-\delta_{x_{s-}^i} \mathbf{1}_{\{w \leq W_1^i(\mathbf{x}_{s-})\}} + \delta_{x_{s-}^i} \mathbf{1}_{\{W_1^i(\mathbf{x}_{s-}) \leq w \leq W_2^i(\mathbf{x}_{s-})\}} + \delta_{x_{s-}^i + z} \mathbf{1}_{\{W_2^i(\mathbf{x}_{s-}) \leq w \leq W_3^i(\mathbf{x}_{s-})\}} \Big) Q(ds,di,dw,dz). \tag{2.3}$$

The process $(\nu_t)_{t\geq 0}$ is Markovian on M_{FP}, with generator *L* defined by Eq. (2.2).

2.2. Moment equations

Moment equations have been proposed recently as handy analytical models for populations structured by a spatial variable (Bolker and Pacala 1997, 1999; Dieckmann and Law 2000; Law et al. 2003—refered hereafter as BPDL). The analogy with populations structured by an adaptive trait is straightforward: in spatially structured populations, the birth and death transitions depend on the individual's spatial location (analogous to the individual's trait), and an offspring moves to a new location as a result of a migration step at birth (analogous to a mutation step).

The "philosophy" of moment equations is germane to the principle of Monte-Carlo methods: computing the "mean path" of the point process from a large number of independent realizations. (The orthogonal stance, as we shall see in section 3, is to model the behavior of a single trajectory when it is the initial number of individuals which is made large). Moment properties of the point process defined by Eq. (2.3) are studied in detail in Fournier and Méléard (2003). In particular, for any φ bounded and measurable on $\overline{\chi}$, the associated process defined by

$$\begin{aligned}\Lambda_t^{\varphi} = &\int_{\overline{\chi}} \varphi(x)\, \nu_t(dx) - \int_{\overline{\chi}} \varphi(x)\, \nu_0(dx) - \int_0^t ds \int_{\overline{\chi}} \nu_s(dx)\, (1-\mu(x))\, b(x, V*\nu_s(x))\, \varphi(x) \\ &- \int_0^t ds \int_{\overline{\chi}} \nu_s(dx)\, \mu(x)\, b(x, V*\nu_s(x)) \int_{\mathbf{R}^d} \varphi(x+z)\, M(x,z)\, dz \\ &+ \int_0^t ds \int_{\overline{\chi}} \nu_s(dx)\, \varphi(x)\, d(x, U*\nu_s(x))\end{aligned} \tag{2.4}$$

is a càdlàg L^2-martingale starting from 0 with predictable quadratic variation

$$\begin{aligned}\left\langle \Lambda^{\varphi} \right\rangle_t = \int_0^t ds \int_{\overline{\chi}} \nu_s(dx) \Big\{ &\mu(x)\, b(x, V*\nu_s(x)) \int_{\mathbf{R}^d} \varphi^2(x+z)\, M(x,z)\, dz \\ &+ \varphi^2(x) \left((1-\mu(x))\, b(x, V*\nu_s(x)) + d(x, V*\nu_s(x)) \right) \Big\}.\end{aligned} \tag{2.5}$$

Let us define the "deterministic measure" $E(\nu)$ associated with a random measure ν by $\int_{\overline{\chi}} \varphi(x)\, E(\nu)(dx) = E\left(\int_{\overline{\chi}} \varphi(x)\, \nu(dx) \right)$. An important property of the point process is that if the deterministic measure of the initial population admits a density p_0 w.r.t. the Lebesgue measure, then for all $t \geq 0$, the deterministic measure $E(\nu_t)$ of the population has a probability density p_t. (To see this, apply Eq. (2.4) to $\varphi = \mathbf{1}_A$ where A has zero Lebesgue measure; taking expectations then yields $E\left(\int_{\overline{\chi}} \varphi(x)\, \nu(dx) \right) = 0$.) As a consequence, the expectation of the total size of the population at time t is $N(t) = E\left(\int_{\overline{\chi}} \nu_t(dx) \right) = \int_{\overline{\chi}} p_t(x) dx$, and $p_t(x)dx / N(t)$ gives the probability of observing one individual at time t in a small ball (x, dx). Under the assumption (made e.g. in Bolker and Pacala 1997) that the death and birth rates take the particular form $d(x,\zeta) = d(x) + \alpha(x)\, \zeta$, $b(x,\zeta) = b(x)$ and $\mu(x) = 1$, taking expectations on Eq. (2.4) with $\varphi \equiv 1$ yields:

$$N(t) = N(0) + \int_0^t ds\, E\left(\int_{\overline{\chi}} [b(x) - d(x) - \alpha(x) U(0)]\, \nu_s(dx) \right) - E\left(\int_{\overline{\chi} \times \overline{\chi}} \alpha(x)\, \mathbf{1}_{\{x \neq y\}} U(x-y)\, \nu_s(dx)\, \nu_s(dy) \right) \cdot \quad (2.6)$$

Whether this approach may eventually help describe the population dynamics in the trait space is still unclear. It may none-the-less be worth emphasizing the direct connection that the derivation of Eq. (2.6) bears with the yet unresolved problem of moment closure that arises in the context of spatially structured populations (Law et al. 2003): in the case where *b*, *d* and α are independent of (the spatial location) *x*, and *U* is symmetrical, Eq. (2.6) recasts into

$$\dot{N} = (b-d)N - \alpha \int_{\mathbf{R}^d} U(r)\, C_t(dr) \quad (2.7)$$

where C_t is defined at any time *t* as a "spatial covariance measure" (*sensu* BPDL) on $\mathbf{R}^d$, given by

$$\int_{\mathbf{R}^d} \varphi(r)\, C_t(dr) = E\left(\int_{y \in \mathbf{R}^d} \varphi(x-y)\, \nu_t(dx)\, \nu_t(dy) \right). \quad (2.8)$$

for any measurable bounded functions φ on $\mathbf{R}^d$. An evolution equation for this covariance measure then obtains by considering the quantities $\int_{\mathbf{R}^d} \varphi(r)\, C_t(dr)$ as functions $\phi(\nu)$ and applying (2.2). This allows to precisely identify the mathematical issues raised by the problem of moment closure (Law et al. 2003).

3. Large-population renormalizations of the polymorphic process

The moment equation approach outlined above is based on the idea of averaging a large number of independent realizations of the population process initiated with a finite number of individuals. Let *K* denote the initial number of individuals – a measure of the "system size", *sensu* Metz *et al.* (1996); the alternative approach is to study the exact process by letting that system size become very large and making some appropriate renormalization—it is now as if the *population* process was averaging by itself over a large number of *individual* realizations. Several types of approximations can then be derived, depending on the renormalization of the process. A "polymorphic deterministic"

approximation is presented in section 3.1, germane to the Fisher-Wright-Kimura equation for mutation-selection balance (e.g. Burger 2000). In section 3.2, a non-classical stochastic approximation obtains in the form of a measure-valued superprocess.

3.1. Large-population limit

As the system size K goes to infinity, we need to renormalize the interaction kernels as $\frac{1}{K}U(x,y)$ and $\frac{1}{K}V(x,y)$. A biological interpretation of this renormalization is that a larger system is made up of smaller individuals, which may be a consequence of a fixed amount of available resources in the environment. Thus, the biomass of each interacting individual scales as $1/K$, which may imply that the effect of interaction on a focal individual scales as $1/K$ as well.

In effect, the renormalization serves to "decorrelate" the life histories of "nearby" (in trait space) individuals. Let ν_t^K be the counting measure of the population at time t. We define the càdlàg M_{FP}^K-valued Markov process $(X_t^K)_{t\geq 0}$ by $X_t^K = \frac{1}{K}\nu_t^K$, where M_{FP}^K denotes the subset $\left\{\frac{1}{K}\nu, \nu \in M_{FP}\right\}$ of $M_F(\overline{\chi})$. Let us assume that the initial conditions converge in law (for the weak topology) towards some deterministic finite measure ξ_0. For any t, the process $(X_t^K)_{t\geq 0}$ converges in law as K goes to infinity to a deterministic measure ξ_t satisfying

$$\begin{aligned}\int_{\overline{\chi}} \varphi(x)\,\xi_t(dx) &= \int_{\overline{\chi}} \varphi(x)\,\xi_0(dx) \\ &+ \int_0^t\int_{\overline{\chi}} \varphi(x)\,[(1-\mu(x))\,b\big(x,V*\xi_t(x)\big) - d\big(x,U*\xi_t(x)\big)]\,\xi_s(dx)\,ds \\ &+ \int_0^t\int_{\overline{\chi}} \mu(x)\,b\big(x,V*\xi_t(x)\big)\left(\int_{\mathbf{R}^d} \varphi(x+z)\,M(x,z)\,dz\right)\xi_s(dx)\,ds\end{aligned} \tag{3.1}$$

for any bounded $\varphi : \overline{\chi} \to \mathbf{R}$. If the initial condition ξ_0 has a density w.r.t. the Lebesgue measure, then for any t the finite measure ξ_t has a density w.r.t. the Lebesgue measure, and ξ_t is a solution of the functional equation:

$$\partial_t \xi_t(x) = \left[(1-\mu(x))\, b\big(x, V*\xi_t(x)\big) - d\big(x, U*\xi_t(x)\big)\right] \xi_t(x) + \int_{\mathbf{R}^d} \xi_t(y)\, \mu(y)\, b\big(y, V*\xi_t(y)\big)\, M(y, x-y)\, dy \tag{3.2}$$

for all $x \in \overline{\chi}$ and $t \geq 0$. The proof of this result (see Fournier and Méléard (2003)) strongly relies on arguments of tightness in finite measure spaces (Roelly 1986). Desvillettes et al. (2003) suggest to refer to ξ_t as the population "number density"; then the quantity $n(t) = \int_{\overline{\chi}} \xi_t(x)\, dx$ can be interpreted as the "total population density" over the whole trait space. This means that if the population is initially seeded with *K* individuals, $K \cdot n(t)$ approximates the number of individuals alive at time *t*, all the more closely as *K* is larger.

Just as we did for moment equations (*cf.* section 2.2), an instructive parallel can be drawn with models of spatially structured populations, in which case the simplifying assumptions that $\overline{\chi} = \mathbf{R}^d$, and that the birth, death, and interaction rates be independent of *x*, are meaningful. In this context, Eq. (3.1) leads to the following equation on $n(t)$:

$$\dot{n} = (b-d)n - \alpha \iint_{\overline{\chi}} U(x-y)\, \xi_t(dx)\, \xi_t(dy). \tag{3.3}$$

With $U \equiv 1$, which amounts to the so-called "mean-field" assumption in population ecology, we recover the classical mean-field logistic equation of population growth:

$$\dot{n} = (b-d)n - \alpha n^2. \tag{3.4}$$

Comparing Eq. (3.4) with the first-moment equation obtained previously (Eq. (2.7)) stresses out the "decorrelative" effect of the large system size renormalization: in Eq. (2.7), the correction term capturing the effect of spatial correlations in the population remains, even if one assumes $U \equiv 1$.

From Eq. (3.1) the path towards adaptive dynamics is still largely unbeaten, but a natural step forward is to involve the timescale separation of mutation and selection. This can be done by accelerating birth and death (of the order of ε^{-1}, where ε is small) and rescaling the mutation rate accordingly (of the order of ε). Namely we write Eq. (3.2) in the general form:

$$\partial_t \xi_t^\varepsilon(x) = \frac{1}{\varepsilon} \rho(x, \xi_t^\varepsilon)\, \xi_t^\varepsilon(x) + \mathbf{M} \xi_t^\varepsilon \tag{3.5}$$

where $\rho(x,\xi) = b(x, V*\xi(x)) - d\big(x, U*\xi(x)\big)$ stands for the population growth rate in the absence of mutation, and $\mathbf{M}$ is the mutation operator given by

$$\begin{aligned}\mathbf{M}\xi &= \int_{\bar{\chi}} \xi(y)[\mu(y)\varepsilon]\frac{b(y,V*\xi(y))}{\varepsilon} M(y,x-y)\,dy - \xi(x)[\mu(x)\varepsilon]\frac{b(x,V*\xi(x))}{\varepsilon} \\ &= \int_{\bar{\chi}} \xi(y)\,\mu(y)\,b(y,V*\xi(y))\,M(y,x-y)\,dy - \xi(x)\,\mu(x)\,b(x,V*\xi(x)).\end{aligned} \tag{3.6}$$

As a first, preliminary step for the study of this equation when ε goes to zero, Jabin and Mischler (unpublished) have considered the special case where $\mu = 0$.

3.2. Large-population limit with accelerated births and deaths

Adaptive dynamics models proceed essentially by making mutations extremely rare in a very large population, and then by making the mutation step extremely small and rescaling time (see section 4). Since mutations are to be considered infinitesimal eventually, the alternative limit of accelerating the timescale of mutations can also be envisaged: it sounds biologically sensible to assume that mutations occur on the same timescale as birth, as long as their effects are extremely small. One merit of this approach is that it does not require to perform different renormalizations in a specific order. The limits of a large system size, accelerated birth and death (hence accelerated mutation), and infinitesimal mutation steps are taken all at once.

Specifically, the trait space $\bar{\chi}$ is assumed to be the whole $\mathbf{R}^d$. The boundedness assumptions on the rates *d*, *b*, and on the interaction kernel *U* (*cf.* section 2) are maintained. Furthermore, the mutation step density is taken as the density of a centered vector of independent Gaussian variables with mean 0 and variance $\frac{\sigma^2(x)}{K^\alpha}$:

$M_K(x,z) = \left(\frac{K^\alpha}{2\pi\sigma^2(x)}\right)^{d/2} \exp[-K^\alpha |z|^2 / 2\sigma^2(x)]$ where $\sigma^2(x)$ is positive and bounded over $\bar{\chi}$, and $\alpha \in (0,1]$. Thus, as *K* goes to infinity, mutant traits become more concentrated around their progenitors'. We accelerate the pace of mutation by making birth more and more frequent as *K* increases. To keep the population demographic balance unaffected, the timescale of death is made accordingly faster. Namely, we write $b_K(x,\zeta) = K^\alpha r(x) + b(x,\zeta)$ and $d_K(x,\zeta) = K^\alpha r(x) + d(x,\zeta)$, where *r* is positive and

bounded over $\overline{\chi}$. As before (section 3.2), the interaction kernels *U* and *V* are renormalized by *K*.

Let us assume that the initial condition $X_0^K = \dfrac{\nu_0^K}{K}$ converges in law and for the weak topology on $M_F(\mathbf{R}^d)$ toward a finite measure $X_0 \in M_F(\mathbf{R}^d)$. When $\alpha < 1$, one can show as in section 3.1 that for all $T > 0$, the sequence of processes $\left(\dfrac{\nu^K}{K}\right)_{K\in\mathbf{N}}$ converges in law in $\mathbf{D}([0,T], M_F(\mathbf{R}^d))$ to a solution of the deterministic reaction-diffusion equation:

$$\partial_t\, \xi_t(x) = \left[\, b\big(x, V*\xi_t(x)\big) - d\big(x, U*\xi_t(x)\big)\,\right]\xi_t(x) + \frac{1}{2}\sigma^2(x)\,\mu(x)\,r(x)\,\Delta\xi_t(x). \tag{3.7}$$

This equation generalizes the Fisher equation known from classical population genetics (Burger 2000).

When $\alpha = 1$, the resulting model is a measure-valued (random) process. Fournier and Méléard (2003) show that for all $T > 0$, the sequence of processes $(X^K)_{K\in\mathbf{N}}$ converges in law in $\mathbf{D}([0,T], M_F(\mathbf{R}^d))$ to the unique (in law) "superprocess" $X \in C([0,T], M_F(\mathbf{R}^d))$, such that for any $\varphi \in C_b^2(\mathbf{R}^d)$

$$\begin{aligned}\overline{\Lambda}_t^{\varphi} = {} & \int_{\overline{\chi}} \varphi(x)\, X_t(dx) - \int_{\overline{\chi}} \varphi(x)\, X_0(dx) - \int_0^t\!\!\int_{\overline{\chi}} \frac{1}{2}\sigma^2(x)\,\mu(x)\,r(x)\,\Delta\varphi(x)\, X_s(dx)\, ds \\ & - \int_0^t\!\!\int_{\overline{\chi}} \varphi(x)\,[\, b(x, V*X_s(x)) - d(x, U*X_s(x))\,]\, X_s(dx)\, ds\end{aligned} \tag{3.8}$$

is a continuous martingale with quadratic variation $\left\langle \overline{\Lambda}^{\varphi} \right\rangle_t = 2\int_0^t\!\!\int_{\overline{\chi}} r(x)\,\varphi^2(x)\, X_s(dx)\, ds$.

The proof of this statement is in many respects similar to that of Eq. (3.1), with the additional use of specific results on superprocesses (Evans and Perkins 1994) to establish the uniqueness of the solution to the martingale problem. The superprocess characterized by Eq. (3.8) appears as a generalization of the model of spatially structured populations which was constructed by Etheridge (2001). Formally, Eq. (3.8) is the weak form of the stochastic partial differential equation

$$\partial_t X_t = [b(\,\cdot\,, V*X_t) - d(\,\cdot\,, U*X_t)]\,X_t + \frac{1}{2}\sigma^2\,\mu\, r\,\Delta X_t + \sqrt{2\, r\, X_t}\,\dot{W} \tag{3.9}$$

where $\dot{W}$ is a space-time white noise, which reflects the demographic stochasticity of this fast birth-and-death process, that is, faster than the accelerated birth-and-death process which led to the deterministic reaction-diffusion approximation, Eq. (3.7).

4. Renormalization of the monomorphic process and adaptive dynamics

Metz et al. (1996) have proposed to approximate the polymorphic stochastic model of adaptive evolution with a monomorphic jump process describing evolutionary trajectories as "trait substitution sequences". Dieckmann and Law (1996) have further developed insightful heuristics to achieve a deterministic approximation for the jump process, solution to the so-called "canonical equation of adaptive dynamics". Metz' notion of trait substitution sequences and Dieckmann and Law's canonical equation form the core of the current theory of "adaptive dynamics". In this section, we present the current status of the mathematical derivation of the monomorphic stochastic process from the individual point process—a derivation that is still incomplete; and we summarize how the deterministic process driven by the canonical equation can be recovered rigorously as an approximation of the jump process by means of appropriate renormalization. Detailed proofs are expounded in Champagnat et al. (2001) and Champagnat (2003a, b). The mathematical approach allows us to extend the standard canonical equation in several directions—most noticingly, to polymorphic populations in which the "invasion implies fixation" principle is enforced, that is, away from the so-called "branching points" and "extinction points" of the trait space.

4.1. Process construction

Heuristically, the monomorphic stochastic model assumes that the population state is described by a single trait value at any time. The trait may change instantaneously as a result of a "mutant invasion". The model assumes that if a population where all individuals carry the trait value x is invadible by a mutant with trait y, then there is a positive probability that the population state jumps to y; otherwise the population state remains x, at least until the next invasion attempt occurs. The "trait substitution sequence" (Metz et al. 1996) so described by successive mutation-invasion events is stochastic in three ways: mutations occur at random times, mutational effects are random

(as prescribed by the mutation law *M* defined in section 2.1), and mutant success is subject to the stochasticity of birth and death in small populations. This in effect yields a Markov jump process in the trait space.

We now proceed to the mathematical construction of this process. To this end, we keep using the notation introduced in sections 2.1 and 3.1, and add $\overline{n}(x)$ to the notation list, which is the "ecological population equilibrium" (see section 3.1) of a monomorphic population with trait *x*. The notion of an "ecological population equilibrium" can be understood in the context of large populations to which the deterministic modeling framework designed in section 3.1 applies. The term "ecological" refers to the absence of genetic effects on population dynamics. This means that no mutation occurs, i.e, $\mu \equiv 0$. Thus, if only trait *x* is present at time $t = 0$, i.e. $\xi_0 = n_0(x)\,\delta_x$, we can write $\frac{\nu_t^K}{K} = \frac{n_t^K(x)}{K}\,\delta_x$ for any time *t*, with $\frac{n_t^K(x)}{K} \to n_t(x)$ when *K* goes to infinity. Hence $\xi_t = n_t(x)\,\delta_x$ at any time *t*, and Eq. (3.1) recasts in this case into

$$(4.1) \qquad \frac{d}{dt} n_t(x) = \rho_1(x, n_t(x))\, n_t(x)$$

where $\rho_1(x, n_t(x)) = b(x, V(0)\, n_t(x)) - d(x, U(0)\, n_t(x))$. The ecological population equilibrium $\overline{n}(x)$ is then given as a putative stable equilibrium solution of Eq. (4.1), necessarily satisfying $d(x, U(0)\,\overline{n}(x)) = b(x, V(0)\,\overline{n}(x))$. This definition of an ecological population equilibrium $\overline{n}(x)$ allows us to construct the first steps of the jump process:

- Start with a population with trait *x* (chosen possibly at random), characterized by the ecological population equilibrium $\overline{n}(x)$.
- After waiting an amount of time drawn from the exponential law with parameter $\mu(x)\, b(x, V(0)\overline{n}(x))\, \overline{n}(x)$, pick a mutant trait $y = x + z$ according to the law $M(x, dz)$.

The next issue is to design an invasion rule. To this end, we formulate a deterministic model for the interaction of two populations, characterized respectively by trait values *x* and *y*. The model again stems from Eq. (3.1) with $\xi_0 = n_0(x)\,\delta_x + n_0(y)\,\delta_y$, assuming no other mutation occurs. We define $n_t(x)$ and $n_t(y)$ for any *t* as before. Then

Eq. (3.1) yields a system of coupled ordinary differential equations for the dynamics of $n_t(x)$ and $n_t(y)$:

(4.2a) $$\frac{d}{dt} n_t(x) = \rho_2(x, y, n_t(x), n_t(y))\, n_t(x)$$

(4.2b) $$\frac{d}{dt} n_t(y) = \rho_2(y, x, n_t(y), n_t(x))\, n_t(y)$$

where $\rho_2(u,v,n,m) = b(u, V(0)\,n + V(u-v)\,m) - d(u, U(0)\,n + U(u-v)\,m)$. Notice that $\rho_2(u,v,n,0) = \rho_1(u,n)$. Assuming that $\bar{n}(x)$ is well *and uniquely* defined by Eq. (4.1), and that $\bar{n}(y)$ can be analogously defined, then the dynamical system Eq. (4.2) possesses two equilibria on the boundary of $\mathbf{R}_+^* \times \mathbf{R}_+^*$, $(\bar{n}(x), 0)$ and $(0, \bar{n}(y))$, which must be stable in the horizontal and vertical direction, respectively. We then state as a rule that "*y* invades *x* deterministically" if the equilibrium $(\bar{n}(x), 0)$ of Eq. (4.2) is unstable in the vertical direction (for an example, see Fig. 2, panel I); this can be shown to occur if $\rho_2(y, x, 0, \bar{n}(x)) > 0$ (Hastings 1985, Rand et al. 1994, Ferriere and Gatto 1995). Geritz et al. (2002) showed that for *y* sufficiently close to *x*, "invasion implies fixation", that is, if $\rho_2(y, x, 0, \bar{n}(x)) > 0$ then all orbits of the dynamical system (4.2) issued from sufficiently small perturbations of the equilibrium $(\bar{n}(x), 0)$ converge to $(0, \bar{n}(y))$—except in the neighborhood of special trait values called "branching points" of the trait space $\bar{\chi}$. Biologists view the quantity $\rho_2(y, x, 0, \bar{n}(x))$ as the "fitness of mutant *y* in a resident population of trait *x* at equilibrium" (Metz et al. 1992), and often use the notation $f(y, x)$ for it—to which we will hereafter adhere and refer to as the "fitness function" defined over $\bar{\chi} \times \bar{\chi}$.

To account for the stochasticity of individual birth and death, Dieckmann and Law (1996) have developed a heuristic argument to measure the probability that an initially small population of individuals with trait *y* actually invades trait *x* at ecological population equilibrium. They assume that if the criterion for deterministic invasion is not fulfilled, the probability that invasion actually occurs is zero; otherwise, they use elementary results on birth-and-death processes to obtain the probability

$[f(y,x)]_+/b(y,V(y-x)\bar{n}(x))$ that invasion does occur. Thus, the next step of the jump process that we are constructing can be specified as follows.

- The process jumps to state y with probability $[f(y,x)]_+/b(y,V(y-x)\bar{n}(x))$ (where $[z]_+ = z \vee 0$), or stays in state x with probability $1-[f(y,x)]_+/b(y,V(y-x)\bar{n}(x))$; the process then returns to the first step.

Notice that at this stage the rigorous flow from a population microscopic model to the desired macroscopic approximation, has been disrupted by mixing the large system size approximation (3.1), needed to define the ecological population equilibrium and recover the invasion-implies-fixation principle, with a microscopic description of the growth of a finite mutant population. However, the jump process has been fully specified by now, and the search for a deterministic approximation can be pursued.

To determine the infinitesimal generator L of the jump process, we need to extend the process to the boundary of $\bar{\chi}$, which we do by assuming that the process stays constant (no evolution) if it starts from or hits that boundary. The generator L is then given, for all $\varphi \in B_b(\bar{\chi})$, by

$$(4.3) \qquad L\varphi(x) = \int_{\mathbf{R}^d} (\varphi(x+z)-\varphi(x))\, g(x+z,x)\, M(x,dz)$$

where $g(y,x) = \mu(x)\, b(x,V(0)\bar{n}(x))\, \bar{n}(x)\, [f(y,x)]_+/b(y,V(y-x)\bar{n}(x))$. Under the assumption that g is bounded on $\bar{\chi}\times\bar{\chi}$ by a constant $\bar{g}$, the generator L defines a unique semigroup, so that the process is unique in law. To prove the existence, we proceed as in section 2.1 by providing an explicit pathwise representation. To this end, we assume that $M(x,\cdot)$ has finite and bounded third-order moments on $\bar{\chi}$, and is absolutely continuous w.r.t. the Lebesgue measure on $\mathbf{R}^d$: $M(x,dz) = M(x,z)\,dz$, with the additional property that there exists a function $\overline{M}:\mathbf{R}^d \to \mathbf{R}$ such that $M(x,z) \le \overline{M}(z)$ for any $x \in \bar{\chi}$.

Let us introduce the Poisson point measure $Q(dt,dw,dz)$ on $\mathbf{R}_+ \times [0,1] \times \mathbf{R}^d$ with intensity $q(dt,dw,dz) = \overline{M}(z)\,\bar{g}\,dt\,dw\,dz$. For x_0 being a random variable on $\bar{\chi}$, independent of Q, we define for any $t \ge 0$

$$(4.4) \qquad x_t = x_0 + \iiint_{[0,t]\times[0,1]\times\mathbf{R}^d} z\,\mathbf{1}_{\left\{w \le \frac{[g(x_{s-}+z,x_{s-})]_+}{\bar{g}}\,\frac{M(x_{s-},z)}{\overline{M}(z)}\right\}}\, Q(ds,dw,dz)\,.$$

The Markov process $(x_t)_{t\geq 0}$ is well defined thanks to the assumptions made on *g* and *M*. An application of Itô's formula then straightforwardly establishes *L* as the infinitesimal generator of the process.

4.2. Canonical equation and extensions

In order to perform the "small mutation" renormalization of the jump process constructed in the previous section, we introduce a (small) parameter $\varepsilon > 0$ and substitute $M(x, dz/\varepsilon)$ to $M(x, dz)$. Now let us define a family of random variables $\{x_0^\varepsilon\}_{0<\varepsilon\leq 1}$ and a family of Markov jump processes $\{(x_t^\varepsilon)_{t\geq 0}\}_{0<\varepsilon\leq 1}$ with paths in $\mathbf{D}([0,\infty), \overline{\chi})$ such that

$$(4.5) \qquad x_t^\varepsilon = x_0^\varepsilon + \iiint_{[0,t]\times[0,1]\times\mathbf{R}^d} \varepsilon z \mathbf{1}_{\left\{w \leq \frac{[g(x_{s-}^\varepsilon + \varepsilon z, x_{s-}^\varepsilon)]_+}{\overline{g}} \frac{M(x_{s-}^\varepsilon, z)}{\overline{M}(z)}\right\}} Q\left(\frac{ds}{\varepsilon^2}, dw, dz\right).$$

As one can see, time is accelerated by a factor ε^{-2}; this is required to avoid the process become constant in the limit $\varepsilon \to 0$. The infinitesimal generator of $(x_t^\varepsilon)_{t\geq 0}$ is

$$(4.6) \qquad L^\varepsilon \varphi(x) = \frac{1}{\varepsilon^2} \int_{\mathbf{R}^d} (\varphi(x+\varepsilon z) - \varphi(x)) [g(x+\varepsilon z, x)]_+ M(x, dz).$$

The same properties that were used to study the renormalizations of the individual point process (sections 3.1 and 3.2)—tightness and weak convergence of semimartingales—then allow us to prove the convergence result whereby the "canonical equation of adaptive dynamics" is recovered. To this end, the following additional assumptions are needed:

- $y \mapsto g(y,x)$ is C^1 on $\overline{\chi}$, and $\nabla_1 g$ is bounded and Lipschitz on $\overline{\chi} \times \overline{\chi}$.
- $\Sigma(x)$, the covariance matrix of $M(x,\cdot)$, has Lipschitz entries on $\overline{\chi}$.

Then, if the family of initial population states $\{x_0^\varepsilon\}_{0<\varepsilon\leq 1}$ is bounded in $L^1(\overline{\chi})$ and converges in law to a random variable $\tilde{x}_0$ as $\varepsilon \to 0$, the family of processes $\{(x_t^\varepsilon)_{t\geq 0}\}_{0<\varepsilon\leq 1}$ converges when $\varepsilon \to 0$ for the Skorohod topology of $\mathbf{D}([0,\infty), \overline{\chi})$ to the process $(\tilde{x}_t)_{t\geq 0}$ with initial condition $\tilde{x}_0$, whose sample paths are given by the unique solution to the (deterministic) ordinary differential equation

$$(4.7) \qquad \frac{d\tilde{x}}{dt} = \int_{\mathbf{R}^d} z [z \nabla_1 g(\tilde{x}, \tilde{x})]_+ M(\tilde{x}, dz).$$

In the case where $M(x,\cdot)$ is a symmetrical measure on $\mathbf{R}^d$ for all $x \in \overline{\chi}$, Eq. (4.7) recasts into the classical form of the canonical equation:

(4.8) $$\frac{d\tilde{x}}{dt} = \frac{1}{2}\Sigma(\tilde{x})\nabla_1 g(\tilde{x},\tilde{x}) .$$

This result has been extended to the case of asymmetrical mutation step distributions (Champagnat et al. 2001). Champagnat (2003a) also proved a similar result for polymorphic populations away from branching points. Thus, the scope of the canonical equation appears to be as broad as the "invasion-implies-fixation" principle can be.

4.3. Higher-order approximation

The large population assumption that goes along with the invasion-implies-fixation principle entails that adaptive change may only be directional—in the direction determined by $\nabla_1 g(x,x)$. However, in large *yet finite* populations, stochasticity may cause a mutant to invade even if its fitness is negative, so that adaptive evolution may proceed in any direction of the trait space. To account for this feature, we introduce a new model of adaptive dynamics in the form of a stochastic differential equation driving a diffusion process. The infinitesimal generator of this diffusion is a first-order approximation of the generator of the directional jump process, in the limit of small mutation jumps. Interestingly, the second-order differential operator obtained in this way possesses degenerate and discontinuous coefficients, rendering the classical theory of diffusion processes non applicable. The weak existence of solutions to this stochastic differential equation has been proved in Champagnat (2003a) under the additional assumptions that the function *g* is differentiable twice w.r.t. the first variable, with bounded derivatives, and that the mutation law $M(x,\cdot)$ has bounded third-order moments and satisfies some continuity properties.

In the special case where $\chi = \mathbf{R}$ and $M(x,\cdot)$ is symmetrical, let $\sigma^2(x)$ be the variance of $M(x,\cdot)$, and $M_3(x) = \int_0^\infty z^3 M(x,z)\,dz$; then the stochastic differential equation writes

(4.9) $$dX_t^\varepsilon = [B_1(X_t^\varepsilon) + \varepsilon B_2(X_t^\varepsilon)]dt + \sqrt{\varepsilon A(X_t^\varepsilon)}\, dW_t$$

where $B_1(x) = \frac{1}{2}\sigma^2(x)\,\partial_1 g(x,x)$, $B_2(x) = \frac{1}{2}M_3(x)\,\mathrm{sgn}[\partial_1 g(x,x)]\,\partial_1^2 g(x,x)$, and $A(x) = M_3(x)\left|\partial_1 g(x,x)\right|$. This formalism suggests to seek a large deviation principle for the sample paths of the diffusion in the limit $\varepsilon \to 0$ (Wentzel 1976a, 1976b, Freidlin and Wentzel 1984). The difficulty lies in the fact that *A* is null at the evolutionary singularities and that B_2 is discontinuous at the same points. The large deviation principle has been obtained by Champagnat (2003b), and implies in particular that the paths of X_t^ε converge in probability to the solution of the canonical equation $\dot{x} = B_1(x)$ when $\varepsilon \to 0$.

This result can be used to study the long-time behavior of the diffusion process when the dimension of the trait space $\overline{\chi}$ is greater than 2. In particular, let us consider the case of multiple attractive evolutionary singularities, i.e. the canonical equation possesses several locally stable equilibrium solutions. Then the time needed to exit the basin of attraction of any one of them can be shown (Champagnat 2003b) to be greater than $\exp[(V-\delta)/\varepsilon]$ with probability converging to 1 when $\varepsilon \to 0$, for any $\delta > 0$; here *V* is a constant called the quasi-potential of the basin of attraction, which depends on the parameters of the diffusion. Moreover, the exit occurs with probability converging to 1 in any neigbourhood of special points of the basin's boundary where the quasi-potential is minimum. On the biological side, we hereby recover a quantitative model for the macroevolutionary pattern of punctuated equilibria (Stanley 1979; Rand and Wilson 1993). The model generally predicts that the order of magnitude of the time spent in the neighborhood of evolutionary equilibria, between rapid evolutionary shifts, is the exponential of the inverse of the mutation step variance. Also, this theory permits to predict the sequence order of evolutionary singularities (equilibria or more generally, ω-limit sets) that the evolutionary process is more likely to visit (Freidlin and Wentzel 1984).

5. Numerical analysis of adaptive dynamics: two examples

We exemplify the numerical analysis of systems of ordinary differential equations involved in adaptive dynamics modeling (section 4), namely Eq. (4.2) describing the

dynamics of resident and mutant populations, and Eq. (4.8) governing trait's adaptive dynamics. Following on from Marrow et al. (1992), Dieckmann and Law (1996) and Dercole (2002), Dercole et al. (2003) have provided a standard layout for such numerical analyses applied to regular models. The two examples that we review here go beyond that framework by including special difficulties with interesting mathematical features and far-reaching biological implications.

5.1. Multiple ecological equilibria, adaptive reversal, and evolutionary cycling

Dercole et al. (2002) have introduced and analysed a simple model for the evolution of competitive ability under asymmetrical competition within a single species. In this model, the ecological equilibrium $\bar{n}(x)$ for Eq. (4.1) undergoes two fold bifurcation as trait x varies in $\bar{\chi} = \mathbf{R}_+^*$. Thus, there is an interval of trait values $[x_l, x_h] \subset \bar{\chi}$ over which Eq. (4.1) possesses two positive, locally stable equilibrium solutions (that we call "low" and "high" ecological equilibria in the sequel). As a consequence, the uniqueness of an ecological equilibrium for the resident population – a critical assumption to properly define the jump process and derive the canonical equation Eq. (4.8) – does not hold over $\bar{\chi}$. In such a case, insights into the species' adaptive dynamics can yet be gained from the numerical bifurcation analysis of the two-trait system Eq. (4.2). In fact, all possible outcomes of the x, y interaction governed by Eq. (4.2) can be classified by means of a bifurcation analysis w.r.t the traits x and y, carried out near the diagonal $y = x$ if we view y as a small mutant of x (Figure 4.2).

The particular bifurcation structure of this model induces the remarkable behavior of adaptive reversal and evolutionary cycling. This happens because the "invasion-implies-fixation" principle does not hold around x_l and x_h, where fold bifurcations of the ecological equilibrium $\bar{n}(x)$ occur (Fig. 2, transitions between regions II and III, and VI and VII, respectively). In fact, consider a point (x, y) in region VI close to the diagonal, where the resident trait is still slightly smaller than x_h while the mutant trait is slightly greater than x_h, and assume that the resident population is settled at its high ecological equilibrium. In this case, after an initial increase, the mutant population starts

declining and eventually goes extinct, while the resident population "swings" to the low ecological equilibrium (see panel VI in Fig. 2). Dercole et al. (2002) suggest that the resulting evolutionary dynamics never comes to a halt. The resident trait is expected to oscillate between a minimum (x_l) and a maximum (x_h) value, and the population should switch periodically between a low and a high ecological equilibrium.

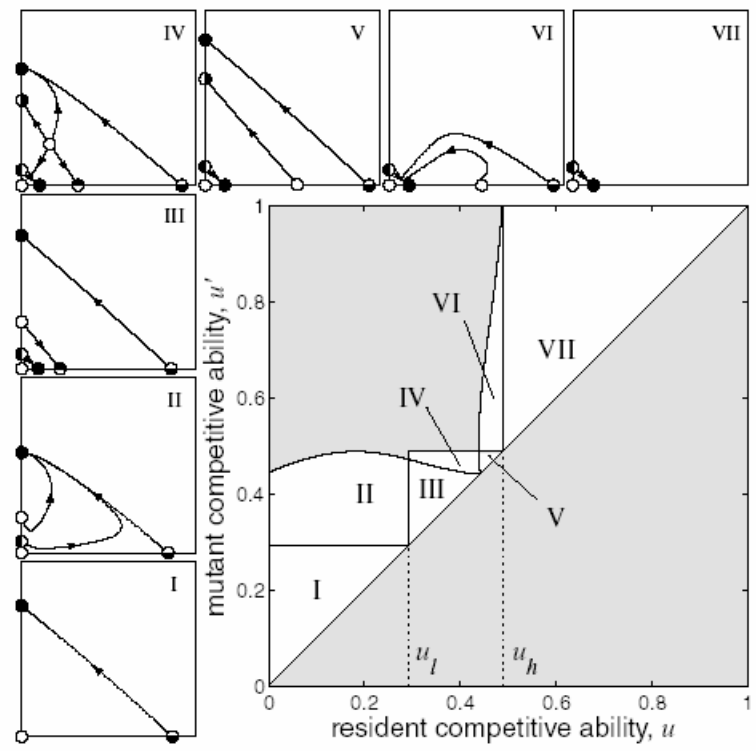

Fig. 2. Bifurcation analysis of the mutant-resident model for a population in which competitive ability evolves under asymmetrical competition (see Dercole et al. (2002)). The jump process underlying the population's adaptive dynamics can be thought of as taking place along the diagonal. The existence of region VI violates the "invasion-implies-fixation" principle: the far-right equilibrium is transversally unstable (hence invadable), yet the process of invasion causes the resident population to swing to its alternative equilibrium, which turns out to be resistant to invasion (transversally stable). As a consequence, the population experiences adaptive reversal. A similar phenomenon occurs when the adaptive dynamics reach region II from above. In the long term, successive evolutionary reversals drive the adaptive dynamics along a limit cycle.

5.2. Slow-fast ecological cycles and evolutionary sliding

Gragnani et al.'s (in prep.) investigates the co-evolutionary dynamics of two species, prey and predator. Each species is characterized by a single adaptive trait.

Monomorphic population dynamics (i.e. ecological dynamics) can be constructed as in section 4.1, which yields a system of two coupled nonlinear ODEs (one for prey number density, and one for predator). Solutions in $\mathbf{R}_+ \times \mathbf{R}_+$ are of three possible types, depending on the traits' values (Fig. 3): convergence to a locally stable equilibrium on the boundary of $\mathbf{R}_+ \times \mathbf{R}_+$ (i.e. extinction the the predator) (outter light region in Fig. 3), convergence to a locally stable positive equilibrium (shaded region, denoted by **E**), or convergence to a locally stable limit cycle (inner light region, denoted by **C**). Thus, the biologically relevant trait space is $\overline{\chi} = \mathrm{int}(\mathbf{E} \cup \mathbf{C})$.

For trait values lying in region **C**, the construction of a fitness function (function f in section 4.1) and calculation of the probability of mutant fixation, are problematic: such trait values violate the assumption that the resident population settles at a point equilibrium (which should be solution to Eq. (4.1) or an appropriate extension thereof in the case of multiple species). Gragnani et al. circumvent the difficulty by focusing on the special case of a "slow-fast" ecological model: birth and death in the predator take place on a much slower timescale than in the prey. Then one can use the singular perturbation approach (Hoppensteadt 1974), to approximate cycles in monomorphic population dynamics with the so-called "singular cycle" (Rinaldi and Scheffer 2000) which can usually be constructed using simple geometric rules (Muratori and Rinaldi 1991). Once the singular cycle has been characterized, it becomes possible to derive the fitness function explicitly, hence the corresponding canonical equation Eq. (4.8).

Because of the singular approximation, however, the fitness function turns out to be only *piecewise* differentiable on $\overline{\chi}$ – it is differentiable on $\mathrm{int}\,\mathbf{E}$ and $\mathrm{int}\,\mathbf{C}$, but not on $\overline{\chi}$. In such a case, the jump process converges to the canonical equation only on time intervals over which the solution to the canonical equation remains in $\mathrm{int}\,\mathbf{E}$ or $\mathrm{int}\,\mathbf{C}$. Thus, the canonical equation is a "piecewise smooth system", also called Filippov system (Filippov 1988), formulated as follows

$$\text{(5.1)} \qquad \dot{x} = \begin{cases} G^{(1)}(x), & x \in \mathbf{E} \\ G^{(2)}(x), & x \in \mathbf{C} \end{cases}$$

where $x = (x_1, x_2)$ denotes the pair of prey and predator trait values. In words, two different vectors $\dot{x}$ are associated to each point x of the boundary **B**: one is $G^{(1)}(x)$,

tangent to the orbit obeying the equations valid in region **E**, and the other is $G^{(2)}(x)$, tangent to the orbit obeying the equations valid in region **C**. If the transversal components of these two vectors w.r.t. the boundary have the same sign, the orbit crosses **B** and the population switches from an equilibrium to a cyclic regime, or vice versa. On the contrary, if the transversal components of the two vectors are of opposite signs, i.e. if the two vector fields are "pushing" in opposite directions, the traits are forced to remain on the boundary and "slide" on it, i.e. the traits evolve in such a way that the populations remain pending for very long periods of time, if not forever, between equilibrium and cyclic coexistence. The ending points of segments of **B** along which sliding occurs can be determined precisely.

Sliding segments play the biological role of "adaptive ridges" in the landscape of evolutionary dynamics. Adaptive ridges possess the remarkable property of canalizing evolutionary trajectories issued from various ancestral phenotypic states, resulting in the uniformization of these trajectories once they leave the adaptive ridge. On the mathematical side, although bifurcation analysis of Filippov systems is important in many applications in various fields of science and engineering, they are not yet fully understood: the classification of bifurcations of Filippov systems (called "sliding bifurcations") is still incomplete, and effective numerical tools to detect them remain to be developped. However, promising steps have been taken by Dercole (2002) and Kuznetsov et al. (2003).

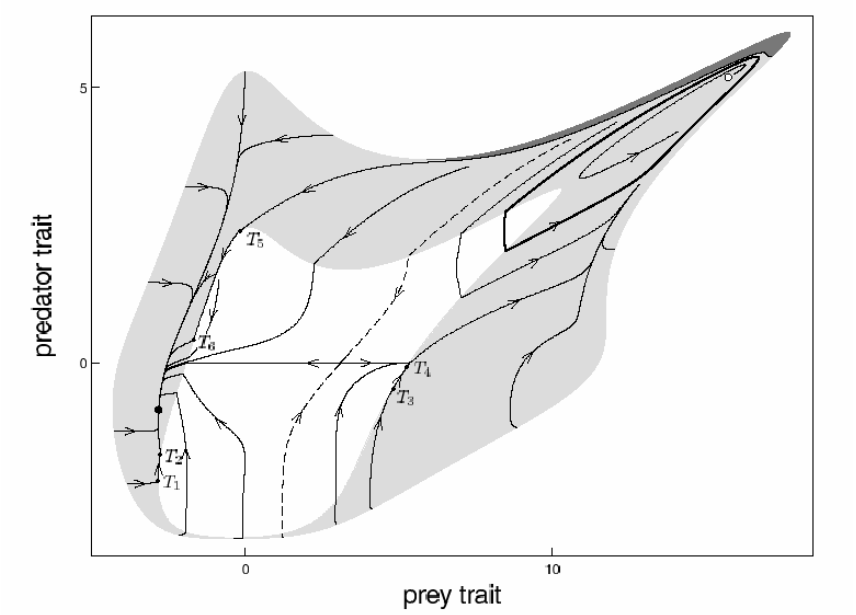

Fig. 3. A state portrait of the Filippov system Eq. (5.1) obtained by Gragnagi et al. (2003) as a model of slow-fast predator-prey coevolution. Trajectories represent orbits of adaptive trait dynamics. Outter light area, predator's ecological dynamics converge to extinction; shaded area, predator-prey ecological dynamics converge to a stable positive equilibrium; inner light region, predator-prey ecological dynamics converge to a stable limit cycle. There are three equilibria for adaptive trait dynamics: a stable node (filled circle) and an unstable focus (open circle) in region **E**, and a saddle in region **C**; and one limit cycle (overlapping regions **E** and **C**). There are two attractors: the node and the cycle, and their basins of attraction are separated by the stable manifold of the saddle. There are three sliding segments: T_1T_2, T_3T_4 and T_5T_6. Predator evolutionary suicide, i.e. predator trait's dynamics toward extinction, occurs in the dark region.

6. Concluding remarks

This review has opened and followed several mathematical directions for the analysis of stochastic individual processes of birth, mutation and death. The basic model takes the form of a point process, to which theoretical biologists often refer to as "individual-based model". The mathematical construction of the model yields a rigorous algorithm for numerical simulations. Different renormalizations lead to different approximations, which write as non-linear integro-differential equations or stochastic partial differential equations. At this moment, we are in the situation where very little is known about the transitory and long-term behavior of these approximations. In contrast, although the link between "adaptive dynamics" models and the underlying individual

point process have not yet been fully established, numerical bifurcation analyses of adaptive dynamics models have unraveled the extreme richness of evolutionary dynamics. Lesson from this investigation is that rigorous mathematical modeling leads to the discovery of novel evolutionary phenomena: adaptive reversal, evolutionary suicide, evolutionary sliding along adaptive ridges, and a quantitative approach to "punctuated" evolutionary trajectories.

6.1. The issue of evolutionary branching

Among issues left opened by this review, one of uttermost biological relevance is to obtain a rigorous characterization of the so-called "evolutionary branching" phenomenon: the qualitative change in trait dynamics from attractiveness to disruption and divergence (Metz et al. 1992, 1996; Geritz et al. 1998; Doebeli and Dieckmann 2000). Evolutionary branching provides a powerful metaphor for evolutionary diversification driven by ecological forces which are internal to the population (e.g. Schluter 2000). Although adaptive dynamics models that have been analysed so far give a sense that evolutionary branching should be widespread, a better mathematical understanding of this phenomenon is urgent. Detecting evolutionary branching amounts to tracking the number of "modes" of the population's trait distribution. To this end, we are envisioning two possible approaches: constructing a model for the dynamics of the support in trait space of the point process introduced in section 2; applying methods from signal processing (e.g. spectral analysis, wavelets techniques) to the integro-differential equations obtained from the renormalizations presented in section 3 (for a conceptually related approach, see Noest 1997). This work is currently under way.

6.2. The notion of fitness

The crux of constructing the adaptive dynamics approximation lies in the definition of the so-called fitness function, which determines the direction and magnitude of steps taken by the jump process in trait space (cf. section 4.1). Jumps correspond to successful invasion of the "resident" population by a "mutant" population originating as a single individual. The heuristics of adaptive dynamics assume a hybrid situation where a large-population renormalization is applied to the resident population, whereas the growth of the mutant population follows a stochastic birth-and-death process, parametrized by the

resident population number density predicted from the renormalized model, Eq. (4.1). Fitness can then be derived from the probability of persistence (or, equivalently, of extinction in finite time) of the mutant population. Beyond the problem of making these heuristics rigorous, this already points out several extensions that will be worth pursuing. First, defining fitness along these lines has been made by Dieckmann and Law (1996) in the simplest possible case of a constant environment; what happens when there are fluctuations in the mutant parameters? Such fluctuations could arise as small random variations driven by the external environment; or as deterministic oscillations in the resident population number density. The latter case could result from the resident population being structured by physiological (e.g. individual age or size) or environmental (e.g. individual spatial location) variables. This calls for extending the whole framework further to the case of structured populations.

6.3. General variation-transmission processes

Another desirable extension of this framework should aim at capturing notions of variation and transmission broader that germ-line mutations and genetic heritability. Recombination, in particular, is a paramount source of genetic variation associated with sexual reproduction (in a broad sense: recombination may occur even in viruses). Recombination raises the need to complicate the basic models with "mating kernels". From a biological perspective, such extensions are eagerly awaited for at least two motives. First, evolutionary branching provides a metaphor of speciation when occuring in sexual populations (Dieckmann and Doebeli 1999; Geritz and Kisdi 2000). Thus, the modeling framework presented here becomes a toolbox to investigate one of the deepest challenge of biology: understanding the ecological and genetic conditions for the formation of new species. Second, the further assumption that sexes are differenciated (into males and females) would allow to investigate another major question of contemporary evolutionary biology—that of conditions and scope for the evolution of sexual dimorphism, and its potential to being an alternative to speciation through evolutionary branching.

Other types of genetic effects need be accomodated by a comprehensive mathematical theory of adaptive evolution (Ancel Meyers and Bull 2002). The dichotomy between germ-line mutations (between-generation inheritance) vs. somatic mutations

(within-organism inheritance) is suggestive of incorporating multi-level selection in the theory by developing new forms of slow-fast models – the fast timescale being that of mutation-selection among somatic cells within the organism, as a potential driver of the organism's developmental process. Timescales themselves may also vary in the course of evolution. "Mutator" genes and "adaptive capacitors" have been discovered in a range of organisms, from bacteria to fruitflies (Rutherford and Lindquist 1998; Tenaillon et al. 1999; see Imasheva and Loeschke 2004 for a review). At times when environmental conditions become adverse, such mechanisms lead to an elevated mutation rate in individual bacteria, or to the sudden expression of phenotypic variation in individual flies. Thus, mutation parameters can vary in time and respond to the population state (e.g. number density). This should affect the type of renormalizations that can be applied to mathematical models of the evolutionary process.

6.4. More complex trait space topologies

The current implementation of Darwinian mathematical models of evolution assumes that the phenotypic trait space is organized into a highly symmetric and regular space equipped with a metric (e.g. a Euclidian vector space). Recent computational work on molecular evolution suggests a different picture. By incorporating an explicit genotype-phenotype map, Stadler et al. (2001) show that the resulting phenotypic space lacks a metric and is better formalized by a pre-topology. Qualitative consequences for evolutionary dynamics can be profound. Stadler et al. have introduced the mathematical concepts and tools necessary to formalize the notion of "accessibility pre-topology" relative to which one can speak of continuity in the genotype-phenotype map and evolutionary trajectories. Incorporating these notions into the quantitative framework presented here raises a major challenge, likely to enhance the nascent synergy of novel mathematics and advanced biological understanding.

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