

Dynamics of fitness distributions in the presence of a phenotypic optimum: an integro-differential approach*

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Abstract

We propose an integro-differential description of the dynamics of the fitness distribution in an asexual population under mutation and selection, in the presence of a phenotypic optimum. Due to the presence of this optimum, the distribution of mutation effects on fitness depends on the parent's fitness, leading to a non-standard equation with "context-dependent" mutation kernels.

Under general assumptions on the mutation kernels, which encompass the standard n -dimensional Gaussian Fisher's geometrical model (FGM), we prove that the equation admits a unique time-global solution. Furthermore, we derive a nonlocal nonlinear transport equation satisfied by the cumulant generating function of the fitness distribution. As this equation is the same as the equation derived by Martin and Roques (2016) while studying stochastic Wright-Fisher-type models, this shows that the solution of the main integro-differential equation can be interpreted as the expected distribution of fitness corresponding to this type of microscopic models, in a deterministic limit. Additionally, we give simple sufficient conditions for the existence/non-existence of a concentration phenomenon at the optimal fitness value, i.e, of a Dirac mass at the optimum in the stationary fitness distribution. We show how it determines a phase transition, as mutation rates increase, in the value of the equilibrium mean fitness at mutation-selection balance. In the particular case of the FGM, consistently with previous studies based on other formalisms (Waxman and Peck, 1998, 2006), the condition for the existence of the concentration phenomenon simply requires that the dimension n of the phenotype space be larger than or equal to 3 and the mutation rate U be smaller than some explicit threshold.

The accuracy of these deterministic approximations are further checked by stochastic individual-based simulations.

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1 Introduction

Understanding the complex interplay between mutation and selection in asexuals is a central issue of evolutionary biology. Recently, several modeling approaches have been proposed, to describe the evolution of a population under the effects of these two forces. Most of these modeling approaches assume that the fitness of the individuals depends on a single quantitative trait (e.g., [2, 23, 36]). Other approaches, as in this study, directly focus on the dynamics of fitness distributions (e.g., [1, 29]).

A rich literature (reviewed in [33]) has also focused on the interplay between drift selection and mutation in asexuals. These theories focus mainly on the expected mean fitness of the population as it reaches a stationary regime, using models that directly focus on fitness distributions. A few also considered transient behaviors of these models (e.g. [31, 35]), which can be seen as an approximation for the expected distribution of fitness, over time (discussed in [29]).

As fitness is a concept of fundamental importance to our study, we begin with an intuitive definition of this concept. In an asexual population made of K genotypes, we say that the genotype i has *absolute* Malthusian fitness m_i if the abundance $N_i(t)$ of the genotype at time t satisfies $N_i'(t) = m_i N_i(t)$. Summing over all the indexes $i = 1, \dots, K$, we observe that the total population size satisfies $N'(t) = \bar{m}(t) N(t)$, with $\bar{m}(t)$ the mean fitness in the population at time t . If we focus on the frequency $p_i(t) = N_i(t)/N(t)$, we get $p_i'(t) = p_i(t) (m_i - \bar{m}(t))$.

In this study, following the standard framework of Wright-Fisher or Moran models [25], we assume a constant population size N and a continuum of fitness classes $m \in \mathbb{R}$. In this case, only *relative* Malthusian fitness matters. If we first neglect the effects of mutations, the changes in genotype frequencies due to selection are determined by their relative fitness m through the expression (see, e.g., [35]):

$$\partial_t p(t, m) = p(t, m) (m - \bar{m}(t)), \quad (1)$$

where $m \in \mathbb{R}$ is the relative Malthusian fitness, $p(t, m)$ the distribution of fitness at time t , and $\bar{m} : \mathbb{R}_+ \rightarrow \mathbb{R}$ is the mean fitness, defined for any $t \in \mathbb{R}_+$ by

$$\bar{m}(t) = \int_{\mathbb{R}} m p(t, m) dm. \quad (2)$$

As we can observe in (1), contrarily to other traits, fitness determines its own evolution. We can also note that the notion of relative fitness is defined by (1) up to an additive constant.

A second key step is to describe the distribution of mutation effects on fitness (or DFE, in short). Most mathematical models of asexual evolution (e.g. all those reviewed in [33]) neglect the dependence of the DFE on the fitness of the parent, as discussed e.g. in [18]. Some also ignore deleterious mutations and focus only on the contribution from beneficial ones [33]. However, accumulating data from evolution experiments, often in asexual microbes, has shown that fitness epistasis is pervasive, i.e. that the fitness effects of mutations (individual effects or full distributions) depend on the genetic background in which they arise (e.g. [9, 18, 24]). This has led to the idea that epistasis, once taken into account, might actually make evolution predictable in spite of stochastic effects due to drift and mutation, at least in large populations and at the fitness level [18, 27, 29]. This may explain why observed fitness trajectories, in large asexual populations, appear relatively repeatable (across biological replicates), in spite of non-repeatable patterns at the sequence level (e.g. [24]). This conjecture partly motivates the present study of phenotypic adaptation as a deterministic dynamical system.

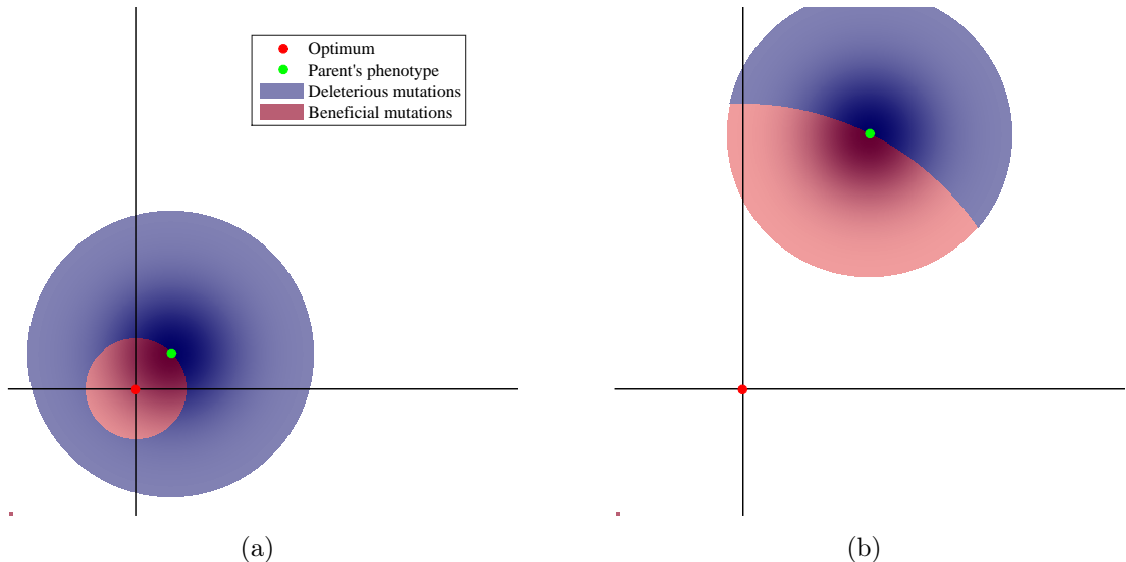


Figure 1: Proportions of beneficial and deleterious mutations, in a two-dimensional phenotypic space with a phenotypic optimum. In panel (b) the parent’s phenotype is farther from the optimum than in panel (a), so that beneficial mutations are more frequent and of larger effect on average in (b).

One option to implement epistasis into fitness dynamics models is by using Fisher’s Geometrical Model (FGM) with a single optimum, where a complex form of epistasis arises naturally. The FGM has been shown to lead to fairly realistic DFEs (e.g., [28]) in their shape, dependence on the environment or epistatic pattern (reviewed in [34]). It is a phenotype-fitness landscape model: it assumes n -dimensional (breeding values for) phenotype, described by vectors $\mathbf{z} \in \mathbb{R}^n$. The connection between phenotypes and relative Malthusian fitness is made through a quadratic function $m = -\|\mathbf{z}\|^2/2$, with $\|\cdot\|$ the Euclidian norm in \mathbb{R}^n . A standard way of describing the effects of mutations on phenotypes is to assume that, given a parent with phenotype \mathbf{z} , the mutant offspring has a phenotype $\mathbf{z} + d\mathbf{z}$, where $d\mathbf{z}$ follows an n -dimensional isotropic Gaussian distribution with variance $\lambda > 0$ at each trait (Gaussian FGM). In this case, even if the distribution of mutation effects on phenotype is independent of the parent phenotype, the DFE on fitness does depend on the parent fitness (because of the non-linear relationship between \mathbf{z} and m). This is illustrated in Fig. 1. These effects can be summarized by a mutation kernel J_y : given a parent with fitness y , the mutant offsprings have fitness $y + s$, with s a random variable with density J_y . We say that this DFE is *context-dependent* because of its dependence on y . In spite of this complication, fitness still entirely determines its own evolution, in the FGM under selection and mutation, because epistasis is mediated by fitness alone.

Combining the equation (1) with the general assumption of a DFE that depends on background fitness, we obtain the following integro-differential equation:

$$\partial_t p(t, m) = U (J_y \otimes p - p) (t, m) + p(t, m) (m - \bar{m}(t)), \quad t \geq 0, \quad m \in \mathbb{R}, \quad (3)$$

where $U > 0$ is a given constant corresponding to the mutation rate and $J_y \otimes p$ is defined, for

any $(t, m) \in \mathbb{R}_+ \times \mathbb{R}$, by

$$(J_y \circledast p - p)(t, m) = \int_{\mathbb{R}} J_y(m - y) p(t, y) dy - p(t, m). \quad (4)$$

This equation corresponds to a generalization of the equations studied in [17], where $J_y = J$ was supposed to be independent of the fitness y of the parent, leading to a standard convolution product instead of the operator \circledast . These previous approaches with context-independent DFEs ignore all forms of epistasis, including, for example, that generated by the presence of a fitness optimum. Similarly, other approaches where the mutation effects are modeled with a diffusion approximation, i.e., when $U(J_y \circledast p - p)(t, m)$ is replaced by $D \partial_{mm} p(t, m)$ for some $D > 0$ also ignore epistasis ([1, 35]). In these two cases (as soon as the support of J intersects \mathbb{R}_+ , i.e., in the presence of beneficial mutations), the mean fitness $\bar{m}(t)$ converges to $+\infty$ at large times, in a non-realistic (superlinear) way, see [31] for a discussion on this aspect.

A closely related work has been proposed in [29]. Their study focuses on a stochastic individual-based Wright-Fisher model combined with the FGM for the description of mutation effects on fitness. Based on formal computations, they derived nonlocal nonlinear transport equations satisfied by some generating function of the fitness distribution. Under some assumptions corresponding to a diffusion approximation of the mutation effects on phenotype, approximate linear transport equations arise that can be solved analytically, allowing to infer the corresponding dynamics of the multivariate phenotype and fitness distribution. Another related work has been developed by [2]. Their approach describes the dynamics of the distribution of a 1-dimensional trait x , with corresponding fitness value $-x^2$, i.e., in the presence of a fitness optimum at $x = 0$. They managed, under a diffusion approximation for the mutation effects on phenotypes, to give a full analytical description of the dynamics of the trait distribution.

From a mathematical perspective, the equation (3) combines several difficulties, compared to standard reaction-diffusion equations $\partial_t u = D \partial_{xx} u + f(u)$ with local diffusion and local reaction terms. The mutation term $U(J_y \circledast p - p)$ is nonlocal, has no regularizing properties, and is not a standard convolution product. The selection term (1) is also nonlocal due to the term $\bar{m}(t)$. Equations of the type $\partial_t u = (J \star u - u) + f(u)$, with \star the convolution product and a local reaction term $f(u)$, have been extensively studied, especially regarding the existence/nonexistence of traveling wave solutions and other spreading properties [3, 7, 11, 14, 15, 32, 39, 40, 41]. In the work [17] that was mentioned above, we considered nonlocal reaction terms of the form (1), but again with a standard convolution product. In the recent work [5], a reaction-diffusion equation with a general reaction term of the form $f(x) - \int_{\mathbb{R}} f(y)u(t, y) dy$ with $f(x) \rightarrow -\infty$ as $|x| \rightarrow \infty$, generalizing the results in [2], has also been thoroughly studied. Reaction-diffusion equations with other types of nonlocal reaction terms have also been investigated in recent works [4, 6, 12, 13, 16, 19, 21]. Lastly, we mention that operators of the type $J_y \circledast p - p$, which can equivalently be written as $\int_{\Omega} K(m, y)p(t, y)dy - p(t, m)$ have also been considered in [8, 10] with an emphasis on the study of the stationary states. Moreover, the existence of stationary states and travelling waves for equations of the form $\partial_t u = \partial_{xx} u + \mu(M \circledast u - u) + f(u)$, with $f(u)$ a nonlocal reaction term, has been studied in [20].

The paper is organized as follows. In Section 2, we detail all the assumptions on the initial condition $p(0, \cdot) = p_0$ and on the mutation kernels J_y . In Section 3, we present our main results on equation (3). In particular, we derive some a priori estimates on the solutions (Section 3.1); we state an existence and uniqueness result (Section 3.2); we connect this equation with

the formal theory developed in [29] for asexual models with selection and epistatic mutation (Section 3.3); we give a qualitative description of the stationary states of (3), and we apply these results to the particular case of the Gaussian FGM (Section 3.4). In Section 4, we present some numerical computations of the solutions of (3) under the assumptions of the Gaussian FGM, and we compare the corresponding distributions with observed distributions from individual-based simulations of the Wright-Fisher model. Lastly, we discuss our results in Section 5. Our results are proved in Section 6.

2 Assumptions

Initial condition. We assume throughout this paper that the initial distribution of fitness $p_0 \in L^\infty(\mathbb{R}) \cap L^1(\mathbb{R})$ is a probability density function, that is,

$$p_0(m) \geq 0 \text{ for all } m \in \mathbb{R} \text{ and } \int_{\mathbb{R}} p_0(m) dm = 1. \quad (5)$$

Additionally, we assume that p_0 satisfies

$$\lim_{m \rightarrow -\infty} p_0(m) e^{\alpha|m|} = 0 \text{ for all } \alpha > 0. \quad (6)$$

As mentioned in the introduction, we assume that there is a fitness optimum m^* and, without loss of generality as we work with relative fitnesses, we can assume that $m^* = 0$. Thus, at $t = 0$, all fitnesses must be less than or equal to 0. This means that the initial distribution p_0 is such that:

$$\text{supp } p_0 \subset \mathbb{R}_- := (-\infty, 0]. \quad (7)$$

General mutation kernels. We begin with the general assumptions that we use for our existence and uniqueness result. For each fitness $y \in \mathbb{R}_-$, we assume that $J_y \in L^1(\mathbb{R})$ is a probability density function:

$$J_y \geq 0 \text{ in } \mathbb{R} \text{ and } \int_{\mathbb{R}} J_y(s) ds = 1. \quad (8)$$

For mathematical convenience, we also set $J_y = 0$ in \mathbb{R} for each $y \in (0, +\infty)$ and we assume that, for each $m \in \mathbb{R}$, the function $y \mapsto J_y(m - y)$ is measurable in \mathbb{R} and finite almost everywhere (a.e. for short) in \mathbb{R} . As 0 is the fitness of the optimum, mutant offspring from any parent with fitness y cannot have a fitness larger than 0. It follows that, for each $y \leq 0$, $-y$ is an upper bound of the support of the mutation kernel J_y , that is,

$$J_y = 0 \text{ a.e. in } (-y, +\infty). \quad (9)$$

When $y = 0$, the parent has the optimal fitness and all mutations lead to fitnesses $m \leq 0$. This is consistent with the assumption (9): the kernel J_0 is supported in $(-\infty, 0]$, and therefore leads to deleterious mutations only.

For technical reasons, we may also assume that the kernels $(J_y)_{y \leq 0}$ are uniformly bounded in \mathbb{R} by a nonnegative function $\bar{J} \in L^1(\mathbb{R})$ which decays faster than any exponential function at $-\infty$, in the sense that

$$J_y \leq \bar{J} \text{ a.e. in } \mathbb{R} \text{ for all } y \leq 0, \text{ and } \int_{-\infty}^0 \bar{J}(m) e^{\alpha|m|} dm < +\infty \text{ for all } \alpha \geq 0. \quad (10)$$

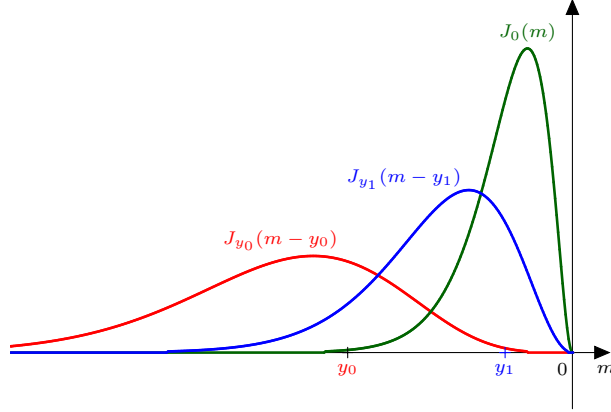


Figure 2: Mutation kernels J_y corresponding to the Gaussian Fisher's geometric model, with phenotype dimension $n = 6$ and variance $\lambda = 1$, for parents with fitnesses $y_0 < 0$, $y_1 < 0$ and 0.

Kernels with log-linear moment generating function. In order to connect our results with the theory described in [29], and to derive additional properties on the stationary states of (3), we require some additional assumptions on the kernels J_y . We assume here that these kernels have log-linear moment generating function in the sense that

$$\int_{-\infty}^{-y} J_y(m) e^{mz} dm = M_{\star}(z) e^{\omega(z)y} \quad \text{for all } y \leq 0 \text{ and } z \geq 0, \quad (11)$$

where

$$M_{\star}(z) = \int_{-\infty}^0 J_0(s) e^{sz} ds$$

is the moment generating function of the mutation kernel at the optimal fitness and $\omega \in \mathcal{C}^1(\mathbb{R}_+)$ satisfies

$$\omega \not\equiv 0 \quad \text{and} \quad \omega'(0) \leq 0. \quad (12)$$

The assumptions (11)-(12) are satisfied in several standard models (discussed in [29]). For example, in the Gaussian Fisher's Geometric model (FGM) mentioned in Section 1, we have [29]:

$$\omega(z) = -\frac{\lambda z^2}{1 + \lambda z} \quad \text{and} \quad M_{\star}(z) = \frac{1}{(1 + \lambda z)^{n/2}}, \quad (13)$$

with $\lambda > 0$ being the variance of mutation effects per phenotypic trait, and n the dimension of the phenotype space. The mutation kernels J_y are uniquely defined by their moment generating function $z \mapsto M_{\star}(z)e^{\omega(z)y}$ and, in the Gaussian FGM, their probability density function (pdf) takes explicit form:

$$J_y(m) = \frac{2}{\lambda} f_{\chi_n^2\left(\frac{-2y}{\lambda}\right)}\left(-\frac{2(m+y)}{\lambda}\right) \quad (14)$$

for all $y \leq 0$ and $m \leq -y$, where $f_{\chi_n^2\left(\frac{-2y}{\lambda}\right)}$ denotes the pdf of the noncentral chi-square distribution with n degrees of freedom and noncentrality $-2y/\lambda$; see Fig. 2 for an illustration. Notice that these kernels also fulfill the assumptions (8)-(10).

The assumption $\omega \neq 0$ in (12) simply means that the kernels J_y do depend on the fitness of the parents. The assumption $\omega'(0) \leq 0$ in (12) can be interpreted as follows. Using (11), we get that:

$$\mathcal{C}_y(z) = \mathcal{C}_*(z) + \omega(z)y \quad (15)$$

for all $y \leq 0$ and $z \geq 0$, where

$$\mathcal{C}_y(z) = \ln \left(\int_{-\infty}^{-y} J_y(m) e^{mz} dm \right) \quad \text{and} \quad \mathcal{C}_*(z) = \ln M_*(z) = \ln \left(\int_{-\infty}^0 J_0(m) e^{mz} dm \right) \quad (16)$$

are the cumulant generating functions of J_y and J_0 respectively. Then, from assumption (10), the functions \mathcal{C}_y and $\mathcal{C}_* = \mathcal{C}_0$ are of class $C^\infty(\mathbb{R}_+)$ and they satisfy

$$\mathcal{C}'_y(0) = \mathcal{C}'_*(0) + \omega'(0)y \quad \text{for all } y \leq 0. \quad (17)$$

It follows that the mean effect of mutations on fitness y , namely $\mathcal{C}'_y(0) = \int_{-\infty}^{-y} m J_y(m) dm$, is a non-increasing function of the fitness of the parent y : $\frac{d}{dy} \mathcal{C}'_y(0) = \omega'(0) \leq 0$. In the special case of the FGM (Fig. 1), the parent fitness does not affect the expected fitness effect of mutations ($\omega'(0) = 0$).

3 Main results

3.1 Support of the solution

Under the assumption (9) on the mutation kernel, it is natural to expect that the upper bound of the support of the solution p of (3) remains below the fitness optimum 0. As stated by the proposition below, this is true even without assumptions (6) and (10) on the exponential decay of p_0 and J_y at $-\infty$.

Proposition 3.1 *Assume that $p_0 \in L^\infty(\mathbb{R}) \cap L^1(\mathbb{R})$ satisfies assumption (7) and the mutation kernels $J_y \in L^1(\mathbb{R})$ satisfy assumptions (8) and (9). Then, for any $T \in (0, +\infty]$ and any nonnegative solution p of (3) such that*

$$p \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R})) \quad \text{and} \quad \bar{m} \in \mathcal{C}([0, T]),$$

there holds

$$\text{supp } p(t, \cdot) \subset (-\infty, 0] \quad \text{for all } t \in [0, T].$$

The assumptions and conclusion of Proposition 3.1 show that the integral in (2) is computed over $(-\infty, 0]$, as is the integral in (4), since $J_y = 0$ in \mathbb{R} for all $y > 0$. From now on, we may therefore define \bar{m} and $J_y \otimes p$ as

$$\bar{m}(t) = \int_{-\infty}^0 m p(t, m) dm \quad \text{and} \quad (J_y \otimes p)(t, m) = \int_{-\infty}^0 J_y(m - y) p(t, y) dy.$$

Moreover, for every $t \in [0, T]$, the function $(J_y \otimes p)(t, \cdot)$ belongs to $L^1(\mathbb{R})$ from Fubini's theorem together with (8) and Proposition 3.1, and therefore the integral defining $(J_y \otimes p)(t, m)$ converges for almost every $m \in \mathbb{R}$ (notice that it converges for every $m \in \mathbb{R}$ if (10) is also

assumed). We also point out that, under the regularity assumptions on p and \bar{m} in Proposition 3.1, the equation (3) is satisfied at each time $t \in [0, T)$ for almost every $m \in \mathbb{R}$.

Furthermore, the distribution $p(t, \cdot)$ may or may not reach the fitness optimum 0. The proposition below shows that if the kernels J_y include some beneficial mutations for any $y < 0$, in some strong sense, then the optimum is instantaneously reached. In other words, the following result gives sufficient conditions for the upper bound of the support of the solution $p(t, \cdot)$ to be equal to 0.

Proposition 3.2 *Assume that the mutation kernels $J_y \in L^1(\mathbb{R})$ satisfy assumptions (8)-(9). For any $y < 0$, set*

$$S_y = \sup \{s > 0 \text{ s.t. } J_y > 0 \text{ a.e. in } (0, s)\} \leq -y,$$

and assume that

$$S_y > 0 \text{ for all } y < 0 \text{ and the map } y \mapsto S_y \text{ is continuous in } (-\infty, 0). \quad (18)$$

Assume that $p_0 \in L^\infty(\mathbb{R}) \cap L^1(\mathbb{R})$ satisfies assumptions (5) and (7) and assume that, for some $T \in (0, +\infty]$, equation (3) admits a nonnegative solution $p \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ such that $\bar{m} \in \mathcal{C}([0, T])$. Then

$$\sup\{\text{supp } p(t, \cdot)\} = 0 \text{ for all } t \in (0, T). \quad (19)$$

The above result is reminiscent of the strong parabolic maximum principle in parabolic equations (see e.g. [30]): it shows that, provided that each kernel J_y (for $y < 0$) includes some beneficial mutations in the sense of (18), the support of the solution propagates with infinite speed, so that it instantaneously reaches the optimum $m = 0$. This property may not be satisfied without the assumption (18).

3.2 Global existence and uniqueness

We are now in position to state our existence and uniqueness result.

Theorem 3.3 (Existence, uniqueness, exponential decay) *Assume that $p_0 \in L^\infty(\mathbb{R}) \cap L^1(\mathbb{R})$ satisfies assumptions (5)-(7) and the kernels J_y satisfy assumptions (8)-(10). Then problem (3) with initial condition p_0 admits a unique solution $p \geq 0$ such that $t \mapsto p(t, \cdot) \in \mathcal{C}^1([0, +\infty), L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ and p decays faster than any exponential function as $m \rightarrow -\infty$ in the sense that, for every $\alpha > 0$ and $T > 0$, there is $\Gamma_{\alpha, T} > 0$ such that:*

$$0 \leq p(t, m) \leq \Gamma_{\alpha, T} e^{\alpha m} \text{ for all } t \in [0, T] \text{ and a.e. } m \in (-\infty, 0]. \quad (20)$$

Furthermore, $\bar{m} \in \mathcal{C}([0, +\infty))$, $\text{supp } p(t, \cdot) \subset (-\infty, 0]$ for all $t \in [0, +\infty)$,

$$\int_{\mathbb{R}} p(t, m) dm = \int_{-\infty}^0 p(t, m) dm = 1 \text{ for all } t \geq 0,$$

and the same decay property (20) is valid for $|\partial_t p(t, m)|$ as well.

The decay assumptions (6) and (10) on p_0 and J_y seem purely technical in the proof. It is an interesting but still open question to prove the same type of result without these hypotheses.

3.3 Cumulant generating function

Our goal here is to connect the equation (3) with the formal theory developed in [29] for Wright-Fisher individual-based models. In [29], the authors derived a nonlocal transport equation approximately satisfied by the expected *cumulant generating function* (CGF, for short) of the fitness distribution.

In the sequel, we assume that the kernels J_y satisfy the assumptions (11)-(12), in addition to the properties (8)-(10). Under the assumptions and notations of Theorem 3.3, we consider the nonnegative solution $p \in \mathcal{C}^1([0, +\infty), L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ of (3), and we define the cumulant generating function $C \in \mathcal{C}^1([0, +\infty) \times [0, +\infty))$ of the fitness distribution by

$$C(t, z) := \ln \left(\int_{\mathbb{R}} p(t, m) e^{mz} dm \right) = \ln \left(\int_{-\infty}^0 p(t, m) e^{mz} dm \right), \quad (21)$$

for $t \geq 0$ and $z \geq 0$. Notice that, from Theorem 3.3, the map $t \mapsto C(t, \cdot)$ is actually of class $\mathcal{C}^1([0, +\infty), \mathcal{C}^\infty([0, +\infty)))$. Notice also that the quantity $C(t, z)$ could be defined for all $t \geq 0$ and all $z \in \mathbb{R}$ due to the decay properties (20). The CGF is a very useful tool to analyze the properties of a distribution. In particular, it is easily seen that

$$\partial_z C(t, 0) = \int_{-\infty}^0 m p(t, m) dm$$

is the mean fitness $\bar{m}(t)$ at a time $t \geq 0$ and

$$\partial_{zz} C(t, 0) = \int_{-\infty}^0 m^2 p(t, m) dm - (\bar{m}(t))^2$$

is the variance in fitness within the population.

We now derive the equation satisfied by C . For any given $t \geq 0$ and $z \geq 0$, by multiplying equation (3) by e^{mz} and integrating over $(-\infty, 0]$ with respect to m (all integrals below converge due to the decay properties of $p(t, \cdot)$ and $\partial_t p(t, \cdot)$ given in Theorem 3.3), we obtain:

$$\begin{aligned} \int_{-\infty}^0 e^{mz} \partial_t p(t, m) dm &= U \int_{-\infty}^0 e^{mz} \left(\int_{-\infty}^0 J_y(m-y) p(t, y) dy - p(t, m) \right) dm \\ &+ \int_{-\infty}^0 m e^{mz} p(t, m) dm - \bar{m}(t) \int_{-\infty}^0 e^{mz} p(t, m) dm. \end{aligned} \quad (22)$$

Then, using the assumption (11), we get that:

$$\begin{aligned} \int_{-\infty}^0 e^{mz} \int_{-\infty}^0 J_y(m-y) p(t, y) dy dm &= \int_{-\infty}^0 \left(\int_{-\infty}^{-y} J_y(s) e^{sz} ds \right) p(t, y) e^{yz} dy \\ &= M_\star(z) \int_{-\infty}^0 e^{y(z+\omega(z))} p(t, y) dy. \end{aligned}$$

Dividing the equality (22) by $\int_{-\infty}^0 e^{mz} p(t, m) dm$ and using Lebesgue's dominated convergence theorem, we then get the following proposition. In the statement, we point out that $z+\omega(z) \geq 0$ for all $z \geq 0$, as follows from the assumptions (8), (9) and (11), see (67) and Appendix B below.

Proposition 3.4 *The function $C \in \mathcal{C}^1([0, +\infty) \times [0, +\infty))$ is a classical solution of the following nonlocal equation*

$$\begin{cases} \partial_t C(t, z) = \partial_z C(t, z) - \partial_z C(t, 0) + U(e^{C(t, z + \omega(z)) - C(t, z)} M_\star(z) - 1), & t \geq 0, z \geq 0, \\ C(0, z) = C_0(z), & z \geq 0, \\ C(t, 0) = 0, & t \geq 0, \end{cases} \quad (23)$$

with initial condition

$$C_0(z) = \ln \left(\int_{-\infty}^0 p_0(m) e^{mz} dm \right).$$

We obtain the same equation as equation (7) in [29]. The consequences of this result are twofold. First, it shows that the solution $p(t, m)$ of (3) can be interpreted as the expected (expectation among replicate populations) distribution of fitness corresponding to Wright-Fisher-type individual-based models, in a deterministic limit. Second, it gives a rigorous mathematical basis to the statements in [29], which were based on formal computations. In particular, it shows that the solution of (23) (provided that it is unique) is truly a cumulant generating function, in the sense that it satisfies (21), with the following immediate consequences: (i) $C(t, \cdot)$ is convex (from Theorem 3.3 and the Cauchy-Schwarz inequality, see (76) below), (ii) $C(t, \cdot)$ is a non-increasing function. These two properties were conjectured without proof in [29].

Previous studies have shown that equations of the form (23) can be more analytically tractable than the original integro-differential equation (3), in part because the nonlocal term $\bar{m}(t)$ is transformed into $\partial_z C(t, 0)$. For instance, when $\omega(z) \equiv 0$ (which is excluded here because of assumption (12)), the results in [17] show that the solution of (3) can be computed explicitly, leading to analytic expressions for the mean and the variance of the distribution $p(t, \cdot)$. The CGF method can be applied as well to diffusion equations, e.g., $\partial_t p = \partial_{mm} p + p(m - \bar{m}(t))$. This diffusion equation was already solved explicitly in [1], with a method based on involved changes of unknown functions to remove the term $p(m - \bar{m}(t))$. With the CGF approach, we simply get $\partial_t C(t, z) = \partial_z C(t, z) - \partial_z C(t, 0) + z^2$, whose solution is $C_0(z + t) - C_0(t) + t^2 z + t z^2$, leading to an analytic characterization of p . Coming back to (3), with $\omega(z) \not\equiv 0$, we were not able to derive an explicit solution of (23). However, the CGF approach leads to sharp a priori estimates of the stationary states of (3). These results are presented in the next section.

3.4 Stationary states

This section is devoted to the study of the stationary states of equation (3). Namely, we focus on weak solutions p_∞ of

$$U(J_y \otimes p_\infty - p_\infty) + (m - \bar{m}_\infty) p_\infty = 0, \quad (24)$$

where

$$(J_y \otimes p_\infty)(m) = \int_{-\infty}^0 J_y(m - y) dp_\infty(y) \quad \text{and} \quad \bar{m}_\infty = \int_{-\infty}^0 m dp_\infty(m). \quad (25)$$

In the section, in addition to the assumptions (5)-(12), we assume that the family $(p(t, \cdot))_{t \geq 0}$ converges weakly as $t \rightarrow +\infty$ to a Radon measure p_∞ in the sense that:

$$\lim_{t \rightarrow +\infty} \int_{\mathbb{R}} \phi(m) p(t, m) dm = \int_{\mathbb{R}} \phi(m) dp_\infty(m) \in \mathbb{R} \quad (26)$$

for any continuous function $\phi : \mathbb{R} \rightarrow \mathbb{R}$ such that $|\phi(m)| = O(|m|)$ as $|m| \rightarrow +\infty$. It then follows from Proposition 3.1 and Theorem 3.3 that p_∞ is nonnegative and satisfies

$$\text{supp } p_\infty \subset (-\infty, 0] \quad \text{and} \quad \int_{-\infty}^0 dp_\infty(m) = 1.$$

Notice also from (26) that \bar{m}_∞ defined in (25) is a real number. Furthermore, the following properties hold.

Proposition 3.5 *Assume that (5)-(12), (18) and (26) hold and that, for any continuous function $\phi : \mathbb{R} \rightarrow \mathbb{R}$ with compact support, the function $(-\infty, 0] \ni y \mapsto \psi(y) = \int_{\mathbb{R}} J_y(m - y) \phi(m) dm$ is continuous. Then the measure p_∞ satisfies*

$$\text{sup}\{\text{supp } p_\infty\} = 0 \quad \text{and} \quad \bar{m}_\infty \geq -U.$$

We are now interested in the existence of a positive mass at the optimal fitness (that is, 0). To do so, notice that the measure p_∞ can be written as a sum of two measures:

$$p_\infty = \rho \delta_0 + (1 - \rho) p^*, \tag{27}$$

where $\rho \in [0, 1]$ (if $\rho = 1$, then we set $p^* = 0$), δ_0 is the Dirac measure at 0, and p^* is a nonnegative measure supported in $(-\infty, 0]$ such that $p^*((-\infty, 0]) = 1$ (if $\rho \neq 1$) and p^* has no mass at 0 in the sense that $p^*([-\varepsilon, 0]) \rightarrow 0$ as $\varepsilon \rightarrow 0$. The following result shows in particular that p^* has no mass at any value $m < 0$ either (thus, the optimum fitness 0 is the unique possible concentration point of p_∞), and it provides a relationship between the existence of a positive mass at 0 and the value of the equilibrium mean fitness \bar{m}_∞ .

Proposition 3.6 *Under the same assumptions as in Proposition 3.5, the measure p_∞ , written as in (27), satisfies*

$$\rho = 0 \quad \text{or} \quad \bar{m}_\infty = -U.$$

Furthermore, p^* and the restriction of p_∞ on $(-\infty, 0)$ are $L^1((-\infty, 0))$ functions. In particular, for every $m < 0$, there holds

$$\lim_{\varepsilon \rightarrow 0} p_\infty([m - \varepsilon, m + \varepsilon]) = \lim_{\varepsilon \rightarrow 0} p^*([m - \varepsilon, m + \varepsilon]) = 0.$$

It turns out that the existence of a positive mass at 0 depends on the mutation rate U and on the harmonic mean $-s_H^*$ of the kernel at the optimal fitness J_0 defined by

$$-s_H^* := \left(\int_{-\infty}^0 \frac{J_0(s)}{s} ds \right)^{-1} = - \left(\int_0^{+\infty} M_\star(z) dz \right)^{-1} \in (-\infty, 0]. \tag{28}$$

More precisely, the next proposition shows that p_∞ admits a positive mass at 0 – meaning that a positive proportion ρ of the population has the best possible phenotype – if $s_H^* \neq 0$ and U is not too large.

Proposition 3.7 *Under the same assumptions as in Proposition 3.5, the measure p_∞ , written as in (27), is such that:*

(i) if $s_H^* = 0$, then $\rho = 0$; furthermore, if $s_H^* = 0$ and

$$\lim_{z \rightarrow +\infty} z + \omega(z) \in [0, +\infty), \quad (29)$$

then $\bar{m}_\infty > -U$;

(ii) if $s_H^* \neq 0$, then

(a) if $U < s_H^*$, then $\rho > 0$ and $\bar{m}_\infty = -U$;

(b) if

$$U > U_c := \inf \{U \geq s_H^* : \text{there is } z > 0 \text{ with } 1 + U \omega(z) M_*(z) = 0\}, \quad (30)$$

then $\rho = 0$ and $\bar{m}_\infty > -U$.

These results on the conditions of existence of a positive mass $\rho > 0$ at the optimum are not straightforward to interpret intuitively (see also [37, 38] for a discussion of this issue for the particular case of the FGM). If $s_H^* = 0$ (case (i)), the distribution of mutation effects s from the optimal phenotype (kernel J_0) typically decays exponentially or faster around $s = 0$. This means that the optimal phenotype produces an amount of infinitely mild deleterious mutants. These are so mildly counter-selected, relative to their optimal parent, that a population of optimal phenotypes cannot build up, even when the mutation rate is infinitely small (albeit non-zero). On the other hand, when $s_H^* \neq 0$ (case (ii)), optimal phenotypes always generate non-vanishingly deleterious mutants, which tend to be counter-selected relative to their optimal parent, thus allowing the maintenance/build-up of a class of optimal phenotypes. However, even then, a large enough mutation rate leads to the erosion of this optimal class ($\rho = 0$), because selection is not strong enough to maintain it, in the face of constant mutation destroying it. This occurs a minima when $U > U_c$ (we point out that U_c is finite from the assumptions made on J_y and ω), and cannot occur when $U < s_H^*$.

The assumption (29) on $\omega(z)$ is more technical. As shown in Appendix A, (29) implies that, for every $y < 0$, the upper bound of the support of the kernel J_y is equal to $-y$. In other words, this means that any suboptimal parent (fitness $y < 0$) can yield mutant offspring with the optimal phenotype (fitness 0, mutation effect $s = -y$).

Consider finally Fisher's geometrical model. Namely, assume that the mutation kernels satisfy assumptions (11) and (13)-(14). Then

$$s_H^* = \left(\int_0^{+\infty} M_*(z) dz \right)^{-1} = \left(\int_0^{+\infty} \frac{dz}{(1 + \lambda z)^{n/2}} \right)^{-1} = \begin{cases} 0, & \text{if } n \leq 2, \\ \frac{\lambda(n-2)}{2}, & \text{if } n > 2. \end{cases} \quad (31)$$

In other words, $s_H^* > 0$ if and only if the phenotype space has more than two dimensions. The following corollary is an immediate consequence of Proposition 3.7 under the assumptions of the Fisher's geometrical model.

Corollary 3.8 *Assume (5)-(14) and (26).*

(i) *If $n \leq 2$, then $\rho = 0$ and $\bar{m}_\infty > -U$;*

(ii) *if $n > 2$, then*

- (a) if $U \leq s_H^* = \lambda(n-2)/2$, then $\rho > 0$ and $\bar{m}_\infty = -U$;
(b) if $U > U_c = \frac{\lambda(n+2)^{n/2+1}}{16(n-2)^{n/2-1}}$, then $\rho = 0$ and $\bar{m}_\infty > -U$.

One of the main ingredients in the proofs of the results of this section is the CGF C_∞ of p_∞ defined by:

$$C_\infty(z) = \ln \left(\int_{\mathbb{R}} e^{mz} dp_\infty(m) \right) = \ln \left(\int_{-\infty}^0 e^{mz} dp_\infty(m) \right) \quad (32)$$

for $z \geq 0$. Assumption (26) shows that $C(t, z) \rightarrow C_\infty(z)$ as $t \rightarrow +\infty$ for all $z \geq 0$ and that C_∞ is of class $\mathcal{C}^1([0, +\infty))$ and is convex in $[0, +\infty)$ as a limit of the convex functions $C(t, \cdot)$ in $[0, +\infty)$. Passing to the limit as $t \rightarrow +\infty$ in (23), we also obtain that C_∞ is a stationary state of (23) in the sense that C_∞ is a classical solution of the following equation:

$$C'_\infty(z) - C'_\infty(0) + U (e^{C_\infty(z+\omega(z))-C_\infty(z)} M_\star(z) - 1) = 0, \quad z \geq 0. \quad (33)$$

Indeed, for any $s \geq 0$, integrating (23) with respect to t over $[s, s+1]$ leads to:

$$C(s+1, z) - C(s, z) = \int_s^{s+1} \left(\partial_z C(t, z) - \partial_z C(t, 0) + U (e^{C(t, z+\omega(z))-C(t, z)} M_\star(z) - 1) \right) dt. \quad (34)$$

As the function C is of class $\mathcal{C}^1(\mathbb{R}_+ \times \mathbb{R}_+)$, the mean value theorem implies that, for each $z \geq 0$ and $s \geq 0$, there is $t_{z,s} \in [s, s+1]$ such that

$$\begin{aligned} \int_s^{s+1} \left(\partial_z C(t, z) - \partial_z C(t, 0) + U (e^{C(t, z+\omega(z))-C(t, z)} M_\star(z) - 1) \right) dt \\ = \partial_z C(t_{z,s}, z) - \partial_z C(t_{z,s}, 0) + U (e^{C(t_{z,s}, z+\omega(z))-C(t_{z,s}, z)} M_\star(z) - 1). \end{aligned}$$

Then, using assumption (26), we get that, for all $z \geq 0$,

$$\lim_{t \rightarrow +\infty} \partial_z C(t, z) = \lim_{t \rightarrow +\infty} \frac{\int_{-\infty}^0 m e^{mz} p(t, m) dm}{\int_{-\infty}^0 e^{mz} p(t, m) dm} = \frac{\int_{-\infty}^0 m e^{mz} dp_\infty(m)}{\int_{-\infty}^0 e^{mz} dp_\infty(m)} = C'_\infty(z).$$

Consequently, passing to the limit as $s \rightarrow +\infty$ in (34) and using $\lim_{t \rightarrow +\infty} C(t, z) = C_\infty(z)$, equation (33) follows. Equation (33) will be used directly in some of the proofs, rather than (24). Notice finally that

$$C'_\infty(0) = \bar{m}_\infty.$$

4 Numerical computations

The objectives of this section are (i) to check numerically the convergence of the solution of (3) towards an equilibrium; (ii) to illustrate the results of Section 3.4 on the stationary states; and (iii) to compare the distributions p obeying the integro-differential equation (3) with empirical individual-based simulations given by a Wright-Fisher model. Namely, we assume that the kernels J_y satisfy the assumptions (8)-(14). For the sake of clarity, we recall these assumptions, which can be summarized as:

$$\left\{ \begin{array}{l} \int_{-\infty}^{-y} J_y(m) e^{mz} dm = M_\star(z) e^{\omega(z)y}, \\ J_y(m) = \frac{2}{\lambda} f_{\chi_n^2(\frac{-2y}{\lambda})} \left(-\frac{2(m+y)}{\lambda} \right), \quad \omega(z) = -\frac{\lambda z^2}{1 + \lambda z} \text{ and } M_\star(z) = \frac{1}{(1 + \lambda z)^{n/2}} \end{array} \right. \quad (35)$$

for all $y \leq 0$, $m \leq -y$ and $z \geq 0$.

Description of a Wright-Fisher individual-based model. As mentioned in the introduction, we assume a constant population size N . Under the assumptions of the FGM, each individual $i = 1, \dots, N$ is characterized by a phenotype $\mathbf{z}_i \in \mathbb{R}^n$. Its relative Malthusian fitness (exponential growth rate) is $m_i = -\|\mathbf{z}_i\|^2/2$ and its corresponding Darwinian fitness is e^{m_i} (geometric growth rate, a discrete time counterpart of the Malthusian fitness). We assume non-overlapping generations of duration $\delta_t = 1$. Each generation, selection and genetic drift are jointly simulated by the multinomial sampling of N individuals from the previous generation, each with weight given by their Darwinian fitnesses. Mutations are then simulated by randomly drawing, for each individual, a Poisson number of mutations, with rate U . We use a classic Gaussian FGM, following e.g. [22, 26]: each single mutation has a random phenotypic effect $d\mathbf{z}$ drawn into an isotropic multivariate Gaussian distribution: $d\mathbf{z} \sim \mathcal{N}(0, \lambda I_n)$, where $\lambda > 0$ is the mutational variance at each trait, and I_n is the identity matrix of size $n \times n$. Multiple mutations in a single individual have additive effects on phenotype. In all our simulations, we started with a clonal population (all of the individuals in the population initially share the same phenotype \mathbf{z}_0), and assumed a population size of $N = 10^5$ individuals.

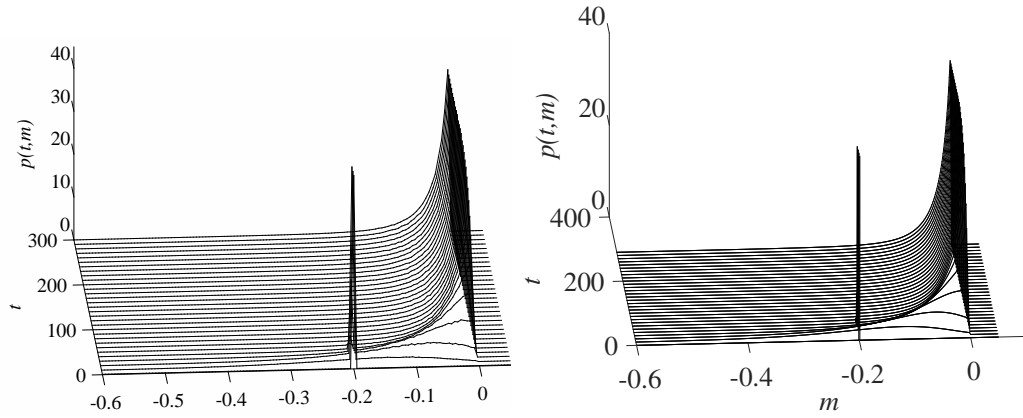
Numerical computations. For our simulations, we considered three sets of values of the parameters (n, λ, U) , each set of value corresponding to a different scenario in Corollary 3.8. The first set of parameters is $(n, \lambda, U) = (2, 1/30, 0.05)$. It corresponds to the assumptions of the first part of Corollary 3.8 (since $n = 2$). The second set of parameters is $(n, \lambda, U) = (6, 1/30, 0.05)$, so that $U < U_c \approx 0.067$, corresponding to the second case in Corollary 3.8. The third set of parameters is $(n, \lambda, U) = (6, 1/30, 0.55)$, corresponding to the last case in Corollary 3.8, with $U > U_c \approx 0.533$. We solved (3) in a bounded interval $[-1.2, 0.05]$ (but only the values of the solutions in the interval $[-0.6, 0.05]$ are displayed in the figures), using an explicit scheme in time with a time step $\delta t = 0.1$. The space was discretized, with a uniform step $\delta m = 0.001$. The simulations were performed using the software Matlab[®].

Fig. 3 depicts the dynamics of the fitness distribution obtained with the individual-based and integro-differential approaches, for the three sets of parameter values (n, λ, U) . In all cases, starting from a clonal population with initial fitness -0.2 (that is, for (3), we consider an initial condition p_0 close to the Dirac mass at -0.2) we observe that the distributions $p(t, \cdot)$ obtained by solving (3) seem to converge towards a stationary distribution. The predictions of the integro-differential approach are close to the empirical distribution given by the individual-based model, from qualitative and quantitative viewpoints.

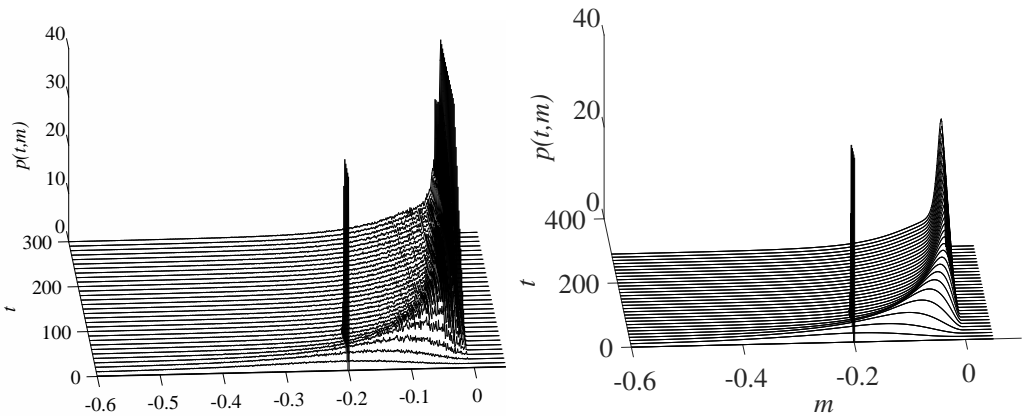
The predictions of the two approaches at large time ($t = 5000$) are depicted in Fig. 4. Consistently with the result of Corollary 3.8, the distributions in Fig. 4a satisfy $\rho = 0$ and $\bar{m}_\infty > -U$, the distributions in Fig. 4b satisfy $\rho > 0$ and $\bar{m}_\infty \approx -U$, while the distributions in Fig. 4c satisfy $\rho = 0$ and $\bar{m}_\infty > -U$. We also note in all cases a good agreement of the distributions obtained from the integro-differential model with those obtained from the individual-based approach.

5 Discussion

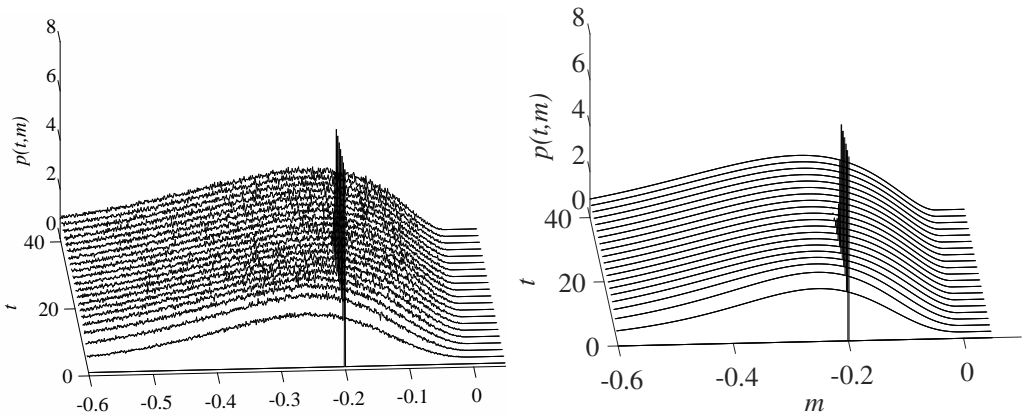
We proposed an integro-differential description of the dynamics of the fitness distribution in a population under mutation and selection, in the presence of a phenotype optimum. Under



(a) $n = 2, U = 0.05$

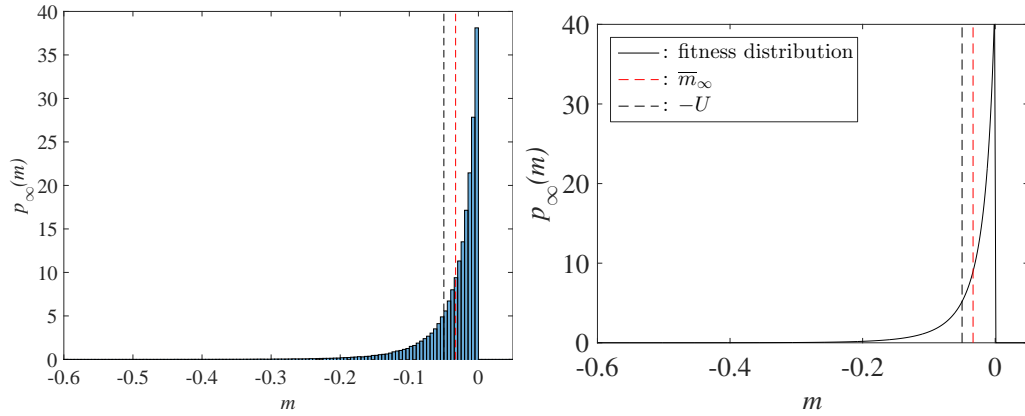


(b) $n = 6, U = 0.05$

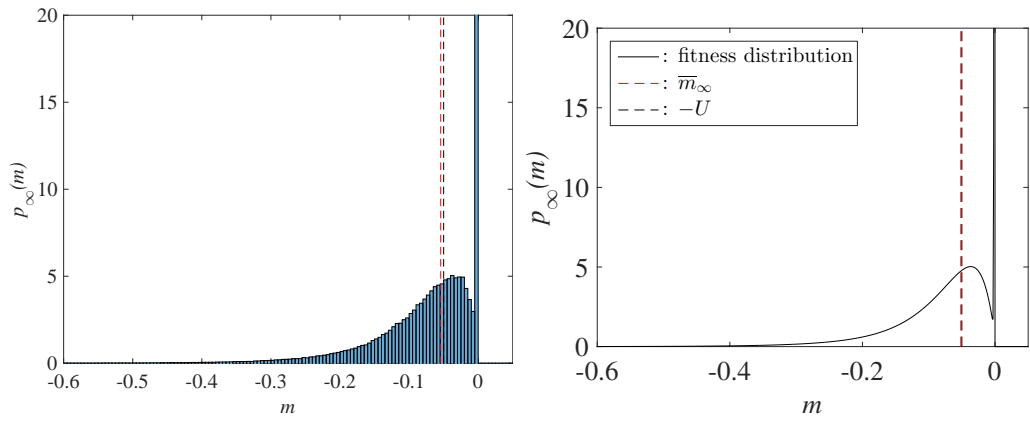


(c) $n = 6, U = 0.55$

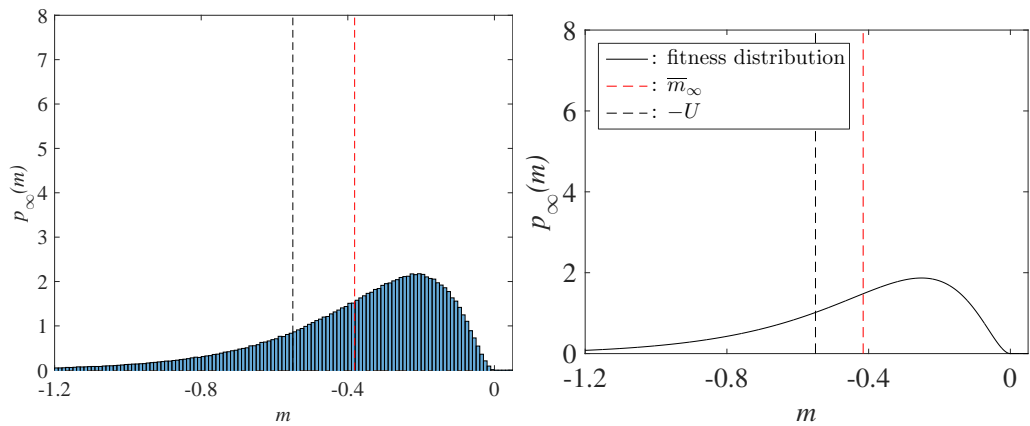
Figure 3: Dynamics of the fitness distribution $p(t, m)$: individual-based simulations with $N = 10^5$ individuals (left column: the distributions are averaged over 10 replicate simulations) vs numerical solution of (3) with the assumption (35) (right column). In all cases, we fixed $\lambda = 1/30$ for the mutational variance at each trait, and we assumed a clonal initial population with fitness -0.2 .



(a) $n = 2, U = 0.05$



(b) $n = 6, U = 0.05$



(c) $n = 6, U = 0.55$

Figure 4: Distribution $p(t, m)$ at large time $t = 5000$, individual-based simulations (left column: the distributions are averaged over 10 replicate simulations) vs numerical solution of (3) with the assumption (35) (right column). The parameter values are the same as in Fig. 3.

general assumptions on the mutation kernels, which encompass the standard Gaussian Fisher's Geometrical Model, we proved that the corresponding Cauchy problem (i.e., initial value problem) was "well posed": it admits a unique time-global solution and the support of the solution remains included in $(-\infty, 0]$, consistently with the existence of a fitness optimum at $m = 0$.

Furthermore, we were able to define the cumulant generating function $C(t, z)$ of the fitness distribution, and to derive a nonlocal nonlinear transport equation satisfied by $C(t, z)$. This equation is the same as the equation derived in [29] while studying stochastic Wright-Fisher-type individual-based models. We illustrated the connection between equation (3) and a Wright-Fisher-type individual-based model by performing numerical simulations. Under the assumptions of the Gaussian FGM, these simulations showed that equation (3) accurately describes the individual-based dynamics of fitness distributions. Additionally, the simulations suggest that the fitness distribution converges towards a stationary state.

The equation satisfied by $C(t, z)$ leads to a precise description of these stationary states. In particular, it leads to simple sufficient conditions for the existence/non-existence of a concentration phenomenon at the optimal fitness value $m = 0$ (i.e., of a Dirac mass at $m = 0$ in the stationary fitness distribution). Under the assumptions of the Gaussian FGM, the condition for the existence of the concentration phenomenon simply means that the dimension n of the phenotype space is larger than or equal to 3 and the mutation rate U is smaller than some explicit threshold. The condition on the dimension of the phenotype space is also a necessary condition: if $n \leq 2$, a positive mass at 0 can no longer exist. This is reminiscent of the results of [37] who stated that "when three or more characters are affected by each mutation, a single optimal genetic sequence may become common".

These results on the stationary states also give important clues on the equilibrium value of the mean fitness (\bar{m}_∞) at mutation-selection balance, called "mutation load": if a concentration phenomenon occurs at $m = 0$ then, necessarily, $\bar{m}_\infty = -U$, where U denotes the mutation rate. In the absence of concentration phenomenon, we conjecture that $\bar{m}_\infty > -U$ (this is true in the case of the Gaussian FGM, and in the general case under the technical assumption (29)). The determination of the exact value of \bar{m}_∞ in this case remains a challenging open problem, although approximate treatments are proposed in [29].

The main motivation for this study was to derive rigorous mathematical results when the DFE is given by the Gaussian FGM. It is noteworthy that all of our results remain true for another standard model of context-dependent DFE: the "House of Cards" model. With this approach, given a parent with fitness y , the mutant offspring have fitness s , where s is a random variable with a nonnegative fixed density $J_H \in L^1(\mathbb{R})$ supported in $(-\infty, 0]$. This means that the mutation kernels J_y are given by

$$J_y = J_H(y + \cdot) \text{ in } \mathbb{R} \text{ for every } y \leq 0.$$

Thus, the family J_y satisfies the same assumption (11) as the Gaussian FGM, with this time

$$M_\star(z) = \int_{-\infty}^0 J_H(s) e^{sz} ds \text{ and } \omega(z) = -z,$$

thus, Proposition 3.7 can be applied. In this case, the assumption (29) is always fulfilled, and the occurrence of a concentration phenomenon at the optimum depends on the harmonic mean of J_H .

6 Proofs of the main results

This section is devoted to the proof of the main results announced in Section 3 on the solutions of (3), (23) and (33).

6.1 Proof of Propositions 3.1 and 3.2 on the support of $p(t, \cdot)$

Proof of Proposition 3.1. Assume that $p_0 \in L^\infty(\mathbb{R}) \cap L^1(\mathbb{R})$ and the mutation kernels $J_y \in L^1(\mathbb{R})$ satisfy assumptions (7)-(9). Let $T \in (0, +\infty]$ and $p \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ be a nonnegative solution of (3) such that \bar{m} defined by (2) belongs to $\mathcal{C}([0, T])$. Let $A > 0$ and denote

$$Q_A(t) = \int_0^A p^2(t, m) dm \quad \text{for } t \in [0, T].$$

The assumptions on J_y and p and Fubini's theorem imply that, for every $t \in [0, T]$, the function $(J_y \otimes p)(t, \cdot)$ belongs to $L^1(\mathbb{R})$ and that

$$\int_a^b (J_y \otimes p)(t, m) dm = \int_a^b \int_{\mathbb{R}} J_y(m-y) p(t, y) dy dm = 0$$

for every $0 \leq a < b$, hence $(J_y \otimes p)(t, m) = 0$ for a.e. $m > 0$. Therefore, for every $t \in [0, T]$, by multiplying (3) by $p(t, m)$ and integrating over $(0, A)$, we get that

$$\frac{1}{2} \int_0^A \partial_t(p^2)(t, m) dm = -U Q_A(t) - \bar{m}(t) Q_A(t) + \int_0^A m p^2(t, m) dm.$$

Since

$$\int_0^A m p^2(t, m) dm \leq A \int_0^A p^2(t, m) dm = A Q_A(t),$$

it follows that

$$\frac{1}{2} Q_A'(t) \leq (A - U - \bar{m}(t)) Q_A(t)$$

for every $t \in [0, T]$. As $Q_A(0) = 0$ according to assumption (7), and since $\bar{m}(t)$ depends continuously on t and $Q_A \geq 0$ on $[0, T]$, Grönwall's lemma implies that $Q_A(t) = 0$ for all $t \in [0, T]$. Since $A > 0$ can be arbitrarily large, the proof of Proposition 3.1 is thereby complete. \square

Proof of Proposition 3.2. Assume that p_0 and the mutation kernels $J_y \in L^1(\mathbb{R})$ satisfy assumptions (5), (7)-(9) and (18). Let $T \in (0, +\infty]$ and $p \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ be a nonnegative solution of (3) such that \bar{m} defined by (2) belongs to $\mathcal{C}([0, T])$. First of all, Proposition 3.1 implies that $\text{supp } p(t, \cdot) \subset (-\infty, 0]$ for all $t \in [0, T]$.

Consider any $t \in (0, T)$ and assume by way of contradiction that $\sup\{\text{supp } p(t, \cdot)\} \neq 0$. Then there is $\delta > 0$ such that $p(t, \cdot) = 0$ almost everywhere in $(-\delta, 0)$ and $\int_{-\delta-\varepsilon}^{-\delta} p(t, y) dy > 0$ for all $\varepsilon > 0$. Since $p \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ is a nonnegative solution of (3), it follows that $\partial_t p(t, \cdot) = 0$ almost everywhere in $(-\delta, 0)$ and that, by integrating (3) at time t over $(-\delta, 0)$, there holds

$$\int_{-\delta}^0 (J_y \otimes p)(t, m) dm = 0.$$

From the assumption (18) on the positivity and continuity of $y \mapsto S_y$ on $(-\infty, 0)$, there is $\varepsilon \in (0, \delta)$ such that $2\varepsilon < S_y$ for all $y \in [-\delta - \varepsilon, -\delta]$. It then follows from the previous displayed equation and the nonnegativity of J_y and $p(t, \cdot)$, together with Fubini's theorem, that

$$\int_{-\delta-\varepsilon}^{-\delta} \left(\int_{-\delta}^{-\delta+\varepsilon} J_y(m-y) dm \right) p(t, y) dy = 0. \quad (36)$$

On the other hand, for each $y \in [-\delta - \varepsilon, -\delta]$ and each $m \in [-\delta, -\delta + \varepsilon]$, one has $0 \leq m - y \leq 2\varepsilon < S_y$. Hence, for every $y \in [-\delta - \varepsilon, -\delta]$, one has $J_y(\cdot - y) > 0$ almost everywhere in $[-\delta, -\delta + \varepsilon]$ and $\int_{-\delta}^{-\delta+\varepsilon} J_y(m-y) dm > 0$. Since $p(t, \cdot) \geq 0$ almost everywhere in \mathbb{R} , one then infers from (36) that $p(t, \cdot) = 0$ almost everywhere in $[-\delta - \varepsilon, -\delta]$, contradicting $\int_{-\delta-\varepsilon}^{-\delta} p(t, y) dy > 0$.

Therefore, one has shown that $\sup\{\text{supp } p(t, \cdot)\} = 0$ for every $t \in (0, T)$ and the proof of Proposition 3.2 is thereby complete. \square

6.2 Global existence: proof of Theorem 3.3

In order to show Theorem 3.3 on the global existence of solutions of (3), the general strategy consists in applying Cauchy-Lipschitz theorem in some suitably chosen function space. To do so, we first prove the local existence, with an existence time which is quantitatively defined in terms of the kernels $(J_y)_{y \in \mathbb{R}_-}$ and the initial probability density p_0 .

Proposition 6.1 (Local existence) *Let $\beta \geq 1$, let the kernels J_y satisfy assumptions (8)-(10) and let $p_0 \in L^\infty(\mathbb{R}) \cap L^1(\mathbb{R})$ satisfy (5), (7) and*

$$0 < K := \text{ess sup}_{m \in \mathbb{R}} (p_0(m) e^{-\beta m}) < +\infty. \quad (37)$$

Let \bar{J} be given in (10) and

$$T = \min \left\{ \beta, \left(U \int_{-\infty}^0 \bar{J}(m) e^{2\beta|m|} dm + U \|\bar{J}\|_{L^1(\mathbb{R})} + 3Ke \right)^{-1} \right\} > 0. \quad (38)$$

Then problem (3) admits a solution $p \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ such that $\bar{m} \in \mathcal{C}([0, T])$ and p decays at least like $e^{t/T + \beta m + tm}$ as $m \rightarrow -\infty$, in the sense that

$$0 \leq p(t, m) \leq Ke^{t/T + (\beta+t)m} \leq Ke^{1+\beta m} \leq Ke^{1+Tm} \text{ for all } t \in [0, T] \text{ and a.e. } m \in \mathbb{R}.$$

Furthermore, this solution is unique.

Remark 6.2 Notice that $\text{supp } p(t, \cdot) \subset \mathbb{R}_-$ for every $t \in [0, T)$ from Proposition 3.1 and for $t = T$ too from the continuity of the map $t \in [0, T] \mapsto p(t, \cdot)$ in $L^\infty(\mathbb{R}) \cap L^1(\mathbb{R})$.

Proof of Proposition 6.1. Step 1: an auxiliary problem. Let β , p_0 and K be defined as in the statement of Proposition 6.1. We first show the local existence, for some well chosen $T > 0$, of a solution v of the following nonlinear Cauchy problem:

$$\begin{cases} \partial_t v(t, m) &= U (J_y^t \otimes v - v)(t, m) - \bar{m}_v(t) v(t, m), & t \in [0, T], m \in \mathbb{R}, \\ v(0, m) &= p_0(m), & m \in \mathbb{R}, \end{cases} \quad (39)$$

with J_y^t defined by

$$J_y^t(s) = e^{-ts} J_y(s) \quad (40)$$

and

$$\bar{m}_v(t) = \int_{\mathbb{R}} m e^{tm} v(t, m) dm. \quad (41)$$

To do so, let us first introduce the Banach space

$$L^\infty(\mathbb{R}) = \{f \in L^\infty(\mathbb{R}); \text{supp } f \subset \mathbb{R}_-\},$$

pick any real number T such that $0 < T \leq \beta$, and consider the set

$$E = \{f \in \mathcal{C}([0, T], L^\infty(\mathbb{R})); f(0, \cdot) = p_0 \text{ and} \\ 0 \leq f(t, m) \leq K e^{t/T + \beta m} \text{ for all } t \in [0, T] \text{ and a.e. } m \in \mathbb{R}\},$$

and denote¹

$$\|f\|_E = \|f(t, m) e^{-t/T - \beta m}\|_{L^\infty([0, T] \times \mathbb{R})}.$$

Notice that the set E is not empty since the function f defined by $f(t, m) = p_0(m)$ belongs to E , as p_0 satisfies (5), (7) and (37). Let us now define a map F as follows:

$$F : E \rightarrow \mathcal{C}^1([0, T], L^\infty(\mathbb{R})), \\ v \mapsto h,$$

where $h = F(v)$ is the solution of the following linear Cauchy problem

$$\begin{cases} \partial_t h(t, m) = U \left(\int_{\mathbb{R}} J_y^t(m-y) h(t, y) dy - h(t, m) \right) - \bar{m}_v(t) h(t, m), & t \in [0, T], m \in \mathbb{R}, \\ h(0, m) = p_0(m), & m \in \mathbb{R}. \end{cases} \quad (42)$$

Notice that, since $v \in E$, the function \bar{m}_v defined in (41) exists and belongs to $\mathcal{C}([0, T])$. Furthermore, Lemma 6.3 below states that h is well defined as well.

Lemma 6.3 *For any given $v \in E$ with $0 < T \leq \beta$, the Cauchy problem (42) admits a unique solution $h \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}))$.*

In order not to slow down the proof of Proposition 6.1, the proof of Lemma 6.3 is postponed in Section 7.

Step 2: F maps E to E for $T > 0$ small enough. Consider any function $v \in E$, for some $T \in (0, \beta]$. Since $\text{supp } v(t, \cdot) \subset \mathbb{R}_-$ for all $t \in [0, T]$ and since $0 \leq v(t, m) \leq K e^{t/T + \beta m}$ for all $t \in [0, T]$ and a.e. $m \in \mathbb{R}_-$ with $\beta \geq 1$, it follows that, for all $t \in [0, T]$,

$$|\bar{m}_v(t)| \leq \int_{-\infty}^0 |y| e^{ty} v(t, y) dy \leq K \int_{-\infty}^0 |y| e^{ty} e^{t/T + \beta y} dy = \frac{K e^{t/T}}{(\beta + t)^2} \leq K e. \quad (43)$$

Now, set

$$\bar{h}(t, m) = \begin{cases} K e^{t/T + \beta m} & \text{for } (t, m) \in [0, T] \times \mathbb{R}_-, \\ 0 & \text{for } (t, m) \in [0, T] \times (0, +\infty). \end{cases}$$

¹With a slight abuse of notation, we also use this notation for functions which are not necessarily in E . Notice that the set E is complete for the topology induced by $\|\cdot\|_E$.

Using assumption (9) and the fact that $J_y = 0$ in \mathbb{R} for all $y > 0$, we observe that

$$\int_{\mathbb{R}} J_y^t(m-y) \bar{h}(t, y) dy = 0 \text{ for any } t \in [0, T] \text{ and } m \in (0, +\infty).$$

On the other hand, for any $(t, m) \in [0, T] \times \mathbb{R}_-$, it follows from (10) and (40) that

$$\begin{aligned} U \left(\int_{\mathbb{R}} J_y^t(m-y) \bar{h}(t, y) dy - \bar{h}(t, m) \right) &= U \bar{h}(t, m) \left(\int_{-\infty}^0 J_y(m-y) e^{(\beta+t)(y-m)} dy - 1 \right) \\ &\leq U \bar{h}(t, m) \int_{-\infty}^0 \bar{J}(m-y) e^{(\beta+t)(y-m)} dy \\ &\leq U \bar{h}(t, m) \int_{\mathbb{R}} \bar{J}(y) e^{-(\beta+t)y} dy \\ &\leq U \bar{h}(t, m) \left(\int_{-\infty}^0 \bar{J}(y) e^{2\beta|y|} dy + \|\bar{J}\|_{L^1(\mathbb{R})} \right). \end{aligned} \quad (44)$$

Consider any real number T such that

$$0 < T \leq \min \left\{ \beta, \left(U \int_{-\infty}^0 \bar{J}(y) e^{2\beta|y|} dy + U \|\bar{J}\|_{L^1(\mathbb{R})} + Ke \right)^{-1} \right\}. \quad (45)$$

Therefore, using the inequalities of the previous paragraph together with (43), we get that, for all $(t, m) \in [0, T] \times \mathbb{R}$,

$$\partial_t \bar{h}(t, m) = \frac{\bar{h}(t, m)}{T} \geq U \left(\int_{\mathbb{R}} J_y^t(m-y) \bar{h}(t, y) dy - \bar{h}(t, m) \right) + |\bar{m}_v(t)| \bar{h}(t, m).$$

Observe also that $\bar{h} \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}))$. In other words, $\bar{h} \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}))$ is a supersolution of problem (42) satisfied by $h = F(v)$. From the definition (37) of K and from (7), we also know that $0 \leq h(0, m) = p_0(m) \leq \bar{h}(0, m)$ for a.e. $m \in \mathbb{R}$.

In order to conclude that $0 \leq h(t, \cdot) \leq \bar{h}(t, \cdot)$ a.e. in \mathbb{R} for every $t \in [0, T]$, we will apply the following comparison principle, whose proof is postponed in Section 7.

Lemma 6.4 (Comparison principle) *Let $\tau \in (0, +\infty)$, $\varpi \in \mathcal{C}([0, \tau])$ and $h_1, h_2 \in \mathcal{C}^1([0, \tau], L^\infty(\mathbb{R}))$ be such that, for every $t \in [0, \tau]$, $h_1(t, \cdot) = h_2(t, \cdot) = 0$ a.e. in $(0, +\infty)$ and*

$$\begin{aligned} \partial_t h_1(t, m) - U \left(\int_{\mathbb{R}} J_y^t(m-y) h_1(t, y) dy - h_1(t, m) \right) + \varpi(t) h_1(t, m) \\ \leq \partial_t h_2(t, m) - U \left(\int_{\mathbb{R}} J_y^t(m-y) h_2(t, y) dy - h_2(t, m) \right) + \varpi(t) h_2(t, m) \end{aligned} \quad (46)$$

for a.e. $m \in \mathbb{R}_-$, with J_y^t defined in (40). Assume that $h_1(0, \cdot) \leq h_2(0, \cdot)$ a.e. in \mathbb{R} . Then, for every $t \in [0, \tau]$, $h_1(t, \cdot) \leq h_2(t, \cdot)$ a.e. in \mathbb{R} .

Using this lemma, we obtain that, for every $t \in [0, T]$, $0 \leq h(t, m) \leq \bar{h}(t, m)$ for a.e. $m \in \mathbb{R}$. Together with Lemma 6.3, it follows that $h = F(v) \in E$.

Step 3: F is a contraction mapping. Let $T > 0$ be as in (45), let $v_1, v_2 \in E$ and define $H = F(v_1) - F(v_2)$. Notice that the function H belongs to $\mathcal{C}^1([0, T], L^\infty(\mathbb{R}))$ from Lemma 6.3 and that it satisfies, for all $t \in [0, T]$ and a.e. $m \in \mathbb{R}$,

$$\begin{cases} \partial_t H(t, m) = U (J_y^t \circledast H - H) (t, m) - (\bar{m}_{v_1}(t) - \bar{m}_{v_2}(t)) F(v_1)(t, m) - \bar{m}_{v_2}(t) H(t, m), \\ H(0, m) = 0. \end{cases} \quad (47)$$

Define

$$\bar{H}(t, m) = \begin{cases} \frac{\|v_1 - v_2\|_E}{2} e^{t/T + \beta m} & \text{for } (t, m) \in [0, T] \times \mathbb{R}_-, \\ 0 & \text{for } (t, m) \in [0, T] \times (0, +\infty). \end{cases}$$

Similar computations as for \bar{h} and v above imply that

$$U \left(\int_{\mathbb{R}} J_y^t(m - y) \bar{H}(t, y) dy - \bar{H}(t, m) \right) \leq U \bar{H}(t, m) \left(\int_{-\infty}^0 \bar{J}(y) e^{2\beta|y|} dy + \|\bar{J}\|_{L^1(\mathbb{R})} \right) \quad (48)$$

for all $(t, m) \in [0, T] \times \mathbb{R}$, and that $|\bar{m}_{v_1}(t) - \bar{m}_{v_2}(t)| \leq e \|v_1 - v_2\|_E$ for all $t \in [0, T]$. Since $F(v_1) \in E$, it then follows that

$$|(\bar{m}_{v_1}(t) - \bar{m}_{v_2}(t)) F(v_1)(t, m)| \leq K e \|v_1 - v_2\|_E e^{t/T + \beta m} = 2K e \bar{H}(t, m), \quad (49)$$

for all $t \in [0, T]$ and a.e. $m \in \mathbb{R}_-$.

Finally, let us consider the real number T defined by (38). Using (43), (48) and (49), we get that

$$\partial_t \bar{H}(t, m) = \frac{\bar{H}(t, m)}{T} \geq U (J_t \circledast \bar{H} - \bar{H})(t, m) + |(\bar{m}_{v_1}(t) - \bar{m}_{v_2}(t)) F(v_1)(t, m)| + |\bar{m}_{v_2}(t)| \bar{H}(t, m)$$

for all $t \in [0, T]$ and $m \in \mathbb{R}_-$ (and also for $m > 0$ since all quantities are then equal to 0). As above, this implies that \bar{H} is a supersolution of equation (47) satisfied by H , while $\bar{H} \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}))$. The functions $h_1 := H$ and $h_2 := \bar{H}$ then satisfy some inequalities of the type (46) with $\varpi = -\bar{m}_{v_2}$ and $\tau := T$. Using again the comparison principle of Lemma 6.4, we get that

$$H(t, \cdot) \leq \bar{H}(t, \cdot) \text{ a.e. in } \mathbb{R} \text{ for all } t \in [0, T].$$

Similarly, one has $-H(t, \cdot) \leq \bar{H}(t, \cdot)$ a.e. in \mathbb{R} for all $t \in [0, T]$. This immediately yields

$$\|F(v_1) - F(v_2)\|_E \leq \frac{1}{2} \|v_1 - v_2\|_E.$$

Thus, $F : E \rightarrow E$ is a contraction mapping.

Step 4: conclusion. Consider now $T > 0$ as defined in (38). The Banach fixed point theorem implies that F admits a unique fixed point $v \in E$. This function v then belongs to $\mathcal{C}^1([0, T], L^\infty(\mathbb{R}))$ from Lemma 6.3, it satisfies

$$0 \leq v(t, m) \leq K e^{t/T + \beta m} \text{ for all } t \in [0, T] \text{ and a.e. } m \in \mathbb{R}$$

with $\text{supp } v(t, \cdot) \subset \mathbb{R}_-$ for every $t \in [0, T]$. This function v is also the unique such solution of (39). Furthermore, with similar estimates as in (43) and (44), there is $K' > 0$ such that

$|\partial_t v(t, m)| \leq K' e^{t/T + \beta m}$ for all $t \in [0, T]$ and a.e. $m \in \mathbb{R}_-$, and $\partial_t v(t, m) = 0$ for all $t \in [0, T]$ and a.e. $m > 0$.

Finally, letting

$$p(t, m) = e^{tm} v(t, m)$$

for $(t, m) \in [0, T] \times \mathbb{R}$, it is straightforward to check that $p \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}))$ is a solution of (3) in $[0, T] \times \mathbb{R}$, with $\text{supp } p(t, \cdot) \subset \mathbb{R}_-$ for every $t \in [0, T]$. Additionally, as $v \in E$, it follows that $p(t, \cdot) \in L^1(\mathbb{R})$ for all $t \in [0, T]$. Lastly, $p \in \mathcal{C}^1([0, T], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$, the function

$$t \mapsto \bar{m}(t) = \int_{\mathbb{R}} m p(t, m) dm = \int_{-\infty}^0 m p(t, m) dm$$

is continuous in $[0, T]$, and

$$0 \leq p(t, m) \leq K e^{t/T + (\beta+t)m} \text{ for all } t \in [0, T] \text{ and a.e. } m \in \mathbb{R}_-.$$

The proof of Proposition 6.1 is thereby complete. \square

Proof of Theorem 3.3. We are now in position to prove the global existence and uniqueness result of Theorem 3.3. Let $T_{max} > 0$ be the largest time such that equation (3) admits a unique solution $p \in \mathcal{C}^1([0, T_{max}], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ with $\bar{m} \in \mathcal{C}([0, T_{max}))$ and, for every $T \in (0, T_{max})$, there is $C_T > 0$ such that

$$0 \leq p(t, m) \leq C_T e^{Tm} \text{ for all } t \in [0, T] \text{ and a.e. } m \in \mathbb{R}. \quad (50)$$

Notice that Proposition 3.1 then implies that $\text{supp } p(t, \cdot) \subset \mathbb{R}_-$ for every $t \in [0, T_{max})$. It follows from the local existence and uniqueness result of Proposition 6.1 applied with, say, $\beta = 1$ that

$$T_{max} \in (0, +\infty].$$

Notice that T_{max} does not depend on the choice $\beta = 1$ in Proposition 6.1, since (50) does not involve any β . Our goal is to show that $T_{max} = +\infty$.

We begin with some fundamental estimates stated in the following lemma, whose proof is postponed in Section 7.

Lemma 6.5 (Mass preservation and estimates on the mean fitness) *We have:*

$$\int_{\mathbb{R}} p(t, m) dm = \int_{-\infty}^0 p(t, m) dm = 1 \text{ for all } t \in [0, T_{max}) \quad (51)$$

and

$$\bar{m}(t) \geq \bar{m}(0) + tU\mu \text{ for all } t \in [0, T_{max}), \quad (52)$$

with

$$\mu = \int_{-\infty}^0 m \bar{J}(m) dm \in (-\infty, 0).$$

Assume now by contradiction that $T_{max} < +\infty$. Define

$$v(t, m) = p(t, m) e^{-tm}$$

for $(t, m) \in [0, T_{max}) \times \mathbb{R}$. The function v is a solution of the Cauchy problem (39) for all $T \in [0, T_{max})$ and, from (50) and the regularity properties of p , the function v belongs to $\mathcal{C}^1([0, T_{max}), L_-^\infty(\mathbb{R}))$. Set now

$$\beta_0 = T_{max} + 1$$

and let

$$K_0 = \operatorname{ess\,sup}_{m \in \mathbb{R}} (p_0(m) e^{-\beta_0 m})$$

be defined as in (37) in Proposition 6.1 with the choice $\beta = \beta_0$. Denote

$$\bar{v}(t, m) = \begin{cases} K_0 e^{\lambda t + \beta_0 m} & \text{for } (t, m) \in [0, T_{max}) \times \mathbb{R}_-, \\ 0 & \text{for } (t, m) \in [0, T_{max}) \times (0, +\infty), \end{cases}$$

where $\lambda \in \mathbb{R}$ is to be chosen later. Using (52) and the property $\bar{m}(t) = \bar{m}_v(t)$ for all $t \in [0, T_{max})$, it is easily seen (as in Step 2 of the proof of Proposition 6.1) that, for every $T \in (0, T_{max})$, \bar{v} is a supersolution of the equation (39) (for which $\bar{m}_v(t) = \bar{m}(t)$ is considered as a fixed coefficient) satisfied by v on $[0, T]$, provided that

$$\lambda \geq U \int_{-\infty}^0 \bar{J}(m) e^{2\beta_0 |m|} dm + U \|\bar{J}\|_{L^1(\mathbb{R})} - \bar{m}(0) - T U \mu. \quad (53)$$

Indeed, for every $T \in (0, T_{max})$, one has $\bar{v} \in \mathcal{C}^1([0, T], L_-^\infty(\mathbb{R}))$ and it follows from (53) that, for any $t \in [0, T]$,

$$\begin{aligned} \partial_t \bar{v}(t, m) - U \left(\int_{\mathbb{R}} J_y^t(m - y) \bar{v}(t, y) dy - \bar{v}(t, m) \right) + \bar{m}(t) \bar{v}(t, m) \\ \geq \lambda \bar{v}(t, m) - U \int_{\mathbb{R}} J_y^t(m - y) \bar{v}(t, y) dy + (\bar{m}(0) + t U \mu) \bar{v}(t, m) \\ \geq \left(\lambda - U \int_{-\infty}^0 \bar{J}(m) e^{2\beta_0 |m|} dm - U \|\bar{J}\|_{L^1(\mathbb{R})} + \bar{m}(0) + T U \mu \right) \bar{v}(t, m) \\ \geq 0 \end{aligned}$$

for almost every $m \in \mathbb{R}$, since $\mu < 0$.

Let then

$$\lambda^* = U \int_{-\infty}^0 \bar{J}(m) e^{2\beta_0 |m|} dm + U \|\bar{J}\|_{L^1(\mathbb{R})} + |\bar{m}(0)| + T_{max} U |\mu| > 0.$$

Using the comparison principle of Lemma 6.4 applied with every $\tau \in (0, T_{max})$, we obtain that

$$\begin{cases} 0 \leq v(t, m) \leq K_0 e^{\lambda^* t + \beta_0 m} & \text{for all } t \in [0, T_{max}) \text{ and a.e. } m \in \mathbb{R}_-, \\ \operatorname{supp} v(t, \cdot) \subset \mathbb{R}_- & \text{for all } t \in [0, T_{max}). \end{cases} \quad (54)$$

Now, for any $\theta \in (0, 1)$, set $p_\theta = p(\theta T_{max}, \cdot)$. We have

$$0 \leq p_\theta(m) = v(\theta T_{max}, m) e^{\theta T_{max} m} \leq K_0 e^{\lambda^* T_{max} + (\theta T_{max} + \beta_0) m} = K_0 e^{\lambda^* T_{max} + (\theta T_{max} + T_{max} + 1) m}$$

for a.e. $m \in \mathbb{R}_-$, while $\operatorname{supp} p_\theta \subset \mathbb{R}_-$. For any $\theta \in (0, 1)$, the function p_θ satisfies (5), owing to (50) and (51). Furthermore,

$$0 < K_\theta := \operatorname{ess\,sup}_{m \in \mathbb{R}} (p_\theta(m) e^{-(\theta T_{max} + T_{max} + 1) m}) \leq K_0 e^{\lambda^* T_{max}} < +\infty. \quad (55)$$

As a consequence, we can apply Proposition 6.1 with

$$\beta = \theta T_{max} + T_{max} + 1 \quad (56)$$

and the initial condition p_θ . Thus, for any $\theta \in (0, 1)$, there exist a time $T_\theta > 0$, defined as in (38) with K_θ instead of K , and a unique solution $\tilde{p} \in \mathcal{C}^1([0, T_\theta], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ of (3) with initial condition p_θ , such that

$$0 \leq \tilde{p}(t, m) \leq K_\theta e^{t/T_\theta + (\theta T_{max} + T_{max} + 1 + t)m}$$

for all $t \in [0, T_\theta]$ and a.e. $m \in \mathbb{R}_-$, and $\text{supp } \tilde{p}(t, \cdot) \subset \mathbb{R}_-$ for every $t \in [0, T_\theta]$. Therefore, for any $\theta \in (0, 1)$, problem (3) with initial condition p_0 has a solution $p \in \mathcal{C}^1([0, \theta T_{max} + T_\theta], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ such that, for all $t \in [\theta T_{max}, \theta T_{max} + \min(T_\theta, 1)]$

$$0 \leq p(t, m) \leq K_\theta e^{(t - \theta T_{max})/T_\theta + (\theta T_{max} + T_{max} + 1 + t - \theta T_{max})m} \leq K_0 e^{\lambda^* T_{max} + 1 + (\theta T_{max} + T_{max} + 1)m}$$

for a.e. $m \in \mathbb{R}_-$, and $\text{supp } p(t, \cdot) \subset \mathbb{R}_-$.

On the other hand, from (55) and from the definitions (56) of β and (38) of $T_\theta > 0$ with K_θ instead of K , it follows that

$$\liminf_{\theta \rightarrow 1, \theta < 1} T_\theta > 0.$$

Therefore, there exist $\theta' \in (0, 1)$ and $T' \in (T_{max}, T_{max} + 1)$ for which problem (3) with initial condition p_0 has a solution $p \in \mathcal{C}^1([0, T'], L^\infty(\mathbb{R}) \cap L^1(\mathbb{R}))$ such that, for all $t \in [\theta' T_{max}, T']$,

$$0 \leq p(t, m) \leq K_0 e^{\lambda^* T_{max} + 1 + (\theta' T_{max} + T_{max} + 1)m} \leq K_0 e^{\lambda^* T_{max} + 1 + T' m} \quad (57)$$

for a.e. $m \in \mathbb{R}_-$, together with $\text{supp } p(t, \cdot) \subset \mathbb{R}_-$. Furthermore, (54) (remember that $\beta_0 = T_{max} + 1$) implies that, for all $t \in [0, \theta' T_{max}]$ and a.e. $m \in \mathbb{R}_-$,

$$0 \leq p(t, m) = v(t, m) e^{tm} \leq K_0 e^{\lambda^* \theta' T_{max} + (T_{max} + 1)m} \leq K_0 e^{\lambda^* \theta' T_{max} + T' m},$$

and $\text{supp } p(t, \cdot) \subset \mathbb{R}_-$ for all $t \in [0, \theta' T_{max}]$. Together with (57) in $[\theta' T_{max}, T'] \times \mathbb{R}_-$, it follows that the solution p satisfies (50) for all $T \in (0, T']$. Finally, one infers that $\bar{m} \in \mathcal{C}([0, T'])$. The fact that T' is larger than T_{max} contradicts the definition of T_{max} .

As a conclusion, $T_{max} = +\infty$ and, from (50) holding for any $T > 0$, property (20) holds with $\Gamma_{\alpha, T} = C_{\max(\alpha, T)}$. From the equation (3) itself and from (10), it also follows that $|\partial_t p(t, m)|$ decays faster than any exponential function as $m \rightarrow -\infty$ in the sense that (20) holds for $|\partial_t p(t, m)|$ as well. The proof of Theorem 3.3 is thereby complete. \square

6.3 Proof of the results on the stationary states of (24) and (33)

Proof of Proposition 3.5. Let us first show that $\sup\{\text{supp } p_\infty\} = 0$. Assume not. Then there is $\delta > 0$ such that

$$p_\infty((-\delta, 0]) = 0 \quad \text{and} \quad p_\infty([-\delta - \varepsilon, -\delta]) > 0 \quad \text{for all } \varepsilon > 0. \quad (58)$$

Consider now any nonnegative continuous function $\phi : \mathbb{R} \rightarrow \mathbb{R}$ with compact support. By using (10) with $\bar{J} \in L^1(\mathbb{R})$, and the fact that the function $y \mapsto \int_{\mathbb{R}} J_y(m - y) \phi(m) dm$ is continuous (and bounded), it follows (as in the derivation of (33)) that

$$\begin{aligned} 0 &= \int_{\mathbb{R}} \int_{\mathbb{R}} J_y(m - y) \phi(m) dm dp_\infty(y) - U \int_{\mathbb{R}} \phi(m) dp_\infty(m) \\ &\quad + \int_{\mathbb{R}} m \phi(m) dp_\infty(m) - \bar{m}_\infty \int_{\mathbb{R}} \phi(m) dp_\infty(m). \end{aligned} \quad (59)$$

Assume moreover that the support of ϕ is included in $[-\delta, 0]$, and that

$$\int_{-\delta}^{-\delta+\eta} \phi(m) dm > 0 \text{ for all } \eta > 0. \quad (60)$$

Since the measure p_∞ is supported in $(-\infty, -\delta]$, one infers from (59) that

$$\int_{\mathbb{R}} \int_{\mathbb{R}} J_y(m-y) \phi(m) dm dp_\infty(y) = 0. \quad (61)$$

From the assumption (18) on the positivity and continuity of $y \mapsto S_y$ on $(-\infty, 0)$, there is $\varepsilon \in (0, \delta)$ such that $2\varepsilon < S_y$ for all $y \in [-\delta - \varepsilon, -\delta]$. It then follows from (61) and the nonnegativity of J_y , ϕ and p_∞ that

$$\int_{-\delta-\varepsilon}^{-\delta} \int_{-\delta}^{-\delta+\varepsilon} J_y(m-y) \phi(m) dm dp_\infty(y) = 0. \quad (62)$$

As in the proof of Proposition 3.2, by using with (60) and the nonnegativity of ϕ , it follows that

$$\int_{-\delta}^{-\delta+\varepsilon} J_y(m-y) \phi(m) dm > 0 \text{ for all } y \in [-\delta - \varepsilon, -\delta].$$

Together with (62) and the nonnegativity of p_∞ , one gets that $p_\infty([-\delta - \varepsilon, -\delta]) = 0$, a contradiction with (58). Therefore, one has shown that

$$\sup\{\text{supp } p_\infty\} = 0.$$

Lemma 4.5 in [17]² then implies that the CGF C_∞ of p_∞ satisfies $C'_\infty(z) \rightarrow 0$ as $z \rightarrow +\infty$.

Finally, let us prove that $\bar{m}_\infty \geq -U$. Using equation (33) satisfied by C_∞ and the fact that $\bar{m}_\infty = C'_\infty(0)$, we obtain that

$$\bar{m}_\infty + U = C'_\infty(0) + U = C'_\infty(z) + U e^{C_\infty(z+\omega(z))-C_\infty(z)} M_\star(z) \geq C'_\infty(z)$$

for all $z \geq 0$. Thus, by passing to the limit as $z \rightarrow +\infty$, one immediately gets that $\bar{m}_\infty + U \geq 0$. The proof of Proposition 3.5 is thereby complete. \square

Proof of Proposition 3.6. Equation (33) satisfied by C_∞ can be rewritten as

$$e^{C_\infty(z)} (C'_\infty(0) + U - C'_\infty(z)) = U e^{C_\infty(z+\omega(z))} M_\star(z) \quad (63)$$

for all $z \geq 0$. On the one hand we have

$$\lim_{z \rightarrow +\infty} e^{C_\infty(z)} = \lim_{z \rightarrow +\infty} \int_{-\infty}^0 e^{zm} dp_\infty(m) = \rho$$

from the definition of $\rho \in [0, 1]$ in (27). On the other hand, as mentioned in the proof of the previous proposition, we know that $C'_\infty(z) \rightarrow 0$ as $z \rightarrow +\infty$. By passing the limit as $z \rightarrow +\infty$ in (63), we get that the right-hand side has a limit and that

$$\rho (C'_\infty(0) + U) = U \lim_{z \rightarrow +\infty} e^{C_\infty(z+\omega(z))} M_\star(z).$$

²It is immediate to see that the proof and the conclusion of [17, Lemma 4.5] hold good even if the nonnegative probability measure p_∞ is not in $L^\infty(\mathbb{R})$.

Since

$$M_\star(z) = \int_{-\infty}^0 J_0(m) e^{mz} dm$$

is the MGF of the mutation kernel J_0 at the optimal fitness, with $J_0 \in L^1(\mathbb{R})$, one has $\lim_{z \rightarrow +\infty} M_\star(z) = 0$. Moreover, the function $s \mapsto e^{C_\infty(s)}$ is continuous in $[0, +\infty)$ and converges to $\rho \in [0, 1]$ at $+\infty$. Thus, it is bounded in $[0, +\infty)$. Therefore, we get that $\lim_{z \rightarrow +\infty} e^{C_\infty(z+\omega(z))} M_\star(z) = 0$ and

$$\rho(\bar{m}_\infty + U) = \rho(C'_\infty(0) + U) = 0,$$

that is to say that $\rho = 0$ or $\bar{m}_\infty = -U$.

Consider now any $A > 0$ and let us show that the restriction of p_∞ on $(-\infty, -A)$ is an $L^1((-\infty, -A))$ function. Together with the notation (27) (under the convention that $p^\star = 0$ if $\rho = 1$) and the fact that p_∞ is a nonnegative measure with unit mass, this will then imply that both p^\star and the restriction of p_∞ on $(-\infty, 0)$ are $L^1((-\infty, 0))$ functions. Fix an arbitrary $\varepsilon > 0$. Consider any integer $n \geq 1$, any real numbers $a_1 < \dots < a_n < a_{n+1} = -A$, any $0 < \eta < \max_{1 \leq i \leq n} (a_{i+1} - a_i)/4$, and set

$$\phi_{a_1, \dots, a_n, \eta} = \sum_{i=1}^n \phi\left(\frac{\cdot - a_i}{\eta}\right),$$

where ϕ is the nonnegative continuous compactly supported function defined by $\phi = 1$ on $(-1, 1)$, $\phi(x) = 2 - |x|$ if $1 \leq |x| \leq 2$ and $\phi = 0$ on $\mathbb{R} \setminus [-2, 2]$. Formula (59), together with the nonnegativity of $\bar{m}_\infty + U \geq 0$ (from Proposition 3.5) and that of $\phi_{a_1, \dots, a_n, \eta}$ and p_∞ , yields

$$\begin{aligned} \sum_{i=1}^n \int_{a_i - 2\eta}^{a_i + 2\eta} m \phi\left(\frac{m - a_i}{\eta}\right) dp_\infty(m) &= - \int_{\mathbb{R}} \int_{\mathbb{R}} J_y(m - y) \phi_{a_1, \dots, a_n, \eta}(m) dm dp_\infty(y) \\ &\quad + (\bar{m}_\infty + U) \int_{\mathbb{R}} \phi_{a_1, \dots, a_n, \eta}(m) dp_\infty(m) \\ &\geq - \int_{\mathbb{R}} \int_{\mathbb{R}} J_y(m - y) \phi_{a_1, \dots, a_n, \eta}(m) dm dp_\infty(y). \end{aligned}$$

Hence, by definition of ϕ and η , there holds

$$A \sum_{i=1}^n p_\infty([a_i - \eta, a_i + \eta]) \leq \int_{\mathbb{R}} \int_{\mathbb{R}} J_y(m - y) \phi_{a_1, \dots, a_n, \eta}(m) dm dp_\infty(y). \quad (64)$$

But, by (10), one has

$$\begin{aligned} &\int_{\mathbb{R}} \int_{\mathbb{R}} J_y(m - y) \phi_{a_1, \dots, a_n, \eta}(m) dm dp_\infty(y) \\ &\leq \int_{\mathbb{R}} \int_{\mathbb{R}} \bar{J}(m - y) \phi_{a_1, \dots, a_n, \eta}(m) dm dp_\infty(y) \\ &\leq \int_{\mathbb{R}} \|\bar{J}\|_{L^1((a_1 - 2\eta - y, a_1 + 2\eta - y) \cup \dots \cup (a_n - 2\eta - y, a_n + 2\eta - y))} dp_\infty(y). \end{aligned}$$

Since $\bar{J} \in L^1(\mathbb{R})$, there holds $\sup_{y \in \mathbb{R}} \|\bar{J}\|_{L^1((a_1 - 2\eta - y, a_1 + 2\eta - y) \cup \dots \cup (a_n - 2\eta - y, a_n + 2\eta - y))} \rightarrow 0$ as $n\eta \rightarrow 0$, and since p_∞ is a nonnegative measure with finite mass, one infers that there exists $\delta > 0$ such that, if $n\eta \leq \delta$, then

$$\int_{\mathbb{R}} \int_{\mathbb{R}} J_y(m - y) \phi_{a_1, \dots, a_n, \eta}(m) dm dp_\infty(y) \leq A\varepsilon,$$

hence $p_\infty([a_1 - \eta, a_1 + \eta]) + \cdots + p_\infty([a_n - \eta, a_n + \eta]) \leq \varepsilon$ by (64).

Since the real numbers $a_1 < \cdots < a_n \in (-\infty, -A)$ are arbitrary, it easily follows by a covering argument that the nondecreasing bounded function $m \mapsto p_\infty((-\infty, m])$ is absolutely continuous in $(-\infty, -A)$. Therefore, the restriction of p_∞ on $(-\infty, -A)$ is an $L^1((-\infty, -A))$ function and, as already emphasized, the proof of Proposition 3.6 is thereby complete. \square

Proof of Proposition 3.7. Let us consider the MGF of p_∞ , namely the function defined in \mathbb{R}_+ by

$$M_\infty(z) = e^{C_\infty(z)} = \int_{\mathbb{R}} e^{zm} dp_\infty(m) = \int_{-\infty}^0 e^{zm} dp_\infty(m), \text{ for } z \geq 0.$$

Equations (33) and (63) with $C'_\infty(0) = \bar{m}_\infty$ can be rewritten as

$$M_\infty(z) (\bar{m}_\infty + U) - M'_\infty(z) = U e^{C_\infty(z+\omega(z))} M_\star(z). \quad (65)$$

We then consider separately the cases $s_H^\star = 0$ and $s_H^\star \neq 0$, where s_H^\star is defined in (28).

First case: $s_H^\star = 0$. This case means that

$$\int_0^{+\infty} M_\star(z) dz = +\infty. \quad (66)$$

Meanwhile, due to (8), (9) and (11), the function ω necessarily satisfies some properties, whose proof is postponed in Appendix B below:

$$\omega(0) = 0, \quad \omega(z) \geq -z \text{ and } \omega''(z) \leq 0 \text{ for all } z \geq 0. \quad (67)$$

Thus, it follows the function $z \mapsto \omega(z) + z$ is nonnegative and nondecreasing. It then has a limit $l \in [0, +\infty]$ as $z \rightarrow +\infty$. Assume first here that

$$\lim_{z \rightarrow +\infty} z + \omega(z) = l \in [0, +\infty).$$

Thus, $e^{C_\infty(z+\omega(z))} M_\star(z) \sim e^{C_\infty(l)} M_\star(z)$ as $z \rightarrow +\infty$ and

$$\int_0^{+\infty} e^{C_\infty(z+\omega(z))} M_\star(z) dz = +\infty. \quad (68)$$

Since $\int_0^{+\infty} M'_\infty(z) dz = \rho - 1$, it follows from (65) and (68) that $\bar{m}_\infty + U > 0$ (otherwise, from the inequality $\bar{m}_\infty + U \geq 0$ in Proposition 3.5, $\bar{m}_\infty + U$ would be 0 and then the integral of the left-hand side of (65) over $(0, +\infty)$ would be finite, while the integral of the right-hand side is infinite by (68)). From Proposition 3.6, this means that $\rho = 0$.

Assume now that

$$\lim_{z \rightarrow +\infty} z + \omega(z) = +\infty.$$

Since C_∞ is nonincreasing in $[0, +\infty)$ from its definition (32) and since ω is nonpositive in $[0, +\infty)$ by (12) and (67), we get that $e^{C_\infty(z+\omega(z)) - C_\infty(z)} \geq 1$ for all $z \geq 0$. Thus, using (66), one infers that

$$\int_0^{+\infty} e^{C_\infty(z+\omega(z)) - C_\infty(z)} M_\star(z) dz \geq \int_0^{+\infty} M_\star(z) dz = +\infty. \quad (69)$$

Let us then show that $\rho = 0$. If $\bar{m}_\infty + U > 0$, then Proposition 3.6 yields $\rho = 0$. Assume now that $\bar{m}_\infty + U = 0$, in other words $C'_\infty(0) + U = 0$. By integrating (33) over $(0, A)$ with $A > 0$, we obtain that

$$U \int_0^A e^{C_\infty(z+\omega(z))-C_\infty(z)} M_\star(z) dz = C_\infty(0) - C_\infty(A) = -C_\infty(A),$$

that is,

$$M_\infty(A) = e^{C_\infty(A)} = \exp\left(-U \int_0^A e^{C_\infty(z+\omega(z))-C_\infty(z)} M_\star(z) dz\right).$$

Knowing that $\lim_{A \rightarrow +\infty} M_\infty(A) = \rho$ and using (69), we finally get that

$$\rho = \lim_{A \rightarrow +\infty} \exp\left(-U \int_0^A e^{C_\infty(z+\omega(z))-C_\infty(z)} M_\star(z) dz\right) = 0.$$

Second case: $s_H^\star \neq 0$. This case means that

$$0 < \int_0^{+\infty} M_\star(z) dz = \frac{1}{s_H^\star} < +\infty.$$

Since C_∞ is nonpositive by (32) and $p_\infty((-\infty, 0]) = 1$, we also have that

$$0 < \int_0^{+\infty} M_\star(z) e^{C_\infty(z+\omega(z))} dz \leq \int_0^{+\infty} M_\star(z) dz = \frac{1}{s_H^\star} < +\infty.$$

Using the inequality $\bar{m}_\infty + U \geq 0$ and integrating (65) over $(0, +\infty)$ yields

$$0 \leq (\bar{m}_\infty + U) \int_0^{+\infty} M_\infty(z) dz = \rho - 1 + U \int_0^{+\infty} M_\star(z) e^{C_\infty(z+\omega(z))} dz \leq \rho - 1 + \frac{U}{s_H^\star}. \quad (70)$$

Therefore, if $U < s_H^\star$, then $\rho > 0$, and $\bar{m}_\infty = -U$ by Proposition 3.6.

Let us now consider the set

$$E = \{U \geq s_H^\star : \text{there is } z > 0 \text{ with } 1 + U \omega(z) M_\star(z) = 0\}.$$

Remember that $M_\star(z) > 0$ for all $z \geq 0$. Furthermore, as ω satisfies (12) and (67), there is $z_0 > 0$ such that $\omega(z_0) < 0$. Therefore, for every $U \geq s_H^\star$ such that $U > -1/(\omega(z_0)M_\star(z_0))$ (> 0), there holds $1 + U \omega(z_0) M_\star(z_0) < 0$ and, by continuity of ω and M_\star and since $\omega(0) = 0$, there is $z_1 > 0$ such that $1 + U \omega(z_1) M_\star(z_1) = 0$. As a consequence, the set E is not empty and

$$U_c := \inf E \in [s_H^\star, +\infty) \quad (71)$$

is well defined.

Pick any $U > U_c$. We want to show that $\rho = 0$ and $\bar{m}_\infty > -U$. Assume by contradiction that $\bar{m}_\infty = -U$, that is, $C'_\infty(0) = -U$. Using (33), we obtain that, for all $z \geq 0$,

$$-C'_\infty(z) = U e^{C_\infty(z+\omega(z))-C_\infty(z)} M_\star(z) \geq U (1 + C_\infty(z + \omega(z)) - C_\infty(z)) M_\star(z).$$

Using (67) and the convexity of C_∞ in $[0, +\infty)$, one infers that, for all $z \geq 0$, $C_\infty(z + \omega(z)) - C_\infty(z) \geq C'_\infty(z) \omega(z)$, hence $-C'_\infty(z) \geq U(1 + C'_\infty(z)\omega(z))M_\star(z)$, that is,

$$-C'_\infty(z)(1 + U\omega(z)M_\star(z)) - UM_\star(z) \geq 0. \quad (72)$$

On the other hand, as $U > U_c$, there are $U' \in [s_H^*, U) \subset (0, U)$ and $z' > 0$ such that $1 + U'\omega(z')M_*(z') = 0$, hence $\omega(z')M_*(z') = -1/U' < 0$ and $1 + U\omega(z')M_*(z') < 0$. Again by continuity, one infers the existence of $z_1 > 0$ such that

$$1 + U\omega(z_1)M_*(z_1) = 0.$$

Formula (72) at $z = z_1$ yields $-UM_*(z_1) \geq 0$, which is ruled out since $U > 0$ and $M_*(z_1) > 0$. Thus, $\bar{m}_\infty > -U$, and $\rho = 0$ by Proposition 3.6. The proof of Proposition 3.7 is thereby complete. \square

Proof of Corollary 3.8. Using (31), it is easily seen that $s_H^* = 0$ is equivalent to $n \leq 2$. Furthermore, in the Gaussian Fisher's geometric model, $\omega(z) = -\lambda z^2/(1 + \lambda z)$. Thus,

$$\lim_{z \rightarrow +\infty} z + \omega(z) = \frac{1}{\lambda} < +\infty.$$

Together with Proposition 3.7, we get the conclusion (i) of Corollary 3.8 in case $n \leq 2$.

In case $n > 2$, then $s_H^* = \lambda(n-2)/2 > 0$. Using again Proposition 3.7, we immediately get that $\rho > 0$ and $\bar{m}_\infty = -U$ if $U < \lambda(n-2)/2$.

Let us show that the same result holds good with the large inequality $U \leq \lambda(n-2)/2 = s_H^*$ (still with $n > 2$). First of all, by using Proposition 3.6 and equation (65) multiplied by ρ , one has

$$-\rho M'_\infty(z) = \rho U e^{C_\infty(z+\omega(z))} M_*(z)$$

for all $z \geq 0$. Hence, after integration over $(0, +\infty)$, one infers that

$$\rho(1 - \rho) = \rho U \int_0^{+\infty} e^{C_\infty(z+\omega(z))} M_*(z) dz.$$

Therefore, $\rho < 1$. As a consequence, the function C_∞ defined in (32) (with p_∞ written as in (27)) is (strictly) decreasing in $[0, +\infty)$ and thus negative in $(0, +\infty)$. Notice that these properties hold under the general assumptions of Proposition 3.7. On the other hand, since, here in the Gaussian Fisher's geometric model, $\omega(z) = -\lambda z^2/(1 + \lambda z)$ for all $z \geq 0$, one has $z + \omega(z) > 0$ for all $z > 0$, hence $e^{C_\infty(z+\omega(z))} < 1$ for all $z > 0$. Together with the positivity of $M_*(z)$, it follows that

$$0 < \int_0^{+\infty} M_*(z) e^{C_\infty(z+\omega(z))} dz < \int_0^{+\infty} M_*(z) dz = \frac{1}{s_H^*} < +\infty.$$

As a consequence, if $U \leq \lambda(n-2)/2 = s_H^*$, then, as in (70), one gets that

$$0 \leq (\bar{m}_\infty + U) \int_0^{+\infty} M_\infty(z) dz = \rho - 1 + U \int_0^{+\infty} M_*(z) e^{C_\infty(z+\omega(z))} dz < \rho - 1 + \frac{U}{s_H^*} \leq \rho,$$

hence $\rho > 0$, and $\bar{m}_\infty = -U$ by Proposition 3.6.

Lastly, still in case $n > 2$, a straightforward computation, using (13), implies that the quantity U_c defined in (71) is equal to

$$U_c = \frac{\lambda(n+2)^{n/2+1}}{16(n-2)^{n/2-1}}.$$

Conclusion (ii)-(b) of Corollary 3.8 then follows immediately from Proposition 3.7. \square

7 Proof of technical lemmas

This section is devoted to the proof of the technical lemmas, namely Lemmas 6.3, 6.4 and 6.5, used in the proof of the main theorems in the previous sections.

7.1 Existence for the Cauchy problem

Proof of Lemma 6.3. Let $v \in E$. We know by definition of the set E and Lebesgue's dominated convergence theorem that the function

$$t \mapsto \bar{m}_v(t) = \int_{-\infty}^0 m v(t, m) e^{tm} dm$$

is continuous in $[0, T]$. Problem (42) can then be written as an ordinary differential equation

$$\begin{cases} h'(t) = G(t, h), & t \in [0, T], \\ h(0) = p_0, \end{cases} \quad (73)$$

with

$$\begin{aligned} G : [0, T] \times L_-^\infty(\mathbb{R}) &\rightarrow L_-^\infty(\mathbb{R}) \\ (t, X) &\mapsto U(J_y^t \circledast X - X) - \bar{m}_v(t) X. \end{aligned}$$

The function space $L_-^\infty(\mathbb{R}_-)$ is a Banach space for the uniform norm $\|\cdot\|_\infty$ and as in the proof of Lemma 6.4 above, the function G is continuous in $[0, T] \times L_-^\infty(\mathbb{R})$ and Lipschitz continuous with respect to X uniformly in $t \in [0, \tau]$. Therefore, the Cauchy-Lipschitz theorem yields the existence and uniqueness of a solution $h \in \mathcal{C}^1([0, T], L_-^\infty(\mathbb{R}))$ of problem (73). \square

7.2 Comparison principle

Proof of Lemma 6.4. Let τ, ϖ, h_1 and h_2 satisfy the assumptions of the lemma. With a slight abuse of notations, we write $h_1(t) = h_1(t, \cdot) \in L_-^\infty(\mathbb{R})$ and $h_2(t) = h_2(t, \cdot) \in L_-^\infty(\mathbb{R})$ for $t \in [0, \tau]$. Set

$$\mathcal{L}_t(h) := U(J_y^t \circledast h - h) - \varpi(t) h$$

for $t \in [0, \tau]$ and $h \in L_-^\infty(\mathbb{R})$. For any such $h \in L_-^\infty(\mathbb{R})$, one has $\text{supp } \mathcal{L}_t(h) \subset \mathbb{R}_-$ and, from (8), (10), (40) and similar calculations as in (44), there holds

$$\|J_y^t \circledast h\|_{L_-^\infty(\mathbb{R})} \leq \|h\|_{L_-^\infty(\mathbb{R})} \left(\int_{-\infty}^0 \bar{J}(y) e^{t|y|} dy + \|\bar{J}\|_{L^1(\mathbb{R})} \right), \quad (74)$$

hence, $\mathcal{L}_t(h) \in L_-^\infty(\mathbb{R})$. Then let us denote

$$a(t) = (h_2'(t) - \mathcal{L}_t(h_2(t))) - (h_1'(t) - \mathcal{L}_t(h_1(t)))$$

for $t \in [0, \tau]$. Notice that $\text{supp } a(t) \subset \mathbb{R}_-$ for every $t \in [0, \tau]$. Furthermore, for any $i \in \{1, 2\}$, any $t \in [0, \tau]$ any sequence $(t_n)_{n \in \mathbb{N}}$ in $[0, \tau]$ converging to t , any $m \in \mathbb{R}_-$ and any $n \in \mathbb{N}$, one

has

$$\begin{aligned}
|(J_y^{t_n} \otimes h_i)(t_n, m) - (J_y^t \otimes h_i)(t, m)| &\leq \int_{\mathbb{R}} J_y(m-y) e^{-t_n(m-y)} |h_i(t_n, y) - h_i(t, y)| dy \\
&\quad + \int_{\mathbb{R}} J_y(m-y) |e^{-t_n(m-y)} - e^{-t(m-y)}| |h_i(t, y)| dy \\
&\leq \|h_i(t_n, \cdot) - h_i(t, \cdot)\|_{L^\infty(\mathbb{R})} \left(\int_{-\infty}^0 \bar{J}(y) e^{\tau|y|} dy + \|\bar{J}\|_{L^1(\mathbb{R})} \right) \\
&\quad + \|h_i(t, \cdot)\|_{L^\infty(\mathbb{R})} \int_{\mathbb{R}} \bar{J}(y) |e^{-t_n y} - e^{-t y}| dy.
\end{aligned}$$

Therefore, $\|J_y^{t_n} \otimes h_i(t_n) - J_y^t \otimes h_i(t)\|_{L^\infty(\mathbb{R})} \rightarrow 0$ as $n \rightarrow +\infty$ from the assumptions on h_i and \bar{J} and from Lebesgue's dominated convergence theorem. Finally, one infers that the maps $t \mapsto \mathcal{L}_t(h_i(t))$ belong to $\mathcal{C}([0, \tau], L_-^\infty(\mathbb{R}))$, and that $a \in \mathcal{C}([0, \tau], L_-^\infty(\mathbb{R}))$.

Now define, for $t \in [0, \tau]$,

$$w(t) = (h_2(t) - h_1(t)) e^{Kt} \in L_-^\infty(\mathbb{R}),$$

with

$$K = U + \max_{[0, \tau]} |\varpi|.$$

It is straightforward to check that w is a solution of the ordinary differential equation

$$w'(t) = F(t, w), \quad t \in [0, \tau], \quad (75)$$

in $L_-^\infty(\mathbb{R})$, for some function $F : [0, \tau] \times L_-^\infty(\mathbb{R}) \rightarrow L_-^\infty(\mathbb{R})$ defined by

$$F(t, w) = U J_y^t \otimes w + w(K - U - \varpi(t)) + a(t) e^{Kt}.$$

As above, the function F is continuous in $[0, \tau] \times L_-^\infty(\mathbb{R})$. Furthermore, for any $t \in [0, \tau]$ and $w, w' \in L_-^\infty(\mathbb{R})$, one has, as in (74),

$$\begin{aligned}
\|J_y^t \otimes w - J_y^t \otimes w'\|_{L^\infty(\mathbb{R})} &\leq \|w - w'\|_{L^\infty(\mathbb{R})} \left(\int_{-\infty}^0 \bar{J}(y) e^{t|y|} dy + \|\bar{J}\|_{L^1(\mathbb{R})} \right) \\
&\leq \|w - w'\|_{L^\infty(\mathbb{R})} \left(\int_{-\infty}^0 \bar{J}(y) e^{\tau|y|} dy + \|\bar{J}\|_{L^1(\mathbb{R})} \right).
\end{aligned}$$

As a consequence, the function F is Lipschitz-continuous with respect to w uniformly in $t \in [0, \tau]$. We can then define $\tilde{w} \in \mathcal{C}^1([0, \tau], L^\infty(\mathbb{R}))$ as the unique solution of $\tilde{w}'(t) = \max\{F(t, \tilde{w}(t)), 0\}$ in $[0, \tau]$ with $\tilde{w}(0) = w(0)$, that is,

$$\tilde{w}(t) = w(0) + \int_0^t \max\{F(s, \tilde{w}(s)), 0\} ds.$$

We have $\tilde{w}(t) \geq w(0)$ and $w(0) \geq 0$ a.e. in \mathbb{R} by assumption. Additionally, from (46), there holds $a(t) \geq 0$ a.e. in \mathbb{R}_- , for all $t \in [0, \tau]$. As a consequence, and since $K - U - \varpi(t) \geq 0$ for all $[0, \tau]$, one infers that, for all $t \in [0, \tau]$, $F(t, \tilde{w}(t)) \geq 0$ a.e. in \mathbb{R}_- . We deduce that \tilde{w} is also a solution of the equation (75) satisfied by w . From the Cauchy-Lipschitz theorem, we deduce that, for all $t \in [0, \tau]$, $w(t) = \tilde{w}(t) \geq 0$ and therefore $h_1(t, \cdot) \leq h_2(t, \cdot)$ a.e. in \mathbb{R} . The proof of Lemma 6.4 is thereby complete. \square

7.3 Mass preservation and estimates on mean fitness

Proof of Lemma 6.5. Let us first show (51). We consider

$$\phi(t) = \int_{\mathbb{R}} p(t, m) dm = \int_{-\infty}^0 p(t, m) dm$$

for $t \in [0, T_{max})$. This quantity is a well defined nonnegative real number due to (50) and the definition of T_{max} . By using (50) for every $T \in [0, T_{max})$, integrating (3) against m over \mathbb{R}_- , we obtain that ϕ is of class $\mathcal{C}^1([0, T_{max}))$ and, for every $t \in [0, T_{max})$,

$$\phi'(t) = \int_{-\infty}^0 \partial_t p(t, m) dm = U \int_{-\infty}^0 (J_y \circledast p)(t, m) dm - U\phi(t) + \bar{m}(t) - \bar{m}(t)\phi(t).$$

From assumption (8), we have

$$\int_{-\infty}^0 (J_y \circledast p)(t, m) dm = \int_{-\infty}^0 \left(\int_{-\infty}^0 J_y(m-y) dm \right) p(t, y) dy = \int_{-\infty}^0 p(t, y) dy = \phi(t).$$

Finally, $\phi'(t) = \bar{m}(t)(1 - \phi(t))$ for all $t \in [0, T_{max})$. From assumption (5), there holds $\phi(0) = 1$, and since $\bar{m} \in \mathcal{C}([0, T_{max}))$, it follows immediately that $\phi(t) = 1$ for all $t \in [0, T_{max})$.

Let us now turn to the proof of (52). By integrating (3) between 0 and $t \in [0, T_{max})$, multiplying by m , integrating over \mathbb{R}_- and using (50) and Fubini's theorem, we get that, for every $t \in [0, T_{max})$,

$$\begin{aligned} \bar{m}(t) - \bar{m}(0) &= \int_{-\infty}^0 \int_0^t m [U((J_y \circledast p)(s, m) - p(s, m)) + (m - \bar{m}(s))p(s, m)] ds dm \\ &= \int_0^t \int_{-\infty}^0 m [U((J_y \circledast p)(s, m) - p(s, m)) + (m - \bar{m}(s))p(s, m)] dm ds. \end{aligned}$$

From (8), (10), (50), (51) and Fubini's theorem, one infers that, for every $s \in [0, t] (\subset [0, T_{max}))$,

$$\begin{aligned} \int_{-\infty}^0 m (J_y \circledast p)(s, m) dm &= \int_{-\infty}^0 \left(\int_{-\infty}^0 (m-y+y) J_y(m-y) p(s, y) dy \right) dm \\ &= \int_{-\infty}^0 \left(\int_{-\infty}^{-y} m J_y(m) dm \right) p(s, y) dy \\ &\quad + \int_{-\infty}^0 y p(s, y) \left(\int_{-\infty}^0 J_y(m-y) dm \right) dy \\ &= \int_{-\infty}^0 \mu_{J_y} p(s, y) dy + \bar{m}(s), \end{aligned}$$

with

$$\mu_{J_y} = \int_{-\infty}^{-y} m J_y(m) dm.$$

Then, using the fact that the functions $\bar{m} : t \mapsto \int_{-\infty}^0 mp(t, m) dm$ and $t \mapsto \int_{-\infty}^0 m^2 p(t, m) dm$ are continuous in $[0, T_{max})$, we deduce that, for every $t \in [0, T_{max})$,

$$\bar{m}(t) - \bar{m}(0) = U \int_0^t \int_{-\infty}^0 \mu_{J_y} p(s, y) dy ds + \int_0^t \int_{-\infty}^0 m^2 p(s, m) dm ds - \int_0^t (\bar{m}(s))^2 ds.$$

Then, by the Cauchy-Schwarz inequality and (51), we have

$$\begin{aligned} (\bar{m}(s))^2 &= \left(\int_{-\infty}^0 m p(s, m) dm \right)^2 \\ &\leq \left(\int_{-\infty}^0 p(s, m) dm \right) \left(\int_{-\infty}^0 m^2 p(s, m) dm \right) = \int_{-\infty}^0 m^2 p(s, m) dm \end{aligned} \quad (76)$$

for all $s \in [0, t] (\subset [0, T_{max}])$. Therefore,

$$\bar{m}(t) \geq \bar{m}(0) + U \int_0^t \int_{-\infty}^0 \mu_{J_y} p(s, y) dy ds \text{ for all } t \in [0, T_{max}].$$

Finally, using assumptions (8) and (10), we have, for all $y \leq 0$,

$$\mu_{J_y} = \int_{-\infty}^{-y} m J_y(m) dm \geq \int_{-\infty}^0 m J_y(m) dm \geq \int_{-\infty}^0 m \bar{J}(m) dm = \mu.$$

Thus, since p is nonnegative and $\int_{-\infty}^0 p(t, m) dm = 1$ for all $t \in [0, T_{max})$, we get that $\bar{m}(t) \geq \bar{m}(0) + tU\mu$ for all $t \in [0, T_{max})$. The proof of Lemma 6.5 is thereby complete. \square

Appendix A: Interpreting condition (29) on $\lim_{z \rightarrow +\infty} z + \omega(z)$

We here show that the assumption (29) of Proposition 3.7, namely $\lim_{z \rightarrow +\infty} (z + \omega(z)) \in [0, +\infty)$, means that any parent can give mutant offspring with the optimal fitness 0, that is, $\sup\{\text{supp } J_y\} = -y$ for every $y \leq 0$. To do so, differentiating equation (15) with respect to z , we have (as in (17)):

$$\mathcal{C}'_y(z) = \mathcal{C}'_\star(z) + \omega'(z)y \text{ for all } y \leq 0 \text{ and } z \geq 0, \quad (77)$$

where the $\mathcal{C}^\infty(\mathbb{R}_+)$ functions \mathcal{C}_y and \mathcal{C}_\star are defined by (16). Now, [17, Lemma 4.5] yields $\lim_{z \rightarrow +\infty} \mathcal{C}'_y(z) = \sup\{\text{supp } J_y\}$ and $\lim_{z \rightarrow +\infty} \mathcal{C}'_\star(z) = \sup\{\text{supp } J_0\}$. Passing to the limit $z \rightarrow +\infty$ in (77), it follows that $\lim_{z \rightarrow +\infty} \omega'(z)$ exists and

$$\lim_{z \rightarrow +\infty} \omega'(z)y = \sup\{\text{supp } J_y\} - \sup\{\text{supp } J_0\}$$

for all $y \leq 0$. Assumption (29) then implies that $\omega'(z) \rightarrow -1$ as $z \rightarrow +\infty$, hence

$$-y = \sup\{\text{supp } J_y\} - \sup\{\text{supp } J_0\}$$

for all $y \leq 0$. On the other hand, assumption (9) yields in particular $\sup\{\text{supp } J_0\} \leq 0$. If $\sup\{\text{supp } J_0\} = -\alpha < 0$, then $\sup\{\text{supp } J_y\} = -y - \alpha$ for all $y \leq 0$, contradicting assumption (18) for $y > 0$ small. Therefore, $\sup\{\text{supp } J_0\} = 0$, and

$$\sup\{\text{supp } J_y\} = -y$$

for all $y \leq 0$. In other words, any parent can give mutant offspring with the optimal fitness 0.

Appendix B: Proof of property (67) on ω

First of all, by taking $z = 0$ in (11), we immediately get that

$$\omega(0) = 0.$$

Second, since

$$\int_{-\infty}^{-y} J_y(m) e^{zm} dm \leq e^{-zy} \int_{-\infty}^{-y} J_y(m) dm$$

for all $y \leq 0$ and $z \geq 0$, it follows from (8) and (9) that

$$\int_{-\infty}^{-y} J_y(m) e^{zm} dm \leq e^{-zy}$$

for all $y \leq 0$ and $z \geq 0$. Then, using (11), we get that $M_\star(z) e^{\omega(z)y} \leq e^{-zy}$ and, for every $y < 0$, we obtain that $(\ln M_\star(z))/y + \omega(z) \geq -z$ for all $z \geq 0$. The limit as $y \rightarrow -\infty$ then yields $\omega(z) \geq -z$ for all $z \geq 0$.

Third, observe that assumption (11) yields

$$\omega(z) = \frac{\mathcal{C}_y(z) - \mathcal{C}_\star(z)}{y},$$

for all $y < 0$ and $z \geq 0$. Thus, as \mathcal{C}_y and \mathcal{C}_\star belong to $\mathcal{C}^\infty(\mathbb{R}_+)$, the function ω belongs to $\mathcal{C}^\infty(\mathbb{R}_+)$ too. In order to show the concavity of ω , it is then sufficient to prove that $\omega'' \leq 0$ in \mathbb{R}_+ . But since \mathcal{C}_y is convex in \mathbb{R}_+ for every $y \leq 0$, the previous displayed formula implies that

$$\omega''(z) = \frac{\mathcal{C}_y''(z) - \mathcal{C}_\star''(z)}{y} \leq -\frac{\mathcal{C}_\star''(z)}{y}$$

for all $y < 0$ and $z \geq 0$. The limit as $y \rightarrow -\infty$ yields $\omega''(z) \leq 0$ for all $z \geq 0$, and the proof of (67) is thereby complete.

References

- [1] M Alfaro and R Carles. Explicit solutions for replicator-mutator equations: Extinction versus acceleration. *SIAM J. Appl. Math.*, 74(6):1919–1934, 2014.
- [2] M Alfaro and R Carles. Replicator-mutator equations with quadratic fitness. *Proc. Amer. Math. Soc.*, 145:5315–5327, 2017.
- [3] M Alfaro and J Coville. Propagation phenomena in monostable integro-differential equations: Acceleration or not? *J. Diff. Equations*, 263(9):5727–5758, 2017.
- [4] M Alfaro, J Coville, and G Raoul. Bistable travelling waves for nonlocal reaction diffusion equations. *Discrete Contin. Dyn. Syst.*, 34:1775–1791, 2014.
- [5] M Alfaro and M Veruete. Evolutionary branching via replicator-mutator equations. *arXiv preprint arXiv:1802.00501*, 2018.

- [6] H Berestycki, G Nadin, B Perthame, and L Ryzhik. The non-local Fisher-KPP equation: travelling waves and steady states. *Nonlinearity*, 22(12):2813–2844, 2009.
- [7] A Carr and J Chmaj. Uniqueness of travelling waves for nonlocal monostable equations. *Proc. Amer. Math. Soc.*, 132(8):2433–2439, 2004.
- [8] C Cortázar, J Coville, M Elgueta, and S Martínez. A nonlocal inhomogeneous dispersal process. *J. Diff. Equations*, 241(2):332–358, 2007.
- [9] A Couce and O A Tenaillon. The rule of declining adaptability in microbial evolution experiments. *Frontiers in Genetics*, 6:99, 2015.
- [10] J Coville. Singular measure as principal eigenfunction of some nonlocal operators. *Appl. Math. Lett.*, 26(8):831–835, 2013.
- [11] J Coville and L Dupaigne. On a nonlocal equation arising in population dynamics. *Proc. Roy. Soc. Edinburgh Sect. A*, 137:1–29, 2007.
- [12] J Fang and X-Q Zhao. Monotone wavefronts of the nonlocal Fisher-KPP equation. *Nonlinearity*, 24:3043–3054, 2011.
- [13] G Faye and M Holzer. Modulated traveling fronts for a nonlocal Fisher-KPP equation: a dynamical systems approach. *J. Diff. Equations*, 258(7):2257–2289, 2015.
- [14] J Garnier. Accelerating solutions in integro-differential equations. *SIAM J. Math. Anal.*, 43:1955–1974, 2011.
- [15] J Garnier, F Hamel, and L Roques. Transition fronts and stretching phenomena for a general class of reaction-dispersion equations. *Discrete Contin. Dyn. Syst.*, 37:743–756, 2017.
- [16] S Genieys, V Volpert, and V Auger. Pattern and waves for a model in population dynamics with nonlocal consumption of resources. *Math. Model. Nat. Phenom.*, 1:63–80, 2006.
- [17] M-E Gil, F Hamel, G Martin, and L Roques. Mathematical properties of a class of integro-differential models from population genetics. *SIAM J. Appl. Math.*, 77:1536–1561, 2017.
- [18] B H Good and M M Desai. The impact of macroscopic epistasis on long-term evolutionary dynamics. *Genetics*, 199:177–190, 2015.
- [19] S A Gourley. Travelling front solutions of a nonlocal fisher equation. *J. Math. Biol.*, 41:272–284, 2000.
- [20] Q Griette. Singular measure traveling waves in an epidemiological model with continuous phenotypes. *arXiv preprint arXiv:1710.02240*, 2017.
- [21] F Hamel and L Ryzhik. On the nonlocal Fisher-KPP equation: steady states, spreading speed and global bounds. *Nonlinearity*, 27(11):2735–2753, 2014.
- [22] M Kimura. A stochastic model concerning the maintenance of genetic variability in quantitative characters. *Proc. Natl. Acad. Sci. USA*, 54(3):731–736, 1965.

- [23] M Kirkpatrick and N H Barton. Evolution of a species' range. *Am. Nat.*, 150:1–23, 1997.
- [24] S Kryazhimskiy, D P Rice, E R Jerison, and M M Desai. Global epistasis makes adaptation predictable despite sequence-level stochasticity. *Science*, 344(6191):1519–1522, 2014.
- [25] A Lambert. Population dynamics and random genealogies. *Stoch. Models*, 24(S1):45–163, 2008.
- [26] R Lande. The genetic covariance between characters maintained by pleiotropic mutations. *Genetics*, 94(1):203–215, 1980.
- [27] M Lässig, V Mustonen, and A M Walczak. Predicting evolution. *Nat. Ecol. Evol.*, 1(3):77, 2017.
- [28] G Martin, S F Elena, and T Lenormand. Distributions of epistasis in microbes fit predictions from a fitness landscape model. *Nature Genetics*, 39(4):555–560, 2007.
- [29] G Martin and L Roques. The non-stationary dynamics of fitness distributions: Asexual model with epistasis and standing variation. *Genetics*, 204:1541–1558, 2016.
- [30] M H Protter and H F Weinberger. *Maximum Principles in Differential Equations*. Prentice-Hall, Inc., Englewood Cliffs, N.J., 1967.
- [31] L Roques, J Garnier, and G Martin. Beneficial mutation-selection dynamics in finite asexual populations: a free boundary approach. *Sci. Rep.*, 7(1):17838, 2017.
- [32] K Schumacher. Travelling-front solutions for integro-differential equations. I. *J. Reine Angew. Math.*, 316:54–70, 1980.
- [33] P D Sniegowski and P J Gerrish. Beneficial mutations and the dynamics of adaptation in asexual populations. *Philos. Trans. Royal Soc. B*, 365(1544):1255–1263, 2010.
- [34] O A Tenaillon. The utility of Fisher's geometric model in evolutionary genetics. *Annual Review of Ecology, Evolution, and Systematics*, 45(1):179–201, 2014.
- [35] L S Tsimring, H Levine, and D A Kessler. RNA virus evolution via a fitness-space model. *Phys. Rev. Lett.*, 76(23):4440, 1996.
- [36] J Y Wakano and Y Iwasa. Evolutionary branching in a finite population: deterministic branching vs. stochastic branching. *Genetics*, 193(1):229–241, 2013.
- [37] D Waxman and J R Peck. Pleiotropy and the preservation of perfection. *Science*, 279(5354):1210–1213, 1998.
- [38] D Waxman and J R Peck. The frequency of the perfect genotype in a population subject to pleiotropic mutation. *Theoretical Population Biology*, 69(4):409–418, 2006.
- [39] H F Weinberger. Long-time behavior of a class of biological models. *SIAM J. Math. Anal.*, 13(3):353–396, 1982.
- [40] H F Weinberger. On spreading speeds and traveling waves for growth and migration in periodic habitat. *J. Math. Biol.*, 45:511–548, 2002.

- [41] H Yagisita. Existence and nonexistence of travelling waves for a nonlocal monostable equation. *Publ. RIMS*, 45:925–953, 2009.