

Density behavior of spatial birth-and-death stochastic evolution of mutating genotypes under selection rates ^{*}

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1 Description of model

We start with a heuristic discussion of a model, describing spatial evolution of mutating genotypes under selection rates. Each genotype might be characterized by a pair $\hat{x} := (x, s_x)$. Here $x \in \mathbb{R}^d$ is a location in the Euclidian space occupied by this genotype, and a mark s_x is its quantitative characteristic. We will consider, cf. [4, 7], a continuous-gene space model. Namely, $s_x \in \mathbb{R}_+ := [0, +\infty)$ will be understood as a length of a genotype located at x .

We describe an infinite collection of genotypes as a configuration $\hat{\gamma} := \{\hat{x}\}$. Having in mind that in the reality any individual with a given genotype has not only position in space but also non-zero size, we assume that $\gamma := \{x\}$ is a locally finite subset in \mathbb{R}^d . Namely, $\gamma \cap \Lambda$ is a finite set for any compact $\Lambda \subset \mathbb{R}^d$. Let Γ and $\hat{\Gamma}$ be the spaces of such γ 's and $\hat{\gamma}$'s, accordingly.

In the present paper, we deal with mutating genotypes. Omitting the nature of these mutations, we suppose that they lead to a stochastic evolution of marks s_x , given by Brownian motion on \mathbb{R}_+ with absorption at 0. We consider a birth-and-death stochastic dynamics of mutating genotypes. It means that at any random moment of time the existing genotype may disappear (die) from the configuration or may produce a new one. This new genotype will be placed at other location in the space. It has the parent's genotype at the moment of birth, but then it immediately involves in a mutation process. This may be understood as an expansion of genotypes along the space. The probabilistic rates of birth and death of a genotype are independent of the rest of configuration, however, we suppose that they depend on sizes of genotypes. In fact, it means that we have selection in rates of birth and death. It is natural for biological systems that genotypes with very short as well as very long length have less possibilities for surviving and reproduction, see e.g. [3, 1].

The heuristic Markov generator of the dynamics described above may given by

$$\begin{aligned} (LF)(\hat{\gamma}) &= \sum_{x \in \gamma} \int_{\mathbb{R}^d} a(x-y)b(s_x)(F(\hat{\gamma} \cup \{y, s_x\}) - F(\hat{\gamma})) dy \\ &\quad + \sum_{x \in \gamma} d(s_x)(F(\hat{\gamma} \setminus \{x, s_x\}) - F(\hat{\gamma})) + \sum_{x \in \gamma} \frac{\partial^2}{\partial s_x^2} F(\hat{\gamma}). \end{aligned} \quad (1.1)$$

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The first term in (1.1) describes the birth part of the dynamics. This reproduction step involves selection as well as expansion of genotypes along the space. The function a describes an expansion (migration) rate, it is independent on marks s_x, s_y . Function b is associated with stabilizing selection. It prescribes that some lengths may be ranked against the other lengths. Genotypes with optimal (or at least more optimal) length are assumed to breed and to spread more intensively. We assume that $0 \leq a \in L^1(\mathbb{R}^d)$, a is an even function, $b : \mathbb{R}_+ \rightarrow \mathbb{R}_+$ with $b(0) = 0$. Without loss of generality we suppose that $\int_{\mathbb{R}^d} a(x)dx = 1$.

The second term is the death part of the dynamics. We assume here that the death rate $d : \mathbb{R}_+ \rightarrow \mathbb{R}_+$ depends only on a length of a genotype, and does not depend on a location of genotype in the space. The shape of d will be discussed below.

The third term describes mainly mutations of genotypes, but also can include all random changes within the genotype, such as: duplication, genetic drift, etc. This differential operator is a modification of the generator for a random jump mutation model on the continuous space. Let us note that the third term is the direct sum of operators. That means that we assume that each offspring develops independently on others and we do not consider any interaction between existing genotypes.

Note that models of this type (without expansion), so-called mutation-selection models, play an important role in analysis of many problems of population genetics, see e.g. [3, 1].

To give a rigorous meaning to the expression (1.1) we consider the following classes of functions. Let \mathcal{D} consist of all functions $\varphi : \mathbb{R}^d \times \mathbb{R}_+ \rightarrow \mathbb{R}$ which have bounded support in $\mathbb{R}^d \times (0, \infty)$, and φ is a continuous functions in the first variable and twice continuously differentiable in the second variable. For any $\varphi \in \mathcal{D}$ the following expression is well-defined:

$$\langle \varphi, \hat{\gamma} \rangle := \sum_{x \in \gamma} \varphi(x, s_x),$$

since the summation will be over finite set $\gamma \cap \Lambda$ only for some compact $\Lambda \subset \mathbb{R}^d$. Let $\varphi_1, \dots, \varphi_N \in \mathcal{D}$ and $f : \mathbb{R}^N \rightarrow \mathbb{R}$ be twice continuously differentiable function on \mathbb{R}^N bounded together with all its partial derivatives. We consider a function $F(\hat{\gamma}) = f(\langle \varphi_1, \hat{\gamma} \rangle, \dots, \langle \varphi_N, \hat{\gamma} \rangle)$. A class of all such functions F we denote by \mathcal{F} . Then for any $\hat{x} \in \hat{\gamma}$ such that x is outside of the union of supports of $\varphi_1, \dots, \varphi_N$, we have that the value of $F(\hat{\gamma})$ for $F \in \mathcal{F}$ does not depend on \hat{x} . In particular, the summation in the second term in (1.1) will be taken over a finite over subset of each γ only, hence this term is well-defined. Analogously, for each x which is outside of the union of supports above, $\frac{\partial^2}{\partial s_x^2} F(\hat{\gamma}) = 0$. Similarly, the integral in the first term in (1.1) will be taken over a compact set, moreover, if, additionally, a has compact support in \mathbb{R}^d the sum before integral will be also finite. For a general integrable function a , this sum is a series which may converges only a.s. in the following sense.

Let μ by a probability measure (state) on the space $\hat{\Gamma}$ with σ -algebra described e.g. in [6]. A function $k_\mu : \mathbb{R}^d \times \mathbb{R}_+ \rightarrow \mathbb{R}$ is called a density (or a first correlation function) of the measure μ if for any $\varphi : \mathbb{R}^d \times \mathbb{R}_+ \rightarrow \mathbb{R}$ such that $k_\mu \varphi \in L^1(\mathbb{R}^d \times \mathbb{R}_+)$ we have that $\langle \varphi, \cdot \rangle$ defined before belongs to $L^1(\hat{\Gamma}, \mu)$ and

$$\int_{\hat{\Gamma}} \langle \varphi, \hat{\gamma} \rangle d\mu(\hat{\gamma}) = \int_{\mathbb{R}^d} \int_{\mathbb{R}_+} \varphi(x, s) k_\mu(x, s) dx ds.$$

In this case, $\langle \varphi, \hat{\gamma} \rangle$ is well-defined for μ -a.a. $\hat{\gamma} \in \hat{\Gamma}$. It is evident now, that, for $a \in L^1(\mathbb{R}^d)$, the first term in (1.1) with $F \in \mathcal{F}$ is well-defined for μ -a.a. $\hat{\gamma} \in \hat{\Gamma}$ for any probability measure μ such that its density k_μ is bounded.

The problem of construction of evolutions of states with generator (1.1) is usually related with construction and properties of evolution of densities and higher-order correlation functions

(see e.g. [8] for the case without marks). The aim of the present paper is to study the evolution of the density only. Therefore, we suppose that there is an evolution of measures given by

$$\frac{d}{dt} \int_{\hat{\Gamma}} F d\mu_t = \int_{\hat{\Gamma}} LF d\mu_t, \quad F \in \mathcal{F} \quad (1.2)$$

with initial condition μ_0 at $t = 0$. We assume also that k_t be a density of μ_t . Then, choosing $F_\varphi(\hat{\gamma}) := \langle \varphi, \hat{\gamma} \rangle$ for $\varphi \in \mathcal{D}$ we obtain

$$(LF_\varphi)(\hat{\gamma}) = \sum_{x \in \gamma} \int_{\mathbb{R}^d} a(x-y)b(s_x)\varphi(y, s_x)dy - \sum_{x \in \gamma} d(s_x)\varphi(x, s_x) + \sum_{x \in \gamma} \frac{\partial^2}{\partial s_x^2} \varphi(x, s_x).$$

Therefore,

$$\begin{aligned} \int_{\hat{\Gamma}} (LF_\varphi)(\hat{\gamma}) d\mu_t(\hat{\gamma}) &= \int_{\mathbb{R}^d} \int_{\mathbb{R}_+} k_t(x, s) \int_{\mathbb{R}^d} a(x-y)b(s)\varphi(y, s)dy ds dx \\ &\quad - \int_{\mathbb{R}^d} \int_{\mathbb{R}_+} k_t(x, s) d(s)\varphi(x, s) ds dx + \int_{\mathbb{R}^d} \int_{\mathbb{R}_+} k_t(x, s) \frac{\partial^2}{\partial s^2} \varphi(x, s) ds dx. \end{aligned} \quad (1.3)$$

On the other hand,

$$\frac{d}{dt} \int_{\hat{\Gamma}} F_\varphi(\hat{\gamma}) d\mu_t(\hat{\gamma}) = \frac{d}{dt} \int_{\mathbb{R}^d} \int_{\mathbb{R}_+} k_t(x, s) \varphi(x, s) ds dx. \quad (1.4)$$

Since $\varphi \in \mathcal{D}$ is arbitrary, we derive by the changing of variables and by the integration by parts in (1.3), that, by (1.2), (1.3), (1.4), the densities k_t should satisfy (in a weak sense) the following differential equation

$$\frac{\partial}{\partial t} k_t(x, s) = b(s) \int_{\mathbb{R}^d} a(x-y)k_t(y, s)dy - d(s)k_t(x, s) + \frac{\partial^2}{\partial s^2} k_t(x, s). \quad (1.5)$$

Using the assumption $\int_{\mathbb{R}^d} a(x)dx = 1$ we may rewrite (1.5) as follows

$$\frac{\partial}{\partial t} k_t(x, s) = (\mathbf{A}k_t)(x, s) - (\mathbf{H}k_t)(x, s), \quad (1.6)$$

$$(\mathbf{A}k_t)(x, s) := b(s) \int_{\mathbb{R}^d} a(x-y)(k_t(y, s) - k_t(x, s))dy, \quad (1.7)$$

$$(\mathbf{H}k_t)(x, s) := -\frac{\partial^2}{\partial s^2} k_t(x, s) + (d(s) - b(s))k_t(x, s). \quad (1.8)$$

It is worth noting that appearance of effective potential $v(s) = d(s) - b(s)$ is inspired by the evolution mechanism of the spatial microscopic model. The function $v(s)$ has meaning of a fitness function, see e.g. [3].

In the next section we will study the classical solution of (1.6)–(1.8) with an initial condition k_0 in a proper Banach space.

2 Properties of a density

Let $\mathcal{H} = L^2(\mathbb{R}_+)$ be real Hilbert space, and consider the following Banach space \mathcal{X} : a measurable function $k : \mathbb{R}^d \times \mathbb{R}_+ \rightarrow \mathbb{R}$ belongs to \mathcal{X} if, for a.a. $x \in \mathbb{R}^d$, $k(x, \cdot) \in \mathcal{H}$ and $\|k\|_{\mathcal{X}} := \text{ess sup}_{x \in \mathbb{R}^d} \|k(x, \cdot)\|_{\mathcal{H}} < \infty$. Hence one can naturally embed \mathcal{H} into \mathcal{X} as set of functions which are constant in x . We will use the same notations for function $f \in \mathcal{H}$ as an element of \mathcal{X} .

Suppose that there exists $\omega \geq 0$ such that

$$v(s) := d(s) - b(s) \geq -\omega, \quad s \in \mathbb{R}_+. \quad (2.1)$$

Let $C_0^\infty(\mathbb{R}_+)$ consist of all smooth functions f on \mathbb{R}_+ with bounded support such that $f(0) = 0$. Then the operator $(Hf)(s) := -f''(s) + v(s)f(s)$ with a domain $C_0^\infty(\mathbb{R}_+)$ is essentially self-adjoint in \mathcal{H} (see e.g. [2]). Let $(\bar{H}, \text{Dom}(\bar{H}))$ be its self-adjoint closure in \mathcal{H} . Let $\mathbf{D} \subset \mathcal{X}$ consist of all functions $k \in \mathcal{X}$ such that, for a.a. $x \in \mathbb{R}^d$, $k(x, \cdot) \in \text{Dom}(\bar{H})$.

Lemma 1. *Let (2.1) hold and $b \in L^\infty(\mathbb{R}_+)$. Then $(\mathbf{A} - \mathbf{H}, \mathbf{D})$ is a generator of a C_0 -semigroup $S(t)$ in \mathcal{X} .*

Proof. Since v is bounded from below, we have, for any $f \in \text{Dom}(\bar{H})$, $(-\bar{H}f, f)_{\mathcal{H}} \leq \omega \|f\|_{\mathcal{H}}^2$. Therefore, by e.g. [5, Example II.3.27], $(-\bar{H}, \text{Dom}(\bar{H}))$ is a generator of a C_0 -semigroup $T_{\bar{H}}(t)$ in \mathcal{H} , and moreover, $\|T_{\bar{H}}(t)\| \leq e^{t\omega}$, $t \geq 0$. Then, by a version of Hille–Yosida theorem (see e.g. [5, Corollary II.3.6]), for each $\lambda > \omega$, $\lambda \in \rho(-\bar{H})$ and $\|R(\lambda, -\bar{H})\| \leq (\lambda - \omega)^{-1}$. Here and below $\rho(B)$ and $R(\lambda, B)$ denotes a resolvent set and a resolvent of a closed operator B , correspondingly. By (1.8) and the properties of \bar{H} , it is evident that $(-\mathbf{H}, \mathbf{D})$ is a closed densely defined operator in \mathcal{X} , moreover, $\rho(-\mathbf{H}) = \rho(-\bar{H})$, and, for each $\lambda \in \rho(-\mathbf{H})$,

$$(R(\lambda, -\bar{H})k(x, \cdot))(s) = (R(\lambda, -\mathbf{H})k)(x, s), \quad k \in \mathcal{X}, x \in \mathbb{R}^d, s \in \mathbb{R}_+.$$

As a result,

$$\begin{aligned} \|R(\lambda, \mathbf{H})k\|_{\mathcal{X}} &= \text{ess sup}_{x \in \mathbb{R}^d} \|(R(\lambda, -\mathbf{H})k)(x, \cdot)\|_{\mathcal{H}} = \text{ess sup}_{x \in \mathbb{R}^d} \|R(\lambda, -\bar{H})k(x, \cdot)\|_{\mathcal{H}} \\ &\leq (\lambda - \omega)^{-1} \text{ess sup}_{x \in \mathbb{R}^d} \|k(x, \cdot)\|_{\mathcal{H}} = (\lambda - \omega)^{-1} \|k\|_{\mathcal{X}}. \end{aligned}$$

Hence, by the version of Hille–Yosida theorem mentioned above, $(-\mathbf{H}, \mathbf{D})$ is a generator of a C_0 -semigroup $T_{\mathbf{H}}(t)$ in the space \mathcal{X} , and moreover, $\|T_{\mathbf{H}}(t)\| \leq e^{t\omega}$, $t \geq 0$.

Next, since $b \in L^\infty(\mathbb{R}_+)$, we have, for any $k \in \mathcal{X}$ and for a.a. $x \in \mathbb{R}^d$,

$$\begin{aligned} \|(\mathbf{A}k)(x, \cdot)\|_{\mathcal{H}} &\leq \|b\|_{L^\infty(\mathbb{R}_+)} \left(\int_{\mathbb{R}_+} \left(\int_{\mathbb{R}^d} a(x-y)(k(y, s) - k(x, s)) dy \right)^2 ds \right)^{\frac{1}{2}} \\ &\leq \|b\|_{L^\infty(\mathbb{R}_+)} \left(\int_{\mathbb{R}_+} \int_{\mathbb{R}^d} a(x-y) |k(y, s) - k(x, s)|^2 dy ds \right)^{\frac{1}{2}} \\ &\leq \sqrt{2} \|b\|_{L^\infty(\mathbb{R}_+)} \left(\int_{\mathbb{R}_+} \int_{\mathbb{R}^d} a(x-y) |k(y, s)|^2 dy ds + \int_{\mathbb{R}_+} |k(x, s)|^2 ds \right)^{\frac{1}{2}} \\ &\leq 2 \|b\|_{L^\infty(\mathbb{R}_+)} \left(\text{ess sup}_{x \in \mathbb{R}^d} \|k(x, \cdot)\|_{\mathcal{H}}^2 \right)^{\frac{1}{2}} \leq 2 \|b\|_{L^\infty(\mathbb{R}_+)} \|k\|_{\mathcal{X}}. \end{aligned}$$

Therefore, \mathbf{A} is a bounded operator in \mathcal{X} with $\|\mathbf{A}\| \leq 2 \|b\|_{L^\infty(\mathbb{R}_+)}$. Then, by e.g. [5, Theorem III.1.3], the operator $-\mathbf{H} + \mathbf{A}$ with domain \mathbf{D} generates a C_0 -semigroup $S(t)$ in \mathcal{X} , and moreover,

$$\|S(t)\| \leq \exp\{(\omega + 2 \|b\|_{L^\infty(\mathbb{R}_+)})t\}, \quad t \geq 0. \quad \square$$

Our goal is to study the asymptotic behavior of $k_t(x, s) = S(t)k_0(x, s)$ as $t \rightarrow \infty$. Here $k_0 \in \mathcal{X}$. In the particular case then, in fact, $k_0 \in \mathcal{H}$, one can solve this problem in details.

Theorem 2. *Let (2.1) hold and $b \in L^\infty(\mathbb{R}_+)$, $b(s) \geq 0$. Suppose additionally that the operator \bar{H} in \mathcal{H} has either simple discrete spectrum $\lambda_0 < \lambda_1 < \dots$, $\lambda_n \rightarrow \infty$, as $n \rightarrow \infty$, or continuous spectrum $[\lambda, +\infty)$ and a finite number of simple eigenvalues $\lambda_0 < \lambda_1 < \dots < \lambda_n < \lambda$. Consider the initial condition given by $k_0(x, s) = \varrho_0(s)$, for a.a. $x \in \mathbb{R}^d$, $s \in \mathbb{R}_+$, where $\varrho_0 \in \mathcal{H}$. Then*

$$\|S(t)k_0 - e^{-t\lambda_0} c_0 f_0\|_{\mathcal{X}} = o(e^{-t\lambda_0}), \quad t \rightarrow \infty, \quad (2.2)$$

where f_0 is the eigenfunction of the operator \bar{H} corresponding to the eigenvalue λ_0 , and $c_0 = (\varrho_0, f_0)_{\mathcal{H}}$.

Proof. By the proof of Lemma 1, the operator $(-\mathbf{H}, \mathbf{D})$ is a generator of a C_0 -semigroup $T_{\mathbf{H}}(t)$ in \mathcal{X} and \mathbf{A} is a bounded operator in \mathcal{X} . Then, by the Trotter formula (see e.g. [5, Exercise III.5.11]), we have

$$S(t)k_0 = \lim_{n \rightarrow \infty} \left(T_{\mathbf{H}}\left(\frac{t}{n}\right) e^{\frac{t}{n}\mathbf{A}} \right)^n k_0,$$

where the limit is considered in the sense of norm in \mathcal{X} . Note that for any $f \in \mathcal{H} \subset \mathcal{X}$, $\mathbf{A}f = 0$, therefore, $e^{t\mathbf{A}}f = f$ for all $t > 0$. Since k_0 does not depend on x , we have that $T_{\mathbf{H}}\left(\frac{t}{n}\right) e^{\frac{t}{n}\mathbf{A}}k_0 = T_{\mathbf{H}}\left(\frac{t}{n}\right)k_0$, and the latter function does not depend on x also. As a result, $S(t)k_0 = T_{\mathbf{H}}(t)k_0 = T_{\bar{H}}(t)\varrho_0$. Therefore, it is enough to show that

$$\|T_{\bar{H}}(t)\varrho_0 - e^{-t\lambda_0}c_0f_0\|_{\mathcal{H}} = o(e^{-t\lambda_0}) \quad t \rightarrow \infty.$$

The latter asymptotic follows from the general spectral theory of self-adjoint operator, see e.g. [9]. Using spectral decomposition of self-adjoint operator $-\bar{H}$ in the Hilbert space \mathcal{H} , we have:

$$T_{\bar{H}}(t)\varrho_0 = \int e^{-tu}dE_{\bar{H}}(u)\varrho_0,$$

where $E_{\bar{H}}$ is the spectral measure of $-\bar{H}$ and the integral is taken over the spectrum of $-\bar{H}$. Then

$$\|T_{\bar{H}}(t)\varrho_0 - e^{-t\lambda_0}c_0f_0\|_{\mathcal{H}}^2 \leq e^{-2t\lambda_1}\|P_{\mathcal{H}'}\varrho_0\|_{\mathcal{H}}^2 = o(e^{-2t\lambda_0}),$$

where $P_{\mathcal{H}'}$ is the projection on $\mathcal{H}' := \mathcal{H} \ominus \{f_0\}$. (Note that λ_1 may be equal to λ .) The statement is proved. \square

Remark 1. Asymptotic formula (2.2) means, in particular, that starting with any function of the form $k_0(x, s) = \varrho(s)$, $x \in \mathbb{R}^d$, $\varrho \in \mathcal{H}$, we get eventually for $k_t(x, s)$ a shape of the first eigenfunction f_0 of operator H .

Remark 2. The behavior of the populations in whole depends on the sign of λ_0 : if $\lambda_0 > 0$, then populations are vanishing, if $\lambda_0 < 0$, then populations are increasing. The case $\lambda_0 = 0$ ("equilibrium" regime) is of particular interest. As follows from the well-known facts on spectrum of one-dimensional Schrödinger operator, see e.g. [2], the sign of λ_0 depends on the shape of the function $v(s) = d(s) - b(s)$. Let us distinguish two interesting cases.

1. let $0 \leq v(s) \rightarrow +\infty$, $s \rightarrow +\infty$, that means, in particular, $d(s) \geq b(s)$ and $d(s) \rightarrow +\infty$; in this case the spectrum of \bar{H} is discrete and simple and, moreover, $\lambda_0 > 0$;
2. let $v(s) = d(s) - b(s) \rightarrow 0$, $s \rightarrow \infty$ and $b(s) = d(s) + \varepsilon(s)$, $s \in (a, b) \subset R_+$ with $\varepsilon(s) > 0$; in this case the operator \bar{H} may have a discrete spectrum below the continuous one with $\lambda_0 < 0$.

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