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Lookdown Model with Selection and Mutation

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Abstract

The purpose of this article is to study the look-down model with selection and mutation in the case of a population containing two types of individuals, where the population size N is finite and fixed. We show (Theorem 3.6) that the proportion of one of the two types converges, as the population size N tends to infinity, towards the Wright-Fisher diffusion with selection and mutation.

AMS Subject Classification: 62G05; 62G20.

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1 Introduction

In this paper we consider the lookdown (which is usually called by some authors the "modified look-down") model with selection and mutation. We first recall the model from ([3],[7]), and then we will describe the variant which will be the subject of the present paper.

The lookdown construction was first introduced by Donnelly and Kurtz in 1996 ([7]). Their goal was to give a construction of the Fleming–Viot superprocess that provides an explicit description of the genealogy of the individuals in a population. Donnelly and Kurtz subsequently modified their construction in [8] to include more general measure-valued processes. Those authors extended their construction to the selective and recombination case [9].

The author [3] consider a lookdown version of the Muller's ratchet model with compensatory mutations, which have been suggested by Anton Wakolbinger in a personal communication. The model have mutations in addition of selection, and will involve in an infinite number of types of individuals, and in an infinite number of selection rates. The type of one individual is determined by the number of uncanceled mutations he carries. The selection is modeled by a death rate (which is not bounded). The author shows that the infinite model

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is well defined even if the death rate is not bounded. He shows also that the model has a limit when the size of the population tends to infinity.

In this paper we consider the lookdown model with selection and mutation where the size $N \in \mathbb{N} = \{1, 2, \ldots, \}$ of the population is finite and fixed. We consider the case of two alleles b and B, where B has a selective advantage over b. This selective advantage is modeled by a death rate α for the type b individuals. We will consider the proportion of b individuals. The type b individuals are coded by 1, and the type B individuals by 0. We assume that the individuals are placed at time 0 on levels $1, 2, \ldots, N$, each one being, independently from the others, 1 with probability x, 0 with probability $1 - x$, for some $0 < x < 1$. For each $1 \leq i \leq N$ and $t \geq 0$, let $\eta_t(i) \in \{0, 1\}$ denote the type of the individual sitting on level i at time t. The evolution of $\eta_t(i)$ is governed by the three following mechanisms.

1. *Births* For each $1 \leq i < j \leq N$, arrows are placed from i to j according to a rate $c > 0$ Poisson Process, independently of the other pairs $i' < j'$. Suppose there is an arrow from i to j at time t. Then a descendant (of the same type) of the individual sitting on level i at time t^- occupies the level j at time t, while for any $k \in \{j, \ldots, N-1\}$, the individual occupying the level k at time t^- is shifted to level $k+1$ at time t. Since the population size N is finite and fixed, the individuals sitting on site N dies. In other words,
$$\eta_t(k) = \begin{cases} \eta_{t^-}(k), & \text{if } k < j. \\ \eta_{t^-}(i), & \text{if } k = j. \\ \eta_{t^-}(k-1) & \text{if } k \in \{j+1, \ldots, N\}. \end{cases}$$

2. *Deaths* Any type 1 individual dies at rate α, his vacant level being occupied by his right neighbor, who himself is replaced by his right neighbor, etc. We complete the population by an individual type 1 at level N with probability $X^N_{t^-}$, type 0 with probability $1 - X^N_{t^-}$.

3. *Mutation* Independently of reproduction and death, individuals may mutate, at rate $\theta\nu_1$ from type B to type b, and at rate $\theta\nu_0$ in the reverse direction. Equivalently, we can say that every individual B (resp. b) mutates at rate θ, and the ensuing type is b (resp. B) with probability ν_1 (resp. ν_0). Mutations are marked by circles. Suppose that, there is a circle at level i at time t, then
$$\eta_t(k) = \begin{cases} \eta_{t^-}(k), & \text{if } k \neq i; \\ 1 - \eta_{t^-}(k), & \text{if } k = i. \end{cases}$$

Note that in this construction the individual on level one is never shifted to level two, and the genealogy is not exchangeable. However the partition at time t induced by the ancestors at time 0 is exchangeable, since going back each pair coalesces at rate 1. This model is a slight variation of the Moran model with mutation and selection proposed by E. Baake, T. Hustedt, S. Kluth in [4]. We hope to be able to treat the case where we have an finite or infinite number of types of individuals, and where we replace the usual reproduction model by a population model dual to the Λ-coalescent (see [17] for more details). We refer the reader to Fig. 1 for a pictorial representation of our model. The types of the newborn

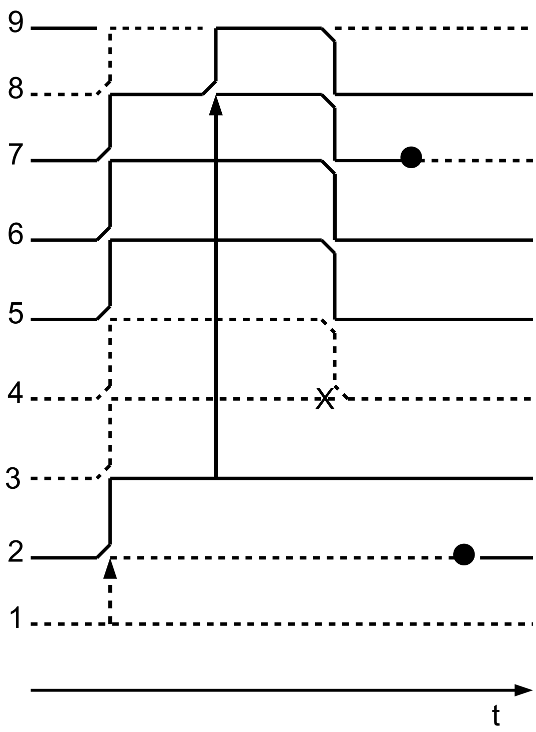

Figure 1. The graphical representation of a lookdown model with selection and mutation of size $N = 9$. Solid lines represent type B individuals, while dotted lines represent type b individuals. Black arrows represent births of type B, and dashed black arrows represent births of type b . Death events are represented by crosses, and mutation by circles. Time flows from the left to the right.

individuals are found by "looking down", while the type of the individual who replaces a dead individual is found by looking up.

Since we have modeled the selection by death events, the evolution of the N individuals $\eta_t(1),\ldots,\eta_t(N)$ depends to the number of deaths between time 0 and t, and $X_t^N = N^{-1}(\eta_t(1),\ldots,\eta_t(N))$, the proportion of type b individuals in the population, is not a Markov process. However for each $t > 0, \{\eta_t(k), k \geq 0\}$ constitutes an exchangeable sequence of $\{0,1\}$-valued random variables. We can then apply Finetti's theorem, and prove that $X_t^N \to X_t$ a.s. for any fixed $t \geq 0$, where $(X_t)_{t\geq 0}$ is a [0, 1]-valued Markov diffusion process, with generator $\mathcal{L}$ given as

$$\mathcal{L}f(x) = \frac{c}{2}x(1-x)f''(x) + \big[-\alpha x(1-x) + \theta\nu_1(1-x) - \theta\nu_0 x\big]f'(x), \tag{1.1}$$

in other word is a solution to the stochastic differential equation (which we call Wright-Fisher SDE with selection and mutation)

$$X_t = x + \int_0^t \sqrt{cX_s(1-X_s)}dB_s + \int_0^t \Big[-\alpha X_s(1-X_s) + \theta\nu_1(1-X_s)ds - \theta\nu_0 X_s\Big]ds, \tag{1.2}$$

where $\alpha \in \mathbf{R}$, B is a realization of a standard Brownian motion, $\theta\nu_1$ and $\theta\nu_0$ are the mutation rates. θ, ν_0, ν_1 are non-negative constants with $\nu_0 + \nu_1 = 1$.

The first part of this equation describes the neutral part of the reproduction. That is the case without selection and mutation. The second term corresponds to the logistic term due to selection and the type follow due to mutation.

When $\alpha > 0$, the process $(X_t)_{t\geq 0}$ represents the frequency of non advantageous allele as time passes. It is well–known (see e.g. Etheridge 2012) that the above continuous time model is the limit of the discrete time Wright-Fisher model with mutation and selection, in the sense that the proportion of advantageous alleles in a population of size N, evaluated in generation $[Nt]$(= the integer part of Nt), converges to the above diffusion process as $N \to \infty$. See [4, 16] for more details.

The paper is organized as follows. Section 2 presents the basic tightness criterion on the space of right continuous functions with left limits $D([0, \infty))$. In section 3, we prove our main result, we establish the convergence of X^N to the solution to (1.2).

In this paper, we assume that $\alpha > 0$, and $c = 1$.

2 Tightness criterion in $D([0, +\infty))$

We remind that the quadratic variation of a scalar discontinuous bounded variation local martingale $(M_t, t \geq 0)$ is the sum of the squares of its jumps and is denoted by :

$$[M]_t = \sum_{s \leq t} |\Delta M_s|^2.$$

Its predictable quadratic variation $\langle M \rangle_t$ is the unique increasing predictable process such that $[M]_t - \langle M \rangle_t$, and hence $M_t^2 - \langle M \rangle_t$ is a martingale.

Consider a sequences $\{X_t^N, t \geq 0\}_{N\geq 1}$ of one dimensional semi-martingale, which is such that for each $N \geq 1$,

$$X_t^N = X_0^N + \int_0^t \varphi_s^N ds + \mathcal{M}_t^N,\ t \geq 0;$$
$$\langle \mathcal{M}_t^N \rangle = \int_0^t \psi_s^N ds,\ t \geq 0;$$

where for each $N \geq 1, \mathcal{M}^N$ is a locally square-integrable martingale, φ^N and ψ^N are progressively measurable processes with value in $\mathbf{R}$ and $\mathbf{R}_+$ respectively. Since our martingales $\mathcal{M}^N$ will be discontinuous, we need to consider their trajectories as elements of $D([0, +\infty))$, the space of right continuous functions with left limits at every point, from $[0, +\infty)$ into $\mathbf{R}$, which we equip with the Skorohod topology, see Billingsley [6] for more details. The following statement can be deduced from Theorem 13.4 and 16.10 of [6].

Proposition 2.1. *A sufficient condition for the above sequence $\{X_t^N, t \geq 0, N \geq 1\}$ of semi-martingales to be tight in $D([0, +\infty))$ is that both*

$$\textit{the sequence of r.v.'s } \{X_0^N, N \geq 1\} \textit{is tight};$$

and for some $c > 0$

$$\sup_{N\geq 1,\, t\geq 0} \Big(|\varphi_t^N| + |\psi_t^N| \Big) \leq C.$$

If moreover, for any $T > 0$, as $N \to \infty$,

$$\sup_{0\le t\le T} | \mathcal{M}_t^N - \mathcal{M}_{t^-}^N | \to 0 \textit{ in probability,}$$

then any limit X of a weakly converging subsequence of the original sequence $\{X^N, N \geq 1, t \geq 0\}$ is a. s. continuous.

We have moreover

Proposition 2.2. *Suppose that all conditions of Proposition* (2.1) *are satisfied, and that moreover, as $N \to \infty$,*

$$(X_0^N, \varphi^N, \psi^N) \Rightarrow (X_0, \varphi, \psi)$$

weakly in $\mathbf{R}_+ \times L^1_{loc}([0,+\infty)) \times L^1_{loc}([0,+\infty))$.
Then X^N converges weakly in $D([0,\infty))$ towards a continuous process X which is such that

$$X_t = X_0 + \int_0^t \varphi_s ds + \mathcal{M}_t,$$

where $\mathcal{M}_t$ is local continuous martingale such that

$$\langle \mathcal{M} \rangle_t = \int_0^t \psi_s ds.$$

3 Tightness and Convergence to the W-F SDE with selection and mutation

3.1 Tightness of $\{X_t^N, t \geq 0, N \geq 1\}$

For each $N \geq 1$ and $t \geq 0$, denote by X_t^N the proportion of type b individuals in the population, i.e.

$$X_t^N = \frac{1}{N}\sum_{i=1}^N \eta_t(i) = \frac{1}{N}\sum_{i=1}^N \mathbf{1}_{(\text{individual sitting on level } i \text{ is b at time } t)}. \tag{3.1}$$

In this part, we will show the tightness of the process $(X^N)_{N\geq 1}$ in $D([0,+\infty))$. For this, we shall write an integral equation for X_t^N.

Let $\left\{P_{b_+}, P_{b_-}, P_{m_+}, P_{m_-}, P_d\right\}$ be standard Poisson point processes on $\mathbf{R}^+$, which are mutually independent.

We first remark that for each $1 \leq i < N$, the individual sitting on level i gives birth at rate $(N-i)$, and

$$\begin{aligned} \mathbf{P}\Big(\eta_t(i) = 1, \eta_t(N) = 0\Big) &= \mathbf{P}\Big(\eta_t(i) = 1 \mid \eta_t(N) = 0\Big)\mathbf{P}(\eta_t(N) = 0) \\ &= X_t(1-X_t)\frac{N}{N-1}. \end{aligned} \tag{3.2}$$

Using the definition of the model and (3.2), it is not hard to see that

$$\begin{aligned} X_t^N &= X_0^N + \frac{1}{N}\Big[P_{b_+}\Big(\int_0^t \frac{N^2}{2} X_s^N(1-X_s^N)ds\Big) - P_{b_-}\Big(\int_0^t \frac{N^2}{2} X_s^N(1-X_s^N)ds\Big)\Big] \\ &+ \frac{1}{N}\Big[P_{m_+}\Big(\int_0^t N(1-X_s^N)\theta\nu_1 ds\Big) - P_{m_-}\Big(\int_0^t N X_s^N \theta\nu_0 ds\Big)\Big] \\ &- \frac{1}{N} P_d\Big(\int_0^t \alpha N X_s^N(1-X_s^N)ds\Big). \end{aligned} \tag{3.3}$$

Let us define the following martingales: $M_{b_+}(t) = P_{b_+}(t) - t$, $M_{b_-}(t) = P_{b_-}(t) - t$, $M_{m_+}(t) = P_{m_+}(t) - t$, $M_{m_-}(t) = P_{m_-}(t) - t$ and $M_d(t) = P_d(t) - t$. We have

$$X_t^N = X_0^N + \int_0^t \Big[\theta\nu_1(1-X_s^N) - \theta\nu_0 X_s^N\Big]ds - \alpha\int_0^t X_s^N(1-X_s^N)ds + \mathcal{M}_t^N, \text{ where}$$

$$\begin{aligned} \mathcal{M}_t^N &= \frac{1}{N}\Big[M_{b_+}\Big(\int_0^t \frac{N^2}{2} X_s^N(1-X_s^N)ds\Big) - M_{b_-}\Big(\int_0^t \frac{N^2}{2} X_s^N(1-X_s^N)ds\Big] \\ &+ \frac{1}{N}\Big[M_{m_+}\Big(\int_0^t N(1-X_s^N)\theta\nu_1 ds\Big) - M_{m_-}\Big(\int_0^t N X_s^N\theta\nu_0 ds\Big] \\ &+ \frac{1}{N} M_d\Big(\int_0^t \alpha N X_s^N(1-X_s^N)ds\Big). \end{aligned}$$

It is clear that $\mathcal{M}_t^N$ is a martingale. Since $X_0^N \in [0,1]$ for each $N \geq 1$, $(X_0^N, N \geq 1)$ is tight. Moreover, we have

Proposition 3.1. *The process* $(X^N, N \geq 1)$ *is tight in* $D([0,+\infty))$

We first prove the following lemma

Lemma 3.2. *For each* $t \geq 0$

$$\langle \mathcal{M}^N \rangle_t = \int_0^t X_s^N(1-X_s^N)ds + \frac{\theta}{N}\int_0^t \Big[\nu_1 + (1-2\nu_1)X_s^N\Big]ds + \frac{\alpha}{N}\int_0^t X_s^N(1-X_s^N)ds$$

Proof : Using the fact that $\mathcal{M}^N$ is a pure-jump martingale, we can deduce that

$$\begin{aligned} [\mathcal{M}^N]_t &= \frac{1}{N^2}\Big[P_{b_+}\Big(\int_0^t \frac{N^2}{2} X_s^N(1-X_s^N)ds\Big) + P_{b_-}\Big(\int_0^t \frac{N^2}{2} X_s^N(1-X_s^N)ds\Big)\Big] \\ &+ \frac{1}{N^2}\Big[P_{m_+}\Big(\int_0^t N(1-X_s^N)\theta\nu_1 ds\Big) + P_{m_-}\Big(\int_0^t N X_s^N\theta\nu_0 ds\Big)\Big] \\ &+ \frac{1}{N^2} P_d\Big(\int_0^t \alpha N X_s^N(1-X_s^N)ds\Big), \end{aligned}$$

and also

$$\begin{aligned} \langle \mathcal{M}^N \rangle_t &= \int_0^t X_s^N(1-X_s^N)ds + \frac{1}{N}\int_0^t \theta\nu_1(1-X_s^N)ds + \frac{1}{N}\int_0^t \theta\nu_0 X_s^N ds + \frac{1}{N}\int_0^t \alpha X_s^N(1-X_s^N)ds \\ &= \int_0^t X_s^N(1-X_s^N)ds + \frac{\theta}{N}\int_0^t \Big[\nu_1 + (1-2\nu_1)X_s^N\Big]ds + \frac{\alpha}{N}\int_0^t X_s^N(1-X_s^N)ds. \end{aligned}$$

The lemma has been established. □

We can now proceed with the

Proof of Proposition 3.1. Let

$$\Phi(x) = \theta\nu_1(1-x) - \theta\nu_0 x - \alpha x(1-x)$$
$$\Psi_N(x) = x(1-x) + \frac{\theta}{N}\Big[\nu_1 + (1-2\nu_1)x\Big] + \frac{\alpha}{N}x(1-x).$$

We have

$$X_t^N = X_0^N + \int_0^t \Phi(X_s^N)ds + \mathcal{M}_t^N, \tag{3.4}$$

where

$$\langle \mathcal{M}^N\rangle_t = \int_0^t \Psi_N(X_s^N)ds.$$

It is a consequence of lemma 3.2 that for each $T > 0$,

$$\sup_{0\le t\le T}\sup_{N\ge 1}\Big(|\Phi(X_t^N)| + |\Psi_N(X_t^N)|\Big) \le C \quad a.s. \tag{3.5}$$

Aldous'tightness criterium (see Aldous [2]) is an easy consequence of (3.5) . □

Using the arguments in [3], it is easy to show if $\{\eta_0(i), i \ge 1\}$ are exchangeable random variables, then for all $t \ge 0, \{\eta_t(i), i \ge 1\}$ are exchangeable. An application of the Finietti's Theorem (see e.g. [1]), yields that

$$X_t = \lim_{N\to\infty} X_t^N \quad \text{exist a.s.} \tag{3.6}$$

Moreover since X^N is tight, there exists a process $X \in D([0,\infty)$ such that for all $t \ge 0$,

$$X^N \Rightarrow X \quad \text{weakly in } D[0,\infty).$$

Using the fact that $\sup_{t\ge 0}|X_t^N - X_{t^-}^N| \le 1/N$, it follows from Proposition 2.1 that X possesses an a. s. continuous modification, and the weak convergence holds for the topology of locally uniform convergence in $[0,+\infty)$.

We have in fact a slight stronger result.

Corollary 3.3. *For any $T \ge 0$, as $N \to \infty$,*

$$\sup_{0\le t\le T}|X_t^N - X_t| \to 0 \textit{ in probability.}$$

Proof : To prove this, we have to show

$$\forall\eta > 0, \forall\varepsilon > 0, \exists N_0 \in \mathbf{N} \text{ such that } \forall N \ge N_0 \quad \mathbf{P}(\sup_{0\le t\le T}|X_t^N - X_t| \ge \eta) \le \varepsilon.$$

To each $\delta > 0$, we associate $n \ge 1$ and $0 = t_0 < t_1 < \cdots < t_n = T$, such that $\sup_{1\le i\le n}(t_i - t_{i-1}) \le \delta$. We have

$$\sup_{0\le t\le T}|X_t^N - X_t| \le \sup_i \sup_{t_{i-1}\le t\le t_i}\{|X_t - X_{t_{i-1}}| \wedge |X_t - X_{t_i}|\}$$
$$+ \sup_i |X_{t_i}^N - X_{t_i}| + \sup_i \sup_{t_{i-1}\le t\le t_i}|X_t^N - X_{t_{i-1}}^N| \wedge |X_t^N - X_{t_i}^N|.$$

Since X is continuous a.s., the first term tends to 0 when δ tends to 0. In other word,

$$\exists\, \delta_0 \text{ such that } \forall \delta \leq \delta_0 \,, \mathbf{P}\Big(\sup_i \sup_{t_{i-1}\leq t\leq t_i} |X_t - X_{t_{i-1}}| \wedge |X_t - X_{t_i}| \geq \frac{\eta}{3}\Big) \leq \frac{\varepsilon}{3}. \tag{3.7}$$

Moreover, since there is a finite number of t_i, and $X^N_{t_i}$ converges a.s towards X_{t_i} . Then the second term tends to 0 when N goes to infinity. That is

$$\exists N_0 \text{ such that } \forall N \geq N_0 \,, \mathbf{P}\Big(\sup_i |X^N_{t_i} - X_{t_i}| \geq \frac{\eta}{3}\Big) \leq \frac{\varepsilon}{3}. \tag{3.8}$$

For the last term, let us define

$$w''(X,\delta) = \sup_{0\leq t_1\leq t\leq t_2\leq T, t_2-t_1\leq\delta} \{|X_t - X_{t_1}| \wedge |X_t - X_{t_2}|\}.$$

and

$$w'(X,\delta) = \inf_{t_i} \max_{1\leq i\leq n} \sup_{t,s\in[t_i,t_{i+1}]} |X_t - X_s|,$$

where the infimum is over all n and all subsets of $[0,T]$ of size $n+1$ such that

$$0 < t_0 < t_1 \cdots < t_n = T \quad \text{with} \quad \min_{1\leq i\leq n}(t_i - t_{i-1}) > \delta.$$

Thanks to (12.28) in [6], we have

$$w'(X^N,\delta) \geq w''(X^N,\delta).$$

Moreover since X^N is tight in $D([0,T))$, by using Theorem 13.2 in [6], we deduce that for each $\eta > 0$,

$$\begin{aligned}
\lim_{\delta\downarrow 0}\lim\sup_{N\to\infty} \mathbf{P}\Big(\sup_i \sup_{t_{i-1}\leq t\leq t_i} \{|X^N_t - X^N_{t_{i-1}}| \wedge |X^N_t - X^N_{t_i}|\} \geq \frac{\eta}{3}\Big) &\leq \lim_{\delta\downarrow 0}\lim\sup_{N\to\infty} \mathbf{P}\Big(w''(X^N,\delta) \geq \frac{\eta}{3}\Big)\\
&\leq \lim_{\delta\downarrow 0}\lim\sup_{N\to\infty} \mathbf{P}\Big(w'(X^N,\delta) \geq \frac{\eta}{3}\Big)\\
&= 0.
\end{aligned}$$

And from this, (3.8) and (3.7), we deduce that

$$\begin{aligned}
\mathbf{P}(\sup_{0\leq t\leq T} |X^N_t - X_t| \geq \eta) &\leq \mathbf{P}\Big(\sup_i \sup_{t_{i-1}\leq t\leq t_i} |X_t - X_{t_{i-1}}| \wedge |X_t - X_{t_i}| \geq \frac{\eta}{3}\Big) + \mathbf{P}\Big(\sup_i |X^N_{t_i} - X_{t_i}| \geq \frac{\eta}{3}\Big)\\
&\quad + \mathbf{P}\Big(\sup_i \sup_{t_{i-1}\leq t\leq t_i} \{|X^N_t - X^N_{t_{i-1}}| \wedge |X^N_t - X^N_{t_i}|\} \geq \frac{\eta}{3}\Big)\\
&\leq \varepsilon.
\end{aligned}$$

Which prove the proposition. □

3.2 Convergence to the W-F SDE with selection and mutation

Our goal is to get a representation of the process $(X_t)_{t\geq 0}$ defined in (3.6) as the unique weak solution of a stochastic differential equation (1.2). We determine the generator $\mathcal{L}^N$ for the process X^N, and take its limit when the size N of the population tends to infinity. This will give an idea about the equation solved by X_t.

Let us prove the following elementary lemma.

Lemma 3.4. *Let f in C^2, then for all $x \in \mathbf{R}$*

$$\lim_{n\to\infty} N^2\Big(f(x+\frac{1}{N})+f(x-\frac{1}{N})-2f(x)\Big) = f''(x)$$

$$\lim_{n\to\infty} N\Big(f(x+\frac{1}{N})-f(x)\Big) = f'(x)$$

$$\lim_{n\to\infty} N\Big(f(x-\frac{1}{N})-f(x)\Big) = -f'(x)$$

Proof : Since $f \in C^2$, by using the Taylor expansion, on can write :

$$f(x+\frac{1}{N}) = f(x)+\frac{1}{N}f'(x)+\frac{1}{2N^2}f''(x)+O(\frac{1}{N^3})$$
$$f(x-\frac{1}{N}) = f(x)-\frac{1}{N}f'(x)+\frac{1}{2N^2}f''(x)+O(\frac{1}{N^3}).$$

Hence

$$N^2\Big(f(x+\frac{1}{N})+f(x-\frac{1}{N})-2f(x)\Big) = f''(x)+O(\frac{1}{N}).$$

Taking the limit $N \to \infty$, the result follows. □

For any $t \geq 0$, $\{X_t^N, t \geq 0\}$ gives the proportion of type b individuals at time t in the population. X^N has a finite number of jumps in a finite time interval, and has transition rates

$$\begin{cases} \gamma \;\to\; \gamma+1/N & \text{at rate } \quad \frac{1}{2}N^2\gamma(1-\gamma)+N\theta(1-\gamma)\nu_1 \\ \gamma \;\to\; \gamma-1/N & \text{at rate } \quad \frac{1}{2}N^2\gamma(1-\gamma)+N\theta\gamma\,\nu_0+\alpha N\gamma(1-\gamma). \end{cases}$$

The process X^N takes values in $\{0, 1/2, \ldots, (N-1)/N, 1\}$ and its generator $\mathcal{L}^N$ is given by

$$\begin{aligned}\mathcal{L}^N f(x) = \frac{N^2}{2}x(1-x)\Big(f(x+\frac{1}{N})+f(x-\frac{1}{N})-2f(x)\Big)+N\,\theta(1-x)\,\nu_1\Big(f(x+\frac{1}{N})-f(x)\Big)\\ +N\,\theta x\,\nu_0\Big(f(x-\frac{1}{N})-f(x)\Big)+\alpha Nx(1-x)\Big(f(x-\frac{1}{N})-f(x)\Big).\end{aligned} \tag{3.9}$$

From Lemma 3.4, we deduce that

$$\lim_{N\to\infty}\mathcal{L}^N f(x) = \frac{1}{2}x(1-x)f''(x)+[-\alpha x(1-x)+(1-x)\theta\nu_1-x\theta\nu_0]f'(x),$$

which is the same generator of the Wright Fisher diffusion with mutation and selection given in (1.1).

Let $(\Omega, \mathcal{F}, \mathbf{P})$ be a fixed probability space with a filtration $(\mathcal{F}_t)_{t\geq 0}$ satisfying the usual condition.

Definition 3.5. We shall call W-F SDE with mutation and selection the following stochastic differential equation

$$\begin{cases} dX_t = -\alpha X_t(1-X_t)dt + \theta\nu_1(1-X_t)dt - \theta\nu_0 X_t dt + \sqrt{X_t(1-X_t)}dB_t, \quad t \geq 0, \\ X_0 = x, \quad 0 < x < 1, \end{cases} \tag{3.10}$$

where B is a realization of a standard Brownian motion, $\alpha \in \mathbf{R}$, $\theta\nu_1$ (resp. $\theta\nu_0$) is the mutation rate towards (resp. from) the focal type from (resp. towards) any other type. The solution $(X_t)_{t\geq 0}$ is $[0,1]-$ valued Markov process with continuous path.

Without loss generality, we assume that $\alpha > 0$, which means that X_t represents the proportion of non-advantageous allele.

Recall the definition of X^N started in (3.4). Let us now prove the main result of this section.

Theorem 3.6. *Suppose that $X_0^N \to x$ a.s, as $N \to \infty$. Then the $[0,1]-$ valued process $\{X_t, t \geq 0\}$ defined by (3.6) is the (unique in law) solution to the W-F SDE with selection and mutation (3.10).*

Proof : Strong uniqueness of the solution to (3.10) follows from a result of Yamada-Watanabe, see e.g. Karatzas and shreve [14].

We now prove that X_t defined by (3.6) is a solution to the W-F SDE (3.10). Recall the decomposition

$$X_t^N = X_0^N + \int_0^t \Phi(X_s^N)ds + \mathcal{M}_t^N.$$

Since $X_t^N \to X_t$ a.s., we have

$$\Phi(X_s^N) \to -\alpha X_s(1-X_s) + \theta\nu_1(1-X_s) - \theta\nu_0 X_s \quad \text{a.s.}, \tag{3.11}$$

and

$$\Psi_N(X_s^N) \to X_s(1-X_s) \quad \text{a.s.} \tag{3.12}$$

From (3.11), (3.12) and Proposition 3.12, we deduce that

$$X_t = X_0 + \int_0^t \Big[-\alpha X_s(1-X_s) + \theta\nu_1(1-X_s) - \theta\nu_0 X_s\Big]ds + \mathcal{M}_t,$$

where $\mathcal{M}$ is a continuous martingale such that

$$\langle \mathcal{M} \rangle_t = \int_0^t X_s(1-X_s)ds.$$

It follows from the martingale representation theorem, there exists, possibly on an enlarged probability space $(\Omega', \mathcal{F}', \mathbf{P}')$, a standard Brownian motion $\{B_t, t \geq 0\}$ such that

$$X_t = X_0 + \int_0^t \Big[-\alpha X_s(1-X_s) + \nu_1(1-X_s)ds - \nu_0 X_s\Big]ds + \int_0^t \sqrt{X_s(1-X_s)}dB_s.$$

Which prove our main Theorem. □

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