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CONVERGENCE OF ONE-DIMENSIONAL DIFFUSION PROCESSES TO A JUMP PROCESS RELATED TO POPULATION GENETICS

by

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and

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CONVERGENCE OF ONE-DIMENSIONAL DIFFUSION PROCESSES TO A JUMP PROCESS RELATED TO POPULATION GENETICS

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Abstract. A conjecture on the convergence of diffusion models in population genetics to a simple Markov chain model is proved. The notion of bi-generalized diffusion processes and their limit theorems are used systematically to prove the conjecture. Three limits; strong selection - weak mutation limit, moderate selection - weak mutation limit, weak selection - weak mutation limit are considered for typical diffusion models in population genetics.

Key words: Diffusion model - Strong selection-weak mutation limit - Markov chain model - Bi-generalized diffusion process

1. Introduction

In population genetics theory, stochastic models are described by discrete time stochastic processes and they are approximated by appropriate continuous time stochastic processes (see Iizuka and Matsuda 1982; Iizuka 1987 and the cited therein). In many cases, these continuous time stochastic processes are diffusion processes and are referred to as diffusion models in population genetics (Crow and Kimura 1970; Ewens 1979). Let $x_i(t)$, $i=1,2,\dots,K$; $t\geq 0$ be the gene frequency of the i-th allele at time t in a population. In the diffusion model, $x(t)=(x_1(t),x_2(t),\dots,x_{K-1}(t))$ is a K-1 dimensional diffusion process with $x_i(t)\geq 0$, $i=1,2,\dots,K$ and $0\leq\sum_{i=1}^{K-1}x_i(t)\leq 1$. The boundary condition, when it is necessary, is usually the reflection boundary condition. The infinitesimal generator of this diffusion process is

$$(1.1) \qquad L = \frac{1}{2}\sum_{i,j=1}^{K-1} a_{ij}(x,\alpha)\frac{\partial^2}{\partial x_i \partial x_j} + \sum_{i=1}^{K-1} b_i(x,\alpha,\theta)\frac{\partial}{\partial x_i},$$

where $x=(x_1,x_2,\dots,x_{K-1})$ with $x_i\geq 0$, $i=1,2,\dots,K-1$ and $\sum_{i=1}^{K-1}x_i\leq 1$. For example, the diffusion terms, $a_{ij}(x,\alpha)$ and the drift terms, $b_i(x,\alpha,\theta)$ are specified in Gillespie (1989) (see Eq. (1)). The parameter α denotes the effect of selection and θ denotes the effect of mutation. From now on, the diffusion processes satisfying the above conditions are called the population genetical diffusion processes. For these diffusion processes in the case of $K \geq 3$ in general, it is difficult to obtain the biologically interesting quantities such as the average homozygosity, $E[\sum_{i=1}^{K} x_i^2(t)]$, the stationary distributions if exist and so on. The exceptions are the case of no selection and the case of pure stochastic selection without mutation and random sampling drift. The reason why it is difficult to obtain the stationary distributions is that population genetical diffusion processes are not time reversible in many cases (in physics term, there is no "flux zero solution" for the Kolmogorov forward equation). The numerical analysis for the diffusion equation or the computer simulation for the corresponding population genetical diffusion process may be applicable, but these methods are again difficult to perform in the case where K is large.

Gillespie (1983a and 1983b) proposed the following conjecture in which K-1 dimensional population genetical diffusion processes with selection, mutation and the random sampling drift are approximated by simple Markov jump processes. Let $X^{\varepsilon}(t)=(X_1^{\varepsilon}(t), X_2^{\varepsilon}(t), \ldots, X_{K-1}^{\varepsilon}(t))$ be a K-1 dimensional population genetical diffusion process with the infinitesimal generator

$$(1.2) \qquad L^{\varepsilon} = \frac{1}{2} \sum_{i,j=1}^{K-1} a_{ij}(x,\alpha_{\varepsilon}) \frac{\partial^2}{\partial x_i \partial x_j} + \sum_{i=1}^{K-1} b_i(x,\alpha_{\varepsilon},\theta_{\varepsilon}) \frac{\partial}{\partial x_i},$$

where $\varepsilon>0$ and $\alpha_{\varepsilon}, \theta_{\varepsilon}>0$.

Conjecture (Gillespie)

Assume that $\alpha_{\varepsilon} \to +\infty$ and $\theta_{\varepsilon} \to 0$ as $\varepsilon \to 0$ where $\alpha_{\varepsilon}\theta_{\varepsilon}$ is fixed. Then $\{X^{\varepsilon}(t)\}$ converges weakly to a Markov chain as $\varepsilon \to 0$.

In this conjecture, the limiting Markov chains are characterized as follows. Assume that there exist two limits $A_{ij}(x)=\lim_{\varepsilon\to 0} a_{ij}(x,\alpha_{\varepsilon})/\alpha_{\varepsilon}$ and $B_i(x)=\lim_{\varepsilon\to 0} b_i(x,\alpha_{\varepsilon},\theta_{\varepsilon})/\alpha_{\varepsilon}$. (1) The case of $A_{ij}(x)=0$ for

$i,j=1,2,\dots,K-1$. The state space of the Markov chain is $\{x;B_i(x)=0, i=1,2,\dots,K-1\}$, that is, a set of the equilibrium points for a deterministic motion $\frac{\partial x(t)}{\partial t}=\sum_{i=1}^{K-1}B_i(x)\frac{\partial x(t)}{\partial x_i}$. (2) The case of $A_{ij}(x)>0$ for some i and j. Assume that there exist the stationary distributions for a diffusion process with the infinitesimal generator $\mathfrak{L} = \frac{1}{2}\sum_{i,j=1}^{K-1}A_{ij}(x)\frac{\partial^2}{\partial x_i \partial x_j}+\sum_{i=1}^{K-1}B_i(x)\frac{\partial}{\partial x_i}$. The state space of the Markov chain is the set of the stationary distributions for this diffusion process, that is, the limiting Markov chain is a measure valued Markov chain.

By the following proposition, however, the conjecture of Gillespie never holds in the sense of weak convergence in the Polish space D with the Skorohod topology (Billingsley 1968).

Proposition

Let $\{y_n(t)\}, n=1,2,\dots$. be a sequence of diffusion processes. The $\{y_n(t\}$ does not converge weakly in D to a jump process.

Proof. Assume that $\{y_n(t)\}$ converges weakly to $y(t)$ in D. Let P_n and P be the induced probability measures on D by $y_n(t)$ and $y(t)$, respectively. The space of the continuous functions C is a closed subset of D (Billingsley 1968). By weak convergence of $\{y_n(t)\}$ to $y(t)$ in D, we have $P(C)\geq\limsup_{n\to+\infty}P_n(C)=1$. This means that $y(t)$ is continuous with probability one. □

By this proposition, the conjecture of Gillespie does not hold in the sense of weak convergence in D. There is, however, a possibility that the conjecture holds in a weaker sense of convergence such as the convergence of the finite dimensional distributions. Indeed, Kipnis and Newman (1985) proved the convergence of one-dimensional diffusion processes related to the metastable behavior in statistical physics to a jump process in the sense of the finite dimensional distributions. In their proof, however, the constancy of the diffusion term is essential and hence not applicable to the conjecture of Gillespie.

It seems us that the proof of the conjecture of Gillespie for $K \geq 3$ is difficult. The results of Fleidlin and Wentzel (1984) are closely related to this problem but their results are rather abstract and do not present limit theorems corresponding to the conjecture of Gillespie. Even the case of $K=2$, there are several questions about the conjecture. First of all, does the conjecture hold in the sense of the convergence of the finite dimensional distributions? What is the appropriate time scaling to obtain a limiting jump process (though Gillespie does not mention about this)? What is the relation between α_ε and θ_ε to obtain a limiting jump process? What is the characterization of the limit process?

In this paper, we will consider the case of $K=2$. Even the case of $K=2$, this is an interesting problems for the limit theorems in the theory of stochastic processes. For example, this is a new type of limit theorem, that is, from the processes with continuous paths to a jump process. Further, the answers for the above questions will be hints for the proof of the conjecture in the case of $K \geq 3$.

The traditional methods to prove the limit theorems are the semigroup approximation theorems (for example, see Kurtz 1975) and the martingale methods (Stroock and Varadham 1979). These methods, however, are not applicable to the present problem. Indeed, the coefficients of the infinitesimal generator have no limit in some cases as we will see later.

Recently, one of the authors proposed a class of one-dimensional stochastic processes called the bi-generalized diffusion processes and proved some limit theorems for this class of processes (Ogura 1989). We will use this method systematically in this paper. In §2, we will review the results on the bi-generalized diffusion processes. We will prove two limit theorems here, since the general results of Ogura (1989) do not cover some cases in this paper. The conjecture of Gillespie for the case of $K=2$ will be described explicitly in §3. Here, we will consider not only the cases of $\alpha_\varepsilon \to +\infty$ and $\theta_\varepsilon \to 0$ but also the cases of $\alpha_\varepsilon \to \alpha\,(0 \leq \alpha < +\infty)$

and $\theta_\varepsilon \to 0$. In §4 the results on the cases introduced in §3 will be obtained using the limit theorems presented in §2. In §5 we will consider the other time scaling to obtain a non-trivial limit process since the time scaling in §4 leads to a trivial limit in some cases. We will discuss the results obtained so far in §6.

2. Bi-generalized diffusion processes and limit theorems

2.1. Feller's canonical form for one-dimensional diffusion processes

Let $x(t), t \geq 0$ be a one-dimensional diffusion process (ODDP for brief) on the state space $(\ell, r), -\infty \leq \ell < r \leq +\infty$, with the infinitesimal generator

$$L = \frac{a(x)}{2} \frac{d^2}{dx^2} + b(x) \frac{d}{dx} \tag{2.1}$$

and given boundary conditions if they are necessary. The representation (2.1) is referred to as Kolmogorov's canonical form and this is equivalent to

$$L = \frac{d}{dm(x)} \frac{d}{ds(x)}, \tag{2.2}$$

$$s(x) = \int_{x_0}^{x} e^{-B(y)} dy, \tag{2.3}$$

$$m(x) = \int_{x_0}^{x} \frac{2}{a(y)} e^{B(y)} dy, \tag{2.4}$$

where $B(x) = 2\int \frac{b(y)}{a(y)} dy$, x_0 is a constant $(\ell < x_0 < r)$ and $\ell \leq x \leq r$. The representation (2.2) is referred to as Feller's canonical form. The continuous and strictly increasing functions $s(x)$ and $m(x)$ are referred to as the scale function and the speed measure, respectively. Note that we can replace a pair $s(x)$ and $m(x)$ by $s_1(x) = cs(x)$ and $m_1(x) = m(x)/c$, where c is a positive constant. Conversely, extending the two functions $s(x)$ and $m(x)$ on (ℓ, r) to $R = (-\infty, +\infty)$ appropriately according to the nature of the boundary points ℓ and r,

$s(x)$ and $m(x)$ which are continuous and strictly increasing on (ℓ,r) determine a unique ODDP on (ℓ,r).

2.2. Generalized diffusion processes

Feller (1959) proposed a class of one-dimensional stochastic processes including ODDPs by means of weakening the conditions on $m(x)$. Let $s(x)$ be a continuous and strictly increasing function on (ℓ,r) and $m(x)$ be a right continuous nondecreasing function on (ℓ,r). Then the pair $s(x)$ and $m(x)$ (after their extension to $\mathbf{R}$) determine a unique strong Markov process. This class of stochastic processes are referred to as the generalized diffusion processes (GDPs for brief). For example, a birth and death process is a GDP. Let $x_n(t)$ be a GDP with the scale function $s_n(x)$ and the speed measure $m_n(x), n=1,2,\ldots$. We may expect limit theorems where the convergence of $\{s_n(x)\}$ and $\{m_n(x)\}$ implies the convergence of a sequence of GDPs $\{x_n(t)\}$ in some sense, for example the sense of the convergence of the finite dimensional distributions. The limit function $s(x)$ of $\{s_n(x)\}$, however, is not continuous nor strictly increasing in general. In other words, the class of GDPs is not suitable to consider the limit theorems. For this reason, it is necessary to extend the class of GDPs by means of defining a new class of one-dimensional stochastic processes by a pair $s(x)$ and $m(x)$ that are not continuous nor strictly increasing in general.

2.3. Bi-generalized diffusion processes

Recently, Ogura (1989) extended the notion of a generalized diffusion process to that of a bi-generalized diffusion process (BGDP for brief), which is a Markov process corresponds to a nondecreasing function $s(x)$ and a right continuous nondecreasing function $m(x)$. In the remaining of this section, we summarize his definition and the analytical construction of BGDPs, and then give two limit theorems for the BGDPs, which are slight extension of those ibid.

2.3.1. Definition and analytical construction of the bi-generalized diffusion processes

In this subsection, we will review the results in Ogura (1989) on the construction of BGDPs and their stopped motions. Let $-\infty\leq\ell_1<\ell_2\leq+\infty$, $Q=(\ell_1,\ell_2)$, $\bar{Q}=[\ell_1,\ell_2]$ and consider two nondecreasing functions s, m on Q. Since we will only be concerned with the Stieltjes measure dm induced by m, we assume that m is right continuous. Under some mild assumptions, we can construct a unique Markov semigroup on Q associated to s and m in the following way (for the rigid statement and its justification, see ibid.).

Let $d\tilde{m}$ the image measure of dm by the map s:

$$\text{(2.5)} \qquad \int_{s(Q)} q(\xi)d\tilde{m}(\xi) = \int_{Q} q\circ s(x)dm(x), \qquad q \in C(s(Q)),$$

where C(S) is the space of all bounded continuous functions on a set S. We want to define a GDP $\tilde{X}$ associated to the speed measure $d\tilde{m}$ and the natural scale $\tilde{s}(\xi)=\xi$. In order to do so we must settle the state space and the boundary conditions when they are necessary. Exploiting Watanabe's convention, however, we can carry over the boundary conditions to the state space by extending it and by setting the trap conditions at the end points (see Watanabe 1975 and Minami *et al.* 1985 for detail). Thus we set $\tilde{Q}=(\tilde{\ell}_1,\tilde{\ell}_2)$, $\tilde{Q}^{\cdot}=[\tilde{\ell}_1,\tilde{\ell}_2]$ and $\int_{\tilde{Q}\setminus s(Q)}d\tilde{m}(\xi)=0$, where $\tilde{\ell}_1\in[-\infty,\inf s(Q)]$ and $\tilde{\ell}_2\in[\sup s(Q),+\infty]$. Notice that $\tilde{\ell}_i$, $i=1,2$ are uniquely determined from s and m in Ogura (1989) by the convention there. More precisely, let $\bar{R}=[-\infty,+\infty]$ and extend s and m to the functions $\bar{R}\rightarrow\bar{R}$ so that i) at least one of $s(\ell_2)$ $[s(\ell_1)]$ and $m(\ell_2)$ $[m(\ell_1-)]$ is equal to $+\infty$ [resp. $-\infty$], ii) ℓ_i is not a common jump point of s and m. In the above and the following we denote $s(a+)=\lim_{x\downarrow a}s(x)$ and $s(a-)=\lim_{x\uparrow a}s(x)$. We then set $\tilde{\ell}_2=s(\ell_2-)$ if $m(\ell_2)=+\infty$, $\tilde{\ell}_2=+\infty$ if $m(\ell_2)<+\infty$, and similarly for $\tilde{\ell}_1$. We also note that the image measure $d\tilde{m}$ is induced by the nondecreasing function $\tilde{m}$ given by

$$\tilde{m}(\xi) = \begin{cases} \sup\{m(x):s(x)\le\xi\}, & \text{if } \{\ \} \neq \phi, \\ m(-\infty), & \text{if } \{\ \} = \phi. \end{cases}$$

We now have the Green function $H(\alpha,\xi,\eta)$, $\alpha>0$, $\xi,\eta\in\tilde{Q}$ and the transition density $q(t,\xi,\eta)$, $t>0$, $\xi,\eta\in\tilde{Q}$ associated to $d\tilde{m}$ (and $\tilde{Q}$) by the standard method, which we give in the following for completeness. Fix a continuity point $\xi_0\in\tilde{Q}$ of $\tilde{m}$, and let $\varphi_1(\xi,\alpha)$, $\varphi_2(\xi,\alpha)$ be the solutions to the following integral equations

$$\varphi_1(\xi,\alpha) = 1 + \alpha\int_{\xi_0+}^{\xi+}(\xi - \eta)\varphi_1(\eta,\alpha)d\tilde{m}(\eta), \qquad \xi \in \tilde{Q},$$

$$\varphi_2(\xi,\alpha) = \xi - \xi_0 + \alpha\int_{\xi_0+}^{\xi+}(\xi - \eta)\varphi_2(\eta,\alpha)d\tilde{m}(\eta), \quad \xi \in \tilde{Q},$$

where $\int_{\xi_0+}^{\xi+}f(\eta)d\tilde{m}(\eta)=\int_{(\xi_0,\xi]}f(\eta)d\tilde{m}(\eta)$ if $\xi\in[\xi_0,\tilde{\ell}_2]$, $=-\int_{(\xi,\xi_0]}f(\eta)d\tilde{m}(\eta)$ if $\xi\in[\tilde{\ell}_1,\xi_0)$. Then, for each $\alpha>0$, there exist the limits

$$h_1(\alpha) = -\lim_{\xi\downarrow\tilde{\ell}_1}\varphi_2(\xi,\alpha)/\varphi_1(\xi,\alpha),$$

$$h_2(\alpha) = \lim_{\xi\uparrow\tilde{\ell}_2}\varphi_2(\xi,\alpha)/\varphi_1(\xi,\alpha),$$

where we use the usual convention $1/\infty=0$, $(\pm a)/0=\pm\infty$ for positive a. Define the function $h(\alpha)$; $\alpha>0$ and $u_i(\xi,\alpha)$, $i=1,2$, $\alpha>0$ by

$$1/h(\alpha) = 1/h_1(\alpha) + 1/h_2(\alpha),$$

$$u_i(\xi,\alpha) = \varphi_1(\xi,\alpha) + (-1)^{i+1}\varphi_2(\xi,\alpha)/h_i(\alpha).$$

It is then known that $u_1(\xi,\alpha)[u_2(\xi,\alpha)]$ is positive and nondecreasing [resp. nonincreasing] in ξ and $u_1(\xi_0,\alpha)=u_2(\xi_0,\alpha)=1$. Further, their Wronskian is equal to $1/h(\alpha)$. We thus obtain the associated Green function $H(\alpha,\xi,\eta)$ and the transition density by

$$H(\alpha,\xi,\eta) = H(\alpha,\eta,\xi) = h(\alpha)u_1(\xi,\alpha)u_2(\eta,\alpha), \quad \tilde{\ell}_1 < \xi \le \eta < \tilde{\ell}_2,$$

$$\int_0^{+\infty} e^{-\alpha t} q(t,\xi,\eta)dt + \Phi(\xi,\eta) = H(\alpha,\xi,\eta), \quad \alpha > 0,\ \xi,\eta \in \tilde{Q},$$

for some function $\Phi(\xi,\eta)$ independent of α. The precise formula of $\Phi(\xi,\eta)$ is given in Minami *et al.* (1985), but we do not use it here.

Now the semigroup T_t for the pair (s,m) is defined by the formula

$$\text{(2.6)} \quad \int_0^{+\infty} e^{-\alpha t} T_t f(x)dt = \int_Q H(\alpha,s(x),s(y))f(y)dm(y), \quad \alpha>0,\ x\in Q,\ f\in B(Q),$$

and the semigroup $T_t^{\bullet}$ for the stopped motion by

$$\text{(2.7)} \quad \int_0^{+\infty} e^{-\alpha t} T_t^{\bullet} f(x)dt = \int_Q H(\alpha,s(x),s(y))f(y)dm(y)$$

$$+ f(\ell_2)\frac{u_1(s(x),\alpha)}{\alpha u_1(\tilde{\ell}_2-,\alpha)} + f(\ell_1)\frac{u_1(s(x),\alpha)}{\alpha u_1(\tilde{\ell}_1+,\alpha)}, \quad \alpha > 0,\ x \in \overline{Q},\ f \in B(\bar{Q}),$$

where $u(\tilde{\ell}_1+,\alpha)=\lim_{\xi\downarrow\tilde{\ell}_1} u(\xi,\alpha)$ and $u(\tilde{\ell}_2-,\alpha)=\lim_{\xi\uparrow\tilde{\ell}_2} u(\xi,\alpha)$ and $B(S)$ is the space of all bounded Borel measurable functions on S. Notice that

$$T_t f(x) = \int_Q q(t,s(x),s(y))f(y)dm(y),$$

$$T_t^{\bullet} f(x) = \int_Q q(t,s(x),s(y))f(y)dm(y)$$

$$+ f(\ell_2)\int_0^t q_{\tilde{\ell}_2}(\tau,s(x))d\tau + f(\ell_1)\int_0^t q_{\tilde{\ell}_1}(\tau,s(x))d\tau,$$

where $q_{\tilde{\ell}_2}(\tau,s(x))[q_{\tilde{\ell}_1}(\tau,s(x))]$ is the inverse Laplace transform of the function $u_1(s(x),\alpha)/u_1(\tilde{\ell}_2-,\alpha)$ [resp. $u_2(s(x),\alpha)/u_2(\tilde{\ell}_1+,\alpha)$]. Although the semigroups T_t and $T_t^{\bullet}$ are not strongly continuous in general, there exist Markov processes $X=(x(t),e_\Delta,P_x)$ on Q and $X^{\bullet}=(x^{\bullet}(t),P_x^{\bullet})$ on $\overline{Q}$ such that

$$E_x[f(x(t));e_\Delta>t] = T_t f(x), \qquad t>0,\ x\in Q,\ f\in B(Q),$$

$$E_x^{\bullet}[f(x^{\bullet}(t))] = T_t^{\bullet} f(x), \qquad t>0,\ x\in\overline{Q},\ f\in B(\overline{Q}),$$

where E_x $[E_x^{\bullet}]$ stands for the expectation with respect to P_x[resp. $P_x^{\bullet}$] (strictly speaking Q is joined with ℓ_1 or ℓ_2 whenever they are reflecting point). We call the process $X^{\cdot}=(x^{\cdot}(t),P_x^{\cdot})$ a stopped BGDP or briefly a SBGDP.

2.3.2. Limit theorems for a sequence of bi-generalized diffusion processes

The question whether the convergence of the sequence of s_n and m_n implies the convergence of that of the associated processes is now on stage. Throughout this subsection, we adopt the convention in the previous subsection and assume that

$$(2.8)\qquad \begin{aligned} &\lim_{n\to\infty} s_n(x) = s(x), \quad && x \in R, \\ &\lim_{n\to\infty} m_n(x) = m(x), \quad && x \in R\setminus J(m), \end{aligned}$$

where $J(m)$ is the set of jump points of m. As is shown in Ogura (1989), if $J(s)\cap J(m)\cap Q=\emptyset$, then the induced measures $d\tilde{m}_n$ converge to $d\tilde{m}$, so that the finite dimensional distributions of the associated processes. However, this is false in general if the condition $J(s)\cap J(m)\cap Q=\emptyset$ fails. Furthermore, in the following applications, we actually encounter with the case of $J(s)\cap J(m)\cap Q\neq\emptyset$, to which we now advance.

Let $X^{(n)}=(x(t),e_\Delta,P_x^{(n)})$ on $Q^{(n)}$ and $X^{\cdot(n)}=(x^{\cdot}(t),P_x^{\cdot(n)})$ on $\bar{Q}^{(n)}$ the BGDPs and SBGDPs associated to s_n and m_n. The corresponding semigroups are denoted by $T_t^{(n)}$ and $T_t^{\cdot(n)}$ respectively. Also the space of continuous functions on Q with compact support is denoted by $C_0(Q)$.

Theorem 2.1. In addition to the condition (2.8), assume that

$$(2.9)\qquad \lim_{n\to\infty} \tilde{m}_n(\xi) = \tilde{m}(\xi), \quad \xi \in R\setminus J(\tilde{m}),$$

$$(2.10)\qquad \lim_{n\to\infty} \int_{[a,b]} q\circ s_n(x)\,dm_n(x)=\int_{[a,b]} q\circ s(x)\,dm(x),$$

$$a,b \in (J(s)\cup J(m))^c\cap Q,\quad q \in C(\tilde{Q}).$$

Then for every $\tau_1,\tau_2,\dots,\tau_N>0$, $f_1,f_2,\dots,f_N\in C_0(Q)$, $N\in\mathbb{N}$, we have

$$(2.11)\qquad \lim_{n\to\infty} T^{(n)}_{\tau_1}(f_1 T^{(n)}_{\tau_2}(\dots(f_{N-1}T^{(n)}_{\tau_N} f_N)\dots))(x)$$

$$= T_{\tau_1}(f_1 T_{\tau_2}(\dots(f_{N-1}T_{\tau_N} f_N)\dots))(x), \qquad x \in Q.$$

Remark 1)Since the conditions (2.9) and (2.10) are automatically satisfied in the case of $J(s)\cap J(m)\cap Q=\phi$, we use Theorem 2.1 in the later without mentioning them in that case.

2)The condition (2.9) does not seem to imply (2.10) in general. Indeed, in view of the relation

$$\int_{s^{-1}((b_1,b_2])} q\circ s_n(x)dm_n(x) = \int_{(b_1,b_2]} q(\xi)d\tilde{m}_n(\xi)$$

in Ogura (1989), we can not expect much information on (2.10) if a or b is the flat point of s_n or s.

Proof of Theorem 2.1. We will show (2.11) only for N=1. The outline of the proof is same as that in Ogura (1989). Indeed, as is shown there, (2.9) implies that $\lim_{n\to\infty}q_n(t,\xi,\eta)=q(t,\xi,\eta)$ uniformly in $\xi,\eta\in K$ for every compact set K in $\tilde{Q}$. Hence we have

$$\lim_{n\to\infty} \left|\int_Q q_n(t,s_n(x),s_n(y))f(y)dm_n(y) - \int_Q q(t,s_n(x),s_n(y))f(y)dm_n(y)\right| = 0.$$

Further, since $q(t,\xi,\eta)$ is uniformly continuous in $\xi,\eta\in K$, we have

$$\lim_{n\to\infty} \left|\int_Q q(t,s_n(x),s_n(y))f(y)dm_n(y) - \int_Q q(t,s(x),s_n(y))f(y)dm_n(y)\right| = 0.$$

Thus the assertion follows from the next Lemma. □

Lemma 2.1. Under the assumption of Theorem 2.1, it holds that

$$(2.12)\quad \lim_{n\to\infty} \int_Q q\circ s_n(x)f(x)dm_n(x)=\int_Q q\circ s(x)f(x)dm(x),\quad q\in C(\tilde{Q}),\quad f\in C_0(Q).$$

Proof. Denote the support of f by sppt(f) and fix an $\varepsilon>0$. Then, due to the uniform continuity of f, we can find a $0<\delta\le\varepsilon$ such that $|f(x)-f(y)|<\varepsilon$ for all $x,y\in\text{sppt}(f)$ with $|x-y|<2\delta$. Also we may assume that $|q(\xi)-q(\eta)|<\varepsilon$ for all $x,y\in\text{sppt}(f)$ with $|x-y|<2\delta$. Let $J_\delta(s)=\{x\in Q: s(x+)-s(x-)\geq\delta\}$. It then follows that

$$\lim_{n\to\infty}\sup\{|q\circ s_n(x)-q\circ s(x)|:x\in K\setminus J_\delta(s)\}\leq\varepsilon \quad \text{for compact } K\subset Q.$$

Denote $J_\delta(s)\cap\text{sppt}(f)=\{x_1<x_2<\cdots<x_k\}$ and let $U=\cup_{i=1}^k I_i$, $I_i=(a_i,b_i)$ where $\ell_1<a_1<x_1<b_1<\cdots<a_i<x_i<b_i<\cdots<x_k<b_k<\ell_2$, $x_i-a_i<\delta/2$, $b_i-x_i<\delta/2$ and all a_i and b_i are continuity point of s and m. We then divide the desired difference as

$$\int_Q q\circ s_n(x)f(x)dm_n(x)-\int_Q q\circ s(x)f(x)dm(x)$$

$$=\left(\int_U q\circ s_n(x)f(x)dm_n(x)-\int_U q\circ s(x)f(x)dm(x)\right)$$

$$+\left(\int_{Q\setminus U} q\circ s_n(x)f(x)dm_n(x)-\int_{Q\setminus U} q\circ s(x)f(x)dm(x)\right)\equiv I_n+II_n.$$

First of all,

$$II_n=\left(\int_{Q\setminus U} q\circ s_n(x)f(x)dm_n(x)-\int_{Q\setminus U} q\circ s(x)f(x)dm_n(x)\right)$$

$$+\left(\int_{Q\setminus U} q\circ s(x)f(x)dm_n(x)-\int_{Q\setminus U} q\circ s(x)f(x)dm(x)\right)\equiv III_n+IV_n,$$

and

$$\overline{\lim_{n\to\infty}}\,|III_n|\leq 2\varepsilon\|f\|_\infty\,\overline{\lim_{n\to\infty}}\,m_n(\text{sppt}(f)).$$

Further, it is easy to show that

$$\overline{\lim_{n\to\infty}}\,|IV_n|\leq 2\varepsilon\|f\|_\infty\,\overline{\lim_{n\to\infty}}\,m_n(\text{sppt}(f)),$$

since the integrand is continuous modulus $\varepsilon\|f\|_\infty$.

Further,

$$I_n=\sum_{i=1}^k\left(\int_{I_i} q\circ s_n(x)f(x)dm_n(x)-\int_{I_i} q\circ s(x)f(x)dm(x)\right)\equiv\sum_{i=1}^k I_n(i),$$

and

$$I_n(i) \le |\int_{I_i} q\circ s_n(x)(f(x)-f(x_i))dm_n(x)|$$

$$+ |f(x_i)(\int_{I_i} q\circ s_n(x)dm_n(x)- \int_{I_i} q\circ s(x)dm(x))|$$

$$+ |\int_{I_i} q\circ s(x)(f(x_i)-f(x))dm(x)|.$$

The first and the third term is dominated by $\varepsilon\sup\{|q\circ s_n(x)|:x\in I_i\}m_n(I_i)$ and $\varepsilon\sup\{|q\circ s(x)|:x\in I_i\}m(I_i)$ respectively. Further, from (2.10), the second term goes to zero as $n\to\infty$, so that

$$\overline{\lim_{n\to\infty}}\ |I_n| \le \varepsilon\ \sup\{|q\circ s(x)|:x\in \mathrm{sppt}(f)\}m(U).$$

Since $\varepsilon>0$ is arbitrary, we obtain (2.12). □

<u>Remark</u> In view of the above proof, (2.10) can be replaced with a weaker condition: for each $x\in J(s)\cap J(m)\cap Q$ and $\delta>0$ there exists an interval $I=(a,b)\subset Q$ such that $x-\delta<a<x<b<x+\delta$, $a,b \in (J(s)\cup J(m))^c\cap Q$ and (2.10) holds.

As is noted in Ogura (1989), Theorem 2.1 does not assure the convergence of the finite dimensional distributions, since $f_k\in C_0(Q)$ is assumed. However, it is not difficult to trace the proof there to obtain the next theorem.

Theorem 2.2. Under the assumption in Theorem 2.1, it holds that

$$\text{(2.13)}\quad \lim_{n\to\infty} P_x^{\cdot(n)}(x(t_1) > a_1,\dots,x(t_N) > a_N)$$

$$= P_x^{\cdot}(x(t_1) > a_1,\dots,x(t_N) > a_N),$$

for every $N\in\mathbb{N}$, $0 <t_1<t_2<\dots<t_N$, $a_1,a_2,\dots,a_N\in Q\setminus J(m)$ and $x\in Q$.

3. Population genetics models

Let $x^\varepsilon(t)$ be a ODDP on $[0,1]$ with the infinitesimal generator

$$\text{(3.1)}\quad L^\varepsilon = \tfrac{1}{2}a_\varepsilon(x)\frac{d^2}{dx^2} + b_\varepsilon(x)\frac{d}{dx},$$

where $a_\varepsilon(x)>0$ $(0<x<1)$, $a_\varepsilon(0)=a_\varepsilon(1)=0$ and $b_\varepsilon(0)\geq 0$, $b_\varepsilon(1)\leq 0$. The concrete functional form of $a_\varepsilon(x)$ and $b_\varepsilon(x)$ will be specified below in (3.10). The ODDP is uniquely determined by $a_\varepsilon(x)$, $b_\varepsilon(x)$ and the boundary conditions if they are necessary. If the boundary 0 or 1 is regular, then we assume the reflection boundary condition as is usually done in population genetics theory. For $a,b\in[0,1]$, we define

$$(3.2)\quad \begin{cases} I_-^\varepsilon(a,b) = \int_a^b e^{-B_\varepsilon(x)}dx \\ \\ I_+^\varepsilon(a,b) = \int_a^b \frac{2}{a_\varepsilon(x)}e^{B_\varepsilon(x)}dx \end{cases}$$

where $B_\varepsilon(x)=2\int\{b_\varepsilon(x)/a_\varepsilon(x)\}dx$, and

$$(3.3)\quad s^\varepsilon(x) = \begin{cases} I_-^\varepsilon(0,x)/I_-^\varepsilon(0,1) & (0\leq x\leq 1) \\ \\ x & (\text{otherwise}), \end{cases}$$

$$(3.4)\quad m^\varepsilon(x) = \begin{cases} 0 & (x\leq 0) \\ I_+^\varepsilon(0,x)I_-^\varepsilon(0,1) & (0\leq x\leq 1) \\ I_+^\varepsilon(0,1)I_-^\varepsilon(0,1) & (x\geq 1). \end{cases}$$

The $s^\varepsilon(x)$ and $m^\varepsilon(x)$ are the scale function and the speed measure of the ODDP $x^\varepsilon(t)$, respectively. The ODDP $x^\varepsilon(t)$ is uniquely determined by the pair $(s^\varepsilon(x),m^\varepsilon(x))$.

We introduce a time scaled process

$$(3.5)\quad X_\varepsilon(t) = x^\varepsilon(\lambda_\varepsilon t)$$

for $x^\varepsilon(t)$, where

$$(3.6)\quad \lambda_\varepsilon = I_-^\varepsilon(0,1)I_+^\varepsilon(0,1).$$

The $X_\varepsilon(t)$ is a ODDP with the scale function $s_\varepsilon(x)$, the speed measure $m_\varepsilon(x)$ and the infinitesimal generator L_ε

$$(3.7)\qquad s_\varepsilon(x) = s^\varepsilon(x)$$

$$(3.8)\qquad m_\varepsilon(x) = m^\varepsilon(x)/\lambda_\varepsilon = \begin{cases} 0 & (x \le 0) \\ I_+^\varepsilon(0,x)/I_+^\varepsilon(0,1) & (0 \le x \le 1) \\ 1 & (x \ge 1) \end{cases}$$

$$(3.9)\qquad L_\varepsilon = \lambda_\varepsilon L^\varepsilon.$$

In the following, we consider the functional form of

$$(3.10)\qquad \begin{cases} a_\varepsilon(x) = x(1 - x) + c\alpha_\varepsilon x^2(1 - x)^2 \\ \\ b_\varepsilon(x) = \alpha_\varepsilon x(1 - x)\{c\beta(1 - 2x) + (1 - c)g(x)\} + \theta_\varepsilon(1 - rx), \end{cases}$$

where $\beta, r \ge 1$, $c=0$ or $c=1$ and $\sup_{0\le x\le 1}|g(x)|<+\infty$. Let $G(x)$ be $G(x)=\int g(x)dx$ with $G(x)\ge 0$ $(0\le x\le 1)$. This functional form of (3.10) covers many models in population genetics as we see in the following. The population genetical meaning of the ODDP $x^\varepsilon(t)$ is the gene frequency of the allele A_1 in the population at time t. The $1-x^\varepsilon(t)$ is the gene frequency of the allele A_2 in the population at time t. Here, we are considering a diploid model with the two alleles, A_1 and A_2. The term $x(1-x)$ in $a_\varepsilon(x)$ denotes the effect of random sampling drift (random effect due to the finiteness of population size). The term $\theta_\varepsilon(1-rx)$ in $b_\varepsilon(x)$ denotes the effect of mutatiom. Let u (resp. v) be the mutation rate from A_2 (resp. A_1) to A_1 (resp. A_2). The parameter $r\ge 1$ is $r=1+v/u$. In the case of symmetric mutation $(u=v)$, $r=2$. In the case of one way mutation from A_2 to A_1, $r=1$. The parameter θ_ε corresponds to $2Nu$, where N is the (effective) size of population. The remaining terms in $a_\varepsilon(x)$ and $b_\varepsilon(x)$ denote the effect of selection. Let S be the order of selection. The parameter α_ε corresponds to $2NS$. The case of $c=1$ is stochastic selection. In the stochastic selection model, the case of $\beta>1$ is the SAS-CFF model proposed by Gillespie (1978). The case of

$\beta=1$ in the stochastic selection model is the TIM model proposed by Takahata *et al.* (1975). The case of $c=0$ is deterministic selection. Two typical examples of $g(x)$ are $g(x)=1$ (genic selection) and $g(x)=1-2x$ (overdominance).

The conjecture of Gillespie in §1 in the case of $K=2$ is to consider the limit of the sequence of ODDPs $\{x^{\varepsilon}(t)\}$ (after an appropriate time scaling) with $\alpha_\varepsilon\to+\infty$ and θ_ε 0. In this paper, we consider three cases including the above. (i) $\alpha_\varepsilon\to+\infty$ and $\theta_\varepsilon\to0$. (ii) $\alpha_\varepsilon\to\alpha(0<\alpha<+\infty)$ and $\theta_\varepsilon\to0$. (iii) $\alpha_\varepsilon\to0$ and $\theta_\varepsilon\to0$. These three limits are referred to as the strong selection - weak mutation limit (SSWM limit), the moderate selection - weak mutation limit and the weak selection - weak mutation limit, respectively. In the next section, we condider the following seven cases with the time scaling λ_ε introduced above. (1) $\alpha_\varepsilon\to\alpha$ $(0\le\alpha<+\infty)$, $\theta_\varepsilon\to0$, $c=0$. (2) $\alpha_\varepsilon\to+\infty$, $\theta_\varepsilon\to0$, $c=0$, $r=2$, $g(x)=1$. (3) $\alpha_\varepsilon\to+\infty$, $\theta_\varepsilon\to0$, $c=0$, $r=2$, $g(x)=1-2x$. (4) $\alpha_\varepsilon\to0$, $\theta_\varepsilon\to0$, $c=1$, $r=2$, $\beta\ge1$. (5) $\alpha_\varepsilon\to\alpha$ $(0<\alpha<+\infty)$, $\theta_\varepsilon\to0$, $c=1$, $r=2$, $\beta\ge1$. (6) $\alpha_\varepsilon\to+\infty$, $\theta_\varepsilon\to0$, $c=1$, $r=2$, $\beta>1$. (7) $\alpha_\varepsilon\to+\infty$, $\theta_\varepsilon\to0$, $c=1$, $r=2$, $\beta=1$. These seven cases are important examlpes in population genetics.

4. Results on population genetics models

We have the following results using the limit theorems in §2. Let $X_\varepsilon(t,x_0)$ be $X_\varepsilon(t)$ defined above with the initial condition $X_\varepsilon(0)=x_0$ where x_0 is a constant $(0\le x_0\le1)$.

(1) Deterministic selection, weak or moderate selection - weak mutation limit ($\alpha_\varepsilon\to\alpha$; $0\le\alpha<+\infty$, $\theta_\varepsilon\to0$, $c=0$)

For simplicity, we consider the case of $r\neq1$. Define $(s(x),m(x))$ by

$$(4.1)\qquad s(x) = \begin{cases} \int_0^x e^{-2\alpha G(y)}dy\Big/\int_0^1 e^{-2\alpha G(y)}dy & (0\le x\le 1) \end{cases}$$

$$\qquad x \qquad\qquad\qquad\qquad \text{(otherwise)}$$

$$(4.2) \qquad m(x) = \begin{cases} 0 & (x < 0) \\ \{1 + \frac{1}{r-1} e^{2\alpha[G(1)-G(0)]}\} & (0 \leq x < 1) \\ 1 & (x \geq 1), \end{cases}$$

where $G(x)$ is defined in the previous section. Then, we have $s_\varepsilon(x) \to s(x)$ for every x and $m_\varepsilon(x) \to m\ (x)$ for every x with $x \neq 0$. Further, for $r \neq 1$, we have

$$(4.3) \qquad \lambda_\varepsilon \sim \frac{1}{\theta_\varepsilon}\{e^{2\alpha G(0)} + \frac{1}{r-1} e^{2\alpha G(1)}\}\int_0^1 e^{-2\alpha G(y)}dy,$$

where $a_\varepsilon \sim b_\varepsilon$ means $a_\varepsilon / b_\varepsilon \to 1$ as $\varepsilon \to 0$. Note that $Q=(-\infty,+\infty)$, $J(s)=\phi$, $J(m)=\{0,1\}$ and $J(s) \cap J(m) \cap Q = \phi$. By Theorem 2.2, $\{X_\varepsilon(t,x_0)\}$ converges to a Markov jump process $X(t,x_0)$ for $t>0$ in the sense of the finite dimensional distributions, where

$$(4.4) \qquad \begin{cases} P(X(t,x_0) = 0) = \rho + (1 - \rho - x_0)\ e^{-t/\rho(1-\rho)} \\ \\ P(X(t,x_0) = 1) = 1 - P(X(t,x_0) = 0) \end{cases}$$

and $\rho = \{1 + \frac{1}{r-1} e^{2\alpha[G(1)-G(0)]}\}^{-1}$. The (4.4) is obtained by the method in §2.3.1. Note that $\lambda_\varepsilon \to +\infty$ by (4.3) and hence $L_\varepsilon = \lambda_\varepsilon L^\varepsilon$ does not have a finite limit. In this case, it is not necessary to put some specific relation between α_ε and θ_ε.

For simplicity, only the case of symmetric mutation (r=2) will be considered in the following.

(2) Deterministic genic selection, strong selection - weak mutation limit ($\alpha_\varepsilon \to +\infty$, $\theta_\varepsilon \to 0$, $c=0$, $g(x)=1$)

In this case, we assume that

$$(4.5) \qquad (\log \theta_\varepsilon)/\alpha_\varepsilon \to 0 \quad \text{as} \quad \varepsilon \to 0.$$

Note that (4.5) holds if $\alpha_\varepsilon\theta_\varepsilon=C$, $0<C<+\infty$. Let $(s(x),m(x))$ be

$$(4.6)\qquad s(x) = \begin{cases} 1 & (0 < x \le 1) \\ x & (\text{otherwise}) \end{cases}$$

$$(4.7)\qquad m(x) = \begin{cases} 0 & (x < 1) \\ 1 & (x \ge 1). \end{cases}$$

Under the condition of (4.5), $s_\varepsilon(x)\to s(x)$ for every x, $m_\varepsilon(x)\to m(x)$ for every x and

$$(4.8)\qquad \lambda_\varepsilon \sim e^{2\alpha_\varepsilon}/2\alpha_\varepsilon\theta_\varepsilon,$$

as $\varepsilon\to 0$. Note that $Q=(-\infty,+\infty)$, $J(s)=\{0\}$, $J(m)=\{1\}$ and $J(s)\cap J(m)\cap Q=\phi$. By Theorem 2.2, $\{X_\varepsilon(t,x_0)\}$ converges to $X(t,x_0)$ in the sense of the finite dimensional distributions, where

$$(4.9)\qquad P(X(t,x_0) = 1) = 1$$

and $t>0$.

(3) <u>Deterministic overdominance, strong selection - weak mutation limit</u> ($\alpha_\varepsilon\to+\infty$, $\theta_\varepsilon\to 0$, $c=0$, $g(x)=1-2x$)

In this case, we assume (4.5). Let $(s(x),m(x))$ be

$$(4.10)\qquad s(x) = \begin{cases} 1/2 & (0 < x < 1) \\ x & (\text{otherwise}) \end{cases}$$

$$(4.11)\qquad m(x) = \begin{cases} 0 & (x < 1/2) \\ 1 & (x \ge 1/2). \end{cases}$$

Under the condition of (4.5), $s_\varepsilon(x) \to s(x)$ for every x, $m_\varepsilon(x) \to m(x)$ for every $x \neq 1/2$ and

$$(4.12) \qquad \lambda_\varepsilon \sim 4\sqrt{2\pi}\ \alpha_\varepsilon^{2\theta_\varepsilon - 3/2}\ e^{\alpha_\varepsilon/2}$$

as $\varepsilon \to 0$. Note that $Q=(-\infty,+\infty)$, $J(s)=\{0,1\}$, $J(m)=\{1/2\}$ and $J(s) \cap J(m) \cap Q = \phi$. By Theorem 2.2, $\{X_\varepsilon(t,x_0)\}$ converges to $X(t,x_0)$ in the sense of the finite dimensional distributions, where

$$(4.13) \qquad P(X(t,x_0) = 1/2) = 1$$

and $t>0$.

(4) Stochastic selection, weak selection - weak mutation limit

($\alpha_\varepsilon \to 0$, $\theta_\varepsilon \to 0$, $c=1$, $\beta \geq 1$)

Let $(s(x), m(x))$ be

$$(4.14) \qquad s(x) = x$$

$$(4.15) \qquad m(x) = \begin{cases} 0 & (x < 0) \\ 1/2 & (0 \leq x < 1) \\ 1 & (x \geq 1) \end{cases}$$

Then, $s_\varepsilon(x) \to s(x)$ for every x, $m_\varepsilon(x) \to m(x)$ for every $x \neq 0$ and

$$(4.16) \qquad \lambda_\varepsilon \sim 2/\theta_\varepsilon^{\,2}$$

as $\varepsilon \to 0$. Note that $Q=(-\infty,+\infty)$, $J(s)=\phi$, $J(m)=\{0,1\}$ and $J(s) \cap J(m) \cap Q = \phi$. By Theorem 2.2, $\{X_\varepsilon(t,x_0)\}$ converges to a Markov jump process $X(t,x_0)$ in the sense of the finite dimensional distributions, where

$$(4.17) \qquad \begin{cases} P(X(t,x_0) = 0) = \{1 + (1 - 2x_0)e^{-4t}\}/2 \\ \\ P(X(t,x_0) = 1) = 1 - P(X(t,x_0) = 0) \end{cases}$$

and $t>0$.

(5) Stochastic selection, moderate selection - weak mutation limit

$(\alpha_\varepsilon \to \alpha;\ 0<\alpha<+\infty,\ \theta_\varepsilon \to 0,\ c=1,\ \beta \ge 1)$

Let $(s(x), m(x))$ be

$$(4.18)\qquad s(x) = \begin{cases} \int_0^x \{\alpha y(1-y)+1\}^{-\beta} dy \Big/ \int_0^1 \{\alpha y(1-y)+1\}^{-\beta} dy & (0 \le x \le 1) \\ x & (\text{otherwise}) \end{cases}$$

$$(4.19)\qquad m(x) = \begin{cases} 0 & (x < 0) \\ 1/2 & (0 \le x < 1) \\ 1 & (x \ge 1). \end{cases}$$

Then, $s_\varepsilon(x) \to s(x)$ for every x, $m_\varepsilon(x) \to m(x)$ for every $x \ne 0$ and

$$(4.20)\qquad \lambda_\varepsilon \sim 2\int_0^1 \{\alpha y(1-y)+1\}^{-\beta} dy/\theta_\varepsilon$$

as $\varepsilon \to 0$. Note that $Q=(-\infty,+\infty)$, $J(s)=\phi$, $J(m)=\{0,1\}$ and $J(s)\cap J(m)\cap Q=\phi$. By Theorem 2.2, $\{X_\varepsilon(t,x_0)\}$ converges to a Markov jump process $X(t,x_0)$ in the sense of the finite dimensional distributions, where

$$(4.21)\qquad \begin{cases} P(X(t,x_0) = 0) = \{1 + (1-2x_0)e^{-4t}\}/2 \\ P(X(t,x_0) = 1) = 1 - P(X(t,x_0) = 0) \end{cases}$$

and $t>0$.

(6) Stochastic selection, SAS-CFF model, strong selection - weak mutation limit $(\alpha_\varepsilon \to +\infty,\ \theta_\varepsilon \to 0,\ c=1,\ \beta>1)$

In this case, we assume that

$$(4.22)\qquad (\log \theta_\varepsilon)/(\log \alpha_\varepsilon) \to 0 \quad \text{as} \quad \varepsilon \to 0.$$

Note that (4.22) is equivalent to

(4.23) $\alpha_\varepsilon{}^b\theta_\varepsilon \to +\infty$ as $\varepsilon \to 0$, for every $b > 0$.

The condition (4.23), hence (4.22) holds if $\theta_\varepsilon \log \alpha_\varepsilon = C$, $0<C<+\infty$. Let $(s(x),m(x))$ be

$$(4.24) \quad s(x) = \begin{cases} 1/2 & (0 < x < 1) \\ x & (\text{otherwise}) \end{cases}$$

$$(4.25) \quad m(x) = \begin{cases} 0 & (x \le 0) \\ \int_0^x \{y(1-y)\}^{\beta-2}dy \,/\, \int_0^1 \{y(1-y)\}^{\beta-2}dy & (0\le x\le 1) \\ 1 & (x \ge 1). \end{cases}$$

Under the condition of (4.22), $s_\varepsilon(x)\to s(x)$ for every x, $m_\varepsilon(x)\to m(x)$ for every x and

$$(4.26) \quad \lambda_\varepsilon \sim \frac{4}{\beta - 1}\, \alpha_\varepsilon{}^{\beta-2}\int_0^1 \{y(1-y)\}^{\beta-2}dy$$

as $\varepsilon\to 0$. Note that $Q=(-\infty,+\infty)$, $J(s)=\{0,1\}$, $J(m)=\phi$ and $J(s)\cap J(m)\cap Q=\phi$. By Theorem 2.2, $\{X_\varepsilon(t,x_0)\}$ converges to $X(t,x_0)$ in the sense of the finite dimensional distributions, where

$$(4.27) \quad P(X(t,x_0) \in A) = \int_A dm(y) = \int_A \{y(1-y)\}^{\beta-2}dy \,/\, \int_0^1 \{y(1-y)\}^{\beta-2}dy,$$

$A\subset[0,1]$ and $t>0$.

<u>(7) Stochastic selection, TIM model, strong selection - weak mutation limit</u> ($\alpha_\varepsilon\to+\infty$, $\theta_\varepsilon\to 0$, $c=1$, $\beta=1$)

In this case, we assume that

(4.28) $\theta_\varepsilon \log \alpha_\varepsilon \to 0$ as $\varepsilon \to 0$.

The condition (4.28) holds if $\alpha_\varepsilon\theta_\varepsilon = C$, $0<C<+\infty$. Let $(s(x),m(x))$ be

$$(4.29) \qquad s(x) = \begin{cases} 1/2 & (0 < x < 1) \\ x & (\text{otherwise}) \end{cases}$$

$$(4.30) \qquad m(x) = \begin{cases} 0 & (x < 0) \\ 1/2 & (0 \le x < 1) \\ 1 & (x \ge 1). \end{cases}$$

Under the condition of (4.28), $s_\varepsilon(x) \to s(x)$ for every x, $m_\varepsilon(x) \to m(x)$ for every $x \neq 0$, $\tilde{m}_\varepsilon(x) \to \tilde{m}(x)$ for $x \in R \setminus J(\tilde{m})$, (2.10) holds and

$$(4.31) \qquad \lambda_\varepsilon \sim \frac{4 \log \alpha_\varepsilon}{\alpha_\varepsilon \theta_\varepsilon}$$

as $\varepsilon \to 0$. Note that $Q=(-\infty,+\infty)$, $J(s)=J(m)=\{0,1\}$ and $J(s) \cap J(m) \cap Q = \{0,1\}$. By Theorem 2.2, $\{X_\varepsilon(t,x_0)\}$ converges to a Markov jump process $X(t,x_0)$ in the sense of the finite dimensional distributions, where

$$(4.32) \qquad \begin{cases} P((X(t,x_0) = 0) = \{1 + (1 - 2x_0)e^{-4t}\}/2 \\ P(X(t,x_0) = 1) = 1 - P(X(t,x_0) = 0) \end{cases}$$

and $t>0$.

5. Other time scalings for population genetics models

In the case of strong selection - weak mutation limit for the deterninistic genic or overdominance selection (the case (2) and (3) in the previous section), the limit process $X(t)$ is trivial since this process is traped at some point instanteniously. The conjecture of Gillespie, however, imlpies that the limit process stays at boundary points with finite holding time then jumps to some trap point. In this section, we will obtain the limit processes with finite holding time at the boundary. The reason why the limit prcesses in the previous section move to the trap point instantinuously is that the time scaling $\lambda_\varepsilon = I_-^\varepsilon(0,1)I_+^\varepsilon(0,1)$ tends to infinity too fast as $\varepsilon \to 0$. In this section, we will introduce a time scaling τ_ε that tends to infinity but slower than λ_ε.

Let $x^\varepsilon(t)$ be the ODDP in the previous section. We define a new time scaling $\tau_\varepsilon = \tau_\varepsilon(\delta)$ by

$$(5.1) \qquad \tau_\varepsilon = \tau_\varepsilon(\delta) = I_-^\varepsilon(0,1)I_+^\varepsilon(0,\delta),$$

for $0<\delta\le 1$. The time scaled process for $x^\varepsilon(t)$ by τ_ε is

$$(5.2) \qquad Y_\varepsilon(t) = x^\varepsilon(\tau_\varepsilon t).$$

The infinitesimal generator, the scale function and the speed measure are denoted by L_ε, $s_\varepsilon(x)$ and $m_\varepsilon(x)$ again. Then

$$(5.3) \qquad L_\varepsilon = \tau_\varepsilon L^\varepsilon = \tau_\varepsilon\{\tfrac{1}{2}a_\varepsilon(x)\frac{d^2}{dx^2} + b_\varepsilon(x)\frac{d}{dx}\}$$

$$(5.4) \qquad s_\varepsilon(x) = \begin{cases} I_-^\varepsilon(0,x)/I_-^\varepsilon(0,1) & (0 \le x \le 1) \\ x & (\text{otherwise}) \end{cases}$$

$$(5.5) \qquad m_\varepsilon(x) = \begin{cases} 0 & (x \le 0) \\ I_+^\varepsilon(0,x)/I_+^\varepsilon(0,\delta) & (0 \le x \le 1) \\ I_+^\varepsilon(0,1)/I_+^\varepsilon(0,\delta) & (x \ge 1) \end{cases}$$

We have the following results. We consider the case of symmetric mutation (r=2) for simplicity.

<u>(8) Deterministic genic selection, strong selection - weak mutation limit</u> ($\alpha_\varepsilon \to +\infty$, $\theta_\varepsilon \to 0$, $c=0$, $g(x)=1$)

In this case, we fix a δ $(0<\delta<1)$ and assume that

$$(5.6) \qquad \lim_{\varepsilon \downarrow 0} \frac{\log \theta_\varepsilon}{\alpha_\varepsilon} \le -2.$$

The condition (5.6) holds if $\theta_\varepsilon e^{2\alpha_\varepsilon} = C$, $0<C<+\infty$. Let $(s(x), m(x))$ be

$$(5.7) \qquad s(x) = \begin{cases} 1 & (0 < x \le 1) \\ x & (\text{otherwise}) \end{cases}$$

$$(5.8) \qquad m(x) = \begin{cases} 0 & (x < 0) \\ 1 & (0 \le x < 1) \\ +\infty & (x \ge 1). \end{cases}$$

Under the condition of (5.6), $s_\varepsilon(x) \to s(x)$ for every x, $m_\varepsilon(x) \to m(x)$ for every $x \ne 0$, $\tilde{m}_\varepsilon(x) \to \tilde{m}(x)$ for $x \in R \setminus J(\tilde{m})$, (2.10) holds and

$$(5.9) \qquad \tau_\varepsilon = \tau_\varepsilon(\delta) \sim \alpha_\varepsilon^{2\theta_\varepsilon - 1}/2\theta_\varepsilon$$

as $\varepsilon \to 0$. Note that $Q=(-\infty, 1]$, $J(s)=\{0\}$, $J(m)=\{0,1\}$ and $J(s) \cap J(m) \cap Q = \{0\}$. By Theorem 2.2, $\{Y_\varepsilon(t, x_0)\}$ converges to a Markov jump process $Y(t, x_0)$ in the sense of the finite dimensional distributions, where $Y_\varepsilon(t, x_0)$ (resp. $Y(t, x_0)$) is the process $Y_\varepsilon(t)$ (resp. $Y(t)$) with $Y_\varepsilon(0) = x_0$ (resp. $Y(t) = x_0$) and

$$(5.10) \qquad \begin{cases} P(Y(t,0) = 0) = e^{-t} \\ P(Y(t,0) = 1) = 1 - e^{-t} \end{cases}$$

$$(5.11) \qquad P(Y(t, x_0) = 1) = 1 \qquad (0 < x_0 \le 1)$$

for $t>0$.

(9) Deterministic overdominance, strong selection - weak mutation limit

$(\alpha_\varepsilon \to +\infty,\ \theta_\varepsilon \to 0,\ c=0,\ g(x)=1-2x)$

In this case, we fix a δ $(0<\delta<1/2)$ and assume that

$$(5.12) \qquad \lim_{\varepsilon \downarrow 0} \frac{\log \theta_\varepsilon}{\alpha_\varepsilon} \le -1/8 \quad \text{and} \quad \theta_\varepsilon e^{\alpha_\varepsilon/2}/\sqrt{\alpha_\varepsilon} \to +\infty \quad \text{as} \quad \varepsilon \to 0.$$

Note that the first condition in (5.12) is equivalent to

$$(5.13)\qquad \theta_\varepsilon e^{\alpha_\varepsilon b} \to 0 \quad \text{as} \quad \varepsilon \to 0 \quad \text{for every} \quad b < 1/8,$$

and (5.12) holds if $\theta_\varepsilon = C\alpha_\varepsilon e^{-\alpha_\varepsilon/8}$, $0<C<+\infty$. Consider x_0 with $0 \le x_0 < 1/2$ for a while. Let $(s(x),m(x))$ be

$$(5.14)\qquad s(x) = \begin{cases} 1/2 & (0 < x < 1) \\ x & (\text{otherwise}) \end{cases}$$

$$(5.15)\qquad m(x) = \begin{cases} 0 & (x < 0) \\ 1 & (0 \le x < 1/2) \\ +\infty & (x \ge 1/2) \end{cases}$$

Under the condition of (5.12), $s_\varepsilon(x) \to s(x)$ for every x, $m_\varepsilon(x) \to m(x)$ for every $x \ne 0$, $\tilde{m}_\varepsilon(x) \to \tilde{m}(x)$, (2.10) holds and

$$(5.16)\qquad \tau_\varepsilon \sim \alpha_\varepsilon^{2\theta_\varepsilon - 1}/\theta_\varepsilon$$

as $\varepsilon \to 0$. Note that $Q=(-\infty,1/2]$, $J(s)=\{0,1\}$, $J(m)=\{0,1/2\}$ and $J(s)\cap J(m)\cap Q=\{0\}$. By Theorem 2.2, $\{Y_\varepsilon(t,x_0)\}$ converges to a Markov jump process $Y(t,x_0)$ in the sense of the convergence of the finite dimensional distributions, where

$$(5.17)\qquad \begin{cases} P(Y(t,0) = 0) = e^{-2t} \\ P(Y(t,0) \in [1/2,1]) = 1 - e^{-2t} \end{cases}$$

$$(5.18)\qquad P(Y(t,x_0) \in [1/2,1]) = 1 \qquad (0 < x_0 < 1/2)$$

for $t>0$. Now, we consider x_0 with $0 \le x_0 \le 1$. By the symmetry at $x=1/2$, $\{Y_\varepsilon(t,x_0)\}$ converges to $Y(t,x_0)$ in the sense of the finite dimensional distributions, where

$$(5.19)\quad \begin{cases} P(Y(t,0) = 0) = e^{-2t} \\ P(Y(t,0) = 1/2) = 1 - e^{-2t} \end{cases}$$

$$(5.20)\quad P(Y(t,x_0) = 1/2) = 1 \qquad (0 < x_0 < 1)$$

$$(5.21)\quad \begin{cases} P(Y(t,1) = 1) = e^{-2t} \\ P(Y(t,1) = 1/2) = 1 - e^{-2t} \end{cases}$$

for $t>0$.

6. Discussion

The natural candidate for the time scaling is that of (3.5) with which the normalization $s_\varepsilon(0) = m_\varepsilon(0) = 0$ and $s_\varepsilon(1) = m_\varepsilon(1) = 1$ holds. This time scaling is used in §4. First, we consider the weak selection - weak mutation limit (see the case (1) and the case (4)). In this case, random sampling drift due to the finite population size predominates over the effect of selection and mutation. The limits are Markov chains with state space $\{0,1\}$, that is, the monomorphic states due to random sampling drift. In the moderate selection - weak mutation limit, the results are very similar to those of weak selection - weak mutation limit (see the case (1) and the case (5)). The reason is that the effect of mutation is very weak in these cases and random sampling drift predominates over selection in the neighborhood of 0 and 1. The effect of moderate selection can be seen only on the time scaling (4.3), (4.20) and ρ in (4.4).

Next, we consider the strong selection - weak mutatiom limit which corresponds to the conjecture of Gillespie. First, we consider the stochastic selection models. In the SAS-CFF model (see the case (6)), the limit is the stationary distribution for the pure stochastic selection model without random sampling drift and mutation. This result is consistent with the conjecture of Gillespie (see §1). Since there is a unique stationary distribution in this case, the state space of the limit is stationary distribution valued but with no jumps. In the TIM model (see the case (7)), the limit is a Markov chain with the state space {0,1}. This result is consistent with the following fact. In the pure TIM model without random sampling drift and mutation, there is no non-trivial stationary distributions and the quasi fixation will occur as t → +∞. The limit process jumps between two trivial stationary points 0 and 1. The results on deterministic selection models, however, are not consistent with the conjecture of Gillespie (see the case (2) and (3)). In the limit, these processes go to some trapped point instanteniously. This trivial results are due to the incorrect choise of the time scaling in these cases. In §5, we have introduced an appropriate time scaling for which non-trivial results are obtained (see the case (8) and (9)). The results for the case (8) and (9) are very consistent with the conjecture. The state space of the limit is stationary points for the ordinary differential equation that describes the pure deterministic selection model without random sampling drift and mutation. The limit process goes to the unique stable stationary point for the ordinary differential equation as t → +∞.

As we have seen in the above, we have proved the conjecture of Gillespie. The convergence is that of the sense of the finite dimensional distributions. We have identifed the limit processes, the appropriate time scaling and the relation between α_ε and θ_ε. We have applied the notion of bi-generalized diffusion processes and their limit theorems systematically. Our method is effective not only for the present problem but also for many models that are described by diffusion equation (for examlpe, a quantitative genetics model in Newman *et al.* (1985)) as far as the model is one-dimensional. For the multidimensional cases, our method is not applicable since the notion of bi-generalized diffusion processes is just for one-dimensional stochastic processes and the proof of the conjecture of Gillespie for the multidimensional cases is an open problem.

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References

Billingsley,P.:Convergence of Probability Measures. New York: Wiley 1968

Crow,J.F.,Kimura,M.:An Introduction to Population Genetics Theory. New York: Harper and Row 1970

Ewen,W.J.:Mathematical Population Genetics. Berlin Heidelberg New York: Springer 1979

Feller,W.:The birth and death processes as diffusion processes. J. Math. Pures Appl., **38**, 301-345 (1959)

Freidlin,M.I.,Wentzel,A.D.:Random Perturbations of Dynamical Systems. Berlin Heidelberg New York: Springer 1984

Gillespie,J.H.:A general model to account for enzyme variation in natural population, V. The SAS-CFF model. Theor. Population Biology, **14**, 1-45 (1978)

Gillespie,J.H.:Some properties of finite populations experiencing strong selection and weak mutation. The American Naturalist, **121**, 691-708 (1983a)

Gillespie,J.H.:A simple stochastic gene substitution model. Theor. Population Biology, **23**, 202-215 (1983b)

Gillespie,J.H.:Molecular evolution and polymorphism: SAS-CFF meets the mutational landscape, The American Naturalist, **134**, 638-658 (1989)

Iizuka,M.:Weak convergence of a sequence of stochastic difference equations to a stochastic ordinary differential equation. J. Math. Biol., **25**, 643-652 (1987)

Iizuka,M.,Matsuda,H.:Weak convergence of discrete time non-Markovian processes related to selecion models in population genetics. J. Math. Biol., **15**, 107-127 (1982)

Kipnis,K., Newman,C.M.:The metastable behavior of infrequently observed random, one-dimensional diffusion processes. SIAM J. Appl. Math., **45**, 972-982 (1985)

Kurtz,T.G.:Semigroups of conditioned shift and approximation of Markov processes. Ann. Probability, **3**, 618-642 (1975)

Minami,N.,Ogura,Y.,Tomisaki,M.:Asymptotic behavior of elementary solutions of one-dimensional generalized diffusion equations. Ann. Probability, **13**, 698-715 (1985)

Newman,C.M.,Cohen,J.E.,Kipnis,C.:Neo-darwinian evolution implies punctuated equilibria. Nature, **315**, 400-401 (1985)

Ogura,Y.:One-dimensional bi-generalized diffusion processes. J. Math. Soc. Japan, **41**, 213-242 (1989)

Stroock,D.W.,Varadhan,S.R.S.:Multidimensional Diffusion Processes. Berlin Heidelberg New York: Springer 1979

Takahata,N.,Ishii,K.,Matsuda,H.:Effect of temporal fluctuation of selection coefficient on gene frequency in a population. Proc. Nat. Acad. Sci. USA, **72**, 4541-4545 (1975)

Watanabe,S.:On time inversion of one-dimensional diffusion processes. Z. Wahrsch. verw. Gebiete, **31**, 115-124 (1975)

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