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Pliska Stud. Math. Bulgar. **22** (2013), 57–70

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SUPERCRITICAL MARKOV BRANCHING PROCESSES WITH NON-HOMOGENEOUS POISSON IMMIGRATION

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Abstract. The paper proposes an extension of Sevastyanov (1957) model allowing an immigration in the moments of a homogeneous Poisson process. Markov branching processes with time-nonhomogeneous Poisson immigration are considered as models in cell proliferation kinetics and limit theorems are proved in the supercritical case. Some of the limiting results can be interpreted as generalizations of the classical result of Sevastyanov (1957) and new effects are obtained due to the non-homogeneity.

1. Introduction. The first model of branching process with immigration was proposed by Sevastyanov (1957). He investigated a Markov branching process admitted an immigration component in the moments of a homogeneous Poisson process.

One of the goals of this paper concerns modeling of renewing cell population. The considered models are based on Markov branching processes allowing immigration in the moments of time-nonhomogeneous Poisson component. For a comprehensive review of branching processes and their biological applications, the reader is referred to Harris (1963), Sevastyanov (1971), Athreya and Ney (1972), Jagers (1975), Yakovlev and Yanev (1989), Kimmel and Axelrod (2002), and Haccou et al. (2005). Some problems of biological models using branching processes with nonhomogeneous Poisson immigration are considered in Yakovlev and Yanev (2006, 2007) and Hyrien and Yanev (2010, 2012).

2010 *Mathematics Subject Classification:* 60J80
Key words: Branching processes, Immigration, Poisson process, Limit theorems

The paper is organized as follows. In Section 2 the biological background and motivation are proposed which gives the general ideas for constructing the corresponding models in Section 3. The basic equations for the p.g.f. and the moments are considered also in Section 3. The asymptotic behavior for the means, variances and covariances of the supercritical processes with immigration is investigated in Section 4 and limit theorems are also proved. The limiting results in Theorems 1 and 2 can be considered as generalizations of the classical result of Sevastyanov (1957) while in Theorems 3 and 4 new effects are obtained due to the non-homogeneity.

2. Biological background and motivation. Recent advances in experimental techniques of flow cytometry have made it possible to collect a wealth of information about the status of individual cells isolated from dissociated tissues.

- The process begins at time zero with N_0 cells. When one is interested in modeling tissue development starting from the earliest embryonic stages it is reasonable to set $N_0 = 0$ because these cells appear only in the course of embryogenesis.
- New type cells (immigrants) of age zero arrive in the population of cells in accordance with a non-homogeneous Poisson process with arrival rate $r(t)$. Upon arrival, these immigrants are assumed to be of age zero.
- Upon completion of its lifespan, every cell either divides into two new cells, or it goes out of the process of proliferation (differentiation or death). These two events occur with probability p and $q = 1 - p$, respectively.
- The time to division or differentiation of any cell is described by a non-negative random variable τ with cumulative distribution function (c.d.f.) $G(x) = \mathbf{P}\{\eta \le x\}$ that satisfies $G(0) = 0$.
- Cells are assumed to evolve independently of each other.

Motivated by the above example, we investigate properties of a class of Markov branching processes with non-homogeneous Poisson immigration. We consider a more general process than the one presented above so that the scope of our work does not remain limited to the study of oligodendrocyte generation.

3. Models and Equations. We consider cell populations (*in vivo)* which proliferation kinetics can de describe as follows. The process begins with immigration of stem cells which appear at the moments of immigration as *progenitors* at zero age. Then every cell has a life-time c.d.f. $G(t) = \mathbf{P}\{\eta \le t\} = 1 - e^{-t/\mu}, t \ge 0$, and at the end of its mitotic cycle η produces an offspring ξ with a p.g.f. $h(s) =$

$\mathbf{E}[s^{\xi}]$, $|s| \leq 1$. We assume that all new born cells are at zero age and continue their evolutions independently and in the same way. Therefore the development of this population can be described in the framework of an Markov branching process with immigration.

The offspring moments

$$m = \mathbf{E}[\xi] = \left.\frac{dh(s)}{ds}\right|_{s=1} \quad \text{and} \quad m_2 = \mathbf{E}[\xi(\xi-1)] = \left.\frac{d^2h(s)}{ds^2}\right|_{s=1}$$

play further an important role as well as the life-span mean $\mu = \int_0^{\infty} x dG(x)$, assuming that all these characteristics are finite.

The models with an offspring p.g.f. $h(s) = 1 - p + ps^2$, $m = 2p = m_2$, are very interesting from biological point of view. It means that at the end of the mitotic cycle every cell can die with probability $1-p$ or it can divide in two cells with probability p. This example may be treated more carefully but now we will investigate the general case.

Let first consider the process without immigration $Z(t)$ (which denotes the number of cells at the moment t) and introduce the corresponding p.g.f. $F(t;s) = E\{s^{Z(t)}|Z(0) = 1\}$. Under the assumptions, it is not difficult to realized that $\{Z(t), t \geq 0\}$ can be considered as Markov branching process well determined by the following nonlinear differential equation:

$$\frac{\partial F(t;s)}{\partial t} = f(F(t;s)), \quad F(0;s) = s, \tag{1}$$

where $f(s) = [h(s) - s]/\mu$ (see e.g. Harris (1963)).

Note that the Malthusian parameter α is determined as usually from the equation $m\int\limits_0^{\infty} e^{-\alpha x} dG(x) = 1$ and in the considered case $\alpha = f'(1) = [m - 1]/\mu$. Introduce also $\beta = f''(1) = m_2/\mu$. Further on we will consider only the supercritical case $\alpha > 0$. Then for corresponding moments one has (see e.g. Harris (1963)):

$$A(t) = \left.\frac{\partial F(t;s)}{\partial s}\right|_{s=1} = \mathbf{E}[Z(t)|Z(0) = 1] = e^{\alpha t}, \tag{2}$$

$$B(t) = \left.\frac{\partial^2 F(t;s)}{\partial s^2}\right|_{s=1} = \mathbf{E}[Z(t)(Z(t)-1)|Z(0) = 1] = \frac{\beta(e^{2\alpha t} - e^{\alpha t})}{\alpha},$$

$$V(t) = Var[Z(t)] = (\beta/\alpha - 1)e^{\alpha t}(e^{\alpha t} - 1). \tag{3}$$

Let now describe the process with immigration. First we will assume that $0 = S_0 < S_1 < S_2 < S_3 < \cdots$ are the time-points of the immigration which form a **non-homogeneous Poisson process** $\Pi(t)$ with a rate $r(t)$, *i.e.* the cumulative rate is $R(t) = \int_0^t r(u)du$, $r(t) \geq 0$, and $\Pi(t) \in Po(R(t))$. Let $U_i = S_i - S_{i-1}$ be the inter-arrival times. Then $S_k = \sum_{i=1}^{k} U_i$, $k = 1, 2, \ldots$.

We will assume also that at every point S_k there is an independent immigration component I_k of cells at zero age, where $\{I_k\}$ are i.i.d. r.v. with the p.g.f. $g(s) = \mathbf{E}[s^{I_k}] = \sum_{i=0}^{\infty} g_i s^i$, $|s| \leq 1$. Let $\gamma = \mathbf{E}[I_k] = \left.\frac{dg(s)}{ds}\right|_{s=1}$ be the immigration mean and introduce the second factorial moment $\gamma_2 = \left.\frac{d^2 g(s)}{ds^2}\right|_{s=1} = \mathbf{E}[I_k(I_k - 1)]$.

Let now $Y(t)$ be the number of cells at the moment t in the process with immigration, where the cell evolution is determined by an (G, h) - Markov branching processes defined above. Then the considered process admits the following representation

$$Y(t) = \begin{cases} \sum_{k=1}^{\Pi(t)} Z^{I_k}(t - S_k), & \text{if } \Pi(t) > 0, \\ Y(t) = 0, & \text{if } \Pi(t) = 0, \end{cases} \tag{4}$$

where $Z^{I_k}(t)$ are i.i.d. branching processes with a given evolution of the cells as $Z(t)$ but started with a random number of ancestors I_k. It is assuming $Y(0) = 0$, but in fact, the process $Y(t)$ begins from the first non-zero immigrants.

Introduce the p.g.f. $\Psi(t; s) = \mathbf{E}[s^{Y(t)} | Y(0) = 0]$. Using (4) Yakovlev and Yanev (2007, Theorem 1) obtained that

$$\Psi(t; s) = \exp\left\{-\int_0^t r(t-u)[1 - g(F(u; s))]du\right\}, \quad \Psi(0, s) = 1, \tag{5}$$

where in our case the p.g.f. $F(u; s)$ satisfies equation (1).

One has to point out that $\{Y(t), t \geq 0\}$ is a time non-homogeneous Markov process. Remark that if $\{U_i\}$ are i.i.d. r.v. with c.d.f. $G_0(x) = \mathbf{P}\{U_i \leq x\} = 1 - e^{-rx}$, $x \geq 0$, then $\Pi(t)$ reduces to an ordinary Poisson process with a cumulative rate $R(t) = rt$ and we obtain the first model with immigration proposed and investigated by Sevastyanov (1957).

Introduce the moments of the process with immigration

$$M(t) = \mathbf{E}[Y(t) | Y(0) = 0] = \left.\frac{\partial \Psi(t; s)}{\partial s}\right|_{s=1},$$

$$M_2(t) = \mathbf{E}[Y(t)(Y(t)-1)|Y(0)=0] = \left.\frac{\partial^2 \Psi(t;s)}{\partial s^2}\right|_{s=1},$$
$$W(t) = Var[Y(t)] = M_2(t) + M(t)(1-M(t)).$$

Then from (5) it is not difficult to obtain that

$$(6) \qquad \begin{aligned} M(t) &= \gamma \int_0^t r(t-u)A(u)du, \\ M_2(t) &= \gamma \int_0^t r(t-u)B(u)du \\ &+ [\gamma \int_0^t r(t-u)A(u)du]^2 + \gamma_2 \int_0^t r(t-u)A^2(u)du, \end{aligned}$$

$$(7) \qquad W(t) = \int_0^t r(t-u)[\gamma V(u) + (\gamma+\gamma_2)A^2(u)]du.$$

To derive also equations for the covariances we have to consider first the joint p.g.f. $F(s_1, s_2; t, \tau) = \mathbf{E}[s_1^{Z(t)} s_2^{Z(t+\tau)}|Z(0)=1]$, $\tau \geq 0$. Conditioning on the evolution of the initial cell and applying the law of the total probability one can obtain the equation:

$$(8) \quad \begin{aligned} F(s_1, s_2; t, \tau) &= \int_0^t h(F(s_1, s_2; t-u, \tau))dG(u) \\ &+ s_1 \int_t^{t+\tau} h(F(1, s_2; t, \tau - v))dG(v) + s_1 s_2 (1 - G(t+\tau)), \end{aligned}$$

with the initial condition $F(s_1, s_2; 0, 0) = s_1 s_2$ (see also Harris(1963)).

Let now introduce the joint p.g.f. for the process with immigration $Y(t)$ defined by (4)

$$\Psi(s_1, s_2; t, \tau) = \mathbf{E}[s_1^{Y(t)} s_2^{Y(t+\tau)}|Y(0)=0], \ \tau \geq 0.$$

Similarly to (5) one can obtain that

$$(9) \qquad \begin{aligned} &\Psi(s_1, s_2; t, \tau) \\ &\quad = \exp\{-\int_0^t r(u)[1 - g(F(s_1, s_2; t-u, \tau))]du \\ &\quad - \int_t^{t+\tau} r(v)[1 - g(F(1, s_2; t, \tau - v))]dv\}. \end{aligned}$$

For the proof one have to consider definition (4) and to follow the method developed in Theorem 1 (Yakovlev and Yanev(2007)) for (5). Introduce the moments

$$A(t,\tau) = \mathbf{E}[Z(t)Z(t+\tau) \mid Z(0)=1] = \left.\frac{\partial^2 F(s_1,s_2;t,\tau)}{\partial s_1 \partial s_2}\right|_{s_1=s_2=1},$$

$$M(t,\tau) = \mathbf{E}[Y(t)Y(t+\tau) \mid Y(0)=0] = \left.\frac{\partial^2 \Psi(s_1,s_2;t,\tau)}{\partial s_i \partial s_j}\right|_{s_1=s_2=1}.$$

Then from (8) and (9) the following equations hold

$$\text{(10)}\quad \begin{aligned} A(t,\tau) &= m\int_0^t A(t-u,\tau)dG(u) + m_2\int_0^t A(t-u)A(t+\tau-u)dG(u) \\ &+ m\int_t^{t+\tau} A(t+\tau-u)dG(u) + 1 - G(t+\tau), \end{aligned}$$

$$\text{(11)}\quad \begin{aligned} M(t,\tau) &= \int_0^t r(u)[\gamma A(t-u,\tau) + \gamma_2 A^2(t-u)]du \\ &+ \gamma^2[\int_0^t r(u)A(t-u)]du]^2, \end{aligned}$$

$$\text{(12)}\quad \begin{aligned} C(t,\tau) &= Cov[Y(t),Y(t+\tau)] = \left.\frac{\partial^2 \log\Psi(s_1,s_2;t,\tau)}{\partial s_i \partial s_j}\right|_{s_1=s_2=1} \\ &= \int_0^t r(u)[\gamma A(t-u,\tau) + \gamma_2 A(t-u)A(t+\tau-u)]du, \end{aligned}$$

with initial conditions $A(0,\tau) = A(\tau)$ and $M(0,\tau) = 0 = C(0,\tau)$.

4. Limit theorems. Recall that we consider the supercritical case $\alpha > 0$. Then from (6) one has

$$\text{(13)}\quad M(t) = \gamma e^{\alpha t}\widehat{r}_t(\alpha),$$

where

$$\text{(14)}\quad \widehat{r}_t(\alpha) = \int_0^t e^{-\alpha u} r(u)du$$

Assume first that

$$\text{(15)}\quad \lim_{t\to\infty} \widehat{r}_t(\alpha) = \widehat{r}(\alpha) < \infty.$$

Remark 1. The relation (15) is fulfilled if, for example, $r(t) = L(t)t^{\theta}$, $-\infty < \theta < \infty$, and a s.v.f. $L(t)$, or $r(t) = O(e^{\rho t}), \rho < \alpha$.

Theorem 1. *Under the condition (15),*

$$\zeta(t) = Y(t)/M(t) \xrightarrow{L_2} \zeta, \ \ as \ \ t \to \infty,$$

where

$$\mathbf{E}[\zeta] = 1 \ \ and \ Var[\zeta] = \widehat{r}(2\alpha)(\alpha\gamma + \beta\gamma_2)/[\alpha\widehat{r}^2(\alpha)\gamma^2].$$

P r o o f. It will be sufficient to show that

$$\Delta(t,\tau) = \mathbf{E}[\zeta(t+\tau) - \zeta(t)]^2 \to 0 \text{ as } t \to \infty,$$

uniformly for $\tau \geq 0$. Note that $\mathbf{E}[\zeta(t)] \equiv 1$,

(16) $\Delta(t,\tau) = Var[\zeta(t+\tau)] + Var[\zeta(t)] - 2Cov[\zeta(t), \zeta(t+\tau)]$,
$Var[\zeta(t)] = W(t)/\ M^2(t)$ and $Cov[\zeta(t), \zeta(t+\tau)] = C(t,\tau)/M(t)M(t+\tau)$.

From (7), using also (2), (3), and (14), one can calculate that

$$W(t) = (\gamma\beta/\alpha + \gamma_2)e^{2\alpha t}\widehat{r}_t(2\alpha) + \gamma(\beta/\alpha - 1)e^{\alpha t}\widehat{r}_t(\alpha).$$

Therefore under the condition (15) and using (13) one gets

$$\lim_{t\to\infty} Var[\zeta(t)] = \widehat{r}(2\alpha)(\alpha\gamma + \beta\gamma_2)/[\alpha\widehat{r}^2(\alpha)\gamma^2]. \tag{17}$$

On the other hand, from (10) and (2) one can obtain the following equation

$$\frac{dA(t,\tau)}{dt} = \alpha A(t,\tau) + \beta e^{\alpha\tau}e^{2\alpha t}, \text{ with } A(0,\tau) = e^{\alpha\tau},$$

which has a solution

$$A(t,\tau) = e^{\alpha(t+\tau)}[\beta(e^{\alpha t} - 1)/\alpha + 1]. \tag{18}$$

The same result can be obtain using the fact that the Markov process $\chi(t) = Z(t)/e^{\alpha t}$ is a martingale (see e.g. Harris (1963)), i.e. $\mathbf{E}[\chi(t+\tau)|\chi(t)] = \chi(t)$. Therefore

$$\mathbf{E}[\chi(t+\tau)\chi(t)] = \mathbf{E}[\chi(t)\mathbf{E}\{\chi(t+\tau)|\chi(t)\}] = \mathbf{E}[\chi^2(t)] = e^{-2\alpha t}\mathbf{E}Z^2(t).$$

On the other hand

$$A(t,\tau) = e^{\alpha(2t+\tau)}\mathbf{E}[\chi(t+\tau)\chi(t)] = e^{\alpha\tau}\mathbf{E}[Z^2(t)] = e^{\alpha\tau}[V(t) + A^2(t)]$$

and using (2) and (3) one obtains again (18). Now from (12) using (18) and (2) one can calculate that

$$C(t,\tau) = (\gamma\beta/\alpha + \gamma_2)e^{2\alpha t+\alpha\tau}\widehat{r}_t(2\alpha) + \gamma(\beta/\alpha - 1)e^{\alpha t}\widehat{r}_t(\alpha).$$

Hence applying (13) and (15) one gets

$$\lim_{t\to\infty} Cov[\zeta(t), \zeta(t+\tau)] = \widehat{r}(2\alpha)(\alpha\gamma + \beta\gamma_2)/[\alpha\widehat{r}^2(\alpha)\gamma^2]. \tag{19}$$

Therefore by (16), (17), and (19) it follows that uniformly for $\tau \geq 0$

$$\lim_{t\to\infty} \Delta(t,\tau) = 0.$$

From this relation and (17) the assertion of the theorem follows. □

Now we will consider more carefully the case

$$r(t) = re^{\rho t}, \quad r > 0, \quad \rho > 0. \tag{20}$$

Then from (6) and (2) one has

$$M(t) = \begin{cases} \gamma re^{\alpha t}/(\alpha - \rho), & \rho < \alpha; \\ \gamma rte^{\alpha t}, & \rho = \alpha; \\ \gamma re^{\rho t}/(\rho - \alpha), & \rho > \alpha. \end{cases} \tag{21}$$

Similarly one can obtain from (7), (3), and (2) that as $t \to \infty$,

$$W(t) \sim \begin{cases} \dfrac{K}{2\alpha - \rho}e^{2\alpha t}, & \rho < 2\alpha; \\ Kte^{2\alpha t}, & \rho = 2\alpha; \\ K_1e^{\rho t}, & \rho > 2\alpha, \end{cases} \tag{22}$$

where $K = r(\gamma\beta/\alpha + \gamma_2)$ and $K_1 = K/(\rho - 2\alpha) + r\gamma(1 - \beta/\alpha)/(\rho - \alpha)$.

On the other hand, from (12), (18), and (2) one gets

$$C(t,\tau) = Ke^{2\alpha t+\alpha\tau}\int_0^t e^{(\rho-2\alpha)u}du + r\gamma(1 - \beta/\alpha)e^{\alpha t+\alpha\tau}\int_0^t e^{(\rho-\alpha)u}du. \tag{23}$$

Now from (23) as $t \to \infty$ one has

$$C(t,\tau)e^{-\alpha\tau} \sim \begin{cases} \dfrac{K}{2\alpha - \rho}e^{2\alpha t}, & \rho < 2\alpha; \\ Kte^{2\alpha t}, & \rho = 2\alpha; \\ K_1e^{\rho t}, & \rho > 2\alpha. \end{cases} \tag{24}$$

Theorem 2. *Assume* (20) *with* $\rho < \alpha$. *If* $t \to \infty$ *then*

$$\zeta(t) = Y(t)/M(t) \xrightarrow{L_2} \zeta \text{ and } \zeta(t) \xrightarrow{a.s.} \zeta,$$

where

$$\mathbf{E}[\zeta] = 1 \text{ and } Var[\zeta] = K(\alpha-\rho)^2/(\gamma r)^2, K = r(\gamma\beta/\alpha + \gamma_2).$$

P r o o f. From (16), (21), (22), and (24) one can obtain that

$$\Delta(t,\tau) = \mathbf{E}[\zeta(t+\tau) - \zeta(t)]^2 \to 0$$

as $t \to \infty$ uniformly for $\tau \geq 0$, which proves L_2-convergence. Note that this fact follows also directly from Theorem 1 because of Remark 1.

On the other hand, from (7), (2), and (3) we have

$$W(t) = \frac{K}{2\alpha-\rho} e^{2\alpha t}(1 - e^{-(2\alpha-\rho)t}) - \frac{K_0}{\alpha-\rho} e^{\alpha t}(1 - e^{-(\alpha-\rho)t}), \tag{25}$$

where $K_0 = r\gamma(\beta/\alpha - 1)$.

From (23) we get

$$C(t,\tau)e^{-\alpha\tau} = \frac{K}{2\alpha-\rho} e^{2\alpha t}(1 - e^{-(2\alpha-\rho)t}) - \frac{K_0}{\alpha-\rho} e^{\alpha t}(1 - e^{-(\alpha-\rho)t}). \tag{26}$$

Therefore, from (16) applying (21), (25), and (26) one obtains

$$\Delta(t) = \lim_{\tau\to\infty} \Delta(t,\tau) = \mathbf{E}[\zeta(t) - \zeta]^2 = e^{-\alpha t}[(\overline{K} + \overline{K}_0)e^{-(\alpha-\rho)t} + \overline{K}_0],$$

where

$$\overline{K} = \frac{K(\alpha-\rho)^2}{(2\alpha-\rho)(\gamma r)^2} \text{ and } \overline{K}_0 = \frac{K_0(\alpha-\rho)}{(\gamma r)^2}.$$

Hence $\int_0^\infty \Delta(t)dt < \infty$ and by Theorem 21.1 of Harris (1963) it follows that $\zeta(t)$ converges with probability 1 to the r.v. ζ as $t \to \infty$. □

Theorem 3. *Assume* (20) *with* $\rho \geq \alpha$. *If* $t \to \infty$ *then*

$$\zeta(t) = Y(t)/M(t) \xrightarrow{L_2} 1 \text{ and } \zeta(t) \xrightarrow{a.s.} 1.$$

P r o o f. Let first note that from (21), (22), and (24) one has

$$\lim_{t\to\infty}\frac{W(t)}{M^2(t)}=\lim_{t\to\infty}\frac{C(t,\tau)}{M(t)M(t+\tau)}=0.$$

Hence from (16) it follows that

$$\Delta(t,\tau)=\mathbf{E}[\zeta(t+\tau)-\zeta(t)]^2\to 0 \text{ as } t\to\infty$$

uniformly for $\tau\geq 0$ which proves the convergence in L_2 to some r.v. ζ. Since $\mathbf{E}[\zeta(t)]=\mathbf{E}[Y(t)/M(t)]\equiv 1$ and $Var[\zeta(t)]=W(t)/\ M^2(t)\to 0$ then $\zeta=1$ *a.s.* Moreover, since for each $\varepsilon>0$,

$$\mathbf{P}\{|\zeta(t)-1|\geq\varepsilon\}\leq\varepsilon^{-2}Var[\zeta(t)]=\varepsilon^{-2}\frac{W(t)}{M^2(t)}\to 0,\quad t\to\infty,$$

then $\zeta(t)\to 1$ in probability.

On the other hand, using (21), (22), and (24) one can prove that

$$\lim_{\tau\to\infty}\frac{W(t+\tau)}{M^2(t+\tau)}=\lim_{\tau\to\infty}\frac{C(t,\tau)}{M(t)M(t+\tau)}=0.$$

Hence

$$\Delta(t)=\lim_{\tau\to\infty}\Delta(t,\tau)=\mathbf{E}\{\zeta(t)-1\}^2=W(t)/M^2(t).$$

Applying again (21) and (22) one can obtain that

$$\Delta(t)=\begin{cases} O(t^{-2}), & \rho=\alpha;\\ O(e^{-2(\alpha-\rho)t}), & \alpha<\rho<2\alpha;\\ O(e^{-2\alpha t}), & \rho=2\alpha;\\ O(e^{-\rho t}), & \rho>2\alpha.\end{cases}$$

Therefore $\int_0^\infty\Delta(t)dt<\infty$ and by Theorem 21.1 of Harris (1963) it follows that $\zeta(t)$ converges to 1 *a.s.* $\square$

Remark 2. Note that Theorem 3 can be interpreted as a LLN because $\dfrac{Y(t)}{M(t)}\to 1$, *a.s.* Hence one can conjecture a CLT.

Theorem 4. *Assume* (20) *with* $\rho\geq\alpha$ *and* $X(t)=[Y(t)-M(t)]/\sqrt{W(t)}$. *Then a CLT holds:*

(*i*) *If* $\alpha \leq \rho < 2\alpha$ *then*

(27) $$X(t) \xrightarrow{d} N(0,1) \ \text{as } t \to \infty;$$

(*ii*) *If* $\rho > 2\alpha$ *then*

$$X(t) \xrightarrow{d} N(0,\sigma^2) \ \text{as } t \to \infty,$$

where $\sigma^2 = (\rho - 2\alpha)[\alpha\beta + \gamma_2(\rho - \alpha)]/(\rho - \alpha)[\gamma\beta + \gamma_2(\rho - \alpha) + \gamma(\rho - 2\alpha)]$.

P r o o f. From (27) one can obtain the characteristic function

$$\begin{aligned} \varphi_t(z) &= \mathbf{E}[e^{izX(t)}] = e^{-izM(t)/\sqrt{W(t)}}\mathbf{E}[e^{izX(t)/\sqrt{W(t)}}] \\ &= e^{-izM(t)/\sqrt{W(t)}}\Psi(t; e^{iz/\sqrt{W(t)}}). \end{aligned}$$

Then using (5) one has

$$\log \varphi_t(z) = -izM(t)/\sqrt{W(t)} - \int_0^t r(t-u)[1 - g(F(u; e^{iz/\sqrt{W(t)}}))]du.$$

Note that as $s \to 1$,

$$\begin{aligned} &1 - g(s) \sim \gamma(1-s) - \gamma_2(1-s)^2/2, \\ &1 - F(u;s) \sim A(u)(1-s) - B(u)(1-s)^2/2. \end{aligned}$$

On the other hand, $1 - e^{cx} \sim -cx$ as $x \to 0$. Therefore as $t \to \infty$,

(28) $$\begin{aligned} &\log \varphi_t(\ z) \sim -izM(t)/\sqrt{W(t)} \\ &- \int_0^t r(t-u)\{\gamma[1 - F(u; e^{iz/\sqrt{W(t)}})] - \gamma_2[1 - F(u; e^{iz/\sqrt{W(t)}}]^2/2\}du. \end{aligned}$$

Since as $t \to \infty$,

$$\begin{aligned} &1 - F(u; e^{iz/\sqrt{W(t)}}) \sim A(u)(1 - e^{iz/\sqrt{W(t)}}) - B(u)(1 - e^{iz/\sqrt{W(t)}})^2/2 \\ \sim\ &-izA(u)/\sqrt{W(t)} + z^2B(u)/\sqrt{W(t)}/2 \end{aligned}$$

then

$$\begin{aligned} D(t) &= \int_0^t r(t-u)\{\gamma[1 - F(u; e^{iz/\sqrt{W(t)}})] - \gamma_2[1 - F(u; e^{iz/\sqrt{W(t)}}]^2/2\}du \\ &\sim -iz\gamma\int_0^t r(t-u)A(u)du/\sqrt{W(t)} + (z^2/2)\gamma\int_0^t r(t-u)B(u)du/W(t) \end{aligned}$$

$$+ \quad (z^2/2)\gamma_2 \int_0^t r(t-u)A^2(u)du/W(t).$$

Now using (6) and (7) one has as $t \to \infty$,

$$D(t) \sim -izM(t)/\sqrt{W(t)} + (z^2/2)[1 - M(t)/W(t)].$$

Hence one gets from (27)

$$\log \varphi_t(z) \sim -(z^2/2)[1 - M(t)/W(t)], \ t \to \infty. \tag{29}$$

As $t \to \infty$ it is not difficult to see from (21) and (22) that $M(t)/W(t) \to 0$ for $\alpha \le \rho < 2\alpha$ and $M(t)/W(t) \to \gamma r/(\rho - \alpha)K_1$ for $\rho > 2\alpha$. One can also show that $\sigma^2 = 1 - \gamma r/(\rho - \alpha)K_1$ is just presented in (ii).

Therefore from (29) we finally obtain that $\lim_{t\to\infty} \varphi_t(\ z) = e^{-z^2/2}$ for $\alpha \le \rho < 2\alpha$ and $\lim_{t\to\infty} \varphi_t(\ z) = e^{-z^2\sigma^2/2}$ for $\rho > 2\alpha$ which are characteristic functions of a corresponding normal distribution. Then by the continuity theorem (see e.g. Feller (1971)) the assertions (i) and (ii) follow. □

Remark 3. It is interesting to note that a LLN and a CLT are obtained for a class of subcritical branching processes with two types of immigration (see Alsmeyer and Slavtchova-Bojkova (2005), Slavtchova-Bojkova (2002, 2011).

Remark 4. Recall that the relation

$$X(t) = [Y(t) - M(t)]/\sqrt{W(t)} \xrightarrow{d} N(0, \sigma^2) \text{ as } t \to \infty$$

is often presented as $Y(t) \in N(M(t), \sigma^2 W(t))$ and one can say that $Y(t)$ has asymptotic normality with a mean $M(t)$ and a variance $\sigma^2 W(t)$. Then from Theorem 4 using (21) and (22) one can obtain the following relations which give more convenient interpretation for the rate of convergence:

(a) If $\rho = \alpha$ then $Y(t)/te^{\alpha t} \in N(\gamma r, Kt^{-2}/\alpha)$;

(b) If $\alpha < \rho < 2\alpha$ then $Y(t)/e^{\rho t} \in N(\gamma r/(\rho - \alpha), Ke^{-2(\rho-\alpha)t}/(2\alpha - \rho))$;

(c) If $\rho = 2\alpha$ then $Y(t)/e^{2\alpha t} \in N(\gamma r/\alpha, Kte^{-2\alpha t})$;

(d) If $\rho > 2\alpha$ then $Y(t)/e^{\rho t} \in N(\gamma r/(\rho - \alpha), \sigma^2 K_1 e^{-\rho t})$;

Note that these relations are also useful for constructing of asymptotically confident intervals.

5. Some Generalizations of the Initial Conditions. In the analysis of renewing cell populations *in vivo* it is important to consider also the situation with a random number of ancestors. Let first assume that the process begins with Z_0^* cells at zero age with a p.g.f. $h^*(s) = \mathbf{E}[s^{Z_0^*}]$. With this initial condition let $Z^*(t)$ be the corresponding process without immigration and let $Y^*(t)$ be the relevant considered process with immigration. Then one can obtain the p.g.f. respectively

$$F^*(t;s) = \mathbf{E}[s^{Z^*(t)}] = h^*(F(t;s), \quad \Psi^*(t;s) = \mathbf{E}[s^{Y^*(t)}] = h^*(F(t;s))\Psi(t;s).$$

Hence it is not difficult to transfer all obtained results from the previous sections. For example, if $m^* = \mathbf{E}[Z_0^*]$ then for the means one has

$$A^*(t) = \mathbf{E}[Z^*(t)] = m^*A(t), \quad M^*(t) = \mathbf{E}[Y^*(t)] = m^*A(t) + M(t).$$

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