

LIMIT THEOREMS FOR SUPERCRITICAL MARKOV  
BRANCHING PROCESSES WITH NON-HOMOGENEOUS  
POISSON IMMIGRATION

Ollivier Hyrien, Kosto V. Mitov\*, Nikolay M. Yanev\*\*

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**Abstract**

This paper deals with Markov branching processes allowing immigration at random time points described by a non-homogeneous Poisson process. This class of processes generalizes a classical model proposed by Sevastyanov, which included a time-homogeneous Poisson immigration. The proposed model finds applications in cell kinetics studies. Limit theorems are obtained in the supercritical case. Some of these results extend the classical results derived by Sevastyanov, others offer novel insights as a result of the non-homogeneity of the immigration process.

**Key words:** branching processes, non-homogeneous Poisson immigration, cell kinetics, statistical inference

**2000 Mathematics Subject Classification:** 60J80

**1. Introduction.** The first branching process model with immigration was proposed by SEVASTYANOV [9]. He investigated a Markov branching process allowing immigration at random time points arising from a homogeneous Poisson process.

In the present paper we study a generalization of Sevastyanov's model. In fact, the model under consideration is also a Markov branching process, but the times at which immigration occurs form a non-homogeneous Poisson process. From a practical standpoint, these processes find applications in modelling the development of renewing cell populations in vivo. For a comprehensive review

of branching processes and their biological applications, the reader is referred to HARRIS [6], SEVASTYANOV [10], ATHREYA and NEY [1], JAGERS [7], YAKOVLEV and YANEV [11], KIMMEL and AXELROD [8], and HACCOU et al. [2]. Some biologically motivated problems relevant to branching processes with non-homogeneous Poisson immigration have been considered in YAKOVLEV and YANEV ([12,13]) and HYRIEN and YANEV ([3,4]).

The paper is organized as follows. Section 2 presents the biological background that introduces the general ideas and motivation behind the construction of the models formulated in Section 3. The basic equations for the probability generating function (p.g.f.) and the moments are also treated in Section 3. Limit theorems for the supercritical processes are presented in Section 4. The limiting results obtained in Theorems 1 and 2 can be regarded as generalizations of the classical result established by Sevastyanov [9]. The results presented in Theorems 3 and 4 offer novel insights that result from the non-homogeneity of the process.

**2. Biological background and motivation.** Continuous-time branching processes have been used to quantify the development of cell populations in cell kinetics studies. In practical applications, the population contains  $N_0$  cells at the onset of the experiment. For example, when studying tissue development during embryogenesis, it is reasonable to set  $N_0 = 0$  if the experiment begins before the first cell of the tissue has been generated. As time increases, cells will begin populating the tissue of interest once precursor cells have started differentiating. We refer to these cells as immigrants and describe their influx using 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 life-span, every cell of the population either divides into two new cells, or it exits the population (due to cell differentiation or cell death). These events occur with probability  $p$  and  $q = 1 - p$ , respectively. The lifespan of any cell is described by a non-negative random variable  $\tau$  with cumulative distribution function (c.d.f.)  $G(x) = \mathbf{P}\{\eta \leq x\}$  that satisfies  $G(0) = 0$ . Cells are assumed to evolve independently of each other. The work presented in this paper was motivated by this example, and we investigated properties of a more general class of Markov branching processes with non-homogeneous Poisson immigration.

**3. Models and equations.** We consider a process that begins with the immigration of differentiating *precursor cells* into the population. Every immigrant is of age zero at the time of immigration. Every cell has a random life-span  $\eta$  with c.d.f.  $G(t) = \mathbf{P}\{\eta \leq t\} = 1 - e^{-t/\mu}, t \geq 0$ . At the end of its life-span, every cell produces a random number of offspring  $\xi$  with p.g.f.  $h(s) = \mathbf{E}[s^\xi], |s| \leq 1$ . We assume that all newborn cells are of zero age and continue their evolutions independently of every other cell and in the same way. Therefore the development of this population can be described within the framework of Markov branching processes with immigration.

The moments of the offspring distribution

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

as well as the mean life-span  $\mu = \int_0^\infty x dG(x)$ , play an important role in the behaviour of the process. We shall assume that these characteristics are finite.

The models with offspring p.g.f.  $h(s) = 1 - p + ps^2$ , and moments  $m = 2p = m_2$ , have a clear biological interpretation: at the end of its mitotic cycle, every cell either dies with probability  $1 - p$  or, it divides in two cells with probability  $p$ . This example could deserve special attention, but we shall investigate the general case.

Let us first consider the process without immigration. Let  $Z(t)$  denote the number of cells at time  $t$ , and introduce the corresponding p.g.f.:  $F(t; s) = \mathbf{E}[s^{Z(t)} | Z(0) = 1]$ . Under the assumptions, it is not difficult to realize that  $\{Z(t), t \geq 0\}$  is a Markov branching process, and its p.g.f. is characterized by the following nonlinear differential equation:

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

where  $f(s) = [h(s) - s]/\mu$  (see e.g. Harris [6]).

Note that the Malthusian parameter  $\alpha$  is determined as usually from the equation  $m \int_0^\infty e^{-\alpha x} dG(x) = 1$ . For the model under consideration, we have  $\alpha = f'(1) = [m - 1]/\mu$ . In what follows we shall consider only the supercritical case  $\alpha > 0$ , corresponding to  $m > 1$ . Introduce also  $\beta = f''(1) = m_2/\mu$ . Then the first two moments of the process are given by (see e.g. Harris [6]):

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

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

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

Let us now describe the process with immigration. First we will assume that  $0 = S_0 < S_1 < S_2 < S_3 < \dots$  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  $S_k = \sum_{i=1}^k U_i$ ,  $k = 1, 2, \dots$

We will also assume that at every point  $S_k$  there is a random number  $I_k$  of cells all of age zero which immigrate into the population, where  $\{I_k\}_{k=1}^\infty$  are

i.i.d. r.v. with p.g.f.  $g(s) = \mathbf{E}[s^{I_k}] = \sum_{i=0}^{\infty} g_i s^i$ ,  $|s| \leq 1$ . Let  $\gamma = \mathbf{E}[I_k] = \frac{dg(s)}{ds}|_{s=1}$  be the immigration mean and introduce the second factorial moment  $\gamma_2 = \frac{d^2g(s)}{ds^2}|_{s=1} = \mathbf{E}[I_k(I_k - 1)]$ .

Let  $Y(t)$  denote the number of cells at time  $t$  in the process with immigration, where the cell evolution is determined by the above-defined  $(G, h)$  – Markov branching processes. The process admits the following representation

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

where  $Z^{I_k}(t)$  are i.i.d. branching processes, which behave like  $Z(t)$ , but started with a random number of ancestors  $I_k$ . We assumed that  $Y(0) = 0$ ; 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 the decomposition (4), Yakovlev and Yanev ([13], Theorem 1) obtained that

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

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

The process  $\{Y(t), t \geq 0\}$  is a time non-homogeneous Markov process. Notice that if  $\{U_i\}_{i=1}^{\infty}$  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 cumulative rate  $R(t) = rt$ . Our model reduces to the model with immigration proposed by Sevastyanov [9].

Introduce the moments of the process with immigration

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

Then it is not difficult to deduce from eqn (5) that

$$\begin{aligned} (6) \quad M(t) &= \gamma \int_0^t r(t-u)A(u)du, \\ M_2(t) &= \gamma \int_0^t r(t-u)B(u)du \\ &\quad + \left[ \gamma \int_0^t r(t-u)A(u)du \right]^2 + \gamma_2 \int_0^t r(t-u)A^2(u)du, \\ (7) \quad W(t) &= \int_0^t r(t-u)[\gamma V(u) + (\gamma + \gamma_2)A^2(u)]du. \end{aligned}$$

In order to derive equations for the covariance of the process, we consider 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 yields the equation

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

with the initial condition  $F(s_1, s_2; 0, 0) = s_1 s_2$  (see also Harris [6]).

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

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

Similarly to (5), one can obtain that

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

To establish this identity, one has to consider definition (4) and follow the method developed in (Yakovlev and Yanev [13], Theorem 1) for (5). Introduce the moments

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

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

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

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

$$M(t, \tau) = \int_0^t r(u)[\gamma A(t-u, \tau) + \gamma_2 A^2(t-u)] du + \gamma^2 \left[ \int_0^t r(u) A(t-u) du \right]^2,$$

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

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

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

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

where

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

Assume first that

$$(12) \quad \lim_{t \rightarrow \infty} \widehat{r}_t(\alpha) = \widehat{r}(\alpha) < \infty.$$

**Remark 1.** The condition (12) is fulfilled if, for example,  $r(t) = L(t)t^\theta$ ,  $-\infty < \theta < \infty$ , and  $L(t)$  is a s.v.f., or  $r(t) = O(e^{\rho t})$ ,  $\rho < \alpha$ .

**Theorem 1.** Assume that condition (12) is satisfied. Then

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

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

We next consider the case where

$$(13) \quad r(t) = r e^{\rho t}, \quad r > 0, \quad \rho > 0.$$

Then it follows from eqns (2) and (6) that

$$(14) \quad M(t) = \begin{cases} \gamma r e^{\alpha t}/(\alpha - \rho), & \rho < \alpha \\ \gamma r t e^{\alpha t}, & \rho = \alpha \\ \gamma r e^{\rho t}/(\rho - \alpha), & \rho > \alpha. \end{cases}$$

Also, we deduce from eqns (2), (3) and (7) that, as  $t \rightarrow \infty$ ,

$$(15) \quad W(t) \sim \begin{cases} \frac{K}{2\alpha - \rho} e^{2\alpha t}, & \rho < 2\alpha \\ K t e^{2\alpha t}, & \rho = 2\alpha \\ K_1 e^{\rho t}, & \rho > 2\alpha, \end{cases}$$

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

Moreover, using eqns (2), (10) and (11), we obtain that

$$(16) \quad C(t, \tau) = K e^{2\alpha t + \alpha \tau} \int_0^t e^{(\rho - 2\alpha)u} du + r\gamma(1 - \beta/\alpha) e^{\alpha t + \alpha \tau} \int_0^t e^{(\rho - \alpha)u} du.$$

Finally, letting  $t \rightarrow \infty$  in eqn (16) yields

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

**Theorem 2.** Assume that condition (13) holds true with  $\rho < \alpha$ . Then, as  $t \rightarrow \infty$ ,

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

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

**Theorem 3.** Assume that condition (13) holds true with  $\rho \geq \alpha$ . Then, as  $t \rightarrow \infty$ ,

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

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

**Theorem 4.** Assume that condition (13) holds true 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

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

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

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

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

**Remark 3.** Recall that the relation

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

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 eqns (14) and (15), one obtains the following relations which give a 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 asymptotic confident intervals.

The proofs of the limit theorems presented herein will appear in [5].

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*Department of Biostatistics  
and Computational Biology  
University of Rochester  
Rochester, NY 14642, USA*  
e-mail: Ollivier\_Hyrien@urmc.rochester.edu

*\*Faculty of Aviation  
National Military University  
“Vasil Levski”  
5856 D. Mitropolia, Pleven, Bulgaria*  
e-mail: kmitov@yahoo.com

*\*\*Department of Probability and Statistics  
Institute of Mathematics and Informatics  
Bulgarian Academy of Sciences  
1113 Sofia, Bulgaria*  
e-mail: yanev@math.bas.bg