Published in final edited form as:
J Appl Probab. 2017 June ; 54(2): 569–587. doi:10.1017/jpr.2017.18.

Subcritical Sevastyanov branching processes with nonhomogeneous Poisson immigration

OLLIVIER HYRIEN[*],
University of Rochester

KOSTO V. MITOV[**], and
Aviation faculty-NMU

NIKOLAY M. YANEV[***]
Bulgarian Academy of Sciences

Abstract

We consider a class of Sevastyanov branching processes with non-homogeneous Poisson immigration. These processes relax the assumption required by the Bellman-Harris process which imposes the lifespan and offspring of each individual to be independent. They find applications in studies of the dynamics of cell populations. In this paper, we focus on the subcritical case and examine asymptotic properties of the process. We establish limit theorems, which generalize classical results due to Sevastyanov and others. Our key findings include novel LLN and CLT which emerge from the non-homogeneity of the immigration process.

Keywords

Branching processes; Immigration; Poisson process; Limit theorems

2010 Mathematics Subject Classification

Primary 60J80; Secondary 60F05; 60J85; 62P10

1. Introduction

Age-dependent branching processes with immigration are well-suited to describe the temporal evolution of populations in which individuals (for example cells) appear randomly over time in accordance with two distinct mechanisms. One mechanism, called immigration, is the influx of new individuals in the population of which they are not natives. The other mechanism, referred to as branching, is the process by which individuals of the population generate new offspring. These models have attracted much attention since Sevastyanov's

[*]Postal address: Department of Biostatistics and Computational Biology, University of Rochester, Rochester, NY 14642, USA Ollivier Hyrien@urmc.rochester.edu
[**]Postal address: Faculty of Aviation, National Military University "Vasil Levski", 5856 D. Mitropolia, Pleven, Bulgaria kmitov@yahoo.com
[***]Postal address: Department of Operations Research, Probability and Statistics, Institute of Mathematics and Informatics, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria, yanev@math.bas.bg

seminal work on continuous-time Markov branching processes with immigration [29]. Jagers [17] established asymptotic properties in the age-dependent (Bellman-Harris) case. Other properties, also for Bellman-Harris processes, were subsequently proven by Radcliffe [28], Pakes and Kaplan [27], Kaplan and Pakes [19], among others. Olofsson considered a process with a more general branching mechanism [25]. These articles dealt with time-homogeneous immigration processes, and Mitov and Yanev [21, 22, 23] investigated a Bellman-Harris process with state-dependent immigration (see also [1], Ch. 3). Age-dependent branching processes with immigration have been proposed to study the dynamics of cell populations developing *in vivo* [33, 34, 11, 14, 12, 13]. We refer to [6, 32, 3, 18, 2, 1] for general monographs on branching processes.

In this paper, we consider a class of age-dependent branching processes with immigration, in which: *(i) the branching mechanism obeys the assumptions of a Sevastyanov process* [25, 26, 27], *an extension of the Bellman-Harris process which allows lifespan and offspring to be dependent; (ii) the immigration process is time-inhomogeneous.* These two extensions are motivated in Section 2 using a cell biology example. Mitov and Yanev [24] and Hyrien et al. [15] studied critical processes for various intensities of the nonhomogeneous Poisson immigration process, while Hyrien et al. [16] investigated the supercritical case. Pakes [26] considered critical and subcritical Bellman-Harris processes with a non-homogeneous Poisson immigration process that converges weakly to an homogeneous Poisson process. Yanev [35, 36] studied the Sevastyanov process when immigration is time-homogeneous. Here, we investigate the subcritical case which is adapted to model the dynamics of terminally differentiated cells.

The asymptotic properties are studied when the intensity of the Poisson immigration process belongs to the class of power and exponential functions.

The process is formulated in Section 3. The asymptotic behavior of its expectation and variance-covariance function is investigated in Section 4. All other limit theorems are stated in Section 5. The conditional limiting distributions of Theorems 5.1, 5.2, and 5.3 are akin to those that have been established for continuous-time branching processes without immigration (e.g., [6, 32, 3, 18, 2, 1]). Theorems 5.4–5.7 uncover behaviors in the form of LLN and CLT that are novel for branching processes and which arise from the non-homogeneity of the immigration process. Theorem 5.8 generalizes a classical result due to Sevastyanov [29] to the more general setting considered herein.

2. A biological motivation

The molecular events and pathways that control cell fate decision (e.g., division, death, differentiation) in multi-cellular systems are not well understood and the subject of intensive basic science research. Experimental set-ups used in these studies often yield observations about the composition of the system at discrete time points only. A viable approach to inferring about cell fate on the basis of such data consists in modeling the dynamics of the cell population in order to relate experimental observations to (unobserved) cell cycle outcomes. Key to the success of this approach is an appropriate modeling framework in which the most prominent features of cell proliferation are properly captured. The Bellman-

Harris process has been successfully used to develop stochastic models in this context. However, the rise of high-throughput, high-dimensional data produced by modern technologies (e.g., flow cytometry, imaging, sequencing) permits a wealth of cellular information to be produced at the single-cell resolution. This information allows teasing apart more subtle models.

An assumption that is central to the make-up of the Bellman-Harris process is that the duration of the lifespan, η, and the number of daughters, ξ, of any cell of the population are independent random variables. This assumption was found inadequate in several studies [7, 8, 9, 10, 5]. One of these studies investigated the generation of terminally differentiated oligodendrocytes from their progenitor cells (PC), known as the oligodendrocytes type-2 astrocytes PC [8]. These cells of the central nervous system produce the myelin sheath that insulate axons which conducts electrical impulses to transmit information between neurons. It was observed in this study that the time to division, the time to death, and the time to differentiation of these cells into oligodendrocytes had dissimilar distributions and that these distributions could be differentially affected by exposure to external signals (see Fig. 1). This finding may be explained by the fact that fate-specific molecular events are triggered in order for cells to reach their ultimate transformation. It also reflects the fact that the time at which a specific fate is detected may be arbitrary and depends on the experimental set-up that is used. The time at which a cell divides may be unambiguously defined as the time at which it splits into two daughter cells at the end of cytokinesis. However, the definition of the time at which a cell dies is debatable because the event that leads to the ultimate disintegration of the cell is not observable, and the time of cell death is instead defined as the time at which an outcome of death (e.g., fragmentation of the cell membrane) becomes experimentally detectable. Relaxing the assumption of independence between η and ξ yields the class of Sevastyanov processes.

Populations of lineage-committed progenitor cells that develop *in vivo* are sustained by influxes of differentiated cells produced by multipotent stem or progenitor cells. This mechanism ensures the maintenance of terminally differentiated tissues which have limited self-renewing capabilities. The influx may vary over time. For example, it may temporarily increase in order to accelerate the repair of damaged downstream cellular compartments. The dynamics of such systems may be described by subcritical branching processes with time-inhomogeneous immigration. Here we ask whether the distribution of the population size can be characterized. We find that the process is asymptotically normal when immigration increases over time under mild assumptions.

To avoid modeling the influx of new cells as a Poisson process, cell kinetics could be alternatively formulated as a two-type reducible Sevastyanov branching process in which the first type of cells would correspond to (unobservable) upstream stem and progenitor cells, while the second one would describe the pool of observable cells (Fig. 2; see also Kesten and Stigum [20] for a discrete-time version of the process). While conceptually simple, this formulation presents several drawbacks, including:

1. It assumes that type-1 cells form a population of homogeneous cells. This assumption may be too rigid in practice. For instance, the hematopoietic

progenitor cells that give rise to the various blood cell lineages (e.g., myeloid (erythrocytes, megakaryocytes, monocytes, neutrophils, basophils, or eosinophils) or lymphoid (T- and B-lymphocytes)) are known to exhibit varying degrees of commitments to these lineages, thereby presenting dissimilar probabilities of further specializing into any of them. By assuming that the offspring distribution is identical among all type-1 cells, the two-type process would be less realistic.

2. It may lack the flexibility needed to capture the plasticity exhibited by stem and progenitor cells in order to respond to the varying needs of the body. Feedback mechanisms between the two cell types could be included in the model to describe this plasticity. Such an extension, however, would define a model that is considerably more challenging to study, especially in the age-dependent case.

In contrast, our model restricts assumptions postulated on the unobservable cell population to its influx into the pool of observable cells. The rate of this influx may be time-dependent, as needed.

3. The process and its equations

3.1. The Sevastyanov process

We consider a branching process in which the joint distribution of the lifespan η and offspring ξ of any cell is specified as $\mathbf{P}\{\eta \in B, \xi = k\} = \int_B p_k(u)dG(u)$ for every Borel set $B \subset \mathbf{R}$, where $G(u) = \mathbf{P}(\eta \le u)$ and $\sum_{k=0}^{\infty} p_k(u) = 1\ (u \ge 0)$, and every cell evolves independently of all other cells. Put $h(u, s) = \sum_{k=0}^{\infty} p_k(u)s^k$, $|s| \le 1$, for the associated probability generating functions (p.g.f.). These assumptions define a (G, h)-Sevastyanov process [32]. Write $\{Z(t)\}_{t \ge 0}$ for the population size at time t.

Define the moments of the offspring and lifespan distributions $a(t) = h_s'(t, s)\mid_{s=1}$, $b(t) = h_{ss}''(t, s)\mid_{s=1}$, $a = \int_0^\infty a(t)dG(t)$, $b = \int_0^\infty b(t)dG(t)$, $\mu = \int_0^\infty t dG(t)$, all assumed finite. This paper is concerned with the subcritical case ($a < 1$), and we assume the existence of $\alpha < 0$, the Malthusian parameter, which solves the equation $\int_0^\infty e^{-\alpha x}a(x)dG(x) = 1$. Let $G(t)$ and $G_a^{(\alpha)}(t) = \int_0^t a(u)e^{-\alpha u}dG(u)$ be non-lattice.

Throughout the paper, we will be assuming that:

$$\int_0^\infty xe^{-\alpha}dG(x) < \infty \quad \text{and} \quad \int_0^\infty xdG_a^{(\alpha)}(x) < \infty, \quad (1)$$

and

$$\int_0^\infty b(u)e^{-\alpha u}dG(u) < \infty \quad \text{and} \quad \int_0^\infty ub(u)e^{-\alpha u}dG(u) < \infty . \quad (2)$$

Another key assumption will be:

Condition 3.1— *The cumulative distribution function (c.d.f.)* $G_a^\alpha(t) = \int_0^t a(u)e^{-\alpha u}dG(u)$ *is of absolutely continuous type; that is, there exists* $k \geq 1$ *for which the k–fold convolution of* $G_a^{(\alpha)}(.)$ *with itself has an absolutely continuous component (see Definition 2, Ch. VIII.7,* [32]).

Put $A(t) = \mathbf{E}[Z(t)|Z(0) = 1]$. When (1) holds true, it is known that ([32], Th. 8.4)

$$A(t) = Ae^{\alpha t}(1 + o(1)), \quad t \to \infty , \quad (3)$$

where

$$A = \frac{\int_0^\infty e^{-\alpha t}(1 - G(t))dt}{\int_0^\infty xe^{-\alpha x}a(x)dG(x)}.$$

Define $B(t, \tau) = \mathbf{E}[Z(t)Z(t + \tau)|Z(0) = 1]$, $B(t) = \mathbf{E}[Z(t)(Z(t) - 1)|Z(0) = 1]$, and $V(t) = \mathrm{Var}[Z(t)|Z(0) = 1]$. Then $V(t) = B(t, 0) - A(t)^2 = B(t) + A(t) - A(t)^2$.

Lemma 3.1— *Assume that* (1), (2), *and Condition 3.1 hold. Then, for every fixed* $\tau \geq 0$, *there exists a constant* $D_\tau > 0$ *such that, as* $t \to \infty$,

$$B(t, \tau) = D_\tau e^{\alpha(t + \tau)}(1 + o(1)). \quad (4)$$

Proof: Write $B_0(t, \tau) = B(t, \tau)e^{-\alpha t}$ and $A_0(t) = A(t)e^{-\alpha t}$. Then, we have that

$$B_0(t, \tau) = \int_0^t B_0(t - u, \tau)dG_a^{(\alpha)}(u) + I(t, \tau),$$

where

$$I(t,\tau) = e^{\alpha t}\int_0^t b(u)A_0(t-u)A_0(t-u+\tau)e^{-2\alpha u}dG(u) + \int_t^{t+\tau} a(u)A_0(t-u+\tau)e^{-\alpha u}dG(u) + e^{-\alpha(t+\tau)}(1 - G(t+\tau))$$
$$= I_1(t,\tau) + I_2(t,\tau) + I_3(t,\tau),$$

(see eq. (23) Ch. VIII.8, [32]). Since $A_0(t)$ is bounded on $[0, \infty)$, there exists $K > 0$ such that

$$I_1(t,\tau) = e^{\alpha t}\int_0^t b(u)A_0(t-u)A_0(t-u+\tau)e^{-2\alpha u}dG(u) \le 2Ke^{\alpha t}\int_0^t b(u)e^{-2\alpha u}dG(u)\,.$$

Applying the line of arguments used in the proof of Theorem 8.10 in [32] gives $I_1(t, \tau) \in L_1[0, \infty)$ and $I_1(t, \tau) \to 0$ as $t \to \infty$ for any fixed τ. Similarly, there exists $K>0$ such that

$$I_2(t,\tau) = \int_t^{t+\tau} a(u)A_0(t-u+\tau)e^{-\alpha u}dG(u) \le K[1 - G_a^{(\alpha)}(t)]\,.$$

The function $K[1 - G_a^{(\alpha)}(t)] \in L_1[0, \infty)$ because of (2), hence so does $I_2(t, \tau)$. We deduce from (1) that $I_3(t, \tau) = e^{-\alpha(t+\tau)}[1-G(t+\tau)] \in L_1[0, \infty)$. Therefore, $I(t, \tau) \in L_1[0, \infty)$ and $I(t, \tau) \to 0$ as $t \to \infty$. Applying Theorem 7.9 from [32] completes the proof.

An immediate consequence of Lemma 3.1 is that the variance satisfies

$$V(t) = D_0e^{\alpha t}(1 + o(1)), \quad t \to \infty\,. \qquad (5)$$

3.2. Sevastyanov process with immigration

Let $\{S_k\}_{k=1}^{\infty}$ be a sequence of increasing time points with $S_0 = 0$ that arises from a non-homogeneous Poisson process $\{\Pi(t)\}_{t\ge 0}$ with instantaneous and cumulative rates $r(t)$ and $R(t) = \int_0^t r(u)du$, with $r(t) \ge 0$. Let, for every $k = 1, 2 \cdots$, I_k be the number of cells immigrating at time S_k, assumed mutually independent. Put $g(s) = \mathbf{E}[s^{I_k}]$, $|s| \le 1$ for its p.g.f., and $\gamma = \mathbf{E}[I_k] = g'(1)$ and $\gamma_2 = g''(1) = \mathbf{E}[I_k(I_k - 1)]$ for its mean and second factorial moment. Let $Y(t)$ denote the number of cells in the population at time t described by a branching process with immigration in which the branching mechanism obeys a (G, h)-Sevastyanov process. We decompose $Y(t)$ as

$$Y(t) = \begin{cases} \sum_{k=1}^{\Pi(t)} \sum_{i=1}^{I_k} Z^{(k,i)}(t - S_k) & \text{if } \Pi(t) > 0 \\ 0 & \text{if } \Pi(t) = 0, \end{cases} \quad (6)$$

where $\{Z^{(k,i)}(t)\}_{t\geq 0}$, $k, i = 1, 2 \cdots$, are independent and identically distributed (i.i.d.) copies of $\{Z(t)\}_{t\geq 0}$.

Define the p.g.f. $\Psi(t; s) = \mathbf{E}[s^{Y(t)} | Y(0) = 0]$. Proceeding as in Yakovlev and Yanev ([34], Theorem 1), we obtain that

$$\Psi(t; s) = \exp\left\{-\int_0^t r(t-u)[1 - g(F(u; s))]du\right\}, \quad \Psi(0, s) = 1, \quad (7)$$

where the p.g.f. $F(t; s) = \mathbf{E}[s^{Z(t)} | Z(0) = 1]$ satisfies the integral equation

$$F(t, s) = s(1 - G(t)) + \int_0^t h(u, F(t-u, s))dG(u)$$

with the initial condition $F(0, s) = s$. Under mild regularity conditions, $F(t, s)$ is the only solution of this equation that belongs to the class of p.g.f.s (see [32]).

We note that $\{Y(t)\}_{t\geq 0}$ is a time-inhomogeneous and non-Markov process. If $\{U_k = S_k - S_{k-1}\}_{k=1}^{\infty}$ are i.i.d. r.v. with c.d.f. $G_0(x) = \mathbf{P}\{U_k \leq x\} = 1 - e^{-x/r_0}$ $(x \geq 0)$, the immigration process $\Pi(t)$ reduces to an ordinary Poisson process with instantaneous and cumulative rates $r(t) \equiv r_0$ and $R(t) = r_0 t$ respectively. Then we obtain the Sevastyanov age-dependent branching process with homogeneous Poisson immigration proposed and investigated by Yanev [35].

Define $M(t) = \mathbf{E}[Y(t) | Y(0) = 0]$. Differentiating both sides of (7), we obtain that

$$M(t) = \Psi_s'(t; s)\,|_{s=1} = \gamma \int_0^t r(t-u)A(u)du. \quad (8)$$

Put $\Psi(s_1, s_2; t, \tau) = \mathbf{E}[s_1^{Y(t)} s_2^{Y(t+\tau)} \mid Y(0) = 0]$, for $t, \tau \geq 0$. Using a line of arguments similar to that used to prove eq. (7) gives

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

where $F(s_1, s_2; t, \tau) = \mathbf{E}[s_1^{Z(t)} s_2^{Z(t+\tau)}]$ is given in eq. (22) Ch. VIII.8, [32].

The proof also uses eq. (6) and the line of arguments used to prove Theorem 1 (Yakovlev and Yanev [34]). Eq. (9) implies that

$$C(t, \tau) = Cov[Y(t), Y(t+\tau)] = \log \Psi(s_1, s_2; t, \tau)''_{s_1 s_2}\Big|_{s_1 = s_2 = 1} \quad (10)$$
$$= \int_0^t r(u)[\gamma B(t-u, \tau) + \gamma_2 A(t-u)A(t+\tau-u)]du,$$

with initial conditions $B(0, \tau) = A(\tau)$ and $C(0, \tau) = 0$. Setting $\tau = 0$ in eq. (10) yields

$$W(t) = Var[Y(t)] = \int_0^t r(t-u)[\gamma V(u) + (\gamma + \gamma_2)A^2(u)]du. \quad (11)$$

4. Asymptotic formulas for the moments

This section is concerned with the expectation, variance, and covariance of $Y(t)$ as $t \to \infty$. We consider 3 cases based on the immigration rate:

Case (i). $\int_0^\infty r(u)e^{-\alpha u}du < \infty$ (Proposition 4.1);

Case (ii). $r(t) = r_0 e^{\rho t}$ where $r_0 > 0$, and $\rho \in \mathbf{R}$ (Propositions 4.2 and 4.3). In this case the asymptotics depend [on how the immigration parameter ρ compares to the Maltusian parameter α;

Case (iii). $r(t) = r_0 \times t^\theta$ or $r(t) = r_0 \times (t+1)^\theta$ where $r_0 > 0$, and $\theta \in \mathbf{R}$. In this case the moments either converge to 0 (if $\theta < 0$) or diverge to infinity (if $\theta > 0$). (Proposition 4.4).

We shall use the lemma and corollary below to derive asymptotics for the moments.

Lemma 4.1—*Let $f(t) \sim Ct^\theta$, as $t \to \infty$, where $C > 0$ and $\theta \in \mathbb{R}$. Assume that $\sup_{0 \le x \le t} f(x) \le Dt^{\max(\theta, 0)}$ for some $D < \infty$. Let $y(\cdot)$ be a function such that $y(t) \ge 0$ ($t \ge 0$), $\bar{y} = \int_0^\infty y(u)du < \infty$, and $y(t) = o(t^{\theta - 1})$ if $\theta < 0$. Then, as $t \to \infty$,*

$$I(t) = \int_0^t f(t-u)y(u)du \sim \bar{y} f(t).$$

Proof: For every $0 < \delta < 1$, we have $I(t) = \int_0^t f(t-u)y(u)du = \int_0^{\delta t} + \int_{\delta t}^t = I_1(t) + I_2(t)$. When the assumptions of the lemma hold, for every $\varepsilon > 0$ and when t is large enough, then $(C - \varepsilon)t^\theta \le f(t) \le (C + \varepsilon)t^\theta$ and

$$(C-\varepsilon)t^\theta \int_0^{\delta t} \left(1 - \frac{u}{t}\right)^\theta y(u)du \le I_1(t) \le (C+\varepsilon)t^\theta \int_0^{\delta t} \left(1 - \frac{u}{t}\right)^\theta y(u)du.$$

To determine the limit of $I_1(t)$ as $t \to \infty$, assume first that $\theta \ge 0$. Then

$$(C-\varepsilon)t^\theta (1-\delta)^\theta \int_0^{\delta t} y(u)du \le I_1(t) \le (C+\varepsilon)t^\theta \int_0^{\delta t} y(u)du,$$
$$\left(1 - \frac{\varepsilon}{C}\right)(1-\delta)^\theta \bar{y} \le \lim_{t \to \infty} \inf \frac{I_1(t)}{f(t)} \le \lim_{t \to \infty} \sup \frac{I_1(t)}{f(t)} \le \left(1 + \frac{\varepsilon}{C}\right)\bar{y}.$$

Therefore, $\lim_{t\to\infty}[I_1(t)/f(t)] = \bar{y}$. Assume next that $\theta \le 0$. Then

$$(C-\varepsilon)t^\theta \int_0^{\delta t} y(u)du \le I_1(t) \le (C+\varepsilon)t^\theta (1-\delta)^\theta \int_0^{\delta t} y(u)du,$$
$$\left(1 - \frac{\varepsilon}{C}\right)\bar{y} \le \lim_{t \to \infty} \inf \frac{I_1(t)}{f(t)} \le \lim_{t \to \infty} \sup \frac{I_1(t)}{f(t)} \le \left(1 + \frac{\varepsilon}{C}\right)(1-\delta)^\theta \bar{y}.$$

Hence $\lim_{t\to\infty}[I_1(t)/f(t)] = \bar{y}$.

Likewise, to study $I_2(t)$ as $t \to \infty$, assume first that $\theta \ge 0$. Then

$$I_2(t) \le \sup_{0 \le x \le t(1-\delta)} f(x) \int_{\delta t}^t y(u)du \le Dt^\theta (1-\delta)^\theta \int_{\delta t}^t y(u)du,$$

which establishes that $\lim\sup_{t\to\infty}[I_2(t)/f(t)] = 0$. Assume next that $\theta < 0$. Then, $I_2(t) \le \sup_{0 \le x \le t(1-\delta)} f(x) \int_{\delta t}^t y(u)du = o(t^\theta)$, and $\lim\sup_{t\to\infty}[I_2(t)/f(t)] = 0$.

We finally deduce that $\lim_{t\to\infty}[I(t)/f(t)] = \bar{y}$, which completes the proof.

Corollary 4.1—*Let $f(t)$ and $y(t)$ be nonnegative functions. Assume that $f(t)$ is bounded in $\mathbb{R}^+$, and that there exists $f^* < \infty$ and $\bar{y} < \infty$ such that $\lim_{t\to\infty} f(t) = f^*$ and $\int_0^\infty y(t)dt = \bar{y}$. Then,*

$$\lim_{t \to \infty} \int_0^t f(u)y(t-u)du = f^* \bar{y}.$$

Define, for every $\alpha < 0$, $\hat{r}_t(\alpha) = \int_0^t r(u)e^{-\alpha u}du$, and assume that

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

Inequality (12) holds if, for example, the intensity of the immigration assumes the form $r(t) = O(e^{\rho t})$ with $\rho < \alpha$.

Proposition 4.1—*Assume* (1), (12), *and* $\gamma_2 < \infty$. *Then, as* $t \to \infty$,

$$M(t) = A\gamma\hat{r}(\alpha)e^{\alpha t}(1 + o(1)) . \quad (13)$$

Moreover, if (2) *and Condition 3.1 hold, then, as* $t \to \infty$,

$$C(t, \tau) = \gamma\hat{r}(\alpha)D_\tau e^{\alpha(t+\tau)}(1 + o(1)) . \quad (14)$$

Proof: Eq. (8) entails that

$$M(t) = \gamma e^{\alpha t} \int_0^t r(t-u)e^{-\alpha(t-u)}A(u)e^{-\alpha u}du .$$

Using eqs. (3) and (12) and applying Corollary 4.1 yields that

$$\int_0^t r(t-u)e^{-\alpha(t-u)}A(u)e^{-\alpha u}du \to A\hat{r}(\alpha),$$

from which eq. (13) follows. The proof of eq. (14) relies on eqs. (3), (4) and (10), but remains otherwise similar to that of eq. (13).

Therefore, when the assumptions of Proposition 4.1 hold, the variance $W(t)$ satisfies

$$W(t) = D_0\gamma\hat{r}(\alpha)e^{\alpha t}(1 + o(1)), \; t \to \infty .$$

Proposition 4.2—*Assume* (1), $r(t) = r_0 e^{\rho t}$ *for some constant* $r_0 > 0$, *and* $t \to \infty$.

i. *If* $\rho > \alpha$, *then* $M(t) = \gamma r_0 \hat{A}(\rho) e^{\rho t}(1 + o(1))$, $\hat{A}(\rho) = \int_0^\infty e^{-\rho u} A(u) du < \infty$;

ii. *If* $\rho = \alpha$, *then* $M(t) = \gamma r_0 A t e^{\alpha t}(1 + o(1))$;

iii. *If* $\rho < \alpha$, *then* $M(t) = \frac{r_0 \gamma A}{\alpha - \rho} e^{\alpha t}(1 + o(1))$.

Proof

i. We have from eq. (8) that $M(t) = \gamma r_0 e^{\rho t} \int_0^t e^{-(\rho - \alpha)u} A(u) e^{-\alpha u} du$. Since $A(u)e^{-\alpha u} \to A$, $u \to \infty$ (by eq. (3)), and $\rho - \alpha > 0$ the integral converges to $\hat{A}(\rho)$ which completes the proof.

ii. In this case $M(t) = \gamma r_0 e^{at} \int_0^t A(u) e^{-\alpha u} du$ and $\int_0^t A(u) e^{-\alpha u} du \sim At$, $t \to \infty$, which completes the proof.

iii. We have that $M(t) = \gamma r_0 e^{\alpha t} \int_0^t e^{(\rho - \alpha)(t - u)} A(u) e^{-\alpha u} du$. Since $A(u)e^{-\alpha u} \to A$, $u \to \infty$, (by eq. (3)) and $\int_0^\infty e^{(\rho - \alpha)t} dt = 1/(\alpha - \rho) > 0$, the proof follows from Corollary 4.1.

Proposition 4.3—*Assume* (1), (2), *Condition 3.1*, $r(t) = r_0 e^{\rho t}$, $r_0 > 0$, *and* $t \to \infty$.

i. *If* $\rho > \alpha$ *then* $C(t, \tau) = C(\tau) r_0 e^{\rho t + \alpha \tau}(1 + o(1))$, *where*

$$C(\tau) = \int_0^\infty e^{-\rho u - \alpha \tau} [\gamma B(u, \tau) + \gamma_2 A(u) A(u + \tau)] du < \infty .$$

ii. *If* $\rho = \alpha$ *then* $C(t, \tau) = r_0 \gamma D_\tau t e^{\alpha(t + \tau)}(1 + o(1))$.

iii. *If* $\rho < \alpha$ *then* $C(t, \tau) = \frac{r_0 \gamma D_\tau}{\alpha - \rho} e^{\alpha(t + \tau)}(1 + o(1))$.

Proof: We deduce from eq. (10) that

$$C(t, \tau) = r_0 e^{\rho t + \alpha \tau} \int_0^t e^{-(\rho - \alpha)u} [\gamma B(u, \tau) + \gamma_2 A(u) A(u + \tau)] e^{-\alpha(u + \tau)} du .$$

In case (i), eqs. (3), (4), and (5) entail that

$$[\gamma B(u, \tau) + \gamma_2 A(u) A(u + \tau)] e^{-\alpha(u + \tau)} \to \gamma D_\tau, \ t \to \infty . \quad (15)$$

Since $\rho > \alpha$, the integral

$$C(\tau) = \int_0^\infty e^{-(\rho - \alpha)u}[\gamma B(u,\tau) + \gamma_2 A(u)A(u+\tau)]\, e^{-\alpha(u+\tau)} du$$

converges. This completes the proof of (i).

In case (ii), it follows from eq. (15) that

$$\int_0^t [\gamma B(u,\tau) + \gamma_2 A(u)A(u+\tau)]\, e^{-\alpha u} du \sim \gamma D_\tau t, \quad t \to \infty,$$

which completes the proof of (ii).

In case (iii), we have that

$$C = \int_0^\infty e^{-(\alpha - \rho)u} du = \frac{1}{\alpha - \rho} \in (0, \infty)$$

and the statement follows from eq. (15) and Corollary 4.1.

Corollary 4.2—*Suppose the assumptions of Proposition 4.3 hold. Then, as* $t \to \infty$:

i. *If* $\rho > \alpha$, *then* $W(t) = We^{\rho t}(1 + o(1))$ *where*

$$W = r_0 \int_0^\infty e^{-\rho u}[\gamma V(u) + (\gamma + \gamma_2)A^2(u)]du < \infty;$$

ii. *If* $\rho = \alpha$, *then* $W(t) = r_0 \gamma D_0 t e^{\alpha t}(1 + o(1))$;

iii. *If* $\rho < \alpha$, *then* $W(t) = \frac{r_0 \gamma D_0}{\alpha - \rho} e^{\alpha t}(1 + o(1))$.

Proposition 4.4—*Suppose that* (1), (2), *and Condition 3.1 hold, and assume further that* $r(t) = r_0 \times t^\theta$, $0 < \theta < \infty$, *or* $r(t) = r_0 \times (t+1)^\theta$, $-\infty < \theta < 0$, *where* $r_0 > 0$ *is a constant. Then, as* $t \to \infty$,

$$M(t) = Mt^\theta(1 + o(1)),\ M = \gamma r_0 \int_0^\infty A(u)du, \quad (16)$$

$$W(t) = Wt^\theta(1 + o(1)),\ W = r_0 \int_0^\infty [\gamma V(u) + (\gamma + \gamma_2)A^2(u)]du \quad (17)$$

and for any $\tau \geq 0$,

$$C(t,\tau) = C(\tau)t^{\theta}(1 + o(1)), \quad (18)$$

where $C(\tau) = r_0 \int_0^{\infty} (\gamma B(u,\tau) + \gamma_2 A(u)A(u+\tau))du$.

Proof: Eq. (3) implies that $\int_0^{\infty} A(u)du < \infty$. Then eq. (16) follows from eq. (8) and Lemma 4.1. Eq. (17) is a consequence of eqs. (11), (3) and (5), and Lemma 4.1. The proof of (18) proceeds similarly using eqs. (10), (3) and (4).

5. Limit theorems

This section presents four classes of limit theorems. The first one is a conditional limit theorem of the form $\lim_{t \to \infty} \mathbf{P}\{Y(t) = k/Y(0) > 0\} = q_k$, with $\sum_{k=1}^{\infty} q_k = 1$, based on the fact that $Y(t) \xrightarrow{\mathbf{P}} 0$ as $t \to \infty$ when $\lim_{t \to \infty} M(t) = 0$. This result is akin to a limit theorem for subcritical processes without immigration (Theorem 2, sect. IX.3, [32]). The second one is a LLN that shows that $Y(t)/M(t)$ converges to 1 in some appropriate sense as $M(t) \to \infty$. The third one is a Central Limit Theorem satisfied by $Y(t)$ when properly normalized. The fourth class of theorems generalizes a classical result on the asymptotic distribution of $Y(t)$ for Markov branching processes with immigration when $\lim_{t \to \infty} r(t) = r_0 > 0$ that is due to Sevastyanov [29].

One of the by-products of these limit theorems is the classification of the process into three subclasses:

- **i.** the subcritical-subcritical case for which conditional limiting distributions are obtained (see Theorems 5.1, 5.2, 5.3);
- **ii.** the subcritical-supercritical case for which LLN and CLT are established (see Theorems 5.4, 5.5, 5.6, and 5.7);
- **iii.** the pure subcritical case for which a stationary distribution exists and is characterized in Theorem 5.8.

It is interesting to point out that in case (i) the probability of non-extinction converges exponentially quickly to zero at rate α, the Malthusian parameter (see Theorem 5.1). In Theorem 5.2, the convergence rate is ρ, the immigration rate, and in Theorem 5.3 it is regular varying at infinity with exponent $\theta < 0$ (the parameter of the immigration intensity).

In case (ii), we show that the asymptotic variance of the normalized process (σ^2) depends on the parameter ρ of the immigration intensity in Theorem 5.5, whereas in Theorem 5.7 it is independent of the corresponding parameter θ. In both cases we show that $0 < \sigma^2 < 1$.

Theorem 5.1

Assume (1), (2), *and* $\lim_{t \to \infty} \hat{r}_t(\alpha) = \hat{r}(\alpha) < \infty$. *Then,*

- **i.** $\mathbf{P}\{Y(t) > 0\} = Ce^{\alpha t}(1 + o(1))$, $C > 0$, *as* $t \to \infty$.

ii. *There exists a conditional stationary distribution*

$$\lim_{t \to \infty} \mathbf{P}\{Y(t) = k \mid Y(t) > 0\} = q_k > 0, k = 1, 2....$$

Proof—Under the assumptions of the theorem, we have ([32], sect. IX.3 Theorem 1 and 2) as $t \to \infty$ and for every $s \in [0, 1]$

$$\mathbf{P}\{Z(t) > 0\} = 1 - F(t, 0) = Qe^{\alpha t}(1 + o(1)), \quad (19)$$

$$1 - F(t, s) = Q(s)e^{\alpha t}(1 + o(1)). \quad (20)$$

Since $1 - g(s) = \gamma(1 - s)(1 + o(1))$, it follows, as $t \to \infty$, that

$$1 - g(F(t, 0)) = \gamma Qe^{\alpha t}(1 + o(1)), \quad (21)$$

and for every $s \in [0, 1]$,

$$1 - g(F(t, s)) = \gamma Q(s)e^{\alpha t}(1 + o(1)). \quad (22)$$

Define the conditional p.g.f.

$$\Psi^*(t; s) = \mathbf{E}\{s^{Y(t)} \mid Y(t) > 0\} = 1 - \frac{1 - \Psi(t; s)}{1 - \Psi(t; 0)}. \quad (23)$$

Note first that $\Psi(t; 0) = e^{-J(t)}$, where $J(t) = \int_0^t r(t - u)[1 - g(F(u; 0))]du$. Then, eq. (21) and Lemma 4.1 entail, as $t \to \infty$, that

$$J(t) = e^{\alpha t}\int_0^t r(t - u)e^{-\alpha(t - u)}e^{-\alpha u}(1 - g(F(u, 0))du \sim e^{\alpha t}\gamma Q\hat{r}(\alpha).$$

Furthermore, $\Psi(t; s) = \exp(-J(t; s))$, where from (22) and Lemma 4.1:

$$
\begin{aligned}
J(t;s) &= \int_0^t r(t-u)(1-g(F(u;s)))du \\
&= e^{\alpha t}\int_0^t r(t-u)e^{-\alpha(t-u)}e^{-\alpha u}(1-g(F(u;s)))du \\
&\sim e^{\alpha t}\gamma Q(s)\hat{r}(\alpha), \quad t\to\infty .
\end{aligned}
$$

Since $\alpha<0$, $J(t)\to 0$ and $J(t;s)\to 0$, uniformly in $s\in[0,1]$. Therefore, as $t\to\infty$

$$
\begin{aligned}
1-\Psi(t;s) &= 1-e^{-J(t;s)} = J(t;s)(1+o(1)) = e^{\alpha t}\gamma Q(s)\hat{r}(\alpha)(1+o(1)), \\
1-\Psi(t;0) &= 1-e^{-J(t)} = J(t)(1+o(1)) = e^{\alpha t}\gamma Q\hat{r}(\alpha)(1+o(1)),
\end{aligned}
$$

The last two relationships show that uniformly in $s\in[0,1]$

$$
\lim_{t\to\infty}\Psi^*(t;s) = \Psi^*(s) = \sum_{k=1}^{\infty} q_k s^k = 1 - Q(s)/Q,
$$

which completes the proof of the theorem by invoking the continuity theorem for p.g.f.

Remark 5.1

The limiting p.g.f. $\Psi^*(s) = \sum_{k=1}^{\infty} q_k s^k$, $0\le s\le 1$, in Theorem 5.1 is similar to that holding for the standard Sevastyanov process without immigration.

Theorem 5.2

Assume (1), (2), *and* $r(t) = r_0 e^{\rho t}$, $r_0>0$, $\alpha<\rho<0$. *Then,*

i. $\mathbf{P}\{Y(t)>0\} = Ke^{\rho t}(1+o(1))$, $K>0$, *as* $t\to\infty$.

ii. *There exists a conditional stationary distribution*

$$
\lim_{t\to\infty}\mathbf{P}\{Y(t)=k \mid Y(t)>0\} = q_k > 0,\ k=1,2,\ldots,
$$

where

$$
\Psi^*(s) = 1 - \frac{\int_0^\infty e^{-\rho u}[1-g(F(u;s))]du}{\int_0^\infty e^{-\rho u}[1-g(F(u;0))]du}, \quad \Psi^*(1)=1.
$$

Proof—Following the proof of the previous theorem we obtain

$$
J(t) = r_0 e^{\rho t}\int_0^t e^{-\rho u}[1-g(F(u;0))]du \sim r_0 K e^{\rho t}, t\to\infty ,
$$

where $K = \int_0^{\infty} e^{-\rho u}[1 - g(F(u; 0))]du < \infty$. Similarly for every $s \in [0, 1)$

$$J(t; s) = r_0 e^{\rho t} \int_0^t e^{-\rho u}[1 - g(F(u; s))]du \sim r_0 K(s) e^{\rho t}, t \to \infty,$$

where $K(s) = \int_0^{\infty} e^{-\rho u}[1 - g(F(u; s))]du < \infty$. Therefore, following the proof of Theorem 5.1, we obtain as $t \to \infty$ that

$$\mathbf{P}\{Y(t) > 0\} = 1 - \Psi(t; 0) \sim r_0 K e^{\rho t}, \quad 1 - \Psi(t; s) \sim r_0 K(s) e^{\rho t}.$$

Hence, by (23), there exists $\Psi^*(s) = \lim_{t\to\infty} \Psi^*(t; s) = 1 - K(s)/K$, which proves the theorem.

Theorem 5.3

Assume (1), (2) *and* $r(t) = r_0 \times (t + 1)^{\theta}$, $\theta < 0$, $r_0 > 0$. *Then*

i. $\mathbf{P}\{Y(t) > 0\} \sim -(r_0 \gamma Q/\alpha) t^{\theta}$ *as* $t \to \infty$.

ii. *There exists a conditional stationary distribution* $\{q_k\}_{k=1}^{\infty}$ *such that*

$$\lim_{t \to \infty} \mathbf{P}\{Y(t) = k \mid Y(t) > 0\} = q_k \quad (k = 1, 2, \ldots)$$

where $\Psi^*(s) = 1 - Q(s)/Q$, $\Psi^*(1) = 1$, *and Q and Q*(*s*) *are defined in* (19) *and* (20).

Proof—Consider the conditional p.g.f. $\Psi^*(t; s)$ as defined in eq. (23) and note that $\Psi(t; s) = \exp\{-r^0 \times (t + 1)^{\theta} J_1(t; s)\}$ where

$$\begin{aligned} J_1(t; s) &= \int_0^t (1 - u/(t + 1))^{\theta}[1 - g(F(u; s))]du \\ &= (t + 1)\int_0^{1 - 1/(t + 1)} (1 - x)^{\theta}[1 - g(F(x(t + 1); s))]dx. \end{aligned}$$

Setting $s = 0$, we deduce from (21) that

$$1 - g(F(x(t + 1); 0)) \sim \gamma[1 - F(x(t + 1); 0) \sim \gamma Q e^{\alpha x(t + 1)}, t \to \infty.$$

Therefore,

$$J_1(t;0) \sim \gamma Q \times (t+1)\int_0^{1-1/(t+1)} (1-x)^{\theta} e^{\alpha x(t+1)}dx, t \to \infty .$$

Furthermore, as $t \to \infty$,

$$(t+1)\int_0^{1-1/(t+1)} (1-x)^{\theta} e^{\alpha x(t+1)}dx = \alpha^{-1}\left[e^{\alpha t}(t+1)^{-\theta} - 1 + \theta\int_0^{1-1/(t+1)} (1-x)^{\theta-1} e^{\alpha x(t+1)}dx\right]$$
$$\to -\alpha^{-1},$$

because Lemma 4.1 ensures that

$$I(t) = \int_0^{1-1/(t+1)} (1-x)^{\theta-1} e^{\alpha x(t+1)}dx = (t+1)^{-\theta}\int_0^{t} (t+1-u)^{\theta-1} e^{\alpha u}du \sim -(\alpha t)^{-1} .$$

Hence $\lim_{t\to\infty} J_1(t; 0) = \gamma Q/(-\alpha)$ such that

$$1 - \Psi(t;0) \sim 1 - \exp\{(r_0\gamma Q/\alpha)t^{\theta}\} \sim -(r_0\gamma Q/\alpha)t^{\theta}, t \to \infty ,$$

which completes the proof of (i).

Similarly, eq. (22) implies, as $t \to \infty$, that

$$1 - g(F(xt;s)) \sim \gamma[1 - F(xt;s)] \sim \gamma Q(s)e^{\alpha xt} .$$

Hence,

$$J_1(t;s) \sim \gamma Q(s)(t+1)\int_0^{1-1/(t+1)} (1-x)^{\theta} e^{\alpha x(t+1)}dx, t \to \infty .$$

Therefore $\lim_{t\to\infty} J_1(t; s) = \gamma Q(s)/(-\alpha)$, and $1-\Psi(t; s) \sim 1-\exp\{(r_0\gamma Q(s)/\alpha)t^{\theta}\} \sim -(r_0\gamma Q(s)/\alpha)t^{\theta}$. Hence, $\lim_{t\to\infty} \Psi^*(t; s) = \Psi^*(s) = 1 - Q(s)/Q$.

Corollary 5.1. [Markov case]

Assume that $G(x) = 1 - e^{-x/\mu}$ $(x \geq 0)$ *for some* $\mu > 0$, $h(\cdot; s) \equiv h(s)$ *for every* $|s| \leq 1$, *and*

$$0 < -\log Q = \int_0^1 \{[\alpha x + f(1-x)]/xf(1-x)\}dx < \infty ,$$

where $f(s) = [h(s) - s]/\mu$ *is the infinitesimal g.f. Then*

$$\Psi^*(s) = 1 - \exp\left\{\alpha \int_0^s dx/f(x)\right\} \ \textit{with}\ \ \Psi^*(1) = 1.$$

Proof—The following asymptotic identities hold as $t \to \infty$ under the assumptions of the theorem (see [32], Ch.II.2, Th.1 and Ch.II.4, Th.1)

$$1 - F(t,0) \sim Qe^{\alpha t}, Q > 0,$$
$$[1 - F(t,s)]/[1 - F(t,0)] \to \exp\left\{\alpha \int_0^s (1/f(x))dx\right\}.$$

Therefore, we deduce from the proof of Theorem 5.3 that $Q(s) = Q\exp\{\alpha\int_0^s dx/f(x)\}$. Hence,

$$\Psi^*(s) = 1 - Q(s)/Q = 1 - \exp\left\{\alpha \int_0^s (1/f(x))dx\right\}.$$

Theorem 5.4

Assume that inequalities (1) *and* (2), *and Condition 3.1 hold. Assume further that* $r(t) = r_0e^{\rho t}$, $r_0 > 0$, $\rho > 0$, $\gamma_2 < \infty$. *Then, as* $t \to \infty$

$$\zeta(t) = Y(t)/M(t) \to 1,\ a.s.\ \textit{and in}\ L_2.$$

Proof—To establish the convergence in L_2, it it is sufficient to show that as $t \to \infty$,

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

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

$$\Delta(t,\tau) = Var(\zeta(t+\tau)) + Var(\zeta(t)) - 2Cov\{\zeta(t), \zeta(t+\tau)\},$$
$$Var(\zeta(t)) = W(t)M(t)^{-2}$$
$$Cov\{\zeta(t), \zeta(t+\tau)\} = C(t,\tau)/(M(t)M(t+\tau)).$$

Since $\rho > \alpha$ we deduce from Proposition 4.2 (i), Corollary 4.2 (i), and Proposition 4.3 (i) as $t \to \infty$, that

$$W(t)M(t)^{-2} = We^{\rho t}(\gamma r_0 \hat{A}(\rho))^{-2}e^{-2\rho t} \to 0,$$
$$W(t+\tau)M(t+\tau)^{-2} = We^{\rho(t+\tau)}(\gamma r_0 \hat{A}(\rho))^{-2}e^{-2\rho(t+\tau)} \to 0,$$
$$C(t,\tau)(M(t)M(t+\tau))^{-1} = C(\tau)r_0 e^{\alpha\tau + \rho t}(\gamma r_0 \hat{A}(\rho))^{-2}e^{-\rho(2t+\tau)} \to 0,$$

where the convergence in the last two relationships are uniform in $\tau \geq 0$. Therefore $\lim_{t\to\infty} \Delta(t, \tau) = 0$ uniformly in $\tau \geq 0$, which proves the convergence in L_2 and

$$\Delta(t) = \lim_{\tau \to \infty} \Delta(t,\tau) = E\{\zeta(t) - 1\}^2 = W(t)/M^2(t) \sim K_1 e^{-\rho t},$$

where $K_1 = W/(\gamma r_0 \hat{A}(\rho))^2$. Therefore $\int_0^\infty \Delta(t)dt < \infty$ and by Theorem 21.1 of Harris [6], we deduce that $\zeta(t)$ converges a.s. to 1.

Theorem 5.5

Assume (1), (2), *Condition 3.1,* $r(t) = r_0 e^{\rho t}$, $r_0 > 0$, $\rho > 0$ *and* $\gamma_2 < \infty$. *Then*

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

where

$$\sigma^2 = \frac{\int_0^\infty e^{-\rho u}\left(\gamma B(u) + \gamma_2 A^2(u)\right)du}{\int_0^\infty e^{-\rho u}(\gamma B(u) + \gamma A(u) + \gamma_2 A^2(u))\,du} \in (0,1)\,. \qquad (24)$$

Proof—Let $\varphi_t(z) = E\{e^{izX(t)}\}$ denote the characteristic function of $X(t)$. Then,

$$\varphi_t(z) = e^{-izM(t)/\sqrt{W(t)}}E\{e^{izY(t)/\sqrt{W(t)}}\}$$
$$= e^{-izM(t)/\sqrt{W(t)}}\Psi(t; e^{iz/\sqrt{W(t)}})\,.$$

We deduce from eq. (7) that

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

The following asymptotic expansions hold as $s \to 1$ (see [32])

$$1 - g(s) \sim \gamma(1-s) - \gamma_2(1-s)^2/2,$$
$$1 - F(u;s) \sim A(u)(1-s) - B(u)(1-s)^2/2.$$

Moreover $1 - e^x = -x(1 + o(1))$ as $x \to 0$. Hence, as $t \to \infty$,

$$\log \varphi_t(z) \sim -\frac{izM(t)}{\sqrt{W(t)}} - \int_0^t r(t-u)\left\{\gamma[1 - F(u; e^{\frac{iz}{\sqrt{W(t)}}})] - \frac{\gamma_2}{2}[1 - F(u; e^{\frac{iz}{\sqrt{W(t)}}}]^2\right\} du, \quad (25)$$

and

$$1 - F(u; e^{\frac{iz}{\sqrt{W(t)}}}) \sim A(u)(1 - e^{\frac{iz}{\sqrt{W(t)}}}) - \frac{B(u)}{2}(1 - e^{\frac{iz}{\sqrt{W(t)}}})^2 \sim -\frac{izA(u)}{\sqrt{W(t)}} + \frac{z^2B(u)}{2W(t)}.$$

Therefore,

$$\int_0^t r(t-u)\left\{\gamma[1 - F(u; e^{\frac{iz}{\sqrt{W(t)}}})] - \frac{\gamma_2}{2}[1 - F(u; e^{\frac{iz}{\sqrt{W(t)}}})]^2\right\} du$$
$$\sim -\frac{iz\gamma}{\sqrt{W(t)}}\int_0^t r(t-u)A(u)du + \frac{z^2\gamma}{2W(t)}\int_0^t r(t-u)B(u)du + \frac{\gamma_2 z^2}{2W(t)}\int_0^t r(t-u)A^2(u)du$$
$$\sim -\frac{izM(t)}{\sqrt{W(t)}} + \frac{z^2}{2}\left[1 - \frac{M(t)}{W(t)}\right].$$

Returning to eq. (25), and letting $t \to \infty$, we find that

$$\log \varphi_t(z) \sim -\frac{z^2}{2}\left[1 - \frac{M(t)}{W(t)}\right]. \quad (26)$$

We deduce from Proposition 4.2 (i) and Corollary 4.2 (i) that

$$\lim_{t \to \infty} \frac{M(t)}{W(t)} = \frac{\int_0^\infty e^{-\rho u}\gamma A(u)du}{\int_0^\infty e^{-\rho u}(\gamma B(u) + \gamma A(u) + \gamma_2 A^2(u))\,du}.$$

from which the expression for σ^2 given in eq. (24) follows. Finally, $\lim_{t\to\infty} \varphi_t(z) = e^{-z^2\sigma^2/2}$, which is the characteristic function of a normal distribution with mean 0 and variance σ^2, and the assertion follows from the continuity theorem [4].

Corollary 5.2

Theorem 5.5, Proposition 4.2 (i) and Corollary 4.2 (i) entail the asymptotic normality:

$$Y(t)e^{-\rho t} \sim N(r_0\gamma\hat{A}(\rho), \sigma^2 W e^{-\rho t}),\ t \to \infty\ .$$

Theorem 5.6

Assume (1), (2), $\gamma_2 < \infty$, *Condition 3.1, and* $r(t) = r_0 t^\theta$ *with* $\theta > 0$ *and* $r_0 > 0$. *Then* $\zeta(t) = Y(t)/M(t) \to 1$ *in* L_2 *as* $t \to \infty$. *The convergence is almost sure if* $\theta > 1$.

Proof—We first deduce from (16), (17), and (18) that, as $t \to \infty$,

$$Var(\zeta(t)) = W(t)M^{-2}(t) \sim WM^{-2}t^{-\theta}, \quad (27)$$

and

$$Cov\{\zeta(t), \zeta(t+\tau)\} = C(t,\tau)(M(t)M(t+\tau))^{-1} \sim C(\tau)M^{-2}(t+t)^{-\theta}. \quad (28)$$

Then eq. (27) and (28) entail that $\Delta(t, \tau) \to 0$ uniformly in $\tau \geq 0$, and the convergence in L_2 follows.

Assume now that $\theta > 1$. Eqs. (27) and (28) entails that $Var(\zeta(t+\tau)) \sim WM^{-2}(t+\tau)^{-\theta} \to 0$ and $Cov\{\zeta(t), \zeta(t+\tau)\} \sim C(\tau)M^{-2}(t+\tau)^{-\theta} \to 0$, $\tau \to \infty$. Hence, $\Delta(t) \sim WM^{-2}t^{-\theta}$, $t \to \infty$, and $\int_0^\infty \Delta(t)dt < \infty$. We deduce from Theorem 21.1 of Harris [6] that $\zeta(t)$ converges to 1 a.s..

Theorem 5.7

Assume (1), (2), $\gamma_2 < \infty$, *Condition 3.1, and* $r(t) = r_0 t^\theta$ *with* $\theta > 0$ *and* $r_0 > 0$. *Then* $X(t) = [Y(t) - M(t)]/\sqrt{W(t)} \xrightarrow{\mathscr{D}} N(0, \sigma^2)$ *as* $t \to \infty$*, where*

$$\sigma^2 = \frac{\int_0^\infty [\gamma B(u) + \gamma_2 A^2(u)]du}{\int_0^\infty [\gamma B(u) + \gamma_2 A^2(u) + \gamma A(u)]du} \in (0, 1)\,.$$

Proof—Following the line of arguments used in the proof of Theorem 5.5 gives

$$\log \varphi_t(z) \sim -\frac{z^2}{2}\left[1 - \frac{M(t)}{W(t)}\right], \quad t \to \infty . \qquad (29)$$

We deduce from eqs. (16) and (17) in Proposition 4.4 that $\lim_{t \to \infty} M(t)/W(t) = M/W$. Finally, we obtain from eq. (29) that $\lim_{t \to \infty} \varphi_t(z) = e^{-z^2\sigma^2/2}$, which is the characteristic function of the normal distribution with mean 0 and variance σ^2. The assertion follows from the continuity theorem (e.g., Feller [4]).

Corollary 5.3

Theorem 5.7 and Proposition 4.4 entail the asymptotic normality: $Y(t)t^{-\theta} \sim N(M, \sigma^2 W t^{-\theta})$, $t \to \infty$.

Theorem 5.8

Assume (1), $\gamma < \infty$ *and that* $\lim_{t \to \infty} r(t) = r_0 > 0$. *Then there exists a limiting distribution* $Q_k = \lim_{t \to \infty} \mathbf{P}\{Y(t) = k\} > 0$ $(k = 0, 1, 2 \cdots)$, *such that*

$$\Psi^*(s) = \sum_{k=0}^{\infty} Q_k s^k = \exp\left\{-r_0 \int_0^{\infty} [1 - g(F(u,s))]du\right\}, \ |s| \le 1.$$

Proof—Under the assumptions of the theorem, $|1-g(s)| \le \gamma|1-s|$ and $|1-F(u;s)| \le A(u)|1-s|$. Therefore

$$\left| \int_0^t r(t-u)[1 - g(F(u,s))]du \right| \le \gamma |1-s| \int_0^t r(t-u)A(u)du .$$

Corollary 4.1 implies that

$$\lim_{t \to \infty} \int_0^t r(t-u)A(u)du = r_0 \int_0^{\infty} A(u)du < \infty .$$

Hence,

$$\lim_{t \to \infty} \Psi(t;s) = \Psi^*(s) = \exp\left\{-r_0 \int_0^{\infty} [1 - g(F(u,s))]du\right\}$$

uniformly in $|s| \le 1$.

Pakes [26] obtained a similar limiting distribution for the Bellman-Harris process.

Author Manuscript

Corollary 5.4

If $G(x) = 1 - e^{-x/\mu}$ $(x \geq 0)$*, for some* $\mu > 0$*, and* $h(u; s) \equiv h(s)$ *then*

$$\Psi^*(s) = \exp\left\{-r_0 \int_s^1 [1 - g(x)]/f(x)dx\right\}.$$

Proof—It follows from the assumptions that $\{Z(t)\}_{t \geq 0}$ is a Markov branching process, and it is characterized by the Kolmogorov differential equations

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

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

$$\begin{aligned} \frac{\partial}{\partial s}\int_0^\infty [1 - g(F(u, s))]du &= -\int_0^\infty g'(F(u; s))\frac{\partial F(u; s)}{\partial s}du \\ &= -\frac{1}{f(s)}\int_0^\infty g'(F(u; s))\frac{\partial F(u; s)}{\partial u}du \\ &= -\frac{1 - g(s)}{f(s)}, \end{aligned}$$

using the fact that $F(\infty; s) = 1$ and $F(0; s) = s$. Hence

$$\int_0^\infty [1 - g(F(u, s))]du = \int_s^1 [1 - g(x)]/f(x)dx,$$

which completes the proof.

Sevastyanov [29] obtained the same p.d.f. when $r(\cdot) \equiv r_0 > 0$.

Acknowledgments

The authors are thankful to the anonymous referee for his valuable suggestions which improve the earlier version of the paper.

The research was partially supported by the NFSR of the Min. Edu. Sci. of Bulgaria, grant No. DFNI-I02/17 and by NIH R01 Grants NS039511, CA134839, and AI069351.

References

1. Ahsanullah, M, Yanev, GP. Records and Branching Processes. Nova Science publishers; New York: 2008.
2. Assmusen, S, Hering, H. Branching Processes. Birkhauser; Boston: 1983.
3. Athreya, KB, Ney, PE. Branching Processes. Springer; New York: 1972.
4. Feller, W. An Introduction to Probability Theory and Its Applications. Vol. 2. Wiley; New York: 1971.

5. Chen R, Hyrien O, Mayer-Proschel M, Noble M. 2010; A composite likelihood approach to the analysis of longitudinal clonal data under an age-dependent branching process. Biostatistics. 12:173–191. [PubMed: 20732974]
6. Harris, TE. The Theory of Branching Processes. Springer; Berlin: 1963.
7. Hyrien O, Mayer-Proschel M, Noble M, Yakovlev A. 2005; A stochastic model to analyze clonal data on multi type cell populations. Biometrics. 61:199–207. [PubMed: 15737094]
8. Hyrien O, Ambeskovic I, Mayer-Proschel M, Noble M, Yakovlev A. 2006; Stochastic modeling of oligodendrocyte generation in cell culture: model validation with time-lapse data. Theoretical Biology and Medical Modelling. 3:21. [PubMed: 16707014]
9. Hyrien O, Chen R, Mayer-Proschel M, Noble M. 2010; Saddlepoint approximations to the moments of age-dependent branching processes with applications. Biometrics. 66:567–577. [PubMed: 19508238]
10. Hyrien O, Dietrich J, Noble M. 2010; Quantitative analysis of the effect of chemotherapy on division and differentiation of glial precursor cells. Cancer Research. 70(24):10051–10059. [PubMed: 21056994]
11. Hyrien O, Yanev NM. 2010; Modeling cell kinetics using branching processes with non-homogeneous Poisson immigration. Compt Rendus l'Acad Bulgar Sci. 63:1405–1414.
12. Hyrien O, Yanev NM, Jordan CT. 2014; A test of homogeneity for age-dependent branching processes with immigration. Electronic Journal of Statistics. 9:898–925.
13. Hyrien O, Peslak S, Yanev NM, Palis J. 2015; A stochastic model of stress erythropoiesis using a two-type age-dependent branching process with immigration. J Math Biol. 70:1485–1521. [PubMed: 24989701]
14. Hyrien, O, Yanev, NM. Age-dependent branching processes with non-homogeneous Poisson immigration as models of cell kinetics. In: Oakes, D, Hall, WJ, Almudevar, A, editors. Modeling and Inference in Biomedical Sciences: In Memory of Andrei Yakovlev. Institute of Mathematical Statistics; Beachwood, Ohio: 2015. IMS Collections Series(in press)
15. Hyrien O, Mitov KM, Yanev NM. 2015; CLT for Sevastyanov branching processes with non-homogeneous immigration. J Appl Stat Sci. 21:229–237.
16. Hyrien, O, Mitov, KM, Yanev, NM. Supercritical Sevastyanov branching processes with non-homogeneous Poisson immigration. In: del Puerto, IM, Gonzales, M, Gutierrez, C, Martinez, R, Minuesa, C, Molina, M, Mota, M, Ramos, A, editors. Branching Processes and their Applications. Vol. 219. Springer; New York: 2016. 151–166. Lecture Notes in Statistics
17. Jagers P. 1968; Age-dependent branching processes allowing immigration. Theory Probab Appl. 13:225–236.
18. Jagers, P. Branching Processes with Biological Applications. Wiley; London: 1975.
19. Kaplan N, Pakes AG. 1974; Supercritical age-dependent branching processes with immigration. Stochastic Process Appl. 2:371–389.
20. Kesten H, Stigum BP. 1967; Limit theorems for decomposable multi-dimensional Galton-Watson processes. J Math Anal Appl. 17:309–338.
21. Mitov KV, Yanev NM. 1982; Bellman-Harris branching processes with state-dependent immigration. J Appl Probab. 22:757–765.
22. Mitov KV, Yanev NM. 1989; Bellman-Harris branching processes with a special type of state-dependent immigration. Adv Appl Probab. 21:270–283.
23. Mitov KV, Yanev NM. 2002; Critical Bellman-Harris branching processes with infinite variance allowing state-dependent immigration. Stoch Models. 18:281–300.
24. Mitov KV, Yanev NM. 2013; Sevastyanov branching processes with non-homogeneous Poisson immigration. Proc Steklov Inst Math. 282:172–185.
25. Olofsson P. 1996; General branching processes with immigration. Journal of Applied Probability. 33:940–948.
26. Pakes AG. 1972; Limit theorems for an age-dependent branching process with immigration. Math Biosci. 14:221–234.
27. Pakes AG, Kaplan N. 1974; On the subcritical Bellman-Harris process with immigration. J Appl Probab. 11:652–668.

28. Radcliffe J. 1972; The convergence of a super-critical age-dependent branching processes allowing immigration at the epochs of a renewal process. Math Biosci. 14:37–44.

29. Sevastyanov BA. 1957; Limit theorems for branching random processes of special type. Theory Probab Appl. 2:339–348.

30. Sevastyanov BA. 1964; Age-dependent branching processes. Theory Probab Appl. 9:577–594.

31. Sevastyanov BA. 1968; Limit theorems for age-dependent branching processes. Theory Probab Appl. 13:243–265.

32. Sevastyanov, BA. Branching Processes. Nauka, Moscow: 1971. (in Russian)

33. Yakovlev A, Yanev NM. 2006; Branching stochastic processes with immigration in analysis of renewing cell populations. Math Biosci. 203:37–63. [PubMed: 16904129]

34. Yakovlev A, Yanev NM. 2007; Age and residual lifetime distributions for branching processes. Statist Probab Lett. 77:503–513.

35. Yanev NM. 1971; Branching processes allowing immigration. Bul Inst Math Acad Bulg Sci. 15:71–88.

36. Yanev NM. 1972; On a class of decomposable age-dependent branching processes. Math Balkanica. 2:58–75.

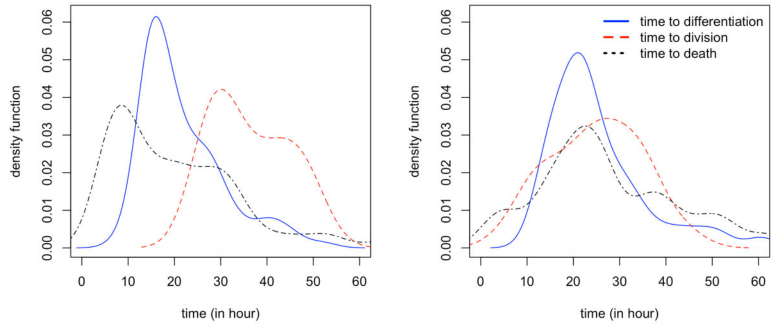

Figure 1.

Kernel density estimates of the distributions of the time to differentiation, the time to division, and the time to death of O-2A/OPCs in the presence (right) and in the absence (left) of thyroid hormone observed in time-lapse experiments (Hyrien et al, [8]). The plots indicate that the distribution of the lifespan depended on the fate of the cell (here: differentiation, division, or death), and that these distributions were affected by thyroid hormone. For example, the presence of thyroid hormone appeared to shorten the time to differentiation and increase the time to death and the time to division. Unlike the Bellman-Harris process, the Sevastyanov process is adapted to describe these features of the cell cycle.

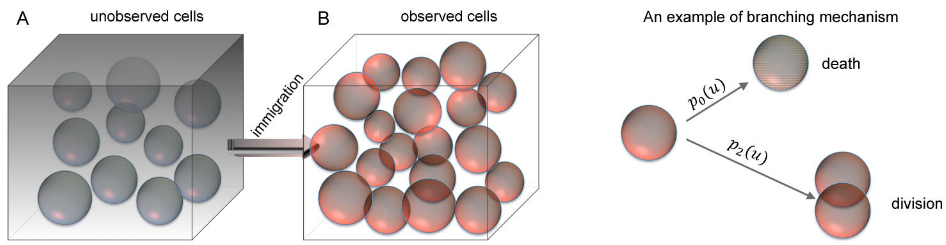

Figure 2.

Left: schematic representation of a population consisting of two types of cells: those in Box B are observed, and those in Box A are unobservable but contribute to the observed population (Box B) via immigration. Our process does not describe population dynamics within Box A, but formulates the influx of cells from Box A into Box B as a non-homogeneous Poisson process, and model the dynamics within Box B as a Sevastyanov process. Right: an example of branching mechanism allowed by the process in which a cell may either die or divide; the Sevastyanov process allows the probabilities of division and death to depend on the age of the cell. For instance, cell death may occur stochastically earlier than cell division.