

Branching Random Walks and their Applications for Epidemic Modelling

Elizaveta Ermakova, Polina Makhmutova, Elena Yarovaya

Dept. of Probability Theory Lomonosov Moscow State University

April, the 11th,
WBPA 2018

Outline

- 1 Introduction
 - Multitype Galton-Watson Branching Process
 - Wright-Fisher Branching Process
 - Bellman-Harris Branching Process
 - Crump-Mode-Jagers process
- 2 Motivation
 - BRWs for Viral Epidemic Modelling
- 3 Main Assumptions
 - Models without Vaccination
 - Models with Vaccination
- 4 BRWs with Finite Number of Initial Particles
 - Main Results
- 5 BRWs with Infinite Number of Initial Particles
 - Duality of BRW Models
- 6 BRW with Infinite Number of Sources and Initial Particles
- 7 References

Introduction

Branching processes are widely used in modelling of populations' behaviour, in particular, the viral epidemic evolution.

The main objects of investigations are the **quantity of infective organisms** or the **number of viral particles** - virions. Depending on aims of research different types of branching processes are used.

- Multitype Galton-Watson process (Antonelly, F., Bosco, F., 2012) Viral evolution and adaptation;
- Wright-Fisher process (Wilke, C., 2003) Probability of fixation of an advantageous mutant in a viral quasispecies;
- Bellman-Harris process (Gonzalez, M., et al., M. 2010) Epidemic modelling and optimal vaccination;
- Crump-Mode-Jagers process (Ball, F., et al., 2014) Application to vaccination in epidemic modelling.

Introduction

Branching processes are more natural for viral modelling under assumptions:

- the quantity of initial infectives is much less than the size of a susceptible population;
- SIR (Susceptible \rightarrow Infected \rightarrow Recovered) or SEIR schemes (Susceptible \rightarrow (Exposed) \rightarrow Infected \rightarrow Recovered) (infection takes place only once during host's lifetime);
- relatively long incubation period and negligible contagious time;

Such assumptions can be used in modelling of measles, mumps, avian influenza and parotit (see Gonzalez et.al., 2010, Ball, F., et.al., 2014).

The main interest is usually to find the best treatment or optimal vaccination, aimed at reducing the number of infected or the duration of outbreaks.

Introduction. Multitype Galton-Watson process (Antonelly, F., Bosco, F., 2012)

Considered a viral population in a host's organism. Particles of a virus are classified by replication capacity.

Branching process is determined by a number of viral particles in the generation n .

$Z_n \in \mathbb{Z}^R$ - a number of viral particles in each class in the generation n .

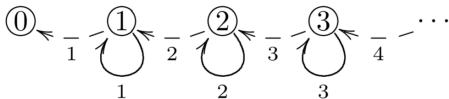
- $Z_0 \neq 0$;
- particles of r types, $0 < r < \infty$;
- a k -type particle produces k offsprings, $k = 1, 2, \dots, r$;

Introduction. Multitype Galton-Watson process

Connection between types: considered three (in general model) or two (in simple model) kinds of mutations - negative, neutral (and positive).

- d, b, c - probabilities of negative, positive and neutral mutations;
- Contiguous for i -type in simple model (a): $i - 1$, $i = 1, 2, \dots, r-1$;
- Contiguous for i -type in general model (b):
 $i - 1, i + 1$,
 $i = 1, 2, \dots, r-1$;

(a) Simple model



(b) General model

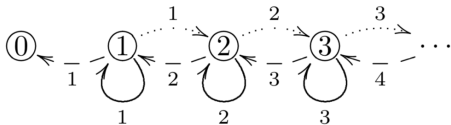


Figure: Transition between types

Introduction. Multitype Galton-Watson process

Results:

- The behaviour of the population depending on the size, the maximum replication capacity of classes and the fraction of the population not affected by deleterious effects;
- The survival probability of a virus population depends on its initial population size;
- The proof, in the context of the theory of branching processes, of the lethal mutagenesis criterion;
- A new proposal for the notion of relaxation time with a quantitative prescription for its evaluation;
- The quantitative description of the evolution of the expected values in four distinct regimes;
- New insights on the dynamics of evolving virus populations can be foreseen.

Probability of fixation of mutations in viral populations.

Authors consider a viral population with n types of particles, divided by a quantity of possible offsprings of a particle per one generation. Each particle is a sequence of genes with length L .

- $X(t) = (X_t^0, \dots, X_t^n), t = 0, 1, 2, \dots$ $X_t^i \in \mathbb{Z}^L$
- $X_t^{ij} \in \{1, \dots, \kappa\}$ $\kappa = 4$.
- N - size of viral population, fixed.

Wright-Fisher branching process:

$$N(t) = \sum_{k=0}^n X_t^k = \text{const}$$

Introduction. Wright-Fisher process

Results:

- Wright-Fisher model allows to investigate the relative quantity of particles of each type;
- The analytic expression for probability of mutant fixation;
- Estimations for fixation probability with different assumption about the mean number of offsprings of invading sequence;
- Estimation based on a small area of genotype space surrounding the invading sequence;
- Importance for investigation the disease dynamics and optimal vaccination;

Introduction. Bellman-Harris branching process (Gonzalez, M., et al., 2010)

Authors investigate the viral epidemic in a large hosts' population under following assumptions:

- SIR-scheme;
- A negligible contagious time;
- The size of population - N ;
- The number a of infectives at the beginning of the outbreak;
- A relatively small number of initial infectives;

Introduction. Bellman-Harris branching process

$Z(t)$ - number of particles at t , $Z(0) = 1$.

Vaccination is presented by the part of organisms, which are resistant to the virus.

Coefficient $\alpha \in [0, 1]$ - the part of immune organisms;

A particle lives during random time with probability function $G(\cdot)$, then produces k offsprings according to replication probability law $\{p_{\alpha,k}\}$;

The main result is **optimal vaccination level**, that guarantees viral distinction not later than after exact time with exact probability value (see Gonzalez, et al.).

Introduction. Crump-Mode-Jagers process (Ball, F., et al., 2010)

A closed population of potential viral hosts, with the size N and with a initial infectives is considered. Authors investigate SEIR-scheme virus.

Particles have IID life stories $H = H_i = (l_i, \xi_i)$, where ξ_i - is a point process of contact moments, l_i is a life length of the particle;

If a particle of i -type with life history $H_i = (l_i, \xi_i)$, $i = 1, \dots, N + a$, appears at the moment b_i and $0 \leq \tau_{i1}, \tau_{i2} \dots \leq l_i$ - points of the process ξ_i , then the particle i has one offspring in each moment $b_i + \tau_{i1}, b_i + \tau_{i2}, \dots$

$$Z(t) = \sum_{i=1}^{N+a} \mathbb{I}\{b_i \leq t, \quad b_i + l_i > t\}$$

$Z(t)$ - quantity of infectives at moment t ;

$Z(0) = a$ - quantity of infectives at $t = 0$.

Results

The main interest is also searching the optimal vaccination level.

Assumptions for vaccination :

- guarantees viral extinction with probability $\geq p$,
- outbreak lasts not longer than time t ,
- dependence on time.

That means, the part $\alpha \in [0, 1]$ of immune organisms is not stable during the outbreak.

The theory is illustrated by applications to the control of the duration of mumps outbreaks in Bulgaria.

BRWs for viral epidemic modelling

We suggest to apply BRWs for viral epidemic modelling. This allows to investigate not only the number of particles (infected individuals), but also their spatial spread.

The transport of infected individuals is described by a symmetric random walk on a multidimensional lattice (see in detail, e.g., Y. (2007)).

Processes of birth and death of infected individuals are represented by a continuous-time Bienayme-Galton-Watson processes at the lattice points (*branching sources*).

A special attention will be paid to the properties of BRWs with one branching source on the entire lattice.

We consider finitely or infinitely many initial particles, and the "duality" of this models. As well as we will shortly introduce BRW model with infinite number of sources and finite number of initial particles.

Each of the models can be considered taking into account the simplest vaccination process.

Main assumptions

Random walk:

$A = (a(x, y))_{x, y \in \mathbb{Z}^d}$ - matrix of transition intensities :

- 1 $a(x, y) \geq 0, \quad x \neq y; \quad a(x, x) < 0;$
- 2 $\sum_y a(x, y) = 0;$
- 3 $a(x, y) = a(y, x)$ (symmetry);
- 4 $\forall z \in \mathbb{Z}^d \quad \exists z_1, \dots, z_k :$
 $z = \sum_{i=1}^k z_i \quad \text{and} \quad a(z_i) \neq 0 \text{ for } i = 1, \dots, k$ (irreducibility)
- 5 $a(x, y) = a(0, y - x) =: a(y - x)$ (spatial homogeneity).

Let $p(t, x, y)$ be a transition probability. Than assume temporary homogeneity of a random walk:

$$p(t_1, x, y) = p(t_2, x, y), \quad \forall t_1 = t_2.$$

Branching process:

$f(u) = \sum_{k=0, k \neq 1}^{\infty} c_k u^k$ - probability generating function,

where c_i defines the probability of producing i by one particle and $c_i \geq 0$ for all $i \neq 1$, $c_1 < 0$, and $\sum_i c_i = 0$.

Assume f to be continuously differentiable:
 $\beta^{(i)} := f^{(i)}(1) < \infty$, $\beta := f'(1)$.

Short-time events in BRW:

I) at point $x = 0$, $h \rightarrow 0$:

- ① moving to $y \neq x$ with probability $a(x, y)h + o(h)$;
- ② producing $k \neq 1$ offsprings with probability $c_k h + o(h)$;
- ③ death with probability $c_0 h + o(h)$;
- ④ remaining at x with probability $1 + a(x, x)h + c_1 h + o(h)$ without offspring.

II) at point $x \neq 0$, $h \rightarrow 0$:

- ① moving to $y \neq x$ with probability $a(x, y)h + o(h)$;
- ② remaining at x with probability $1 + a(x, x)h + o(h)$.

Models with vaccination

Vaccination process takes place at every point of a lattice and reduces the intensity of birth of infected individuals, the intensity of death remains stable (see Gonzalez, et.al. 2010) .

The vaccination process does not depend on time, that allows to investigate spatial properties of viral evolution.

Coefficient $\alpha \in [0, 1]$ presents the vaccination success.
The case with two offsprings:

$$\tilde{c}_2 = \alpha c_2, \quad \tilde{c}_0 = c_0, \quad \tilde{c}_1 = -(c_0 + \alpha c_2)$$

Natural assumption:

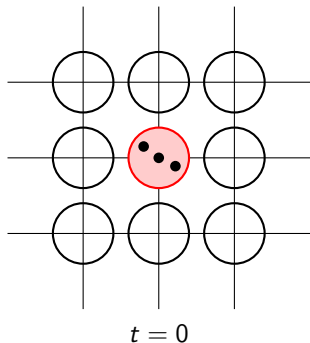
$$\tilde{c}_k = \alpha^{k-1} c_k.$$

Thus, during small time h , a particle at $x = 0$ can:

- 1 move to $y \neq x$ with probability $a(x, x)h + o(h)$;
- 2 remain at x and produces k offsprings with probability $\tilde{c}_k h + o(h) = \alpha^{k-1} c_k h + o(h)$;
- 3 die with probability $\tilde{c}_0 h + o(h) = c_0 h + o(h)$;
- 4 remain at x and have no offspring with probability $1 + a(x, x)h - \sum_{i=0, i \neq 1}^{\infty} \tilde{c}_i h + o(h)$.

Generating Function:
$$\tilde{f}(u) = \frac{(f(\alpha u) - uf(\alpha) + f(0)(1 - \alpha)(u - 1))}{\alpha}$$

Model I



$\mu_x(t)$ - quantity of particles at x in the moment t , $x \in \mathbb{Z}^d$,

$\mu(t)$ - general quantity of particles,

$\mu_x(0) = a\delta_0(x) \quad \forall x \in \mathbb{Z}^d, a \geq a_0 > 0.$

$m_n(t, x) := E_x \mu^n(t),$

$m_n(t, x, y) := E_x \mu_y^n(t), \quad n = 1, 2, \dots$

Let F_x be the Laplas generating function of the process:

$$F_x(z; t, x, y) := E_x e^{-z\mu(t)}$$

Main results

Statement (Differential equations for first moments)

First moment of symmetric random walk $m_1(t, x, y)$ satisfies Cauchy problem

$$\partial_t m_1(t, x, y) = H_x m_1(t, x, y), \quad m_1(0, \cdot, y) = a \delta_y(\cdot),$$

$$\partial_t m_1(t, x, y) = H_y m_1(t, x, y), \quad m_1(0, x, \cdot) = a \delta_x(\cdot),$$

where operators H_x, H_y have the forms:

$$H_x m_1(t, x, y) := (A m_1(t, \cdot, y))(x) + \beta \delta_0(x) m_1(t, x, y),$$

$$H_y m_1(t, x, y) := (A m_1(t, x, \cdot))(y) + \beta \delta_0(y) m_1(t, x, y).$$

Statement (Integral equations for first moments)

First moments of random walk satisfy integral equations:

$$m_1(t, x, y) = ap(t, x, y) + \beta \int_0^t p(t-s, x, 0)m_1(s, 0, y)ds,$$

$$m_1(t, x, y) = ap(t, x, y) + \beta \int_0^t p(t-s, 0, y)m_1(s, 0, y)ds,$$

$$m_1(t, x) = a + \beta \int_0^t p(t-s, x, 0)m_1(s, 0)ds,$$

$$m_1(t, x) = a + \beta \int_0^t m_1(s, x, 0)ds,$$

where $p(t, x, y)$ - solution of Cauchy problem

$$\partial_t p(t, x, y) = Ap(t, x, y), \quad p(t, \cdot, y) = \delta_y(\cdot).$$

Statement (Integral equations for higher moments)

Moments $m_k(t, x, y)$ and $m_k(t, x)$ with $k > 1$ satisfy

$$m_k(t, x, y) = m_1(t, x, y) + \int_0^t m_1(t-s, x, 0) g_k(m_1(s, 0, y), \dots, m_{k-1}(s, 0, y)) ds,$$

$$m_k(t, x) = m_1(t, x) + \int_0^t m_1(t-s, x, 0) g_k(m_1(s, 0), \dots, m_{k-1}(s, 0)) ds,$$

where functions g_n are following:

$$g_n(m_1, m_2, \dots, m_{n-1}) = \sum_{r=1}^n \frac{\beta^{(r)}}{r!} \cdot \sum_{\substack{i_1, \dots, i_r > 0, \\ i_1 + \dots + i_r = n}} \frac{n!}{i_1! \dots i_r!} m_{i_1} \dots m_{i_r}.$$

Limit theorems

The main interest is of asymptotic of first and high-order moments of particle's number with $t \rightarrow \infty$.

To analyze moment's behaviour, consider the Green function, which is Laplas transform of transition probabilities $p(t, x, y)$:

$$G_\lambda(x, y) := \int_0^\infty e^{-\lambda t} p(t, x, y) dt, \quad (1)$$

Let $\beta_c := \frac{1}{G_0(0,0)}$. If $\sigma^2 = -\frac{1}{a(0,0)} \sum_{x \in \mathbb{Z}^d} |x|^2 a(0, x) < \infty$, then $\beta_c := 0$

$d = 1, 2$ and $\beta_c := \frac{1}{G_\lambda(0,0)}$ if $d \geq 3$.

The form of asymptotics of the moments $m_n(t, x, y)$ and $m_n(t, y)$ depends on d -dimension of the lattice and the parameter β_c .

Limit theorems

Theorem

If $\sigma^2 = -\frac{1}{a(0,0)} \sum_{x \in \mathbb{Z}^d} |x|^2 a(0, x) < \infty$, then for all $n \in \mathbb{N}$ and $t \rightarrow \infty$

$$m_n(t, x, y) \equiv C_n(x, y)u_n(t), \quad m_n(t, x) \equiv C_n(x)v_n(t), \quad (2)$$

where $C_n(x, y), C_n(x) > 0$, and functions u_n, v_n are of the form:

a) if $\beta > \beta_c$

$$u_n(t) = e^{n\lambda_0 t}, \quad v_n(t) = e^{n\lambda_0 t};$$

b) if $\beta = \beta_c$

$d = 1$	$u_n(t) = t^{-1/2}(\ln t)^{n-1},$	$v_n(t) = t^{(n-1)/2};$
$d = 2$	$u_n(t) = t^{-1},$	$v_n(t) = (\ln t)^{n-1};$
$d = 3$	$u_n(t) = t^{-1/2}(\ln t)^{n-1},$	$v_n(t) = t^{n-1/2};$
$d = 4$	$u_n(t) = t^{n-1}(\ln t)^{1-2n},$	$v_n(t) = t^{2n-1}(\ln t)^{1-2n};$
$d \geq 5$	$u_n(t) = t^{n-1}(\ln t)^{n-1},$	$v_n(t) = t^{2n-1};$

Limit theorems

Theorem

c) if $\beta < \beta_c$

$$\begin{array}{lll} d = 1 & u_n(t) = t^{-3/2}, & v_n(t) = t^{-1/2}; \\ d = 2 & u_n(t) = (t \ln^2 t)^{-1}, & v_n(t) = (\ln t)^{-1}; \\ d \geq 3 & u_n(t) = t^{-3/2}, & v_n(t) = 1; \end{array}$$

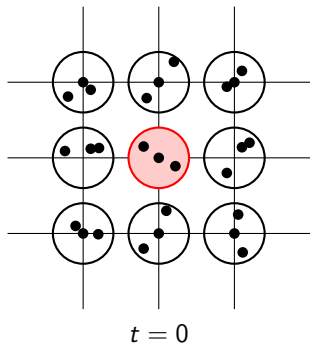
Theorem

If $\beta > \beta_c$, in the sense of moment's convergence

$$\lim_{t \rightarrow \infty} \mu_t(y) e^{-\lambda_0 t} = \xi \phi_0(y), \quad \lim_{t \rightarrow \infty} \mu_t(y) e^{-\lambda_0 t} = \xi, \quad (3)$$

where ξ - is some non-degenerate random variable, such as $E_x \xi^n = C_n(x)$ ($n \in \mathbb{N}$), and moments $C_n(x)$ coincides corresponding ones in 1. If $\beta_r = O(r!r^{r-1})$, moments $C_n(x)$ uniquely determine the distribution ξ , and the relations are valid in the relations are valid in the sense of convergence in distribution.

Model II



Infinite number of particles at $t = 0$

$\eta_t(x)$ - local number of particles at x in the moment t , $x \in \mathbb{Z}^d$,

$\eta_x(0) \equiv a \quad \forall x \in \mathbb{Z}^d, a \geq a_0 > 0.$

$m_n(t, x) := E_x \mu^n(t)$ (in the first model),

$m_n(t, x, y) := E_x \mu_y^n(t)$ (in the first model),

$M_n(t, x) := E_\infty \eta_x^n(t).$

Short-time events in BRW:

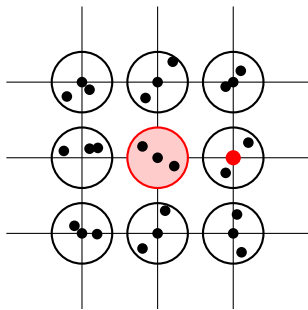
I) at point $x = 0$, $h \rightarrow 0$:

- ① moving to $y \neq x$ with probability $a(x_j, x_k)h + o(h)$;
- ② producing $k \neq 1$ offsprings with probability $c_k h + o(h)$;
- ③ death with probability $c_0 h + o(h)$;
- ④ staying stable at x with probability $1 + a(x_j, x_j)h + c_1 h + o(h)$ without offspring.

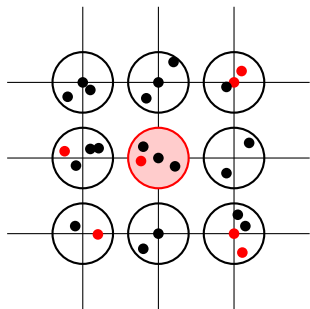
II) at point $x \neq 0$, $h \rightarrow 0$:

- ① moving to $y \neq x$ with probability $a(x_i, x_k)h + o(h)$;
- ② staying at x with probability $1 + a(x_i, x_i)h + o(h)$.

Sub-populations

 $t = 0$ 

$$\eta_x(0) \equiv a$$

 $t > 0$ 

$\eta_{x,x_i}(t)$ - local number of offsprings of particle i ;

$$\eta_{x,x_i}(0) = a\delta_{x_i}(0);$$

$$M_{i,n}(t, x_i, x) := E_{x_i} \eta_{x,x_i}^n(t).$$

Duality of BRW models

Let F_∞ be the Laplas generating functions of the processes:

$$\begin{aligned} F(z; t, x) &:= E_x e^{-z\mu(t)} \\ F(z; t, x, y) &:= E_x e^{-z\mu_y(t)} \\ F_\infty(z; t, x, y) &:= E_\infty e^{-z\eta_y(t)} \\ F_i(z; t, x, y) &:= E_{x_i} e^{-z\eta_{x_i}(t)} \end{aligned}$$

Statement

For all $0 \leq z \leq \infty$ Laplas generating functions $F(z; t, x)$ and $F(z; t, x, y)$ in the first model and $F_\infty(z; t, x, y)$ and $F_i(z; t, x, y)$ in the second model are continuously differentiable and satisfy the same differential equations:

$$\begin{aligned} \partial_t F(z; t, x) &= (AF(z; t, \cdot))(x) + \delta_0(x)f(F(z; t, x)) \\ \partial_t F(z; t, x, y) &= (AF(z; t, \cdot, y))(x) + \delta_0(x)f(F(z; t, x, y)), \\ \partial_t F_\infty(z; t, x, y) &= (AF_\infty(z; t, \cdot, y))(x) + \delta_0(x)f(F_\infty(z; t, x, y)), \\ \partial_t F_i(z; t, x, y) &= (AF_i(z; t, \cdot, y))(x) + \delta_0(x)f(F_i(z; t, x, y)), \end{aligned} \quad (1.4)$$

*with: $F(z; 0, x) = ae^{-z}$, $F(z; 0, x, y) = ae^{-z\delta_x(y)}$,
 $F_\infty(z; 0, x, y) = ae^{-z}$ and $F_i(z; 0, x, y) = ae^{-z\delta_{x_i}(x)}$.*

Statement

First moments of general number of particle in model I and local number of particles in the source in model II satisfy:

$$\begin{cases} \frac{\partial m_1(t,x)}{\partial t} = (Hm_1(t, \cdot))(x) \\ m_1(0, x) = a\delta_0(x) \end{cases}$$

$$\begin{cases} \frac{\partial M_1(t,x,y)}{\partial t} = (HM_1(t, \cdot, y))(x) \\ M_1(0, \cdot, y) \equiv a, \quad y \in \mathbb{Z}^d \end{cases}$$

where $H := A + \beta\delta_0$.

Statement

For all $n \geq 2$ moments of local number of particles satisfy integral equations:

$$m_n(t, x) = m_1(t, x) + \delta_0(x) \int_0^t m_1(t-s, x, 0) g_n(m_1(s, 0), \dots, m_{n-1}(s, 0)) ds,$$

$$M_n(t, x, y) = M_1(t, x, y) + \delta_0(x) \int_0^t M_1(t-s, x, 0) g_n(M_1(s, 0, y), \dots, M_{n-1}(s, 0, y)) ds,$$

where

$$g_n(m_1, m_2, \dots, m_{n-1}) = \sum_{r=1}^n \frac{\beta^{(r)}}{r!} \cdot \sum_{\substack{i_1, \dots, i_r > 0, \\ i_1 + \dots + i_r = n}} \frac{n!}{i_1! \dots i_r!} m_{i_1} \dots m_{i_r},$$

$$g_n(M_1, M_2, \dots, M_{n-1}) = \sum_{r=1}^n \frac{\beta^{(r)}}{r!} \cdot \sum_{\substack{i_1, \dots, i_r > 0, \\ i_1 + \dots + i_r = n}} \frac{n!}{i_1! \dots i_r!} M_{i_1} \dots M_{i_r}.$$

Statement

First moments of local number of particles at a point y (Model I) and a local number of particle of one subpopulation at the source (Model II) satisfy:

$$\begin{cases} \frac{\partial m_n(t,x,y)}{\partial t} = (Hm_n(t, \cdot, y))(x) + \delta_0(x)g_n(m_1(t, x, y), \dots, m_{n-1}(t, x, y)) \\ m_n(0, x, y) = a\delta_0(y) \end{cases}$$

$$\begin{cases} \frac{\partial M_{i,n}(t,x,y)}{\partial t} = (HM_{i,n}(t, \cdot, y))(x) + \delta_0(x)g_n(M_{i,1}(t, x, y), \dots, M_{i,n-1}(t, x, y)) \\ M_{i,n}(0, x_i, y) = a\delta_{x_i}(y) \end{cases}$$

where

$$g_n(m_1, m_2, \dots, m_{n-1}) = \sum_{r=1}^n \frac{\beta^{(r)}}{r!} \cdot \sum_{\substack{i_1, \dots, i_r > 0, \\ i_1 + \dots + i_r = n}} \frac{n!}{i_1! \dots i_r!} m_{i_1} \dots m_{i_r},$$

$$g_n(M_{i,1}, M_{i,2}, \dots, M_{i,n-1}) = \sum_{r=1}^n \frac{\beta^{(r)}}{r!} \cdot \sum_{\substack{i_1, \dots, i_r > 0, \\ i_1 + \dots + i_r = n}} \frac{n!}{i_1! \dots i_r!} M_{i,i_1} \dots M_{i,i_r}.$$

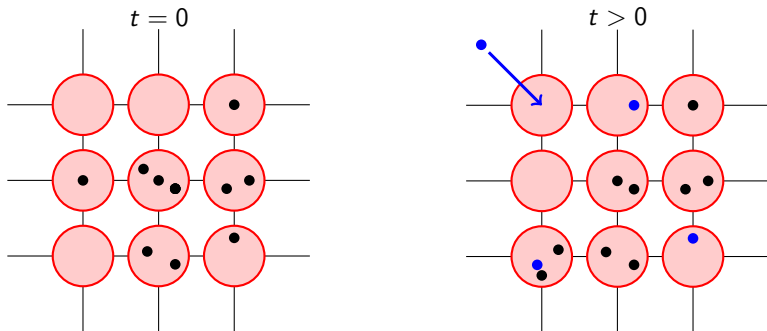
Theorem

For all moments of a total number of particles over the lattice in model I and a local number of particles at the branching source in model II we have: $m_n(t, 0) \equiv M_n(t, 0, 0)$.

Theorem

For all moments of a local number of particles at a point x in model I and a number of offsprings at the branching source of a particle started at a point x (subpopulation size) in model II we have: $m_n(t, x, 0) \equiv M_{x,n}(t, x, 0)$.

BRWs with Immigration (Han, Makarova, Molchanov, Y.



$F(x)$ - the initial distribution of particles on the lattice;

$f(u)$ - probability generating function of BP with $\beta := f'(1) < 0$.

The BP at every lattice point is **subcritical**, but there is **immigration** of new particles into each point of the lattice, so the process will not extinct for $t \rightarrow \infty$.

BRW with Immigration

Immigration influx helps to stabilize the population when the birth rate is less than the mortality rate.

Such a model may describe the demographic situations associated with immigration in different European countries.

This approach was suggested by Molchanov and Whitmeyer in 2016, but only for the case of the binary splitting, i.e. when one particle can produce one offspring at the moment of birth.

We considered the case when particles can produce **an arbitrary number of offsprings** and investigated the asymptotic behaviour of the moments of particle numbers as $t \rightarrow \infty$. We consider the moments $m_n(t, x_1, \dots, x_n) = E(n(t, x_1) \cdot \dots \cdot n(t, x_n))$. The asymptotics of the first two moments $m_1(t, x_1)$ and $m_2(t, x_1, x_2)$ were obtained as $t \rightarrow \infty$.

BRW with Immigration

In the presence of the immigration we have use **forward** Kolmogorov equations. Their derivation is based on the representations:

$$n(t + dt, x) = n(t, x) + \xi(dt, x),$$

where $\xi(dt, x)$ is the random variable and

$$\xi(dt, x) = \begin{cases} n - 1, & \text{with probability } b_n n(t, x) dt, \quad n \geq 3, \\ 1, & \text{with probability } b_2 n(t, x) dt + k dt \\ & + \kappa \sum_{z \neq 0} a(z) n(t, x + z) dt, \\ -1, & \text{with probability } b_0 n(t, x) dt + \kappa n(t, x) dt, \\ 0, & \text{with probability } 1 - \sum_{n \geq 3} b_n n(t, x) dt \\ & - (b_2 + b_0 + \kappa) n(t, x) dt - k dt \\ & - \sum_{z \neq 0} a(z) n(t, x + z) dt. \end{cases}$$

First moment. BRW with Immigration

For the first moment we obtain the explicit formula:






$$m_1(t, x) = \frac{k}{\beta - b_0} (e^{(\beta - b_0)t} - 1) + e^{(\beta - b_0)t} En(0, x).$$

For $t \rightarrow \infty$ we have

- if $\beta \geq b_0$, $k > 0$ then $m_1(t, x) \rightarrow \infty$;
- if $b_0 > \beta$ then $m_1(t, x) \rightarrow \frac{k}{b_0 - \beta}$.

Problems

- Adding of a random walk into models with BPs.
- Generalization BRWs for different types of particles;
- Generalization BRWs for branching sources with different intensities;
- More natural vaccination;
- Vaccination depending on time from beginning of outbreak;
- Including immigration of particles.

-  Gonzalez, M., Martinez, R. and Slavtchova-Bojkova, M. (2010). *Stochastic monotonicity and continuity properties of the extinction time of Bellman-Harris branching processes: an application to epidemic modelling* . J. App. Prob., 47, 58-71.
-  Ball, F., Gonzalez, M., Martinez, R. and Slavtchova-Bojkova, M. (2014) *Stochastic monotonicity and continuity properties of functions defined on Crump-Mode-Jagers branching processes, with application to vaccination in epidemic modelling*. Bernoulli 20(4), 2014, 2076-2101.
-  Antonelly, F., Bosco, F. (2012) *Viral evolution and adaptation as a multivariate branching process*. Biomat., 217-243.
-  Wilke, C. (2014) *Probability of fixation of an advantageous mutant in a viral quasispecies*. Genetics, 163, 457-466.
-  Yarovaya, E. (2007). Branching random walks in non-homogenous environment. Moscow, Center of Applied Investigations of the Faculty of Mechanics and Mathematics of the Moscow State University. (in Russian)