Population dynamics with applications to mathematical biology

Juan Carlos Pardo

CIMAT, Mexico

Cells with parasite infection

Motivation : continuous time model for dividing cells infected by parasites (Bansaye & Tran 2011)

We always assume $\theta \in (0,1)$.

Motivation : continuous time model for dividing cells infected by parasites (Bansaye & Tran 2011)

We assume that parasites proliferate in the cells and that their lifelengths are much less than the one of the cell.

We always assume $\theta \in (0, 1)$.

Motivation : continuous time model for dividing cells infected by parasites (Bansaye & Tran 2011)

We assume that parasites proliferate in the cells and that their lifelengths are much less than the one of the cell.

We also assume that the quantity of parasites in a cell evolves as a specific population dynamic model (which is random) and cells divide (randomly) in continuous time with rate r.

We always assume $\theta \in (0, 1)$.

Motivation : continuous time model for dividing cells infected by parasites (Bansaye & Tran 2011)

We assume that parasites proliferate in the cells and that their lifelengths are much less than the one of the cell.

We also assume that the quantity of parasites in a cell evolves as a specific population dynamic model (which is random) and cells divide (randomly) in continuous time with rate r.

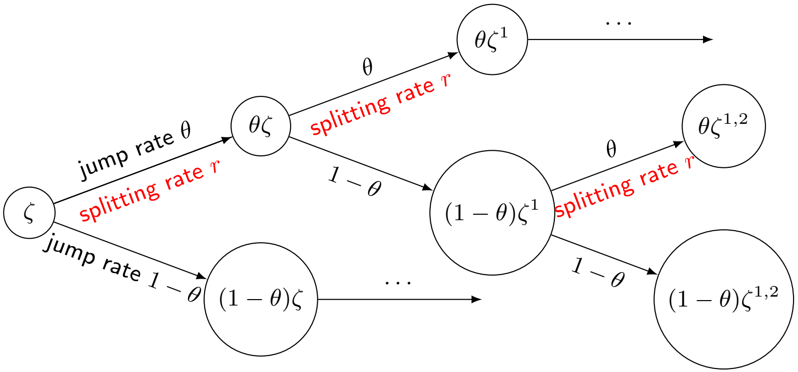
When a cell divides, a random fraction θ of the parasites goes into the 1st daughter cell and a fraction $(1-\theta)$ in the second one. We always assume $\theta \in (0, 1)$.

Motivation : continuous time model for dividing cells infected by parasites (Bansaye & Tran 2011)

We assume that parasites proliferate in the cells and that their lifelengths are much less than the one of the cell.

We also assume that the quantity of parasites in a cell evolves as a specific population dynamic model (which is random) and cells divide (randomly) in continuous time with rate r.

When a cell divides, a random fraction θ of the parasites goes into the 1st daughter cell and a fraction $(1-\theta)$ in the second one. We always assume $\theta \in (0,1)$.


ζ
jump rate θ
splitting rate r
jump rate $1-\theta$
$\theta\zeta$
$(1-\theta)\zeta$
θ
splitting rate r
$1-\theta$
$\theta\zeta^1$
$(1-\theta)\zeta^1$
. . .
. . .
θ
splitting rate r
$1-\theta$
$\theta\zeta^{1,2}$
$(1-\theta)\zeta^{1,2}$

Instead of parasite infection, we can also think in some biological content which grows in the cell and is shared randomly when the cells divide (proteins, nutrients, energy, etc)

Instead of parasite infection, we can also think in some biological content which grows in the cell and is shared randomly when the cells divide (proteins, nutrients, energy, etc)

The biological model is inspired by the experiments conducted in Tamara's Laboratory (Sorbonne University) where bacteria *E-coli* have been infected with bacteriophage lysogens (a virus that infects and replicates within bacteria).

Instead of parasite infection, we can also think in some biological content which grows in the cell and is shared randomly when the cells divide (proteins, nutrients, energy, etc)

The biological model is inspired by the experiments conducted in Tamara's Laboratory (Sorbonne University) where bacteria *E-coli* have been infected with bacteriophage lysogens (a virus that infects and replicates within bacteria).

During the experiment, it was notice that a very infected cell often gives birth to a very infected and a lowly infected daughter cells.

The structure of this model seems to be quite complex, unfortunately. Since it needs a good understanding of *random population dynamics models* which have a tree-like structure that evolves in a random tree. But it is possible to determine some interesting parameters.

The structure of this model seems to be quite complex, unfortunately. Since it needs a good understanding of *random population dynamics models* which have a tree-like structure that evolves in a random tree. But it is possible to determine some interesting parameters.

An example of an important parameter for biology is the expected number of infected cells.

The structure of this model seems to be quite complex, unfortunately. Since it needs a good understanding of *random population dynamics models* which have a tree-like structure that evolves in a random tree. But it is possible to determine some interesting parameters.

An example of an important parameter for biology is the expected number of infected cells.

Such parameter is important because, we say that, a cell population will recover if the asymptotic proportion of contaminated cells vanishes.

Random walks, random trees and Bienayme-Galton-Watson processes

Imagine that a gambler have a fortune of 5 fair coins and he decide to play a coin tossing game.

Imagine that a gambler have a fortune of 5 fair coins and he decide to play a coin tossing game.

On each successive gamble either wins 1 (if the coin shows heads) or loses 1 (if the coin shows tails) independently of the past.

Imagine that a gambler have a fortune of 5 fair coins and he decide to play a coin tossing game.

On each successive gamble either wins 1 (if the coin shows heads) or loses 1 (if the coin shows tails) independently of the past.

Let S_n denote the total fortune after the n-th gamble. Then $S_0 = 5$ and then S_1 is either 6 or 4 (with equal probability) and so on.

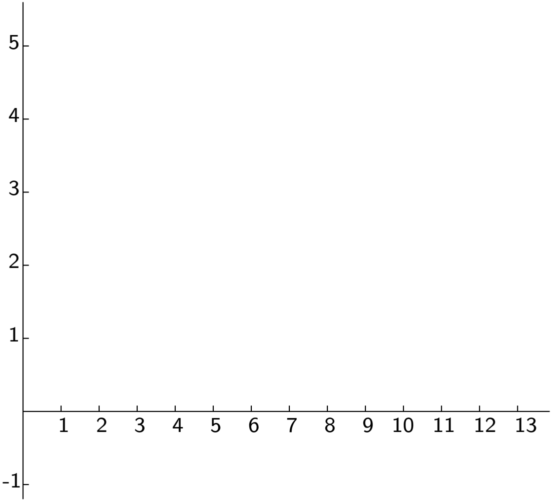
Imagine that a gambler have a fortune of 5 fair coins and he decide to play a coin tossing game.

On each successive gamble either wins 1 (if the coin shows heads) or loses 1 (if the coin shows tails) independently of the past.

Let S_n denote the total fortune after the n-th gamble. Then $S_0 = 5$ and then S_1 is either 6 or 4 (with equal probability) and so on.

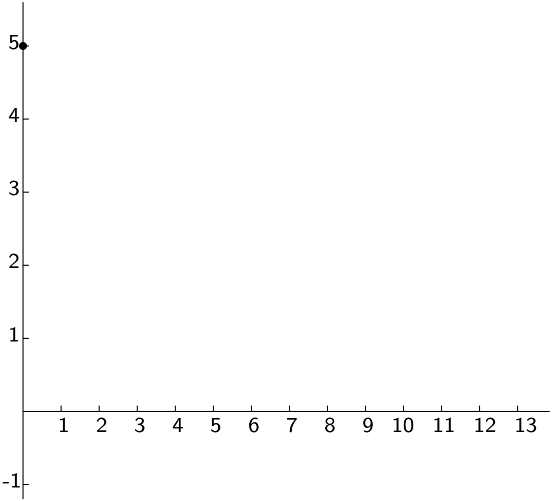
If we denote by τ_0 the time to ruin, in particular $\tau_0 \geq 5$.

A possible realization



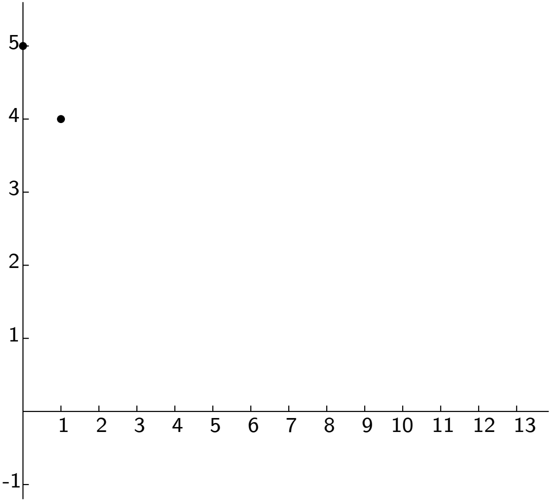
A possible realization

- $S_0 = 5$



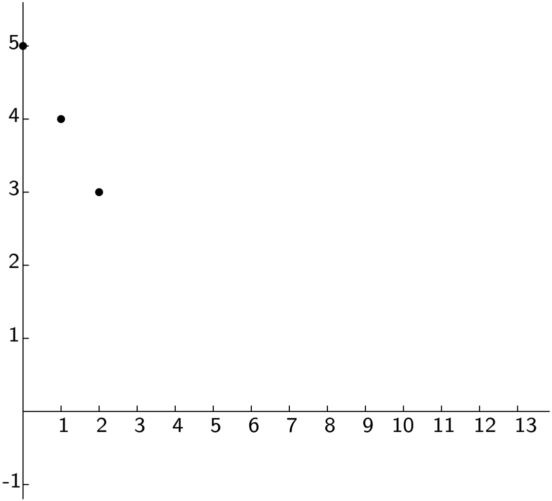
A possible realization

- $S_0 = 5$
- $S_1 = 4$



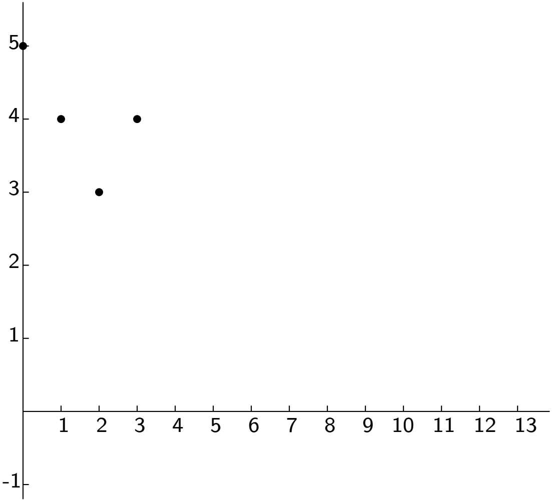
A possible realization

- $S_0 = 5$
- $S_1 = 4$
- $S_2 = 3$



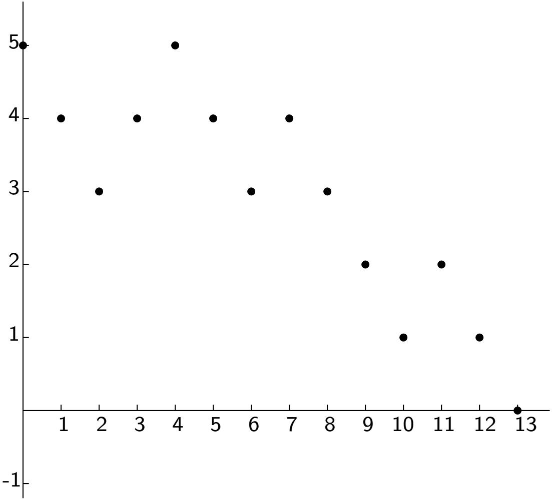
A possible realization

- $S_0 = 5$
- $S_1 = 4$
- $S_2 = 3$
- $S_3 = 4$ and so on ...



A possible realization

- $S_0 = 5$
- $S_1 = 4$
- $S_2 = 3$
- $S_3 = 4$ and so on ...
- $\tau_0 = 13$



$(S_n, n \geq 0)$ is known as the *simple random walk* and in particular, it can be written as follows

$$S_n = S_0 + \sum_{i=1}^{n} \Delta S_i, \qquad n \leq \tau_0$$

where each ΔS_i represents the value 1 or -1 accordingly as the i-th coin tossing shows heads or tails (increments).

$(S_n, n \geq 0)$ is known as the *simple random walk* and in particular, it can be written as follows

$$S_n = S_0 + \sum_{i=1}^{n} \Delta S_i, \qquad n \leq \tau_0$$

where each ΔS_i represents the value 1 or -1 accordingly as the i-th coin tossing shows heads or tails (increments). Moreover, the result of the i-th coin tossing doesn't interfere with the result of the j-th coin tossing, meaning that all increments are mutually independent.

$(S_n, n \geq 0)$ is known as the *simple random walk* and in particular, it can be written as follows

$$S_n = S_0 + \sum_{i=1}^{n} \Delta S_i, \qquad n \leq \tau_0$$

where each ΔS_i represents the value 1 or -1 accordingly as the i-th coin tossing shows heads or tails (increments). Moreover, the result of the i-th coin tossing doesn't interfere with the result of the j-th coin tossing, meaning that all increments are mutually independent.

For constructing our population dynamic model, we introduce

$$Y_i = 1 + \Delta S_i, \qquad \text{for} \quad i \geq 1.$$

In other words, if we flip the i-th coin Y_i takes the value 0 or 2 accordingly as the coin shows tails or heads.

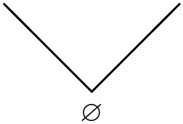
Informally, Y_i will represent the offsprings of my population dynamic model.

Informally, Y_i will represent the offsprings of my population dynamic model. Let us explain this by drawing a random tree as follows. For simplicity, we assume that we start with one individual in the population (the root $\varnothing$).

$\varnothing$

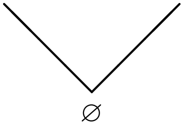
Informally, Y_i will represent the offsprings of my population dynamic model. Let us explain this by drawing a random tree as follows. For simplicity, we assume that we start with one individual in the population (the root $\varnothing$).

- if $Y_1 = 2$, we draw two branches

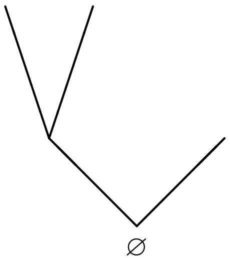


Informally, Y_i will represent the offsprings of my population dynamic model. Let us explain this by drawing a random tree as follows. For simplicity, we assume that we start with one individual in the population (the root $\varnothing$).

- if $Y_1 = 2$, we draw two branches
- we explore the branches from L to R,

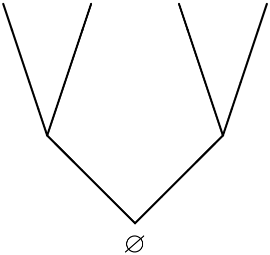


Informally, Y_i will represent the offsprings of my population dynamic model. Let us explain this by drawing a random tree as follows. For simplicity, we assume that we start with one individual in the population (the root $\varnothing$).



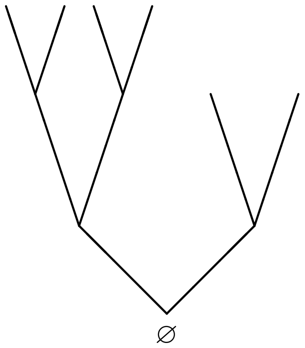
- if $Y_1 = 2$, we draw two branches
- we explore the branches from L to R,
- if $Y_2 = 2$, we draw two branches

Informally, Y_i will represent the offsprings of my population dynamic model. Let us explain this by drawing a random tree as follows. For simplicity, we assume that we start with one individual in the population (the root $\varnothing$).



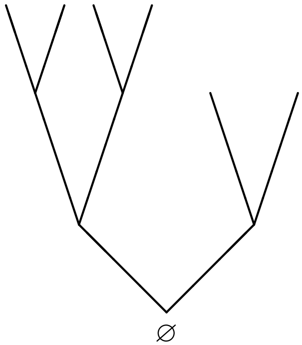
- if $Y_1 = 2$, we draw two branches
- we explore the branches from L to R,
- if $Y_2 = 2$, we draw two branches
- if $Y_3 = 2$, we draw two branches

Informally, Y_i will represent the offsprings of my population dynamic model. Let us explain this by drawing a random tree as follows. For simplicity, we assume that we start with one individual in the population (the root $\varnothing$).

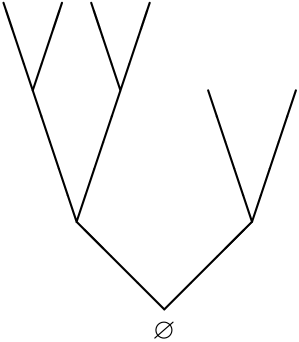


- if $Y_1 = 2$, we draw two branches
- we explore the branches from L to R,
- if $Y_2 = 2$, we draw two branches
- if $Y_3 = 2$, we draw two branches
- and so on ...

The random population dynamic model that we are interested on is embedded in the tree.

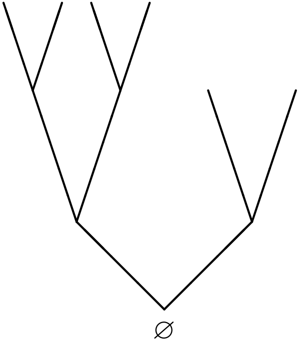


The random population dynamic model that we are interested on is embedded in the tree.



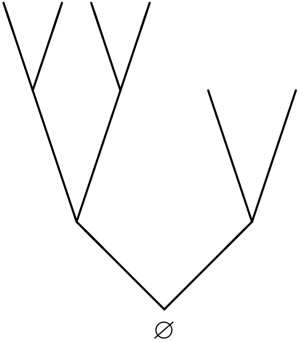
- $Z_0 = \sharp\{\text{nodes at height } 0\} = 1$

The random population dynamic model that we are interested on is embedded in the tree.



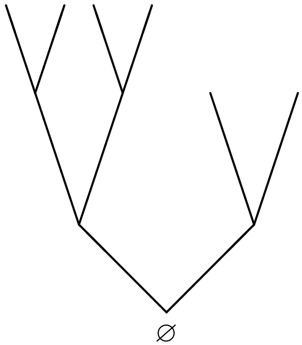
- $Z_1 = \sharp\{\text{nodes at height } 1\} = 2$
- $Z_0 = \sharp\{\text{nodes at height } 0\} = 1$

The random population dynamic model that we are interested on is embedded in the tree.



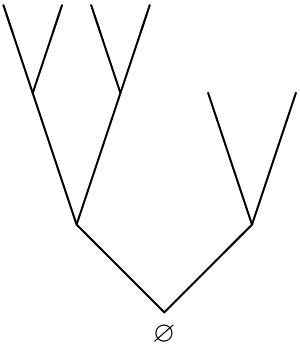
- $Z_2 = \sharp\{\text{nodes at height } 2\} = 4$
- $Z_1 = \sharp\{\text{nodes at height } 1\} = 2$
- $Z_0 = \sharp\{\text{nodes at height } 0\} = 1$

The random population dynamic model that we are interested on is embedded in the tree.



- $Z_3 = \sharp\{\text{nodes at height } 3\} = 4$
- $Z_2 = \sharp\{\text{nodes at height } 2\} = 4$
- $Z_1 = \sharp\{\text{nodes at height } 1\} = 2$
- $Z_0 = \sharp\{\text{nodes at height } 0\} = 1$

The random population dynamic model that we are interested on is embedded in the tree.



- $Z_4 = \sharp\{\text{nodes at height } 4\} = 0$
- $Z_3 = \sharp\{\text{nodes at height } 3\} = 4$
- $Z_2 = \sharp\{\text{nodes at height } 2\} = 4$
- $Z_1 = \sharp\{\text{nodes at height } 1\} = 2$
- $Z_0 = \sharp\{\text{nodes at height } 0\} = 1$

A Bienaymé-Galton-Watson (BGW) process is a random model that describes the evolution of a given population whose individuals reproduce independently of each other and with the same reproduction law.

A Bienaymé-Galton-Watson (BGW) process is a random model that describes the evolution of a given population whose individuals reproduce independently of each other and with the same reproduction law.

We introduce $\{Y_{i,n} : n \geq 0, i \geq 1\}$ a sequence of independent r.v.'s,

A Bienaymé-Galton-Watson (BGW) process is a random model that describes the evolution of a given population whose individuals reproduce independently of each other and with the same reproduction law.

We introduce $\{Y_{i,n} : n \geq 0, i \geq 1\}$ a sequence of independent r.v.'s, that is to say for $n \geq 0$ and $i \neq j$

$$\mathbb{P}(Y_{j,n} = k, Y_{i,n} = \ell) = \mathbb{P}(Y_{j,n} = k)\mathbb{P}(Y_{i,n} = \ell),$$

A Bienaymé-Galton-Watson (BGW) process is a random model that describes the evolution of a given population whose individuals reproduce independently of each other and with the same reproduction law.

We introduce $\{Y_{i,n} : n \geq 0, i \geq 1\}$ a sequence of independent r.v.'s, that is to say for $n \geq 0$ and $i \neq j$

$$\mathbb{P}(Y_{j,n} = k, Y_{i,n} = \ell) = \mathbb{P}(Y_{j,n} = k)\mathbb{P}(Y_{i,n} = \ell),$$

Each $Y_{i,n}$ represents the number of offsprings of the i-th individual of the n-th generation.

In this context, we describe Z_{n+1}, the total amount of individuals at the $n+1$-generation by

$$Z_{n+1} = \sum_{i=1}^{Z_n} Y_{i,n}.$$

In this context, we describe Z_{n+1}, the total amount of individuals at the $n+1$-generation by

$$Z_{n+1} = \sum_{i=1}^{Z_n} Y_{i,n}.$$

From the latter, we observe that if $Z_n = 0$, then $Z_{n+m} = 0$, for any $m > 0$, and in consequence zero is an absorbing state.

In this context, we describe Z_{n+1}, the total amount of individuals at the $n+1$-generation by

$$Z_{n+1} = \sum_{i=1}^{Z_n} Y_{i,n}.$$

From the latter, we observe that if $Z_n = 0$, then $Z_{n+m} = 0$, for any $m > 0$, and in consequence zero is an absorbing state.

The transition probabilities are given by

$$\mathbf{P}_{ij} := \mathbb{P}\Big(Z_{n+1} = j \Big| Z_n = i\Big) = \frac{\mathbb{P}\Big(Z_{n+1} = j, Z_n = i\Big)}{\mathbb{P}\Big(Z_n = i\Big)},$$

$$\mathbf{P}_{ij} = \frac{\mathbb{P}\Big(\sum_{k=1}^{i} X_{k,n} = j, Z_n = i \Big)}{\mathbb{P}\Big(Z_n = i \Big)} = \mathbb{P}\Bigg(\sum_{k=1}^{i} X_{k,n} = j \Bigg).$$

$$\mathbf{P}_{ij} = \frac{\mathbb{P}\Big(\sum_{k=1}^{i} X_{k,n} = j, Z_n = i \Big)}{\mathbb{P}\Big(Z_n = i \Big)} = \mathbb{P}\Bigg(\sum_{k=1}^{i} X_{k,n} = j \Bigg).$$

This property is known as the Markov property or informally speaking the future and the past are independent given that we know the current state of the random process.

$$\mathbf{P}_{ij} = \frac{\mathbb{P}\Big(\sum_{k=1}^{i} X_{k,n} = j, Z_n = i\Big)}{\mathbb{P}\Big(Z_n = i\Big)} = \mathbb{P}\Big(\sum_{k=1}^{i} X_{k,n} = j\Big).$$

This property is known as the Markov property or informally speaking the future and the past are independent given that we know the current state of the random process.

Branching property : the process Z_n starting from $Z_0 = i + j$ has the same law as the stochastic sum of two independent copies $\widetilde{Z}_n$ and $\widehat{Z}_n$ starting from i and j, respectivelly.

The branching property allow us to compute the expected value of the number of individuals at a given generation.

$$\mathbb{E}[Z_n|Z_0 = 1] = \mu^n$$

The branching property allow us to compute the expected value of the number of individuals at a given generation.

$$\mathbb{E}[Z_n|Z_0 = 1] = \mu^n$$

Three different regimes appears depending on the value of μ. We say that the process is supercritical, critical or subcritical accordingly as $\mu > 1$, $\mu = 1$ or $\mu < 1$.

The branching property allow us to compute the expected value of the number of individuals at a given generation.

$$\mathbb{E}[Z_n|Z_0 = 1] = \mu^n$$

Three different regimes appears depending on the value of μ. We say that the process is supercritical, critical or subcritical accordingly as $\mu > 1$, $\mu = 1$ or $\mu < 1$.

The probability that the population becomes extinct equals one if $\mu \leq 1$ and if $\mu > 1$, then it is positive but smaller than one.

Scaling limits

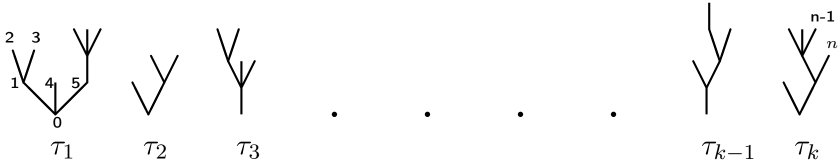
How can we study populations that reproduce very fast and have lots of individuals such as parasites ?

How can we study populations that reproduce very fast and have lots of individuals such as parasites ?

Let us assume that we have a collection of independent trees (forest) as in the picture below.

How can we study populations that reproduce very fast and have lots of individuals such as parasites ?

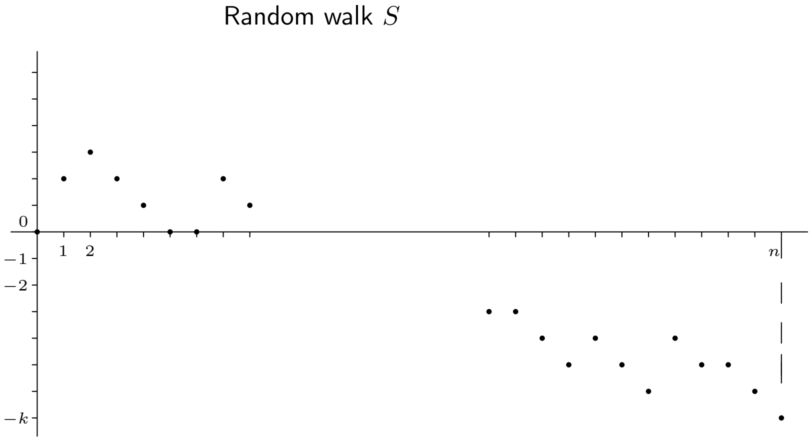
Let us assume that we have a collection of independent trees (forest) as in the picture below.



Forest with k trees and n vertices.

Associated with this forest we have the following random walk

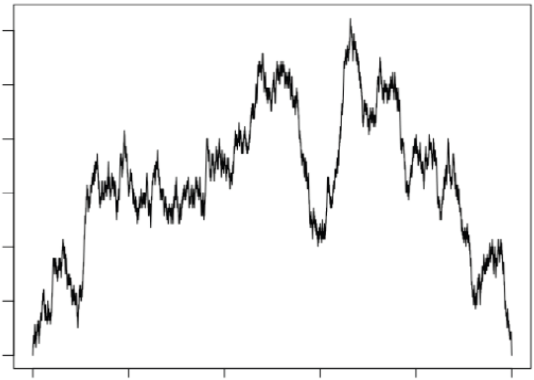
Associated with this forest we have the following random walk



Under an adecuate scaling in time (N) and space $(N^{-1/2})$, the random walk S converges towards the Brownian motion $B = (B_t, t \geq 0)$, (as N increases).

Under an adecuate scaling in time (N) and space $(N^{-1/2})$, the random walk S converges towards the Brownian motion $B = (B_t, t \geq 0)$, (as N increases).

Brownian excursion



BGW $\to$ Feller Diffusion

$$X_t = X_0 + \int_0^t \sqrt{2\sigma^2 X_s} \mathrm{d}B_s, \qquad t \geq 0,$$

with associated infinitesimal operator

$$\mathcal{A}f(x) = \sigma^2 x f''(x).$$

BGW $\to$ Feller Diffusion

$$X_t = X_0 + \int_0^t \sqrt{2\sigma^2 X_s} \mathrm{d}B_s, \qquad t \geq 0,$$

with associated infinitesimal operator

$$\mathcal{A}f(x) = \sigma^2 x f''(x).$$

In other words, Feller diffusion is a natural model for populations which die and multiply fast, randomly, without interaction.

BGW $\rightarrow$ Feller Diffusion

$$X_t = X_0 + \int_0^t \sqrt{2\sigma^2 X_s} \mathrm{d}B_s, \qquad t \geq 0,$$

with associated infinitesimal operator

$$\mathcal{A}f(x) = \sigma^2 x f''(x).$$

In other words, Feller diffusion is a natural model for populations which die and multiply fast, randomly, without interaction.

We also may add a linear drift and the model still makes sense, i.e.

$$X_t = X_0 + g\int_0^t X_s \mathrm{d}s + \int_0^t \sqrt{2\sigma^2 X_s} \mathrm{d}B_s, \qquad t \geq 0,$$

with associated infinitesimal operator

$$\mathcal{A}f(x) = -gxf'(x) + \sigma^2 x f''(x).$$

Simlarlly to the discrete case, we have

$$\mathbb{E}[X_t | X_0 = x] = xe^{gt},$$

and three different regimes appears depending on the value of the parameter g which is known as Malthusian parameter.

Simlarlly to the discrete case, we have

$$\mathbb{E}[X_t|X_0 = x] = xe^{gt},$$

and three different regimes appears depending on the value of the parameter g which is known as Malthusian parameter.

The branching property allow us to compute the probability of extinction at finite time

$$\mathbb{P}(\exists t > 0 : X_t = 0|X_0 = x) = e^{-g/\sigma^2 x},$$

when $g > 0$ and equals one otherwise.

Simlarlly to the discrete case, we have

$$\mathbb{E}[X_t|X_0 = x] = xe^{gt},$$

and three different regimes appears depending on the value of the parameter g which is known as Malthusian parameter.

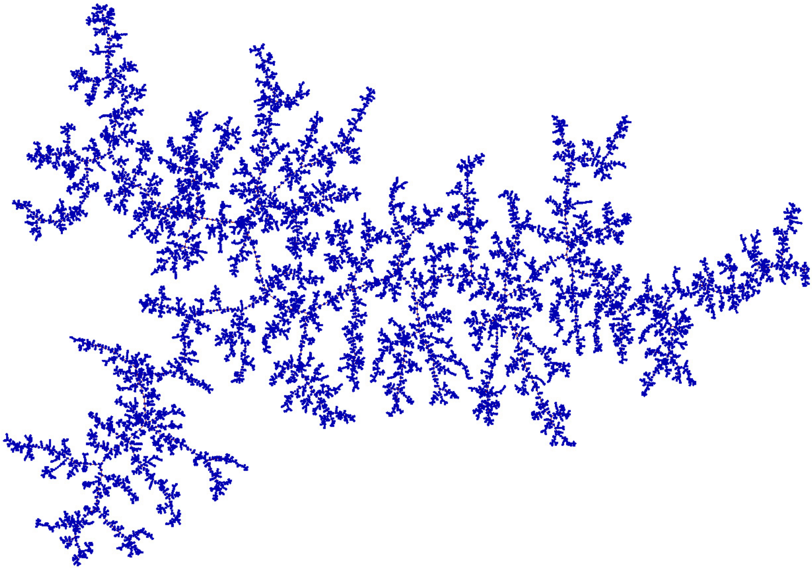
The branching property allow us to compute the probability of extinction at finite time

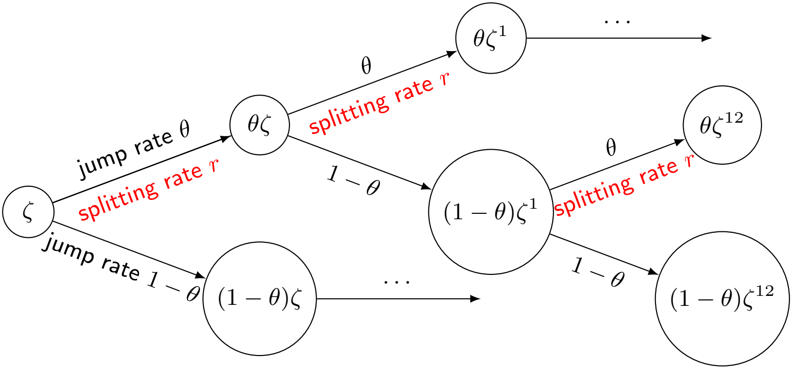
$$\mathbb{P}(\exists t > 0 : X_t = 0|X_0 = x) = e^{-g/\sigma^2 x},$$

when $g > 0$ and equals one otherwise.

The tree structure which is behind is the Continuum Random Tree (g=0).

Continuum random tree (I. Kortchemski)




$\theta\zeta^1$
$\dots$
θ
splitting rate r
$\theta\zeta^{12}$
$\theta\zeta$
jump rate θ
splitting rate r
$1-\theta$
θ
splitting rate r
ζ
$(1-\theta)\zeta^1$
jump rate $1-\theta$
$(1-\theta)\zeta$
$\dots$
$1-\theta$
$(1-\theta)\zeta^{12}$

The cell divides at constant rate r and a random fraction $\theta \in (0, 1)$ of parasites enters the first daughter cell, whereas the remainder enters the second daughter cell.

The cell divides at constant rate r and a random fraction $\theta \in (0, 1)$ of parasites enters the first daughter cell, whereas the remainder enters the second daughter cell.

Following the infection in a cell line, the parasites grow as a Feller diffusion and undergo a catastrophe when the cell divides.

The cell divides at constant rate r and a random fraction $\theta \in (0,1)$ of parasites enters the first daughter cell, whereas the remainder enters the second daughter cell.

Following the infection in a cell line, the parasites grow as a Feller diffusion and undergo a catastrophe when the cell divides.

Then its dynamics must be

$$Z_t = Z_0 + g\int_0^t Z_s \mathrm{d}s + \int_0^t \sqrt{2\sigma Z_s}\mathrm{d}B_s \qquad ,$$

The cell divides at constant rate r and a random fraction $\theta \in (0,1)$ of parasites enters the first daughter cell, whereas the remainder enters the second daughter cell.

Following the infection in a cell line, the parasites grow as a Feller diffusion and undergo a catastrophe when the cell divides.

Then its dynamics must be

$$Z_t = Z_0 + g\int_0^t Z_s \mathrm{d}s + \int_0^t \sqrt{2\sigma Z_s}\mathrm{d}B_s + \int_0^t Z_{s-}\mathrm{d}K_s,$$

where K is a random process that determines the time of splitting of cells and the proportion.

Let N_t and N_t^* be the number of cells and infected cells at time t, respectively.

Let N_t and N_t^* be the number of cells and infected cells at time t, respectively.

If there is one infected cell at time 0, the average number of infected cells must be exponential, i.e. $\mathbb{E}[N_t] = e^{rt}$ and $\mathbb{E}[N_t^*] = e^{rt}\mathbb{P}(Z_t > 0 | Z_0 = x)$

Let N_t and N_t^* be the number of cells and infected cells at time t, respectively.

If there is one infected cell at time 0, the average number of infected cells must be exponential, i.e. $\mathbb{E}[N_t] = e^{rt}$ and $\mathbb{E}[N_t^*] = e^{rt}\mathbb{P}(Z_t > 0|Z_0 = x)$

Five different regimes appears now that depends not only on r but also on the Malthusian parameter and the splitting rule (with C. Smadi and V. Bansaye).

a/ We assume that $g < 2r\mathbb{E}\left[\log(1/\Theta)\right]$. Then there exist positive constants c_1, c_2, c_3 such that

(i) If $g < 2r\mathbb{E}\left[\Theta\log(1/\Theta)\right]$, then

$$\mathbb{E}\left[N_t^*\right] \sim c_1 e^{gt}, \quad \text{as} \quad t \to \infty.$$

(ii) If $g = 2r\mathbb{E}\left[\Theta\log(1/\Theta)\right]$, then

$$\mathbb{E}\left[N_t^*\right] \sim c_2 t^{-1/2} e^{gt}, \quad \text{as} \quad t \to \infty.$$

(iii) If $g > 2r\mathbb{E}\left[\Theta\log(1/\Theta)\right]$, then

$$\mathbb{E}\left[N_t^*\right] \sim c_3 t^{-3/2} e^{\alpha t}, \quad \text{as} \quad t \to \infty.$$

where $\alpha = \min_{\lambda\in[0,1]}\{g\lambda + 2r(\mathbb{E}[\Theta^\lambda] - 1/2)\} < g$.

b/ We now assume $g = 2r\mathbb{E}\left[\log(1/\Theta)\right]$, then there exists $c_4 > 0$ such that,

$$\mathbb{E}\left[N_t^*\right] \sim c_4 t^{-1/2} e^{rt}, \quad \text{as} \quad t \to \infty.$$

c/ Finally, if $g > 2r\mathbb{E}\left[\log(1/\Theta)\right]$, then there exists $0 < c_5 < 1$ such that,

$$\mathbb{E}\left[N_t^*\right] \sim c_5 e^{rt}, \quad \text{as} \quad t \to \infty.$$

Thank you !