CEMRACS 2018: Horizontal gene transfer

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July 30, 2018

Abstract

Write an abstract!

1. Biological application: - antibiotic resistance - evolution dynamics blahblahblah

1 Model

Now, let us introduce a general setting of the problem. Consider a model of a bacteria population with stochastic system of interacting individuals. They are characterized by traits, which summarize the geno- or phenotype of the individual. Each trait x belongs to a compact subset $\mathcal{X} \in \mathbb{R}^d$. Traits can be either inherited from parents to the offspring, either occur in the case of mutation, or transmitted from one individual to another (this phenomena is called a horizontal transfer). The reproduction of the individuals is asexual.

The population is described at each moment of time t by the point measure

$$\nu_t^K(dx) = \frac{1}{K}\sum_{i=0}^{N_t^K} \delta_{X_t(t)}(dx),$$

where parameter K is a scale parameter which determines the size of a population (K can represent, for example, the initial size of population, amount of available resources, carrying capacity etc.), $N_t^K = K\int \nu_t^K(dx)$ is the size of the population at time t, and $x_i(t)$ is the trait of i-th individual living at t.

The demography of the population is regulated, first of all, by birth and death rates. An individual with trait x gives birth to a new individual with rate $b_K(x)$, which carries a trait x with a probability $1 - p_K$. With probability p_K a mutation occurs, and then the trait z of the offspring is chosen from a probability distribution $m(x, dz)$ (mutation kernel). Each x-individual dies either from death rate $d_K(x)$, or from the competition with any other individual with trait y alive at the same time, so that the additional death rate is $C_K(x, y)$ (...) . Finally, an individual x can induce a horizontal transfer to an individual y at rate $h_K(x, y, \nu)$, so that the pair (x, y) becomes $(T_1(x, y), T_2(x, y))$. It can

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also occur that the recipient acquires a trait of the donor, so that (x, y) becomes (x, x). In that case the transfer is called unilateral.

[MORE TEXT] The generator of the process is then given by:

$$\begin{aligned} L^K F(\nu) = &\sum_{i=1}^{N} b_K(x_i)(1-p_K)\left(F\left(\nu + \frac{1}{K}\delta_{x_i}\right) - F(\nu)\right) \\ &+ \sum_{i=1}^{N} b_K(x_i)(p_K)\int_{\mathcal{X}}\left(F\left(\nu + \frac{1}{K}\delta_{z}\right) - F(\nu)\right) m(x_i, dz) \\ &\sum_{i=1}^{N}\left(d_K(x_i) + KC_K * \nu(x_i)\right)\left(F\left(\nu - \frac{1}{K}\delta_{x_i}\right) - F(\nu)\right) \\ \sum_{i=1}^{N} h_K(x_i, x_j, \nu)&\left(F\left(\nu + \frac{1}{K}\delta_{T_1(x_i,x_j)} + + \frac{1}{K}\delta_{T_2(x_i,x_j)} - \frac{1}{K}\delta_{x_i} - \frac{1}{K}\delta_{x_j}\right) - F(\nu)\right) \end{aligned}$$

2 Numerical implementation

The main goal is to conduct a numerical analysis of a behaviour of the stochastic system, which describes the dynamics of a given population of individuals with different traits, with the deterministic systems which are obtained as a limit for large population. Since we do not aim to build a perfect replication of a specific biological symbiosis, we restrict ourselves to a simplified version of the system described in previous section.

First simplification is that we assume that the birth rate b is constant: it does not depend nor on x, nor on the carrying capacity of system K. A newborn individual obtains a new trait with probability $p_K \equiv 1$, picked from a random distribution $\mathcal{N}(x, \sigma)$, where σ is a mutation variance. The probability of death depends on x, the constant death rate d_r, and also the power d_e. In addition, we take into account death from a competition rate (which is constant between all individuals), so finally it is computed as follows:

$$d(x) = d_r|x|^{d_e} + N_t\frac{C}{K},$$

where N_t is a total number of individuals in a population at a given time t.

Finally, we assume that the horizontal transfer rate is unilateral and is computed by the following rule:

$$h(x, y) = \frac{\tau \mathbb{1}_{x>y}}{\beta + \mu x},$$

where τ, β, μ are given constants (we will restrict ourselves to the case when $\beta = 1$ and $\mu = 0$).

Basing on the rates we then compute the expected occurence of each event withing a small time interval Δ. We assume that it is possible that $1, 2$ or 3 events happen within the time step. Then we observe the behaviour of the system over the fixed time interval $[0, T]$

2.1 Stochastic simulation

As a first step, we simulate an initial population of size N_0. We assume that the population is normally distributed around a mean trait X_μ with a standard deviation X_σ, so that the resulting vector $X_0 \in \mathbb{R}^{N_0}$. Note that the choice of the mean trait and the deviation is crucial for survival, since choosing an initially "unfit" individuals they risk to go extinct before they mutate enough.

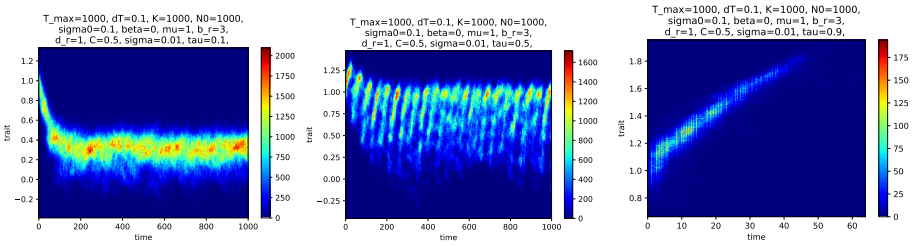
Algorithm 1: Population dynamics on time interval $[0, T]$

```
Random initialization of a population X_0 := N(X_0^mean, σ_0) × N_0 ;
while iΔ ≤ T do
    for ∀x ∈ X_i do
        X_i = X_{i−1};
        R_b := b(x), R_d := d(x), R_HT := h(x);
        T_b := λ(R_b), T_d := λ(R_d), T_HT := λ(R_HT), where λ denotes an
         exponential random law;
        if T_b ≤ Δ then
            pick up a new trait z from N(x, σ);
            add a new individual with trait z to X_i;
        end
        if T_HT ≤ Δ then
            change a trait of a random living individual y to x
        end
        if T_d ≤ Δ then
            remove the individual from X_i
        end
    end
    return X_i
end
```

Depending on the initial parameters we may observe three types of behaviour. First possibility is that after some time the population "converges" to a certain optimal value of trait and then stabilizes with occasional oscillations. Second option is that the population drives itself to extinction. It is the case if the horizontal transfer rate is high, so that the individuals with higher — and, consequently, less fit — traits occur more often, while the birth and mutation rate prevent the system to reach the balance before the extinction occurs.

The last possibility is the cycling behaviour: if the transfer rate τ is high enough with respect to the birth, death and mutation rates, then the population is "pushed" toward the higher trait over time. The side effect of this phenomena is that the individuals become less fit and die with higher rate, until the whole population boils down to its initial state with less individuals, which launches the cycle again.

All three scenarios can be observed on Figure 1. We simulate the population up to time $T = 1000$ with $\Delta = 0.1$, and then plot the density of the population at each time: brighter colors on plot mean that there is a big amount of individuals with very similar traits. On the first plot we see that the population goes very fast to the optimal trait, which is in this case close to 0.4, and keeps reproducing within reached limits. On the last plot high transfer rate pushes the whole population to extinction.



(a) Stabilization: $\tau = 0.1$ (b) Cycles: $\tau = 0.5$ (c) Extinction: $\tau = 0.9$

Figure 1: $b_r = d_r = 1$, $\sigma = 0.01$, τ is changing

[POSSIBLY MOVE TO DISCUSSIONS OR CONCLUSIONS] The question arises — which value of τ is critical for extinction, given the birth and the death rates? [INSERT PICTURES: dependency on birth/date/mutation rate?]

2.2 Integro-differential approach

2.3 smth

3 Conclusions