extinction and Survival

Let $u_i = \mathbb{P}_i(T_0 < +\infty)$ be the extinction probability in finite time, for a process starting from state i. We have $u_0 = 1$.
By conditioning on the first jump $X_{T_1} - X_0 \in \{-1, +1\}$, we obtain the following recurrence relation: for all $k \geq 1$,

$$\begin{aligned} u_k &= \mathbb{P}_k(Extinction) \\ &= \mathbb{P}_k(Extinction|Birth)\,\mathbb{P}_k(Birth) + \mathbb{P}_k(Extinction|Death)\,\mathbb{P}_k(Death) \\ &= u_{k+1}\,\frac{\lambda_k}{\lambda_k+\mu_k} + u_{k-1}\,\frac{\mu_k}{\lambda_k+\mu_k}, \end{aligned}$$

and then

$$\lambda_k u_{k+1} - (\lambda_k + \mu_k) u_k + \mu_k u_{k-1} = 0.$$

By resolving this equation, we prove that

If $U_\infty = \sum_{k=1}^{\infty} \frac{\mu_1 \cdots \mu_k}{\lambda_1 \cdots \lambda_k} = +\infty$, then $u_i = 1$ for any i - Almost-sure Extinction.

If $U_\infty = \sum_{k=1}^{\infty} \frac{\mu_1 \cdots \mu_k}{\lambda_1 \cdots \lambda_k} < +\infty$, then for $i \geq 1$, $u_i = (1 + U_\infty)^{-1} \sum_{k=i}^{\infty} \frac{\mu_1 \cdots \mu_k}{\lambda_1 \cdots \lambda_k}$.
The process has a positive but strictly less than 1 survival probability, for any $i \neq 0$.

Linear and logistic cases

Linear case: $\sum_{k=1}^{\infty} \frac{\mu_1 \cdots \mu_k}{\lambda_1 \cdots \lambda_k} = \sum_{k=1}^{\infty} \left(\frac{d}{b}\right)^k.$

Then : Almost-sure Extinction $\Longleftrightarrow b \leq d$. (subcritical or critical cases)

In the case $b > d$ (super-critical case), then $U_\infty = \frac{d}{b-d}$ and a simple computation shows that $u_i = \left(\frac{d}{b}\right)^i$.

In particular,

$$\mathbb{P}_1(\text{Survival}) = \frac{b-d}{b}.$$

Logistic case. $\lambda_n = bn$; $\mu_n = dn + c\,n(n-1)$ with $b > d$ and $c > 0$. *Without competition, the survival probability is (strictly) positive.*

But with $c > 0$: trade-off between demographic and ecological effects (competition).

Using D'Alembert's criterium, one proves that $U_\infty = \infty$ and then $u_i = 1$ for all i. Extinction almost-surely for any initial state i.

The quadratic death term ($c > 0$) makes the population go to extinction almost surely.

Approximation in large population

- Logistic framework.
- One introduces a scaling size parameter K. (Carrying capacity).
- Assume that $X^K(0) = [n_0 K]$ and that the competition pressure is c/K.

$$\frac{X_t^K}{K} = \frac{[n_0 K]}{K} + M_t^K + \int_0^t (b - d - \frac{c}{K} X_s^K) \frac{X_s^K}{K} ds,$$

and

$$\mathbb{E}((M_t^K)^2) = \frac{1}{K} \int_0^t (b + d + \frac{c}{K} X_s^K) \frac{X_s^K}{K} ds.$$

- Theorem [Kurtz, 1971]

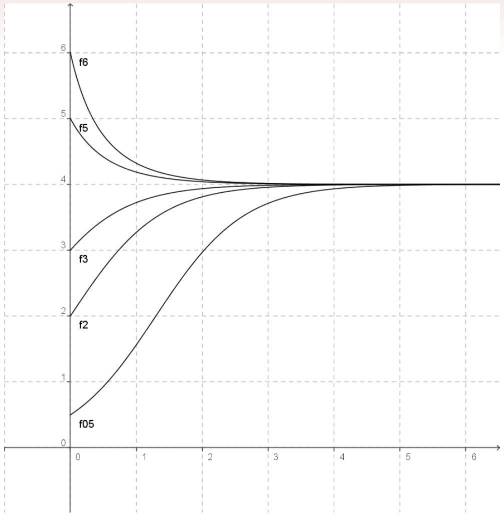
  When $K \to \infty$, *the stochastic process* $(\frac{X^K(t)}{K}, t \geq 0)$ *converges in probability to the deterministic and continuous function* $(n(t), t \geq 0)$ *solution of the logistic differential equation* (Verhulst 1850)

$$n'(t) = n(t) \left(b - d - c\, n(t)\right), \; n(0) = n_0.$$

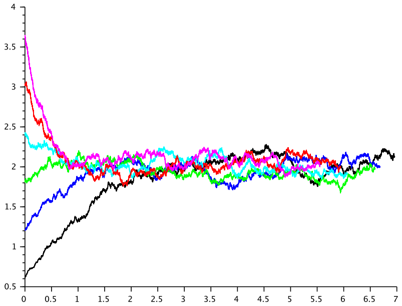
Idea of the proof : Uniform control of moments ; Tightness (compactness of the laws) ; Identification of the limit and uniqueness.

For the ODE, the solution stabilizes :

$$\lim_{t\to\infty} n(t) = \frac{b-d}{c} = n^* > 0.$$



$K = 200$, $b - d = 2$, $c = 1$; $n^* = 2$
(V. Bansaye).



Limits don't commute since for fixed K, $\lim_{t\to\infty} X^K(t) = 0$.

For large K, the process $X^K(t) \approx [K\, n(t)]$ stays a long time near its deterministic equilibrium before extinction : T_0 is of order of magnitude $\exp(CK)$ - arguments of large deviations (Champagnat 2006).

Deterministic or Stochastic Model ?

If we ask questions related to the extinction of a population or the emergence of a population (genetic mutation, space invasion), we will study small populations and stochastic models are suitable.

On the other hand, if we are studying a "large population", we will rather use deterministic models, knowing however that the real dynamics are stochastic.

Often the two are intertwined: the emergence of a new population within a very large population of another type.

Two types Population Dynamics - Horizontal Gene Transfer - Plasmids

We will now focus on populations of bacteria or cells.

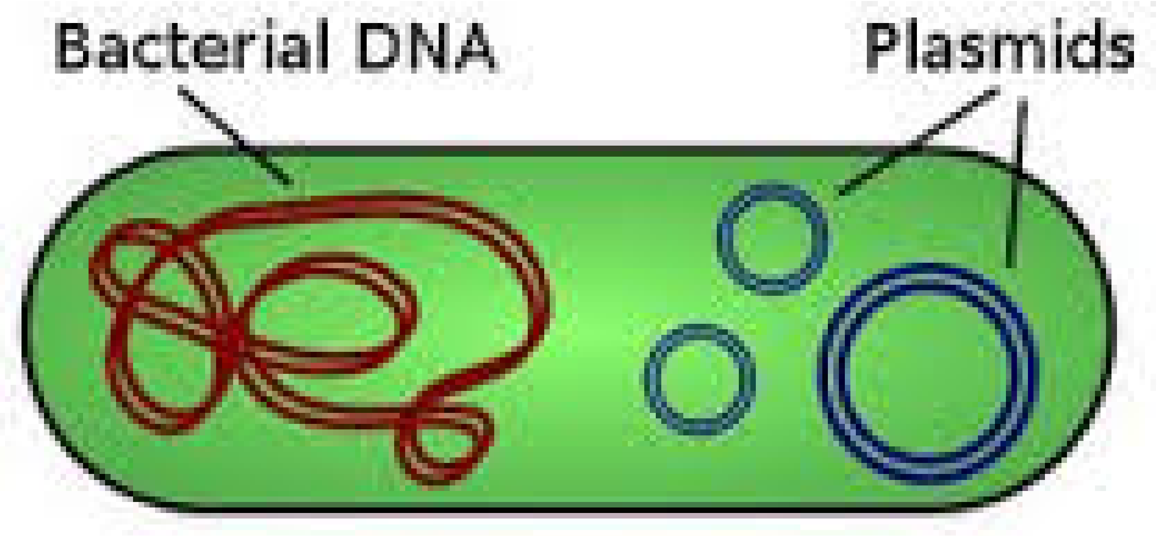
The dynamics of individuals (bacteria) is based on the following mechanisms

- Division
- Death : either intrinsic or due ton competition (fixed resources amount)
- Horizontal gene transfer
    - Transformation : some DNA filaments enters directly the cell.
    - Transduction : DNA moves from a cell to another one through the action of viruses (phages).
    - Conjugation

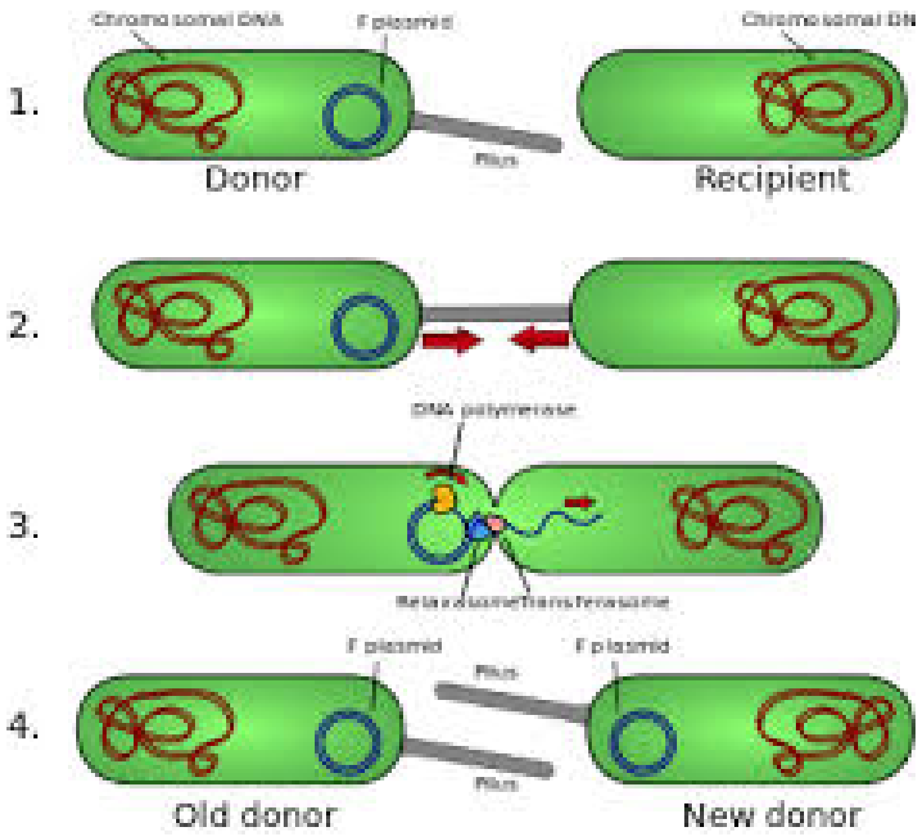
Plasmids - Genes of resistance to antibiotics

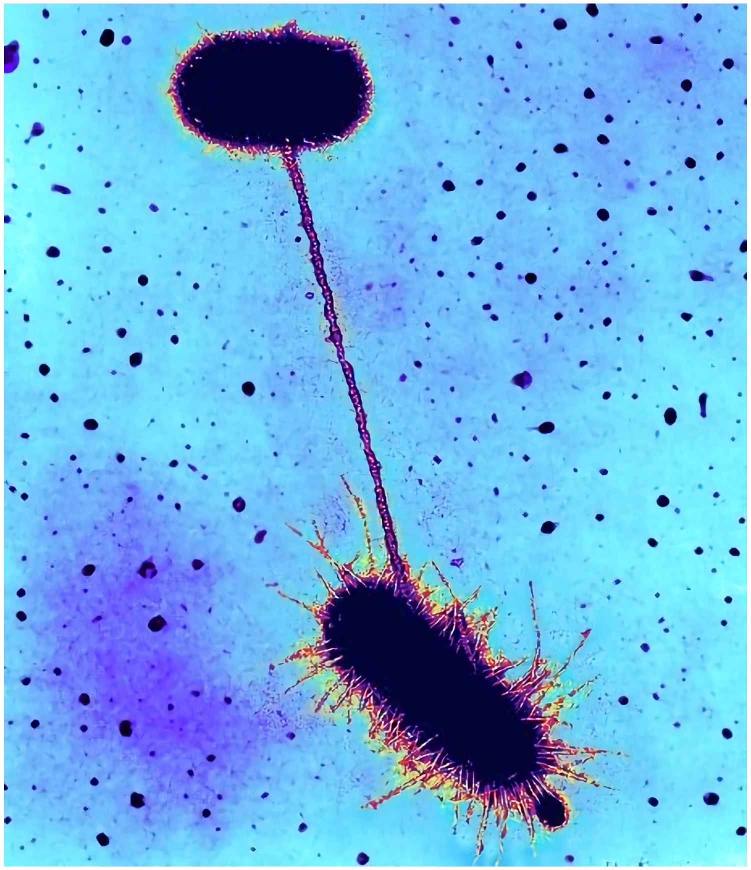
Conjugation : transfer of genetic material between bacteria cells by direct cell-to-cell contact. We will focus on plasmid conjugation.

Plasmids: small circular double-stranded DNA, physically separated from the chromosonal DNA. They replicate from a cell to another one, independently of the chromosome.



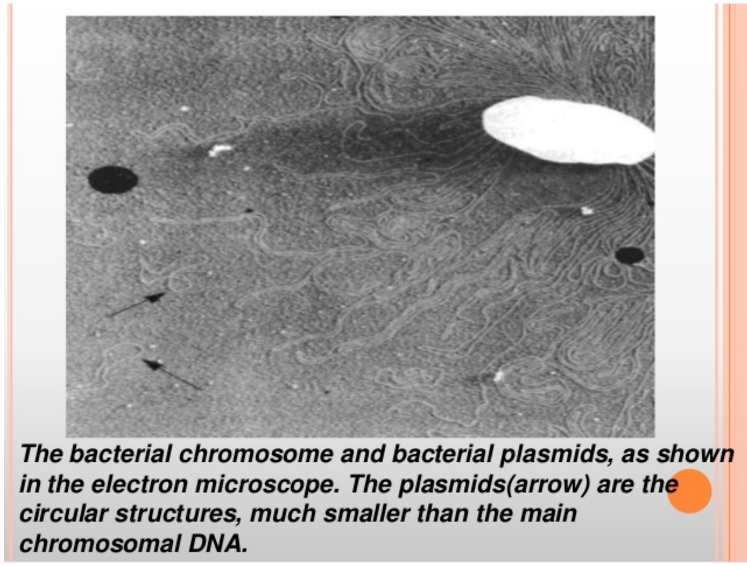
Plasmid transfer



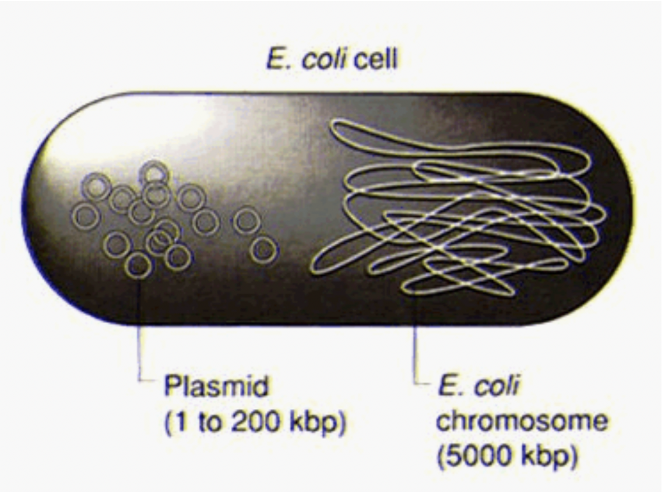


Plasmids in E-Coli

Number of identical plasmids in a cell: from 1 to 1000.



The bacterial chromosome and bacterial plasmids, as shown in the electron microscope. The plasmids(arrow) are the circular structures, much smaller than the main chromosomal DNA.



- Plasmids often carry genes that may benefit the survival of the organisms, for example pathogens or antibiotic resistances.

  HGT is the primary reason for bacterial antibiotic resistance

- Artificial plasmids are widely used as vectors in molecular cloning (CRISPR/Cas 9)
- Important role in the degradation of novel compounds by bacteria (such as human-created pesticides).

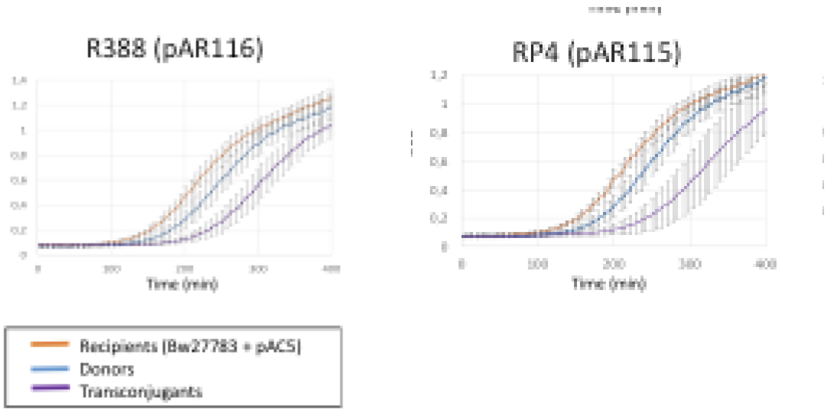
Experiments and data

- Plasmids are costly and cells with plasmids are less efficient for the reproduction.

- Population of recipients (without the plasmid) : cells divide every 20 mn.
- Population of donors (they carry a plasmid coding for antibiotics AB1 resistance) : cell division takes place every 22 mn.

Populations of recipients and donors are isolated and their growth rate is measured by par spectrophotometry.

Data: R. Fernandez-Lopez et al.



A two-traits stochastic birth and death process with transfer

- K scales the population size.
- The population is structured by a gene x with two alleles A and a : $x \in \{A, a\}$.
- The population at time t is modeled by the vector

$$(Z_t^{A,K}, Z_t^{a,K}) = \frac{1}{K}(N_t^{A,K}, N_t^{a,K}),$$

  where $N_t^{A,K}$ and $N_t^{a,K}$ are the numbers oof individuals with alleles respectively A and a.
- Division rate of an individual with trait $x \in \{A, a\}$: $b(x)$.
- Death rate of an individual with trait $x \in \{A, a\}$ at time t ; $y \in \{A, a\}$ is the other trait:

$$d(x) + \frac{C(x,x)}{K} N_t^{x,K} + \frac{C(x,y)}{K} N_t^{y,K}.$$

HGT: Bacterial conjugation

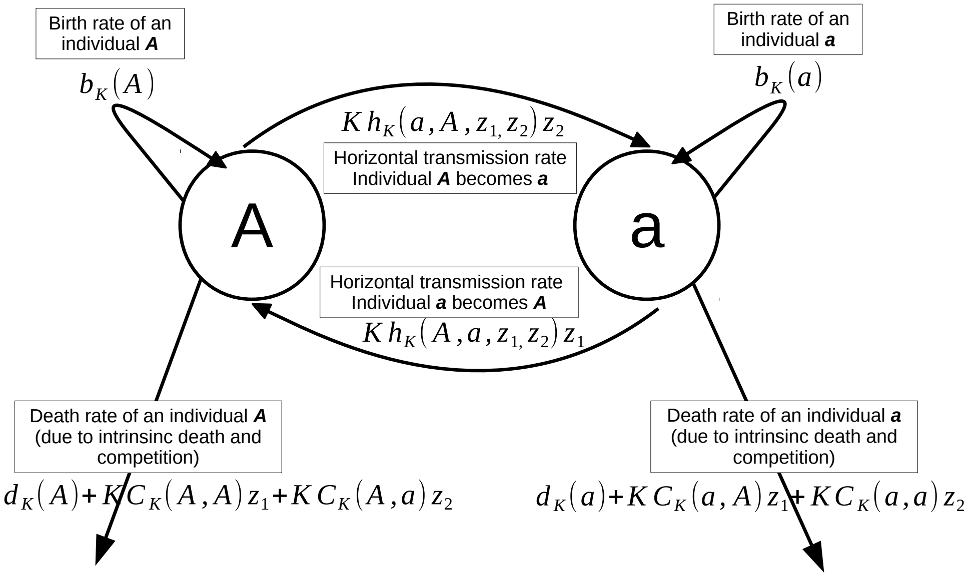
- Transfer rate: in the population (z_1, z_2), a donor transmits its trait x to a recipient with trait y at rate

$$h_K(x, y, z_1, z_2) = \frac{\tau(x, y)}{K(z_1 + z_2)} = \frac{\tau(x, y)}{N}$$

.

- The recipient trait becomes x.

Markovian dynamics



Birth rate of an individual ***A***

$b_K(A)$

Birth rate of an individual ***a***

$b_K(a)$

$K h_K(a, A, z_1, z_2) z_2$

Horizontal transmission rate Individual ***A*** becomes ***a***

Horizontal transmission rate Individual ***a*** becomes ***A***

$K h_K(A, a, z_1, z_2) z_1$

Death rate of an individual ***A*** (due to intrinsinc death and competition)

$d_K(A) + K C_K(A, A) z_1 + K C_K(A, a) z_2$

Death rate of an individual ***a*** (due to intrinsinc death and competition)

$d_K(a) + K C_K(a, A) z_1 + K C_K(a, a) z_2$

The stochastic process

Let $F \in \mathcal{C}_b(\mathbb{R}^2,\ \mathbb{R})$ be a test function. The infiniftesimal generator of $(Z_t^{A,K}, Z_t^{a,K})_{t\geq 0}$ is

$$
\begin{aligned}
LF(z_1, z_2) = {} & K\, z_1\, b(A) \left(F(z_1 + \frac{1}{K}, z_2) - F(z_1, z_2) \right) \\
& + K\, z_2\, b(a) \left(F(z_1, z_2 + \frac{1}{K}) - F(z_1, z_2) \right) \\
& + K\, z_1 \left(d(A) + C(A,A)\, z_1 + C(A,a)\, z_2 \right) \left(F(z^1 - \frac{1}{K}, z_2) - F(z^1, z_2) \right) \\
& + K\, z_2 \left(d(a) + C(a,A)\, z_1 + C(a,a)\, z_2 \right) \left(F(z^1, z_2 - \frac{1}{K}) - F(z^1, z_2) \right) \\
& + K\, z_1\, z_2\, \frac{\tau(A,a)}{z_1 + z_2} \left(F(z_1 + \frac{1}{K}, z_2 - \frac{1}{K}) - F(z^1, z_2) \right) \\
& + K\, z_1\, z_2\, \frac{\tau(a,A)}{z_1 + z_2} \left(F(z_1 - \frac{1}{K}, z_2 + \frac{1}{K}) - F(z^1, z_2) \right).
\end{aligned}
$$

We can decompose the process in semimartingales

$$
\begin{aligned}
Z_t^{A,K} &= Z_0^{A,K} + \int_0^t P_K(Z_s^{A,K}, Z_s^{a,K})ds + M_t^{K,A}, \\
Z_t^{a,K} &= Z_0^{a,K} + \int_0^t Q_K(Z_s^{A,K}, Z_s^{a,K})ds + M_t^{K,a},
\end{aligned}
$$

where $M^{K,A}$ and $M^{K,a}$ are martingales and P_K and Q_K converge as K tends to infinity to P and Q defined by

$$
\begin{aligned}
P(u,v) &= \Big(r(A) - C(A,A)u - C(A,a)v + \frac{\alpha(A,a)}{(u+v)}\,v\Big)u \\
Q(u,v) &= \Big(r(a) - C(a,A)u - C(a,a)v - \frac{\alpha(A,a)}{(u+v)}\,u\Big)v,
\end{aligned}
$$

where

$$\alpha(x,y) = \tau(x,y) - \tau(y,x),$$

denotes the transfer flux. It can be either positive or negative.

One can show that

$$\begin{aligned}
&\mathbb{E}((M_t^{K,A})^2)\\
&= \frac{1}{K}\,\mathbb{E}\Big(\int_0^t b(A)Z_s^{A,K}ds + \int_0^t \left(d(A) + C(A,A)\,Z_s^{A,K} + C(A,a)\,Z_s^{a,K}\right) Z_s^{A,K} ds\\
&\qquad + \int_0^t K\big(h_K(A,a,Z_s^{A,K},Z_s^{a,K}) + h_K(a,A,Z_s^{A,K},Y_s^K)\big) Z_s^{A,K} Z_s^{a,K} ds\Big);\\
&\mathbb{E}((M_t^{K,a})^2)\\
&= \frac{1}{K}\,\mathbb{E}\Big(\int_0^t b(a)Z_s^{a,K}ds + \int_0^t \left(d(a) + C(a,A)\,Z_s^{A,K} + C(a,a)\,Z_s^{a,K}\right)\, Z_s^{a,K} ds\\
&\qquad + \frac{1}{K}\int_0^t K\big(h_K(A,a,Z_s^{A,K},Z_s^{a,K}) + h_K(a,A,Z_s^{A,K},Z_s^{a,K})\big) Z_s^{A,K} Z_s^{a,K} ds\Big);\\
&\mathbb{E}(M_t^{K,A} M_t^{K,a})\\
&= -\frac{1}{K}\,\mathbb{E}\Big(\int_0^t K\big(h_K(A,a,Z_s^{A,K},Z_s^{a,K}) + h_K(a,A,Z_s^{A,K},Z_s^{a,K})\big) Z_s^{A,K} Z_s^{a,K} ds\Big).
\end{aligned}$$

Then

$$\mathbb{E}(\sup_{t\leq T}(M_t^{K,A} + M_t^{K,a})^2) \leq \frac{C}{K}.$$

Large population limit - A law of large numbers

Theorem [Kurtz, 1971]

When $K \to \infty$*, the stochastic process* $(Z_t^{A,K}, Z_t^{a,K})_{t\geq 0}$ *converges in probability to the deterministic and continuous solution* $(n_t^A, n_t^a)_{t\geq 0}$ *of the ODE's system*

$$\frac{dn^A}{dt} = \Big(r(A) - C(A,A)n^A - C(A,a)n^a + \frac{\alpha(A,a)}{(n^A+n^a)}\, n^a\Big)n^A = P(n^A,n^a)$$

$$\frac{dn^a}{dt} = \Big(r(a) - C(a,A)n^A - C(a,a)n^a - \frac{\alpha(A,a)}{(n^A+n^a)}\, n^A\Big)n^a = Q(n^A,n^a).$$

Idea of the proof : Uniform control of moments ; Tightness (compactness of the laws) ; Identification of the limit and uniqueness.

If there is only one type a, we recover the logistic equation

$$\frac{dn^a}{dt} = \Big(r(a) - C(a,a)n^a\Big)n^a.$$

There is a unique stable equilibrium

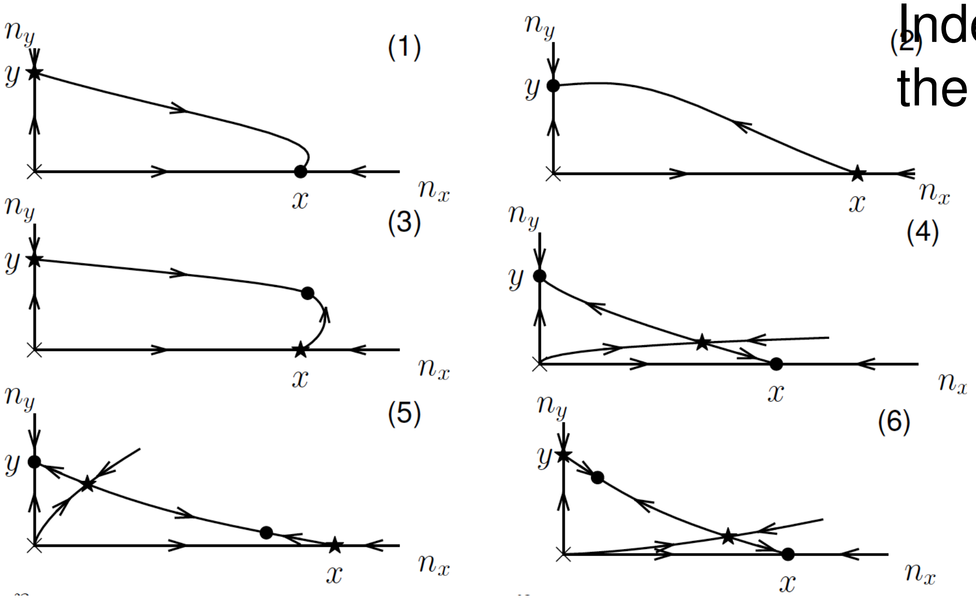
$$\bar{n}^a = \frac{r(a)}{C(a,a)}.$$

Study of the dynamical system

- If $C(A,A) > 0$ and $C(a,a) > 0$, no cycle in $(\mathbb{R}_+^*)^2$. Indeed $\varphi(z^1, z^2) = \frac{1}{z^1 z^2}$ is a Dulac function, i.e.
$$\Big(\partial_u(\varphi P) + \partial_v(\varphi Q)\Big)(u,v)$$
has the same sign on the whole domain $(\mathbb{R}_+^*)^2$. We apply Dulac's Theorem.
- To find the fixed points in the positive quadrant: easier to consider the system " population size and frequencies".
$$n(t) = n^a(t) + n^A(t) \quad ; \quad q(t) = \frac{n^a(t)}{n^a(t) + n^A(t)}.$$

$$\begin{aligned}\frac{dn}{dt} &= n\Big(q\,r(A) + (1-q)\,r(a) - C_{AA}\,q^2 n - (C_{Aa} + C_{aA})\,q(1-q)n \\ &\qquad - C_{aa}\,(1-q)^2 n\Big)\\ \frac{dq}{dt} &= q\,(1-q)\,\Big(r(A) - r(a) + nq(C_{aA} - C_{AA}) + n(1-q)(C_{aa} - C_{Aa}) + \\ &\qquad + \alpha(a,A)\Big).\end{aligned}$$

Stability Analysis



Index Poincaré Theorem to obtain the sinks and sources.

- Without transfer (Lotka-Volterra competitive system): only the four first pictures.

The stability is governed by the function, called invasion fitness function

$$S(y;x) = r(y) - C(y,x)\bar{n}^x + \alpha(y,x) = r(y) - \frac{C(y,x)}{C(x,x)} r(x) + \alpha(y,x).$$

- A can invade a resident population with trait a if $S(A;a) > 0$.
- Trade-off between demography-ecology and transfer.