

1 Biological context

Adaptive dynamics

Chemostat

2 Deterministic approach to adaptive dynamics

The PDE model

Hamilton Jacobi equation with constraint

Closed Hamilton Jacobi equation

Consequences in adaptive dynamics

3 Stochastic approach to adaptive dynamics

Individual-based model

Limit of large population

Limit of rare mutations

The limit of small mutations

4 Conclusion

Darwinian evolution

Three main ingredients:

- **Heredity**: transmissions of individual characteristics from a generation to the next one.
- **Mutation**: cause of the variability in individual characteristics.
- **Selection**: consequence of the interactions between individuals and their environment, including the rest of the population (**ecology**).

First approach: **population genetics** (since the 30s)

- Wright-Fisher, Moran, Flemming-Viot, Kingman coalescent... models
- Put emphasis on the genetic mechanism at the molecular level
- Selection: a **fixed fitness value** is associated to each allele
↪ supposes a **fixed environment** of the population

Adaptive dynamics

Adaptive dynamics (since the 90s): Hofbauer and Sigmund (1990), Metz, Geritz et al. (1992,1996), Dieckmann and Law (1996)...

- Focus on the **interplay between ecology and evolution**
- **Ecological interactions** modeled in detail
- Heredity is simplified as much as possible: **asexual (clonal) reproduction**

↪ Density-dependent individual-based models where **no fitness is given**. The fitness landscape has to be constructed from the parameters of the model.

↪ New phenomenon of **evolutionary branching** (Metz et al., 1996)

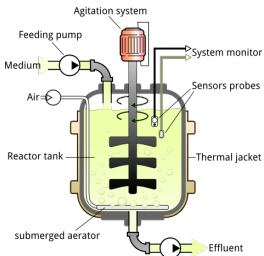
- Transition from a population concentrated around a single phenotype to a population concentrated around several distinct phenotypes, still under ecological interaction
- Mechanism of **diversification**
- Can lead to **speciation** without geographical separation (Dieckmann and Doebeli, 1999)

Chemostat (J. Monod, 1950)

A chemostat is a bioreactor in which liquid is continuously injected while volume is kept constant by an equal outflow:

- allows to control the growth rate of microorganisms in a **controlled environment** (temperature, pH, nutrient concentration...)
- used to grow cells or to perform a biochemical process (e.g. wastewater treatment)

The chemostat is an efficient device to make bacteria **adapt to given environmental conditions**, e.g. to improve nutrients consumption.



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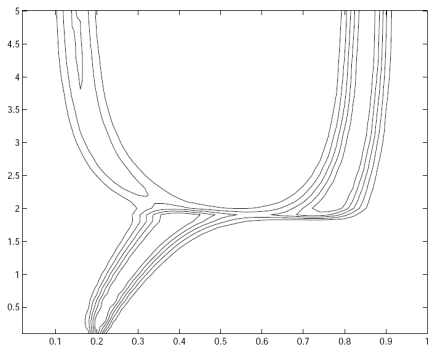
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Simulation



Competition for two resources
(Diekmann, Jabin, Mischler, Perthame, 2005)

Strong selection and small mutations

Non-local interactions favor the concentration of population densities close to the “best” traits. The idea is to strengthen this concentration in order to simplify the dynamics.

Sélection forte et petites mutations :

$$\partial_t u_\varepsilon(t, x) = \frac{1}{\varepsilon} u_\varepsilon(t, x) \left(\sum_{k=1}^r R_k^\varepsilon(t) \eta_k(x) - d(x) \right) + \frac{1}{\varepsilon} \int_{\mathbb{R}} K(z) (u_\varepsilon(t, x + \varepsilon z) - u_\varepsilon(t, x)) dz.$$

WKB ansatz

For reaction-diffusion: Fleming, Souganidis, 1986, Barles, Evans, Souganidis, 1990, Freidlin, 1990.

For adaptive dynamics: Diekmann et al., 2005.

$$u_\varepsilon(t, x) = \exp\left(\frac{\varphi_\varepsilon(t, x)}{\varepsilon}\right).$$

Then $\partial_t u_\varepsilon = \frac{u_\varepsilon}{\varepsilon} \partial_t \varphi_\varepsilon$ and so

$$\begin{aligned} \partial_t \varphi_\varepsilon(t, x) &= \sum_{k=1}^r R_k^\varepsilon(t) \eta_k(x) - d(x) \\ &+ \int_{\mathbb{R}^k} K(z) \left(e^{(\varphi(t, x+\varepsilon z) - \varphi(t, x))/\varepsilon} - 1 \right) dz. \end{aligned}$$

Hamilton-Jacobi equation with constraint

Therefore, one expects $\varphi_\varepsilon \rightarrow \varphi$, where

$$\partial_t \varphi = \sum_{k=1}^r R_k(t) \eta_k(x) - d(x) + H(\partial_x \varphi),$$

where $R_k^\varepsilon(t) \rightarrow R_k(t)$ and

$$H(p) = \int_{\mathbb{R}} K(z) (e^{pz} - 1) dz.$$

By Jensen's inequality, $H(p) \geq 0$ and $H(p) = 0$ iff $p = 0$.

- All the mass of $u_\varepsilon(t, \cdot)$ is concentrated close to $\{x : \varphi(t, x) = 0\}$.
- If $0 < \underline{d} \leq d(\cdot)$ and $0 < \underline{\eta} \leq \eta_k(\cdot) \leq \bar{\eta}$,

$$\frac{d}{dt} \int_{\mathbb{R}} u_\varepsilon(t, x) dx \leq \left(\int_{\mathbb{R}} u_\varepsilon(t, x) dx \right) \frac{1}{\varepsilon} \sum_{k=1}^r \left(\frac{\bar{\eta}}{1 + \underline{\eta} \int_{\mathbb{R}} u_\varepsilon(t, x) dx} - \underline{d} \right).$$

↪ non-explosion of the total population density:

$$\limsup_{\varepsilon \rightarrow 0} \max_x \varphi_\varepsilon(t, x) = 0.$$

Hamilton-Jacobi equation with constraints

One expects $\varphi_\varepsilon \rightarrow \varphi$, where

$$\partial_t \varphi = \sum_{k=1}^r R_k(t) \eta_k(x) - d(x) + H(\partial_x \varphi),$$

and $\sup_{x \in \mathbb{R}} \varphi(t, x) = 0$ for all $t \leq 0$.

How to characterize $R_k(t)$?

In order to satisfy the constraint, one should also have

- $\sum_{k=1}^r R_k(t) \eta_k(x) - d(x) \leq 0$ for all x such that $\varphi(t, x) = 0$,
- $\sum_{k=1}^r R_k(t) \eta_k(x) - d(x) = 0$ for at least one x such that $\varphi(t, x) = 0$.

First approach:

- R_k are Lagrange multipliers associated with these constraints. Works only in particular cases (Diekmann et al., 2005, Barles, Perthame, 2007, 2008, Mirrahimi, Perthame, Wakano, 2012...).
- Difficulty: the number of unknown r can be different from the number of constraints (number of zeroes of φ).

Assumptions

- Smoothness of the parameters.
- For all distinct x_1, \dots, x_{r+1} , the vectors

$$\begin{pmatrix} \eta_1(x_1) \\ \vdots \\ \eta_1(x_{r+1}) \end{pmatrix} \cdots \begin{pmatrix} \eta_r(x_1) \\ \vdots \\ \eta_r(x_{r+1}) \end{pmatrix}, \begin{pmatrix} d(x_1) \\ \vdots \\ d(x_{r+1}) \end{pmatrix}$$

are linearly independent

- For all distinct x_1, \dots, x_r , the vectors

$$\begin{pmatrix} \eta_1(x_1) \\ \vdots \\ \eta_r(x_1) \end{pmatrix} \cdots \begin{pmatrix} \eta_1(x_r) \\ \vdots \\ \eta_r(x_r) \end{pmatrix}$$

are linearly independent.

Under these conditions, one can associate a unique environment (resources) to the set of zeroes of φ , and a unique population measure associated to this environment.

Proposition (C., Jabin, 2011)

For all closed $A \subset \mathbb{R}$, there exists a unique finite positive measure $\mu(A)$ satisfying

(i) $\text{supp } \mu \subset A$

(ii) if we define $\bar{R}_k(\mu) = \frac{g_k}{1 + \int \eta_k(x) d\mu(x)}$,

$$\sum_{k=1}^r \bar{R}_k(\mu) \eta_k(x) - d(x) \leq 0 \text{ in } A,$$

$$\sum_{k=1}^r \bar{R}_k(\mu) \eta_k(x) - d(x) = 0 \text{ in } \text{supp } \mu.$$

The limiting $R_k(t)$ are then obtained as

$$R_k(t) = \bar{R}_k(\mu(\{\varphi(t, \cdot) = 0\})).$$

A remark on the number of coexisting traits

- In view of the previous result, given distinct x_1, \dots, x_n , one says that these traits **coexist** if $\text{supp } \mu(\{x_1, \dots, x_n\}) = \{x_1, \dots, x_n\}$.
- In order to have coexistence of x_1, \dots, x_n , one must have

$$\sum_{k=1}^r \bar{R}_k(\mu) \eta_k(x_i) - d(x_i) \leq 0, \quad 1 \leq i \leq n.$$

Because of our assumptions, **this is impossible if $n > r$** .

- This has the following biological interpretation: one cannot have coexistence of more species than resources. This is related to the concept of **ecological niche**.

Proof of existence

We consider the differential equation in measure space

$$\partial_t \nu = \left(\sum_{i=1}^k \bar{I}_i(\nu) \eta_i(x) - 1 \right) \nu.$$

A stable steady state of this equation should satisfy the conditions of the Proposition.

Since this system has the convex, strict Lyapunov functional

$$L(\nu) = \int_{\mathbb{R}} d(x) \nu(dx) - \sum_{k=1}^r g_k \log(1 + \int \eta_k(x) \nu(dx)),$$

one can define the measure μ as the global minimizer of this functional.

Indeed,

$$\frac{d}{dt} L(\nu_t) + \int \left(\sum_{k=1}^r \frac{g_k \eta_k(x)}{1 + \int \eta_k(y) \nu_t(dy)} - d(x) \right)^2 \nu_t(dx).$$

Theorem (C., Jabin, 2011)

Under the previous assumptions, if $u_\varepsilon(t=0) > 0$ is smooth enough and $\varphi_\varepsilon(t=0)$ converges to φ^0 in $W^{1,\infty}(\mathbb{R})$,

then, up to a subsequence extraction, φ_ε uniformly converges on all compact set and in $W_{\text{loc}}^{1,p}(\mathbb{R}_+ \times \mathbb{R})$ to φ , almost everywhere solution to

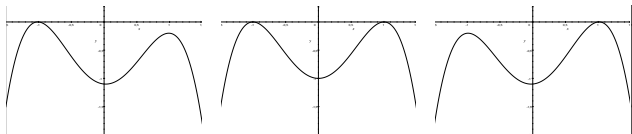
$$\partial_t \varphi = \sum_{k=1}^r R_k(t) \eta_k(x) - 1 + H(\partial_x \varphi),$$

where $R_k(t) = \bar{R}_k(\mu(\{\varphi(t, \cdot) = 0\}))$.

In addition, the functions R_k^ε converge to R_k in L^p for all $p < \infty$.

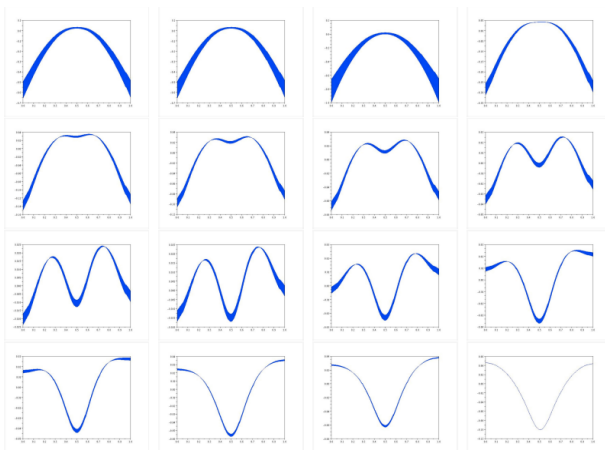
Some elements of the proof of the theorem

- One cannot have existence of a solution to HJ in the strong sense. The $R_k(t)$ need not be continuous.



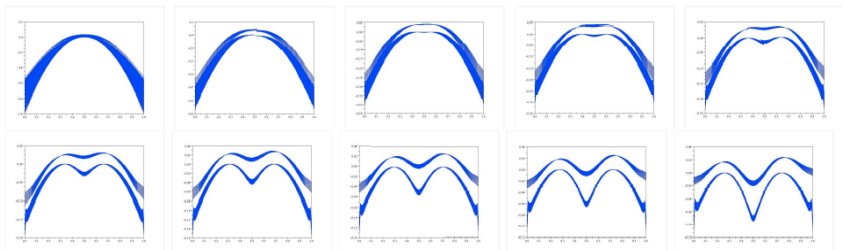
- We use classical a priori estimates for HJ equations, and prove that they hold for φ_ε uniformly in ε . In particular, we prove that $\partial_x \varphi^\varepsilon$ is bounded in $L^\infty([0, T], BV_{\text{loc}}(\mathbb{R}))$ and $\partial_{xx} \varphi_\varepsilon \geq -C$.
- This implies easily the strong convergence of a subsequence of φ_ε .
- The difficult part is the convergence of $R_k^\varepsilon(t)$ to the correct limit. This is done by proving [uniform Lebesgue-right-continuity estimates](#).

Simulation of the PDE for population densities



(Implicit finite differences)

Simulation of the HJ equation with constraints



The fitness function

The fitness function can be defined as the **growth rate of a trait x in the absence of mutation** and in a given environment. For example, in the environment in the HJ equation at time t (the $R_k(t)$),

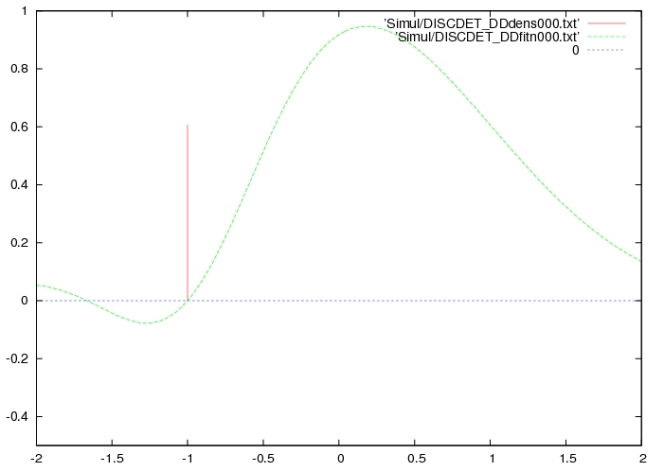
$$f(x, t) = \sum_{k=1}^r R_k(t) \eta_k(x) - d(x).$$

More generally, given a closed subset A of \mathbb{R} , we define the fitness of a trait x in the population characterized by A as

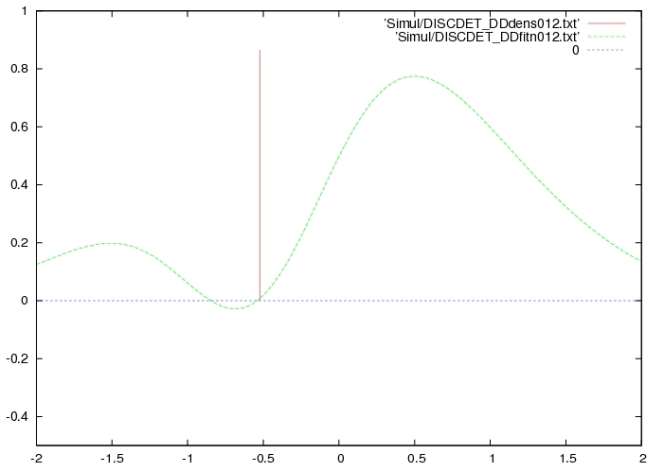
$$f(x, A) = \sum_{k=1}^r \bar{R}_k(\mu(A)) \eta_k(x) - d(x).$$

The sign of this fitness function characterizes the direction of evolution of the population.

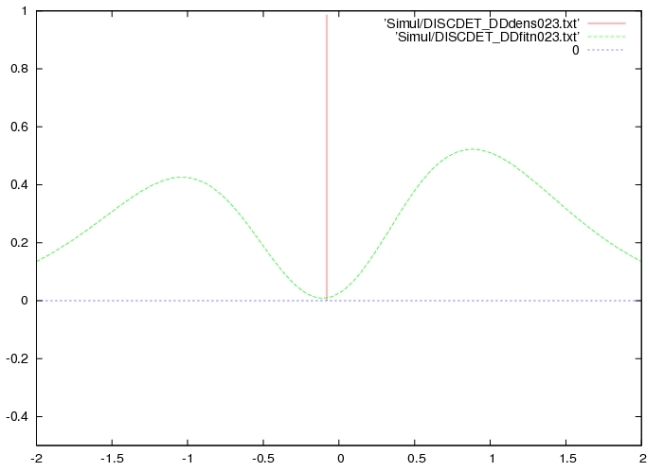
Coevolution with the fitness landscape



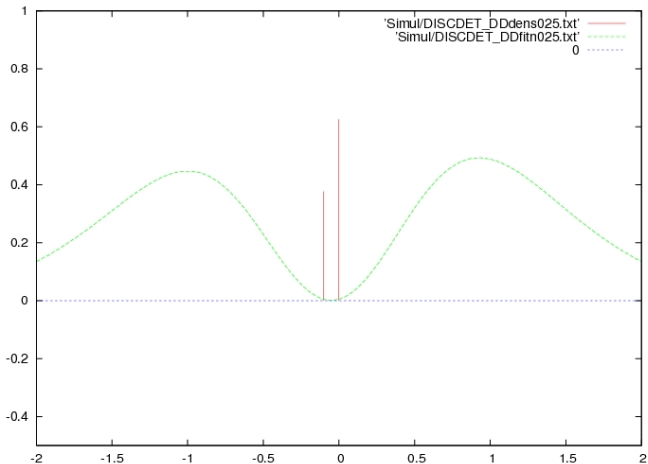
Coevolution with the fitness landscape



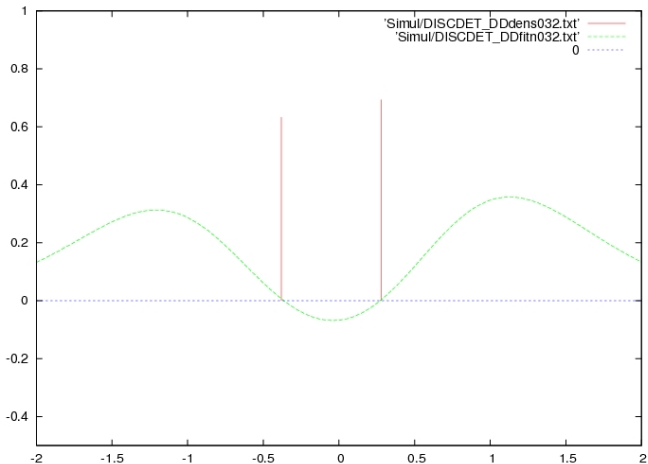
Coevolution with the fitness landscape



Coevolution with the fitness landscape



Coevolution with the fitness landscape



The canonical equation of adaptive dynamics: first form

- As long as there is only a single point in $\{\varphi(t, \cdot) = 0\}$,
 $\mu(\{\varphi(t, \cdot) = 0\}) = \bar{u}(t)\delta_{\bar{x}(t)}$.
- Since $\partial_x \varphi(t, \bar{x}(t)) = 0$, we have

$$\partial_{tx} \varphi(t, \bar{x}(t)) + \partial_{xx} \varphi(t, \bar{x}(t)) \frac{d\bar{x}(t)}{dt} = 0.$$

- Since $\partial_t \varphi(t, x) = f(x, \{\bar{x}(t)\}) + H(\partial_x \varphi(t, x))$,

$$\partial_{tx} \varphi(t, \bar{x}(t)) = \partial_x f(x, \{\bar{x}(t)\}) + H'(\partial_x \varphi(t, \bar{x}(t))) \partial_{xx} \varphi(t, \bar{x}(t)) = \partial_x f(x, t).$$

Therefore

$$\frac{d\bar{x}(t)}{dt} = -(\partial_{xx} \varphi(t, \bar{x}(t)))^{-1} \partial_x f(x, \{\bar{x}(t)\}).$$

This equation is called “canonical equation of adaptive dynamics”.

Adaptive dynamics via the PDE approach

- Until the first time where φ has two distinct zeroes (jump or evolutionary branching), the support of the population evolves according to the canonical equation, and tries to locally increase the fitness.
- Evolutionary branching can only occur at points x^* where $\partial_x f(x, \{x^*\}) = 0$ (evolutionary singularity).
- Evolutionary branching occurs at evolutionary singularities where the fitness function is convex.

Mathematical questions

- Open problem: **well-posedness** of the Hamilton-Jacobi equation with constraint. Only known in special cases (a single resource or no mutation)
 - Jumps in the R_k and in $\partial_x \varphi$ are possible.
 - Viscosity solutions or variational characterizations do not extend easily to this problem.
 - This is also important in simulations.
- **Smoothness of the solution** is only known in special cases
 \rightsquigarrow justification of the canonical equation and of the branching criterion only in special cases.
- Open problems: time of branching, speed of branching, after evolutionary branching...

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2 scaling parameters:

- K scales the size of the population (large K means large population)
- μ_K scales the probability of mutation (small μ_K means rare mutations)

Birth-death-mutation discrete process coupled with r continuous resources with concentrations $R_1^K(t), \dots, R_r^K(t)$:

- each individual is characterized by a **phenotypic trait** x in \mathbb{R}
- a population of $N^K(t)$ individuals holding traits

$$x_1, \dots, x_{N^K(t)} \in \mathcal{X} \text{ is represented by } \nu_t^K = \frac{1}{K} \sum_{i=1}^{N^K(t)} \delta_{x_i}$$

Transitions

- Each individual with trait x gives birth at (inhomogeneous) rate

$$\sum_{k=1}^r \eta_k(x) R_k^K(t) \text{ to a single individual.}$$

$\eta_k(x)$ represents the consumption efficiency of resource k by bacteria with trait x . At each birth time:

- with probability $1 - \mu_K$, clonal reproduction (trait x)
 - with probability μ_K , mutation; the mutant trait is $x + h$ where h has given law $m(x, h)dh$.
- Each individual with trait x dies or is removed from the chemostat at rate $d(x)$.
 - Resources concentrations as before in a quasi-equilibrium

$$R_k^K(t) = \frac{g_k}{1 + \left(\frac{1}{K} \sum_{i=1}^{N(t)} \eta_k(x_i) \right)} = \frac{g_k}{1 + \langle \nu^K, \eta_k \rangle}.$$

$g_k > 0$ is incoming concentration of resource k .

$K \rightarrow +\infty$ (without time scaling)

Theorem

If $\mu_K \rightarrow 0$ when $K \rightarrow +\infty$ and ν_0^K converges in distribution to a deterministic measure $\nu_0 = \sum_{i=1}^n u_i(0)\delta_{x_i}$, then $(\nu_t^K, t \geq 0)$ converges in distribution to the function $(\sum_{i=1}^n u_i(t)\delta_{x_i}, t \geq 0)$, where

$$\dot{u}_i = u_i \left(-d(x_i) + \sum_{k=1}^r \eta_k(x_i) R_k \right), \quad \forall 1 \leq i \leq n,$$

$$R_k = \frac{g_k}{1 + \sum_{i=1}^n \eta_k(x_i) u_i}, \quad \forall 1 \leq k \leq r.$$

This system will be called below **chemostat system**.

Long-time behavior of chemostat systems

Proposition (C., Jabin, Raoul, 2010)

*Under the previous assumptions, for all $n \geq 1$ and all distinct $x_1, \dots, x_n \in \mathcal{X}$, there exists a **unique** \bar{u} in $(\mathbb{R}_+)^{n+r}$ such that any solution $u(t)$ of the chemostat system with $u_i(0) > 0$ for any $1 \leq i \leq n$, converges to \bar{u} .*

With our previous notation, we have $\mu(\{x_1, \dots, x_n\}) = \sum_{i=1}^n \bar{u}_i \delta_{x_i}$.

We shall denote by $\bar{u}(\mathbf{x})$ this equilibrium, where $\mathbf{x} := (x_1, \dots, x_n)$.

Link with the fitness function

The case of two trait:

If $n = 2$, the equilibrium $(\bar{u}(x_1), 0)$ is stable iff $f(x_2, \{x_1\}) \leq 0$.

If both $(\bar{u}(x_1), 0)$ and $(0, \bar{u}(x_2))$ are unstable, i.e. if $f(x_1, \{x_2\}) > 0$ and $f(x_2, \{x_1\}) > 0$, then there exists a stable equilibrium where both traits coexist.

We will write for simplicity $f(x; y)$ for $f(x, \{y\})$.

Limit of rare mutations: biological idea (Metz et al. 1996)

- The selection process has sufficient time between two mutations to eliminate disadvantaged traits (**time scale separation**)
- The assumption of **large populations** allows one to assume a **deterministic** population dynamics
 ↪ one can **predict the outcome of competition** between several traits.
- Succession of phases of **mutant invasion**, and phases of **competition** between traits

Convergence to the PES (C., Jabin, Méléard, 2013)

Theorem

Assume (A). If $\nu_0^K = u_0^K \delta_x$ with $u_0^K \rightarrow \bar{u}(x)$ in probability when $K \rightarrow +\infty$. Assume also

$$\forall C > 0, \quad \log K \ll \frac{1}{K\mu_K} \ll \exp(CK),$$

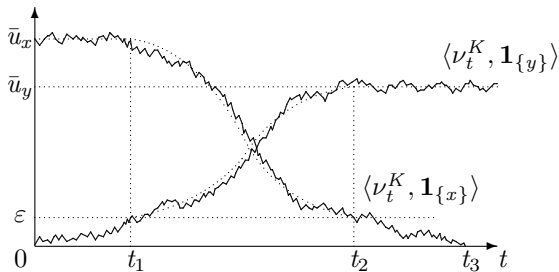
then, the process $(\nu_{t/K\mu_K}^K, t \geq 0)$ converges for f.d.d. to a pure jump Markov process $(\Lambda_t, t \geq 0)$ with explicit jump rates and taking values in

$$\mathcal{M}_0 := \left\{ \sum_{i=1}^d \bar{u}_i(\mathbf{x}) \delta_{x_i}, d \geq 1, x_1, \dots, x_d \in \mathcal{X} \text{ coexist} \right\}.$$

The process Λ_t is called **Polymorphic Evolution Sequence** (PES).

After the first mutation: competition phase

- **between 0 and t_1** : the number of mutant individuals is close to a **branching process** with birth rate $\sum_k \eta_k(y) \bar{R}(x)$ and death rate $d(y)$
 \rightsquigarrow survival probability $[f(y; x)]_+ / (\sum_k \eta_k(y) \bar{R}(x))$
- **between t_1 and t_2** : close to the chemostat system
- **after t_2** : the number of resident individuals is close to a **sub-critical branching process**
- If $\log K \ll \frac{1}{Ku_K}$ the next mutation occurs after this phase with high probability.



The Canonical Equation of Adaptive Dynamics

- **Small mutations:** size of mutations scaled by ε , i.e. $m(x, h)dh$ replaced by $\frac{1}{\varepsilon}m(x, \frac{h}{\varepsilon})dh$.
- **Renormalized PES:** Λ^ε .
- **Rescaled time:** t/ε^2 .

Theorem

The processes $(\Lambda_{t/\varepsilon^2}^\varepsilon, t \geq 0)$ converge in law as $\varepsilon \rightarrow 0$ to $(\bar{u}(x(t))\delta_{x(t)}, t \geq 0)$, where x is solution of the ODE

$$\frac{dx}{dt} = \int h^2 \bar{u}(x) \partial_1 f(x; x) m(x, h) dh.$$

This is the **canonical equation of adaptive dynamics** (Dieckmann and Law, 1996).

\rightsquigarrow Evolutionary branching can only occur in the neighborhood of a point where $\partial_1 f(x, x) = 0$.

A definition of evolutionary branching

Definition

For any $\eta > 0$, we say that there is η -branching at the evolutionary singularity x^* if

- There exist $t > 0$ such that the support of Λ_t^ε is composed of **a single trait** in $(x^* - \eta, x^* + \eta)$.
- There exist $s > t$ such that the support of Λ_s^ε is composed of **two traits** distant of more than η .
- Between s and t , the support of Λ^ε is always a subset of $[x^* - \eta, x^* + \eta]$ composed of at most 2 traits.

Comparison of the two approaches (1)

- We used 3 limits in our two approaches:
 - ① large population
 - ② rare mutations
 - ③ small mutations
- The PDE approach corresponds to (1) then (3).
- The stochastic approach corresponds to (1)+(2) then (3).

Comparison of the two approaches (2)

- The two approaches give qualitatively similar results (convergence to equilibria according to a canonical equation, same branching criterion)...
- ... but quantitatively different results (the two canonical equations are different, the time scales of evolutionary branching are different).
- Both approaches are criticized by biologists: in the PDE approach, very small densities have a strong influence; in the stochastic approach, assumptions are biologically too strong (rare mutations).
- The results seem robust \rightsquigarrow intermediate approaches (e.g. small mutations only, but with simultaneously large populations)

