

Random modeling of adaptive dynamics for diploid populations

Sylvie Méléard, Pierre Collet, Ecole Polytechnique
J.A.J. Metz, Leiden University

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Darwinian or Adaptive Evolution

The population has the propensity to generate as well as to select individual diversity .

Three main ingredients for this :

- ▶ Heredity
- ▶ Mutation
- ▶ Selection

Adaptive Dynamics studies this evolution (Hofbauer-Sigmund 1990, Marrow-Law-Cannings 1992, Metz-Geritz-Meszéna et al. 1992, 1996, Dieckmann-Law 1996)

- ▶ Focus on the interplay between ecology and evolution .
- ▶ Emphasis on the ecological interactions : density-dependent selection model .
- ▶ BUT (up to now)
 - ▶ Asexual (clonal) reproduction
 - ▶ No genetics in the reproduction

Three biological assumptions :

- ▶ (1) large populations
- ▶ (2) rare mutations
- ▶ (3) small mutation steps

and long (evolutive) time scale.

- ▶ In the approach of Metz et al., Champagnat 06 : (1) + (2) then (3) .
- ▶ Individual-based model with stochastic tools mixed with dynamical system arguments .
(Bolker-Pacala 97, Kisdi 99, Dieckmann-Law 00, Fournier-Méléard 04, Ferrière-Champagnat-Méléard 06, Champagnat-Méléard 10)
- ▶ **OUR AIM IN THIS WORK** : To generalise this approach to diploid populations : make a link between ecology, genetics and evolution

The Microscopic Model

- ▶ Each individual i is characterised by two allelic traits (u_1^i, u_2^i) . (u^i real number or vector).
- ▶ The corresponding phenotypic trait is given by a symmetric function $\phi(u_1^i, u_2^i)$.
- ▶ Biologically, all coefficients (except the mutation law) depend on the allelic traits u_1 and u_2 through the phenotypic trait $\phi(u_1, u_2)$. This implies the symmetry of all (rate) functions in (u_1, u_2) . We will forget ϕ and denote $g(u_1, u_2)$ for $g(\phi(u_1, u_2))$.
- ▶ K scales the size of the population : K large .
- ▶ u_K scales the probability of mutation : u_K small. (Only rare mutations affect the phenotype of the individual).
- ▶ Population of $N^K(t)$ individuals and allelic traits $(u_1^1, u_2^1), \dots, (u_1^{N^K(t)}, u_2^{N^K(t)})$. The size ($N^K(t)$) of the allelic trait vector evolves with time.

A model for the reproduction mechanism.

An individual (u_1^i, u_2^i) produces large and small gametes.

The small gametes are far more numerous than the large ones.

The fertility rate for large gametes is $f(u_1^i, u_2^i)$, and $M f(u_1^i, u_2^i)$ for small gametes, with $M \gg 1$.

The large gametes are in a “sea” of small gametes and choose one at random (well mixed sea) with probability

$$\frac{M f(u_1^k, u_2^k)}{M \sum_{j=1}^{N^K} f(u_1^j, u_2^j)} = \frac{f(u_1^k, u_2^k)}{\sum_{j=1}^{N^K} f(u_1^j, u_2^j)}.$$

Note that allelic pairs (u_1, u_2) with larger $f(u_1, u_2)$ are favoured in this choice.

Transitions for an individual with trait (u_1, u_2) in the population, birth rate :

- ▶ An individual i is chosen with probability

$$\frac{f(u_1^i, u_2^i)}{\sum_{j=1}^{N^K} f(u_1^j, u_2^j)}.$$

- ▶ With probability $1 - u_K \mu$, sexual Mendelian reproduction : 4 possibilities

$$(u_1, u_1^i), (u_1, u_2^i), (u_2, u_1^i), (u_2, u_2^i),$$

with probability $1/4$.

- ▶ With probability $u_K \mu$: mutation on an allele . Let σ denote the scale of the mutation .
A mutant from the allelic trait u_1 is $u_1 + \sigma h$, with $|h| = \mathcal{O}(1)$ chosen at random following a distribution $m(u_1, h)dh$.

Transitions for an individual with trait (u_1, u_2) in the population, death rate :

$$D^0(u_1, u_2) + \frac{1}{K} \sum_{j=1}^{N^K} \alpha(u_1, u_2; u_1^j, u_2^j) .$$

D^0 is the natural death and α describes the competition between individuals.

Assumptions :

- ▶ Initial size of order K (**large**).
- ▶ f , D^0 , α , and m smooth enough.
- ▶ f , D^0 and α are bounded.
- ▶ "Natural growth rate" of the population of type (u_1, u_2) :
 $f(u_1, u_2) - D^0(u_1, u_2) > 0$.
- ▶ Interaction rate : $\alpha(u_1, u_2; v_1, v_2) > 0$, $\forall u_1, u_2, v_1, v_2 \in \mathcal{U}$.

Notation : If we consider two alleles A and a , we refer to u_A by A , and u_a by a :

$$f_{AA} = f(u_A, u_A); \quad D_{AA}^0 = D^0(u_A, u_A); \quad \alpha_{AA,AA} = \alpha(u_A, u_A; u_A, u_A),$$

and the same for Aa and aa .

Behaviour for large population and rare mutation. **Time scale of order 1**

Large K ; small mutation probability $u_K \simeq 0$. Denote by $n^K(t, u, v)$ the number of individuals with allelic traits (u, v) at time t .

Theorem 1 (Fournier-Méléard 2004)

When K tends to infinity, the dynamics of the population is almost **deterministic**. The (non random) limit $W_t(u, v)$ of the normalised number $n^K(t, u, v)/K$ of the allelic pair (u, v) is a solution of the equation

$$\begin{aligned} \partial_t W_t(u, v) = & -W_t(u, v) \left(D^0(u, v) + \int \alpha(uv; u'v') W_t(u', v') du' dv' \right) \\ & + \frac{\left(\int f(u, u_1) W_t(u, u_1) du_1 \right) \left(\int f(v, v_1) W_t(v, v_1) dv_1 \right)}{\int f(u_1, u_2) W_t(u_1, u_2) du_1 du_2}. \end{aligned}$$

No mutation appears at this time scale ($u_K \simeq 0$).

Monomorphic homozygote case AA

If the initial population is composed of individuals with allelic trait (u_A, u_A) , it will stay monomorphic with trait (u_A, u_A) at this time scale (i.e. until the first mutation).

The population process is a birth and death process with birth rate f_{AA} and death rate $D_{AA}^0 + \alpha_{AA,AA} N^K(t)/K$.

For large K , the normalised population size $N^K(t)/K$ is close to $n(t)$, solution of the logistic equation

$$\dot{n} = (f_{AA} - D_{AA}^0 - \alpha_{AA,AA} n) n.$$

There is a unique equilibrium

$$\bar{n}_{AA} = \frac{f_{AA} - D_{AA}^0}{\alpha_{AA,AA}},$$

stable since we assumed $f_{AA} - D_{AA}^0 > 0$.

Three genotypes : AA , Aa and aa

Assume there are only two possible alleles, A and a .

- ▶ $t \mapsto (X_t^K, Y_t^K, Z_t^K)$: population process of individuals with genotype AA , Aa and aa .
- ▶ Birth and death process with three types and birth rates b_{AA}, b_{Aa}, b_{aa} and death rates d_{AA}, d_{Aa}, d_{aa} .
- ▶ The birth rates are given by :

$$b_{AA} = \frac{(f_{AA} X + f_{Aa} Y/2)^2}{f_{AA} X + f_{Aa} Y + f_{aa} Z},$$
$$b_{Aa} = \frac{2(f_{AA} X + f_{Aa} Y/2)(f_{aa} Z + f_{Aa} Y/2)}{f_{AA} X + f_{Aa} Y + f_{aa} Z},$$
$$b_{aa} = \frac{(f_{aa} Z + f_{Aa} Y/2)^2}{f_{AA} X + f_{Aa} Y + f_{aa} Z}.$$

Death rates are given by

$$\begin{aligned}d_{AA} &= (D_{AA}^0 + \alpha_{AA,AA} X/K + \alpha_{AA,Aa} Y/K + \alpha_{AA,aa} Z/K) X, \\d_{Aa} &= (D_{Aa}^0 + \alpha_{Aa,AA} X/K + \alpha_{Aa,Aa} Y/K + \alpha_{Aa,aa} Z/K) Y, \\d_{aa} &= (D_{aa}^0 + \alpha_{aa,AA} X/K + \alpha_{aa,Aa} Y/K + \alpha_{aa,aa} Z/K) Z.\end{aligned}$$

Theorem 2

For large K , the normalised population dynamics $(X_t^K/K, Y_t^K/K, Z_t^K/K)$ evolves closely to a solution of the dynamical system $DS(AA, Aa, aa)$ given by the vector field

$$\vec{X}(x, y, z) = \begin{pmatrix} \tilde{b}_{AA} - \tilde{d}_{AA} \\ \tilde{b}_{Aa} - \tilde{d}_{Aa} \\ \tilde{b}_{aa} - \tilde{d}_{aa} \end{pmatrix} (x, y, z).$$

where

$$\tilde{b}_{AA} = \frac{(f_{AA} x + f_{Aa} y/2)^2}{f_{AA} x + f_{Aa} y + f_{aa} z},$$

$$\tilde{d}_{AA} = (D_{AA}^0 + \alpha_{AA,AA} x + \alpha_{AA,Aa} y + \alpha_{AA,aa} z) x, \quad \text{etc.}$$

Long time behaviour of DS(AA,Aa,aa)

The vector field has 15 parameters and generically around 3000 fixed points (most are complex hence irrelevant). There are two main fixed points : $(\bar{n}_{AA}, 0, 0)$, $(0, 0, \bar{n}_{aa})$ with

$$\bar{n}_{AA} = \frac{f_{AA} - D_{AA}^0}{\alpha_{AA,AA}} , \bar{n}_{aa} = \frac{f_{aa} - D_{aa}^0}{\alpha_{aa,aa}} .$$

Theorem 3

The differential $D\vec{X}_{AA}$ is a triangular (3×3) matrix with two negative eigenvalues and the third one is equal to the *invasion fitness* of mutant Aa in the resident population AA :

$$S_{Aa,AA} = f_{Aa} - D_{Aa}^0 - \alpha_{Aa,AA} \bar{n}_{AA} .$$

A similar property holds for $D\vec{X}_{aa}$.

Non linear vector fields in dimension 3 may have complex long time behaviour (E. Lorenz).

It is possible to have AA unstable, aa stable but no fixation of the mutant allele a . This is not possible for a two dimensional Lotka Volterra model.

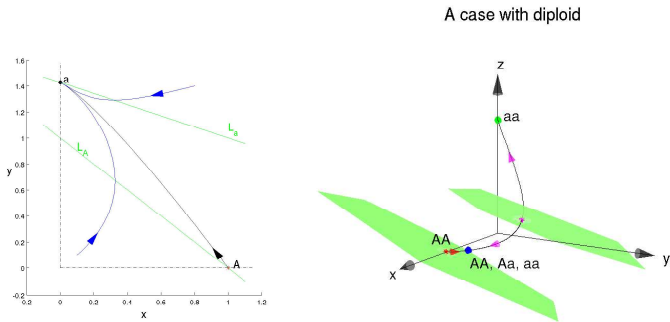


Fig.: Left, Lotka Volterra 2d case, right the vector field \vec{X} for a particular choice of the parameters. In both cases A is unstable and a is stable.

Let $\epsilon = \sigma h$ the (small) variation of the allelic trait, $u_a = u_A + \epsilon$. To study $\vec{X}(\epsilon, \cdot)$, we will assume that mutants have small amplitudes (a is close to A), namely perturb around the neutral case. In any case this is what we are interested in at the end (small mutation steps).

Neutral case.

We start by looking at this simpler case.

All parameters are equal : $AA = aa$, $\epsilon = 0$. Let $\bar{n}_0 = \bar{n}_{AA} = \bar{n}_{aa}$.

Theorem 4

The neutral vector field $\vec{X}(0, \cdot)$ has a curve of fixed points

$$C_0(s) = \begin{pmatrix} \frac{(s - \bar{n}_0)^2}{4 \bar{n}_0} \\ s^2 - \bar{n}_0^2 \\ -\frac{2 \bar{n}_0}{(s + \bar{n}_0)^2} \\ \frac{(s + \bar{n}_0)^2}{4 \bar{n}_0} \end{pmatrix}.$$

This curve is transversally stable (attracting).

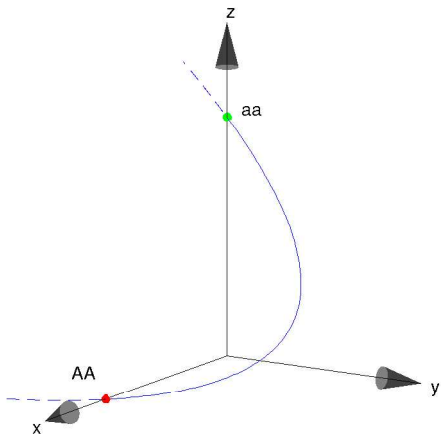


Fig.: The neutral curve.

General perturbations around the neutral case

By the stability of transversally hyperbolic invariant manifolds of Hirsh, Pugh and Shub we know that after a small enough perturbation there is still an invariant attracting curve.

Question : What is the dynamics on this curve ?

General perturbations around the neutral case

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Question : What is the dynamics on this curve ?

Define a function g by

$$g(s) = \det \left(\partial_\epsilon \vec{X}(0, C_0(s)), C_0(s), \frac{d^2}{ds^2} C_0(s) \right) .$$

Theorem 5

Assume the function g satisfies $dg/ds(\pm\bar{n}_0) \neq 0$ and g does not vanish on $] -\bar{n}_0, \bar{n}_0[$. Then there exists $\epsilon_0 = \epsilon_0(\vec{X}(\cdot, \cdot)) > 0$ such that for any $\epsilon \in [-\epsilon_0, \epsilon_0] \setminus \{0\}$, the vector field $\vec{X}(\epsilon, \cdot)$ has only two fixed points in a tubular neighbourhood of C_0 . These two fixed points are $(\bar{n}_{AA}, 0, 0)$ and $(0, 0, \bar{n}_{aa})$.

Remark : $g(\pm\bar{n}_0) = 0$.

This Theorem is for general (small) perturbations, which are not necessarily coming from small mutations.

Small mutations I.

What is special about perturbations coming from small mutations?

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What is special about perturbations coming from small mutations?

$$u_a = u_A + \epsilon \quad \text{with} \quad |\epsilon| \ll 1.$$

$$f_{Aa} = f(u_A + \epsilon, u_A) = f_{AA} + \partial_1 f(u_A, u_A)\epsilon + \mathcal{O}(\epsilon^2).$$

Note that because of the symmetry $\partial_1 f(u_A, u_A) = \partial_2 f(u_A, u_A)$.

Similarly

$$\begin{aligned} f_{aa} &= f(u_A + \epsilon, u_A + \epsilon) = f_{AA} + \epsilon (\partial_1 f(u_A, u_A) + \partial_2 f(u_A, u_A)) + \mathcal{O}(\epsilon^2) \\ &= f_{AA} + 2\epsilon \partial_1 f(u_A, u_A) + \mathcal{O}(\epsilon^2) = f_{AA} + 2\epsilon \partial_2 f(u_A, u_A) + \mathcal{O}(\epsilon^2). \end{aligned}$$

This is sometimes represented by

$$\begin{pmatrix} AA & Aa & aa \\ 1 & 1+s & 1+2s \end{pmatrix}$$

Small mutations II .

$$u_a = u_A + \epsilon \quad \text{with} \quad |\epsilon| \ll 1.$$

The fitness of a mutant Aa in the resident population AA ($S_{Aa,AA} = f_{Aa} - D_{Aa}^0 - \alpha_{Aa,AA} \bar{n}_{AA}$), is a function of ϵ . At neutrality ($\epsilon = 0$) we have $S_{Aa,AA}(0) = 0$. Therefore

$$S_{Aa,AA}(\epsilon) = \epsilon \frac{dS_{Aa,AA}}{d\epsilon}(0) + \mathcal{O}(\epsilon^2).$$

Theorem 6

$$\frac{dS_{Aa,AA}}{d\epsilon}(0) = -\frac{dS_{Aa,aa}}{d\epsilon}(0) = -2 \frac{dg}{ds}(-\bar{n}_0) = 2 \frac{dg}{ds}(\bar{n}_0).$$

In particular, for ϵ small enough, if $\frac{dS_{Aa,AA}}{d\epsilon}(0) \neq 0$ and AA is stable then aa is unstable and vice versa. Moreover the condition $\frac{dg}{ds}(\pm \bar{n}_0) \neq 0$ of the previous theorem can be read on the fitnesses.
Proof : compute.

Small mutations III.

$$u_a = u_A + \epsilon \quad \text{with} \quad |\epsilon| \ll 1.$$

Theorem 7

For ϵ small enough, if $\frac{dS_{Aa,AA}}{d\epsilon}(0) \neq 0$, there are only two equilibria which are the homozygote populations AA and aa .

- ▶ If $\epsilon \frac{dS_{Aa,AA}}{d\epsilon}(0) > 0$, the fixed point AA is unstable and we have invasion (by aa) for the macroscopic dynamics.
- ▶ If $\epsilon \frac{dS_{Aa,AA}}{d\epsilon}(0) < 0$, the fixed point AA is stable and the mutant disappears in the macroscopic dynamics.

Proof :

compute

$$g(s) = \frac{1}{4 \bar{n}_0} \frac{dF_{Aa,AA}}{d\epsilon}(0) (s^2 - \bar{n}_0^2),$$

then apply Theorem 5. ▶

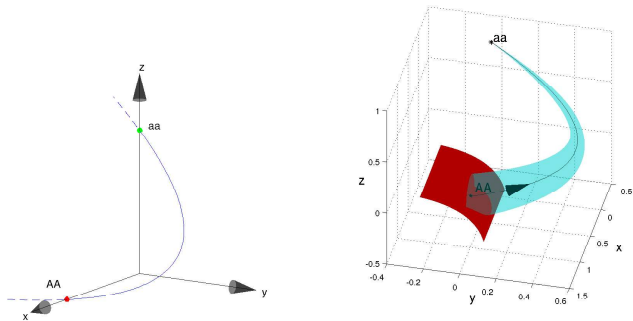


Fig.: Left : neutral case - Right : small mutant case

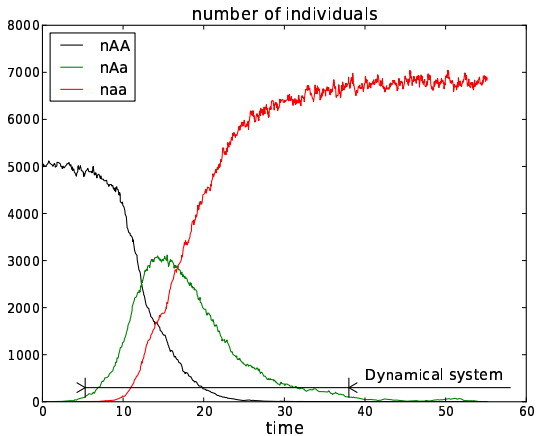


Fig.: Simulation of invasion by a successful mutant.

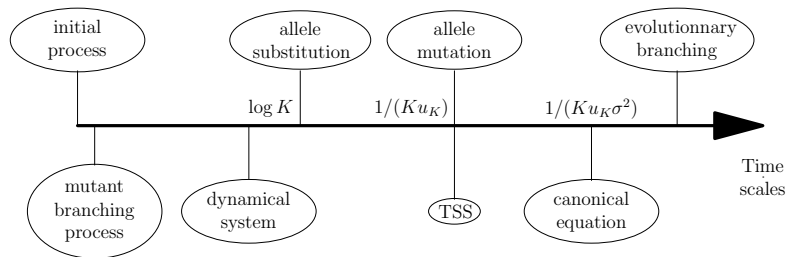
The whole invasion process takes a time of order $\log K$.

The mutation rate is small enough so that during the invasion period no other mutant appears (with large probability).

We can now go to the next (larger) time scale, namely squeeze this picture. We will only see a jump from u_A to u_a .

The time scales

Now that we control the dynamical system, and the invasion by a successful mutant, we can consider the larger time scale of mutation events.



Mutation time scale : **of order** $\frac{t}{K u_K}$

Dynamics of the microscopic process :

Theorem 8

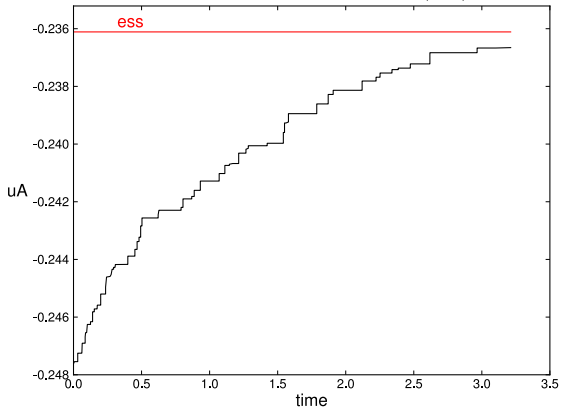
Assume a monomorphic homozygote initial population with trait $A_0 A_0$. Assume that

$$\forall C > 0, \quad \ln K \ll \frac{1}{K u_K} \ll \exp(CK), \quad \text{for large } K. \quad (1)$$

Then, for σ small enough ($\epsilon = \sigma h$), the population process at time $\frac{t}{K u_K}$ is approximated by a jump process defined as follows :

- ▶ Initial configuration : all individuals with traits (u_{A_0}, u_{A_0}) .
- ▶ The process jumps from \bar{n}_{AA} individuals with trait (u_A, u_A) to \bar{n}_{aa} individuals with trait (u_a, u_a) , with $u_a = u_A + \sigma h$.
- ▶ The jumps happen after an exponential time with parameter $2\mu f_{AA} \bar{n}_{AA} \frac{[S_{Aa,AA}]_+}{f_{Aa}}$.
- ▶ The amplitude of the jump is distributed following $m(u_A, h)dh$.

Evolution of the resident allelic trait (TSS)



Generalisation of the trait substitution sequence (TSS) .

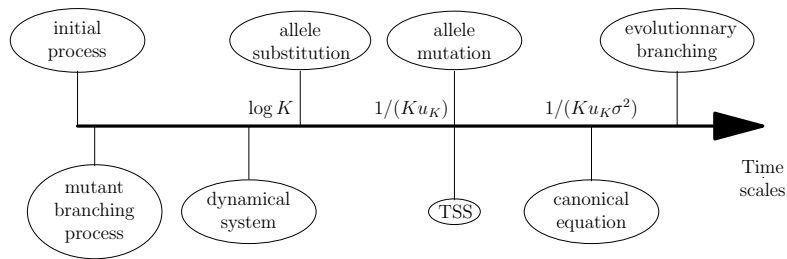
Monomorphic asexual case : Metz et al. 1996 ; Champagnat 06 .

Idea of the proof :

- ▶ The selection process has sufficient time between two mutations to eliminate disadvantaged types (time scale separation).
- ▶ Assumption of large populations : between mutations, the population is close to the deterministic population dynamics , so that one can predict the outcome of competition between the traits.
- ▶ Succession of phases of mutant invasion , and phases of competition between traits

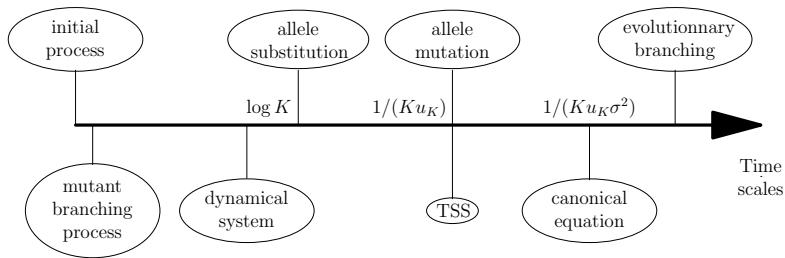
The time scales

Now that we have control on the TSS we can go the next time scale.

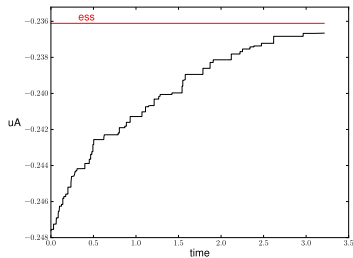


The time scales

Now that we have control on the TSS we can go the next time scale.



We will rescale time and the amplitude of mutations simultaneously. The TSS curve will become a continuous curve.



The Canonical Equation of Adaptive Dynamics

What happens for σ small? (σ : mutation amplitude)

At its time scale, the TSS process disappears (no more jumps). **We need to rescale the time** : longer time $\frac{t}{Ku_K\sigma^2}$.

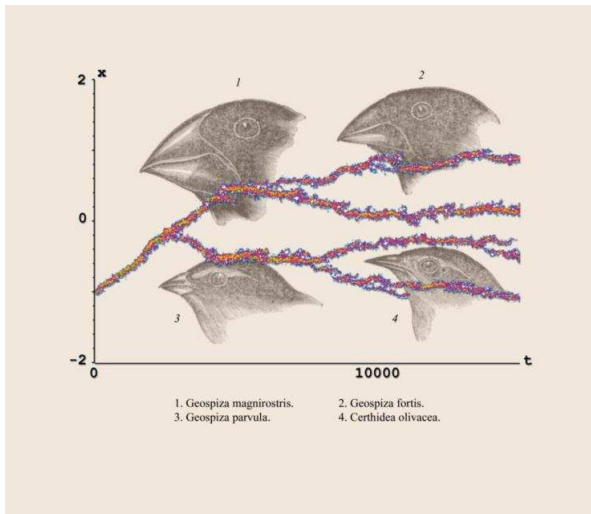
Theorem 9


When σ is small, the dynamics of equilibria allelic traits is given by

$$\frac{du}{dt} = 2\mu \bar{n}_{uu} \partial_1 S(u, u; u, u) \int_{\mathbb{R}} h^2 m(u, h) dh.$$

Canonical equation of the adaptive dynamics.

Evolutionary singularities : points (u, u) such that $\partial_1 S(u, u; u, u) = 0$: possibility of evolutionary branching.



Evolutionary branching for $u \in \mathbb{R}$ beyond $\partial_1 S(u, u; u, u) = 0$.
 Champagnat-Méléard 2010 (asexual case). 

Before the first mutation, K large

- ▶ Monomorphic population with genotype AA : the size of the population for t large enough is close to \bar{n}_{AA} .
- ▶ If $\frac{1}{Ku_K} \ll e^{CK}$, the first mutation occurs before the exit time of a neighbourhood of \bar{n}_{AA} with high probability . (Large deviations).
- ▶ Before this exit time, the rate of mutation from trait (u_A, u_A) is close to $2\mu u_K f_{AA} K \bar{n}_{AA}$.
- ▶ On the time scale $\frac{t}{Ku_K}$: $2\mu f_{AA} \bar{n}_{AA}$.

After the first mutation : competition phase

- ▶ An allelic mutant trait appears at time t_0 .
- ▶ **between t_0 and t_1** : the number of mutant individuals with trait Aa is close to a branching process with birth rate f_{Aa} and death rate $D_{Aa}^0 + \alpha_{Aa,AA} \bar{n}_{AA}$.
- ▶ Growth rate = fitness function :

$$S_{Aa;AA} = f_{Aa} - D_{Aa}^0 - \alpha_{Aa,AA} \bar{n}_{AA}.$$

- ▶ Survival probability : $\frac{[S_{Aa,AA}]_+}{f_{Aa}}$.
- ▶ **After t_1** : close to $DS(AA, Aa, aa)$.

- ▶ Convergence of $DS(AA, Aa, aa)$ to the equilibrium \bar{n}_{aa} .
- ▶ The population density of genotype aa reaches the η -neighbourhood of \bar{n}_{aa} at time t_2 .
- ▶ **After t_2** : the densities of genotypes AA and Aa are approximated by sub-critical branching process .
- ▶ Time scale : $\ln K$.
- ▶ If $\ln K \ll \frac{1}{Ku_K}$, the next mutation occurs after these three phases with high probability.
- ▶ We reiterate the procedure by Markovian arguments.

