

Evolutionary Scenario - No HGT

A toy model : $x \in [0, 4]$. $b(x) = 4 - x$; $d \equiv 1$, $C(x, y) \equiv C$ and

$$\bar{n}_x = \frac{3 - x}{C} .$$

- The invasion fitness is given by

$$f(y; x) = r(y) - r(x) = x - y > 0 \iff y < x.$$

A mutant trait y will invade the population $\iff y < x$.

The evolution leads to trait 0.

Simulations:

- $C = 0,5$; $p = 0,03$; $\sigma = 0,1$; $K = 1000$.
- Initial state: 1000 individuals with trait 1.
Equilibrium : $1000 \times \frac{b(1)-d(1)}{C} = 4000$ individuals.
- Optimal trait 0 . Equilibrium : $1000 \times \frac{b(0)-d(0)}{C} = 6000$ individuals.

$$\tau = 0$$

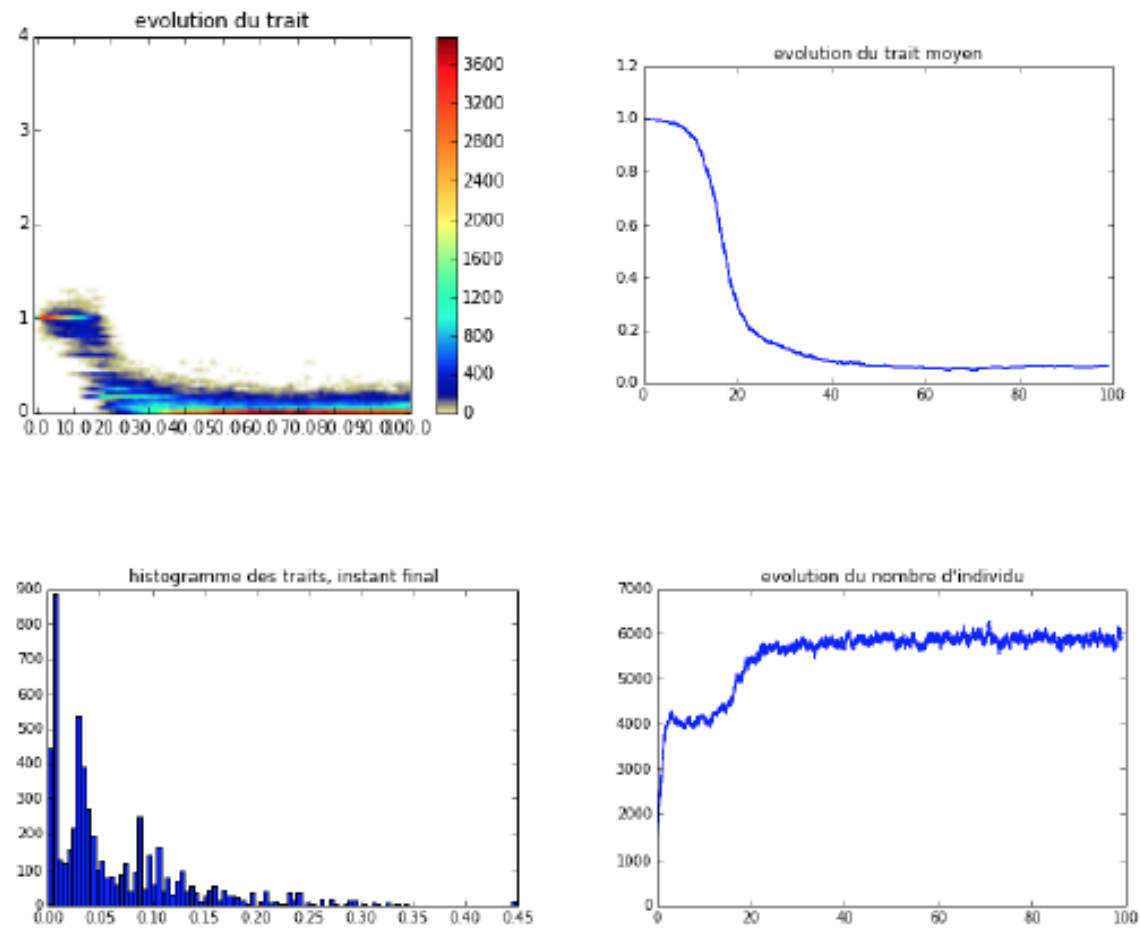


FIGURE 7 – Simulations pour $\tau = 0$.

Evolutionary Scenario - With HGT

- Assume $\tau(x, y) = \tau \mathbf{1}_{x > y}$.

Transfer favors large traits: trade-off between reproduction and transfer.

We have

$$\begin{aligned} S(y; x) &= r(y) - r(x) + \alpha(y, x) \\ &= x - y + \tau \frac{y - x}{|y - x|} \end{aligned}$$

$$S(y; x) > 0 \iff y > x \text{ and } \tau > y - x \text{ or } x > y \text{ and } x - y > \tau.$$

Large values of τ : the evolution can lead the population to traits larger and larger and possibly to evolutionary suicide.

$\tau = 0,2$ - Almost no modification

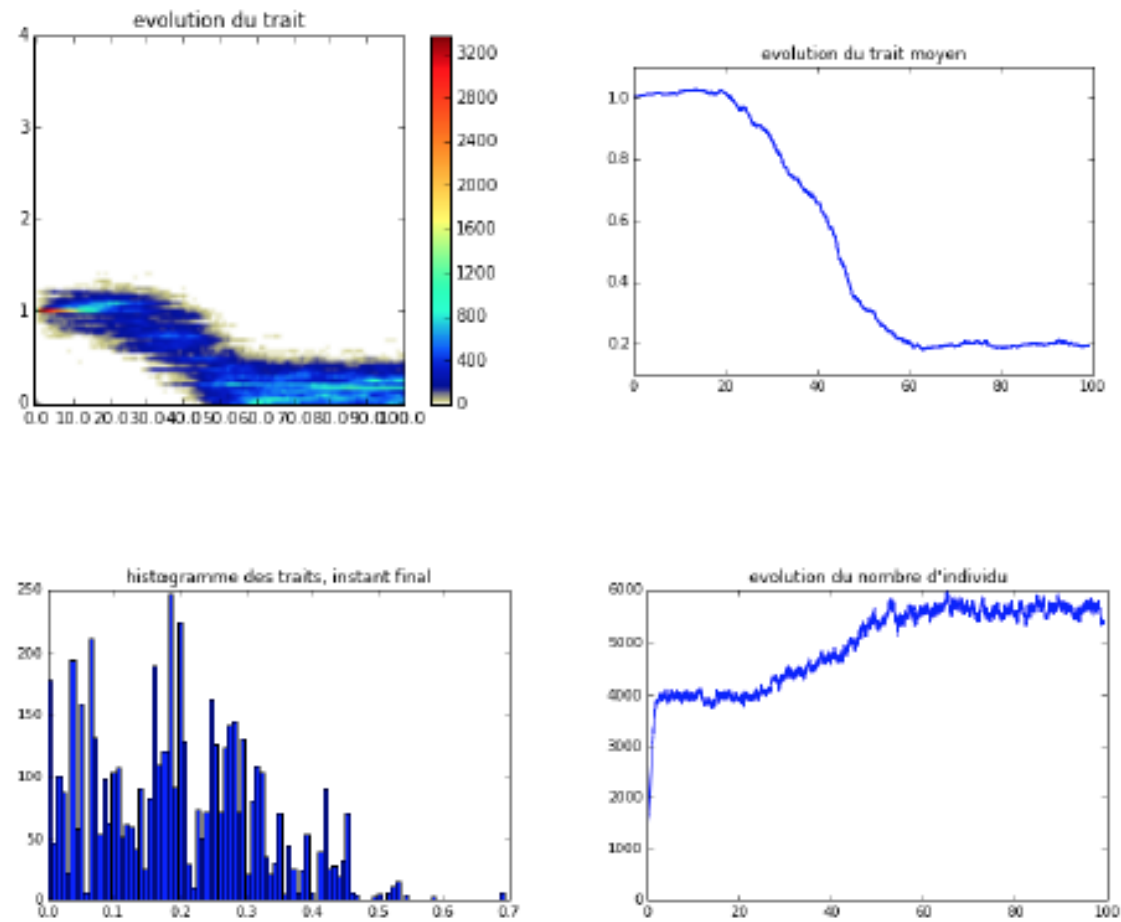


FIGURE 8 – Simulations pour $\tau = 0.2$

$\tau = 1$ - Evolutionary suicide

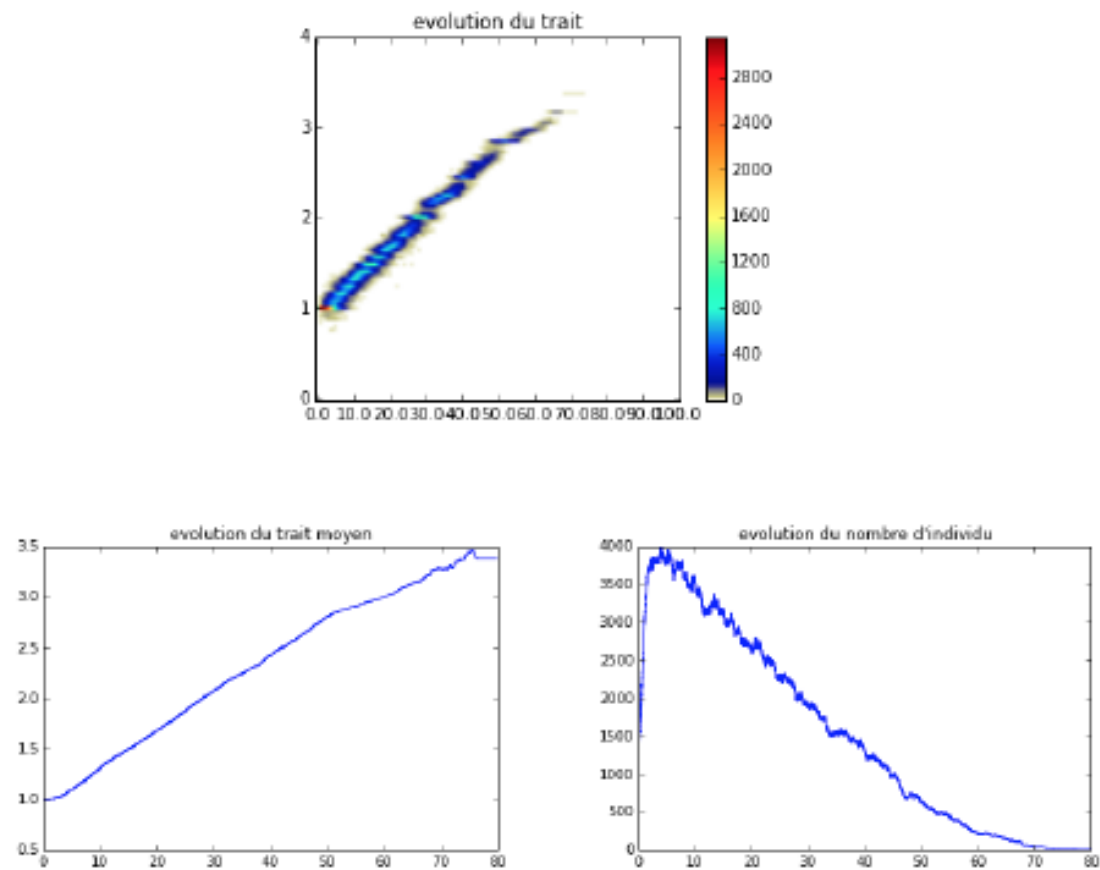


FIGURE 17 – Simulations pour $\tau = 1$

Intermediate rate : $\tau = 0,6$

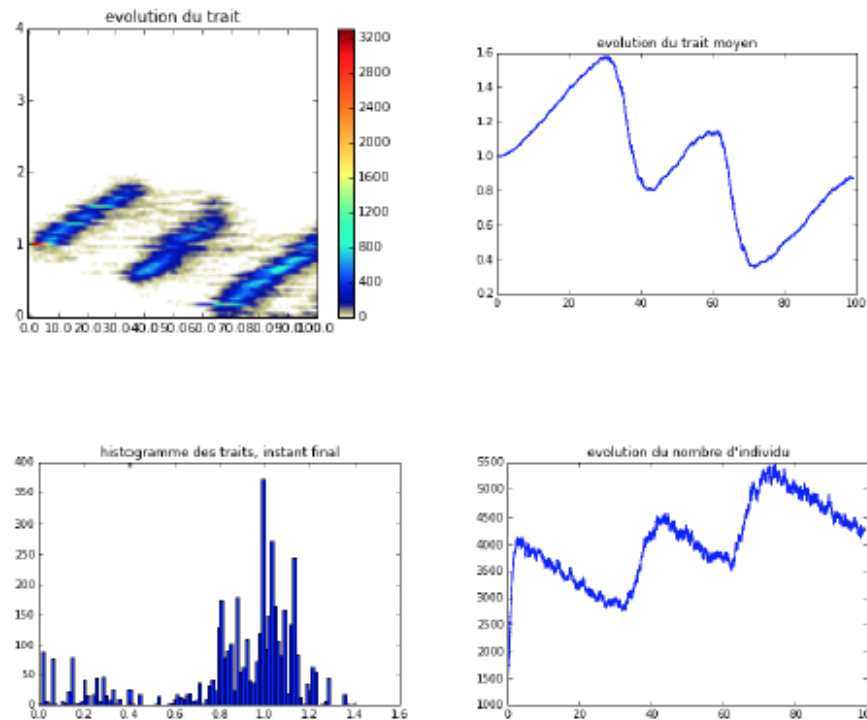
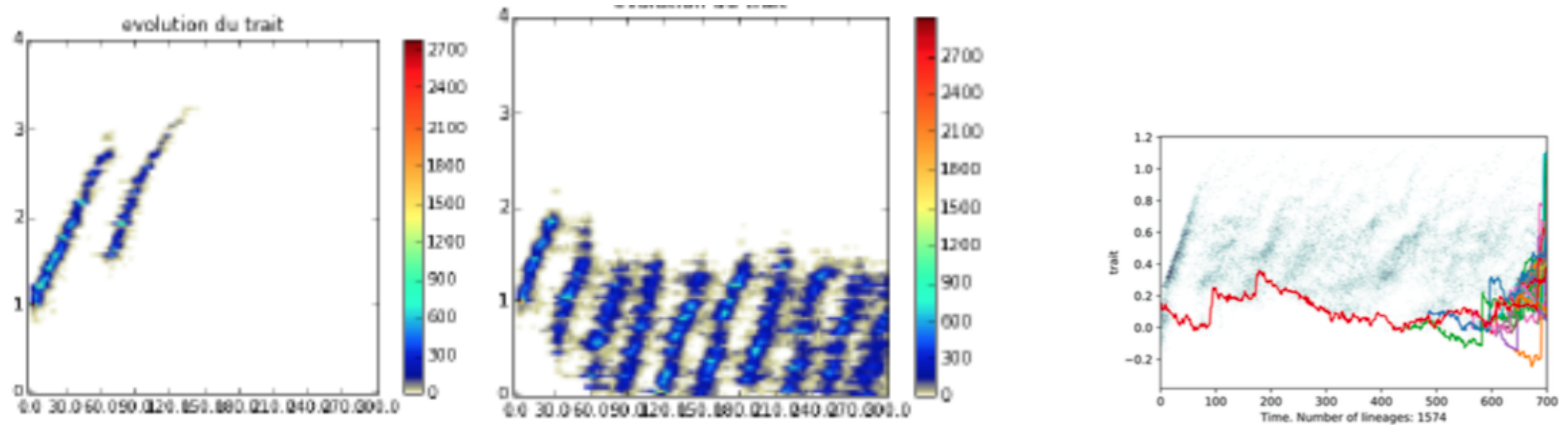


FIGURE 9 – Simulations pour $\tau = 0.6$ sur un temps de 100

- Population size decreases. For a given trait x , the population size at equilibrium is $N_{eq} = \frac{b(x)-d}{c} \times 1000 = 2000(3 - x)$.
- One observes the brutal occurrence of new strains.

$$\tau = 0,7$$

4 simulations with the same parameters. The differences are due to the possibility for a mutant to create a new strain.



Rare mutations but not so rare

For the simulations, the mutation probability is equal to 0.03 and $K = 1000$.

KP_K is not small : the assumptions of the adaptive dynamics are not satisfied.

The emergence of new strains seems to come from a few number of individuals.

Difficulty: To keep track of small populations in large population approximations. It's our actual challenge.

A discrete model to capture evolutionary cyclic behaviors

avec N. Champagnat et C.V. Tran (AAP 2021)
(Durrett, Mayberry 2011 - Bovier, Coquille, Smadi 2019).

- The trait space $[0, 4]$ is discretized. $\delta > 0$ is fixed.

$$x = i\delta \in [0, 4], \quad i \in \{0, \dots, \lfloor \frac{4}{\delta} \rfloor\}.$$

- **Divisions:** rate $b(x) = 4 - x$

- Probability $p_K = K^{-\alpha}$ avec $0 < \alpha < 1$: mutant with trait $x + \delta$.
- Probability $1 - K^{-\alpha}$: clonal reproduction clonal.

Note that $Kp_K = K^{1-\alpha}$ tends to infinity.

- **Death:** taux $d(x) = 1 + C \frac{N_t^K}{K}$.
- **HGT:** unilateral conjugation: $(x, y) \rightarrow (y, y)$ at rate $(\tau/N^K)\mathbf{1}_{y>x}$.
- The fitness is given by $S(y; x) = x - y + \tau \text{sign}(y - x)$.
- **Initial population size:**

$$\lfloor \frac{3K}{C} \rfloor, \quad \lfloor K^{1-\alpha} \rfloor, \dots, \lfloor K^{1-i\alpha} \rfloor, \dots, 0, \dots, 0.$$

Possible resurgences : we will follow small populations,
of size K^β , on the time scale $\log K$.

($\beta = 0$ means extinction).

Remark : if $N_{i\delta}^K \sim CK^{\beta_i^K}$, then $\beta_i^K \sim \frac{\log(1 + N_{i\delta}^K)}{\log K}$.

We want to study, for $i \in \{0, 1, \dots, \lfloor 4/\delta \rfloor\}$, the asymptotic behavior of the process

$$\left(\frac{\log(1 + N_{i\delta}(s \log K))}{\log K}, s \in [0, T] \right)$$

when $K \rightarrow +\infty$.

Exponents for the birth and death processes

- A small population with trait y in a resident population with trait x with $y < x$ behaves as a branching process with birth and death rates respectively :

$$4 - y \quad \text{and} \quad 1 + \frac{CN_x^K(t)}{K} + \tau.$$

- Lemma :

Consider a linear birth and death process $(Z_t^K)_{t \geq 0}$ at rate b and d , with initial condition $[K^\beta - 1]$ (with $\beta \leq 1$).

Then,

$$\left(\frac{\log(1 + Z_{s \log K}^K)}{\log K}, s \in [0, T] \right) \xrightarrow{K \rightarrow +\infty} ((\beta + s(b - d)) \vee 0, s \in [0, T]),$$

uniformly on $[0, T]$, in probability.

Note that $\mathbb{E}(Z_t^K) = K^\beta e^{(b-d)t}$. The proof is easy for $b - d \geq 0$, more technical for $b - d < 0$ since one needs to control the extinction events after some time.

Exponents for the birth and death processes with immigration

- A small population with trait y in a resident population with trait x , with $y = x + \delta$, behaves as a branching process with rates

$$4 - y + \tau \quad \text{and} \quad 1 + \frac{CN_x^K(t)}{K}.$$

- But y can also receive a contribution from x due to mutations: $N_x^K(t)K^{-\alpha}$.

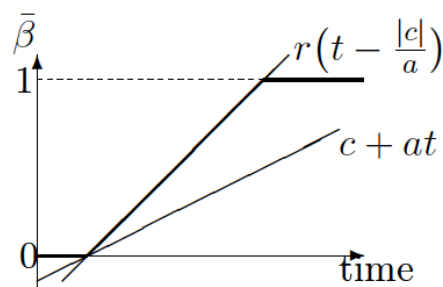
From previous lemma, $N_x^K(s \log K)$ behaves as K^{c+as} for some $a, c \in \mathbb{R}$.

- Lemma :

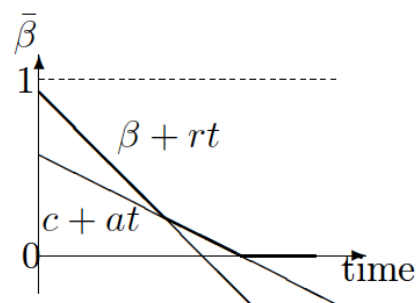
Assumptions of the previous lemma + immigration at rate $K^c e^{at}$, for $a, c \in \mathbb{R}$. We assume that $c \leq \beta$ and either $\beta > 0$, or $c \neq 0$. Then,

$$\left(\frac{\log(1 + Z_{s \log K}^K)}{\log K}, s \in [0, T] \right) \xrightarrow{K \rightarrow +\infty} ((\beta + s(b - d)) \vee (c + as) \vee 0, s \in [0, T]),$$

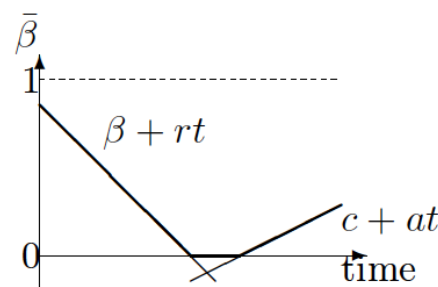
uniformly on $[0, T]$ and in probability.



(a): $c < \beta = 0, 0 < a < r$



(b): $0 < c < \beta, r < a < 0$



(c): $c < 0 < \beta, r < 0 < a$

Case of three traits (1)

Three traits: $0, \delta, 2\delta$, with

$$\delta < \tau < 2\delta < 3 < 4 < 3\delta.$$

Recall that $0 < \alpha < 1$ and that $S(y; x) = x - y + \tau \text{sign}(y - x)$.

At time $s_0 = 0$, $\beta^K(0) = (1, 1 - \alpha, (1 - 2\alpha) \vee 0)$ and $N_0^K(0) = \frac{3K}{C}$.

- **Trait δ :**

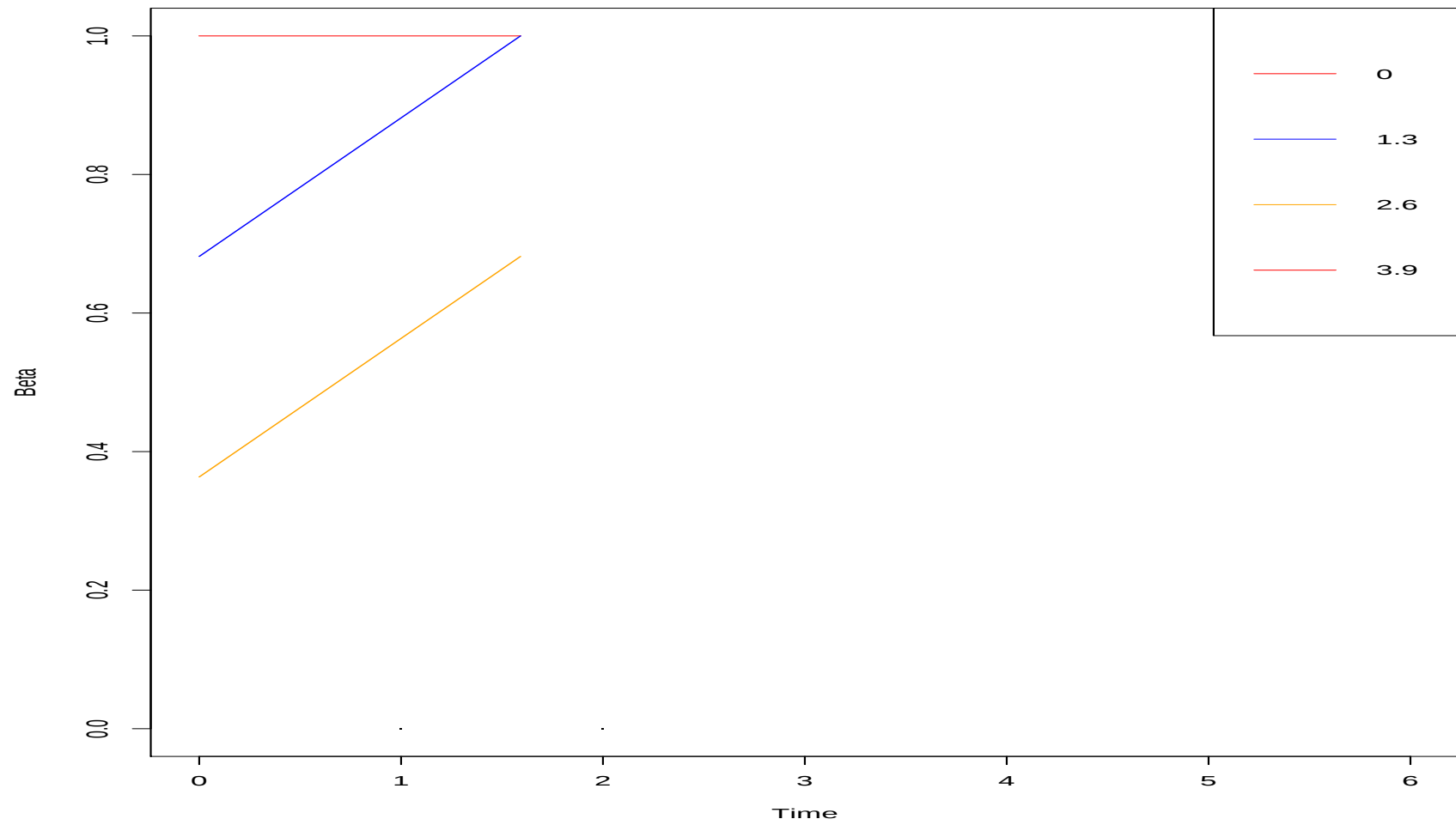
- $\beta_1(0) = 1 - \alpha$
- $S(\delta; 0) = \tau - \delta > 0$

$$\beta_1(s) = (1 - \alpha) + (\tau - \delta)s \quad (\geq 1 - \alpha)$$

- **Trait 2δ :**

- $\beta_2(0) = 1 - 2\alpha$
- $S(2\delta; 0) = \tau - 2\delta < 0 \rightarrow \tilde{\beta}_2(t) = (1 - 2\alpha) + (\tau - 2\delta)t$
- But there are mutations from δ :

$$\beta_2(s) = (1 - 2\alpha) + (\tau - \delta)s \quad (\geq 1 - 2\alpha)$$



$$\delta = 1.3, \alpha = 0.32, \tau = 1.5.$$

Case of three traits (2)

At time $s_1 = \frac{\alpha}{\tau - \delta}$, the traits 0 and δ have both the exponent 1:

$$\beta_0(s_1) = \beta_1(s_1) = 1 ; \beta_2(s_1) = 1 - \alpha.$$

↪ invasion implies fixation: a unique dominant trait.

- **Trait 0:**

- $S(0; \delta) = \delta - \tau < 0$, and $\beta_0(s) = 1 - (\tau - \delta)(s - s_1)$.

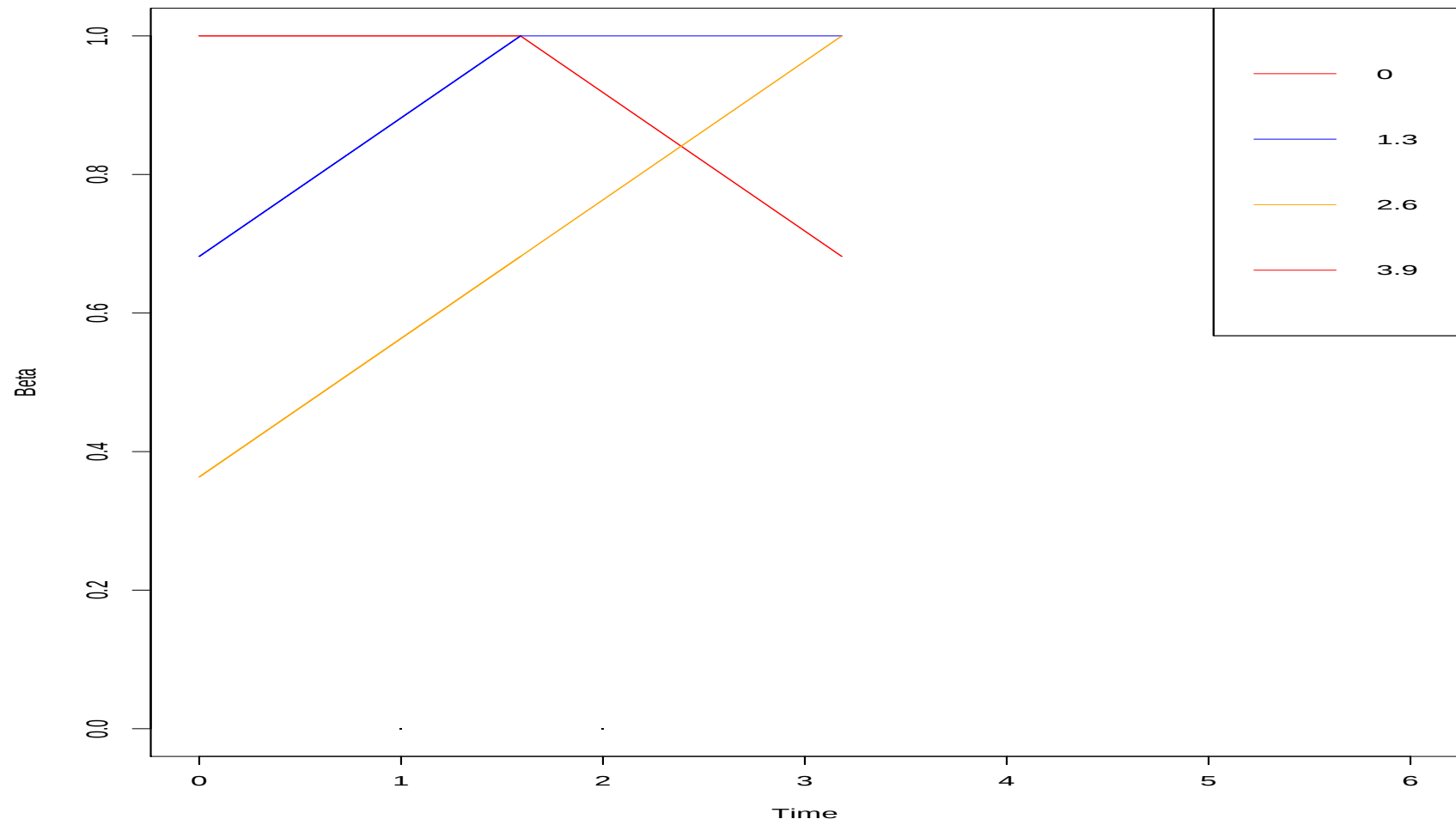
- **Trait δ :**

- $N_1(s_1) = \frac{(3-\delta)K}{C}$

- **Trait 2δ :**

- $S(2\delta; \delta) = \tau - \delta > 0 \rightarrow \beta_2(s) \geq 1 - \alpha$

$$\beta_2(s) = (1 - \alpha) + (\tau - \delta)(s - s_1)$$



$$\delta = 1.3, \alpha = 0.32, \tau = 1.5.$$

Case of three traits (3)

At time $s_2 = \frac{\alpha}{\tau - \delta} + \frac{\alpha}{\tau - \delta}$, $\beta_0(s_2) = 1 - \alpha$; $\beta_1(s_2) = \beta_2(s_2) = 1$.

- **Trait 0:**

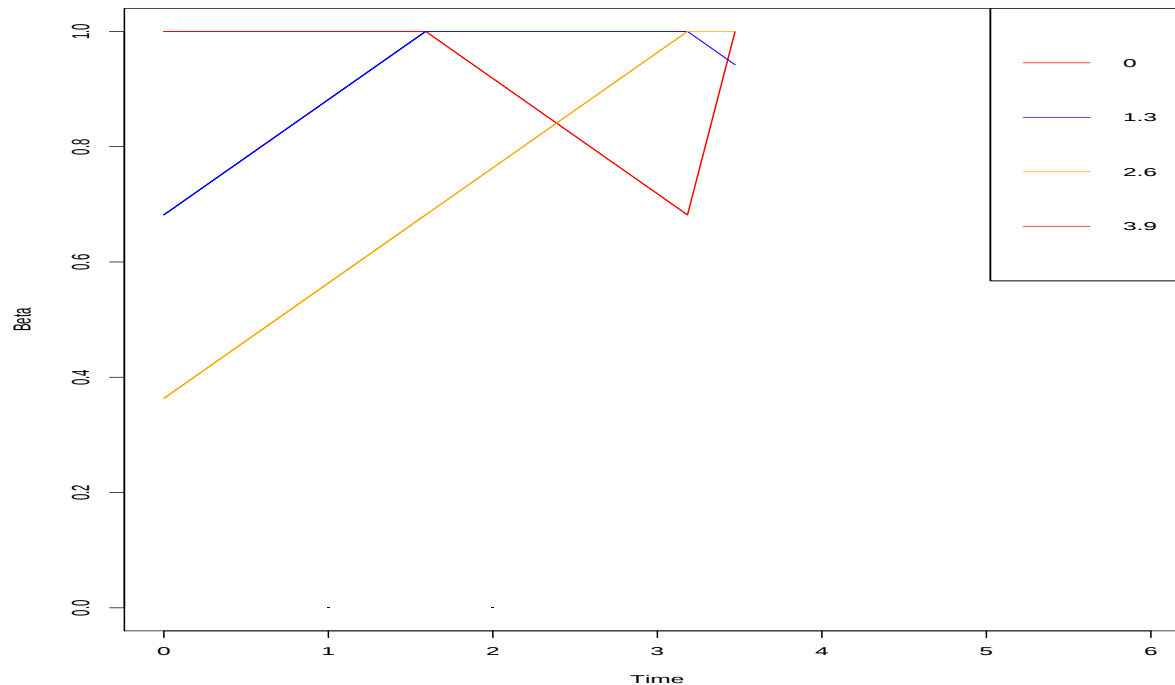
- $S(0; 2\delta) = 2\delta - \tau > 0$,

$$\beta_0(s) = (1 - \alpha) + (2\delta - \tau)(s - s_2)$$

- **Trait δ :**

- $S(\delta; 2\delta) = \delta - \tau < 0$,

$$\beta_1(s) = \max \left[1 - (\tau - \delta)(s - s_2), (1 - 2\alpha) + (2\delta - \tau)(s - s_2) \right]$$



Case of three traits (4)

Assume that $0 < \tau - \delta < 2\delta - \tau$.

At time $s_3 = \frac{2\alpha}{\tau - \delta} + \frac{\alpha}{2\delta - \tau}$, $\beta_0(s_3) = 1 = \beta_2(s_3)$ et $\beta_1(s_3) = 1 - \alpha \frac{\tau - \delta}{2\delta - \tau}$.

- **Trait δ :**

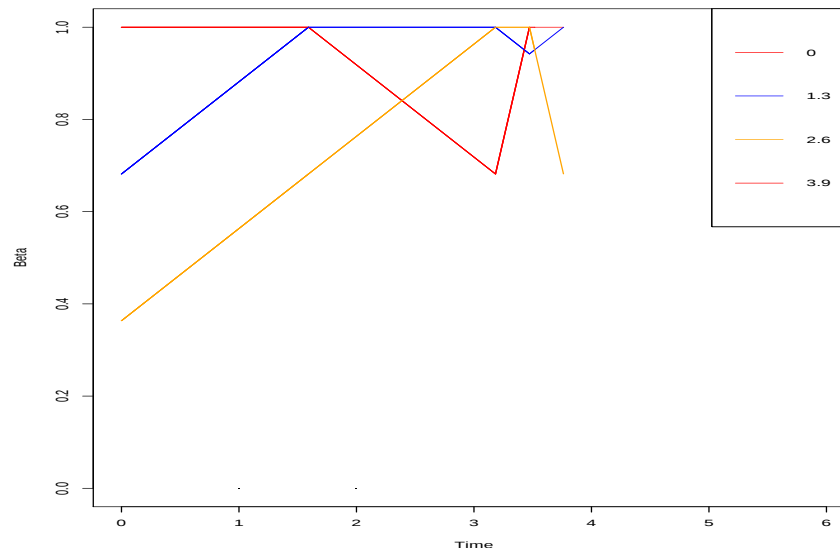
- $S(\delta, 0) = \tau - \delta > 0$,

$$\beta_1(s) = 1 + \frac{\delta - \tau}{2\delta - \tau} \alpha + (\tau - \delta)(s - s_3)$$

- **Trait 2δ :**

- $S(2\delta, 0) = \tau - 2\delta < 0$

$$\beta_2(s) = \max \left[1 + (\tau - 2\delta)(s - s_3), 1 - \frac{\delta\alpha}{2\delta - \tau} + (\tau - \delta)(s - s_3) \right]$$



Case of three traits (5)

At time $s_4 = \frac{2\alpha}{\tau-\delta} + \frac{2\alpha}{2\delta-\tau}$, $\beta_0(s_4) = 1 = \beta_1(s_4)$; $\beta_2(s_4) = 1 - \alpha$.

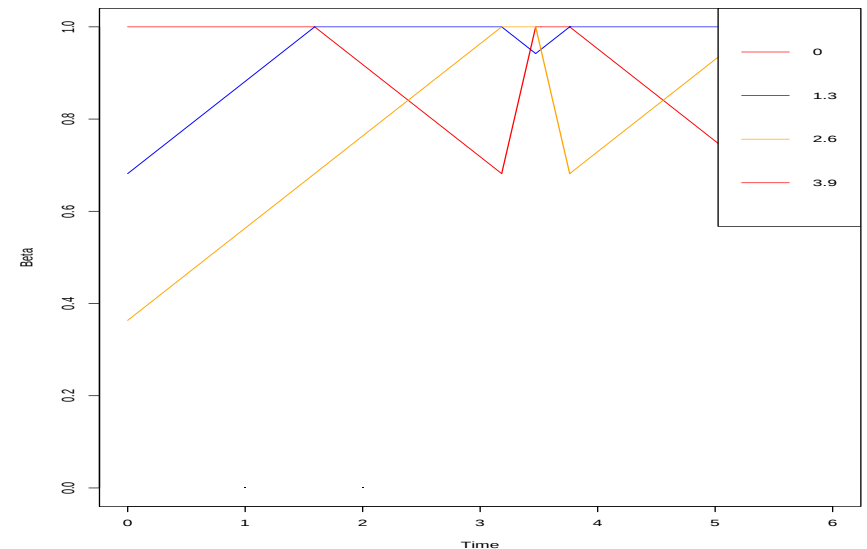
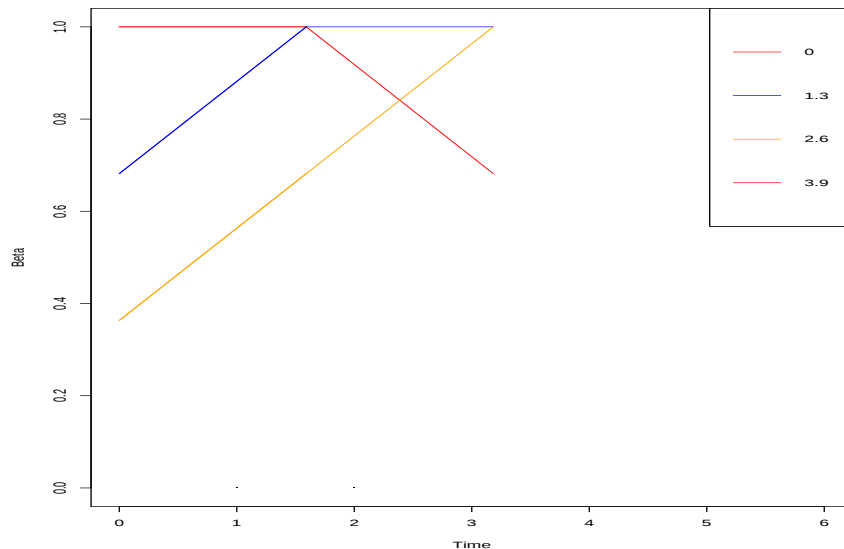
- **Trait 0:**

- $S(0; \delta) = \delta - \tau < 0$,

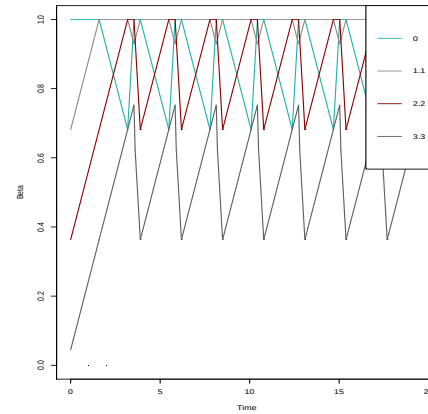
- **Trait 2δ :**

- $S(2\delta; \delta) = \tau - \delta > 0$

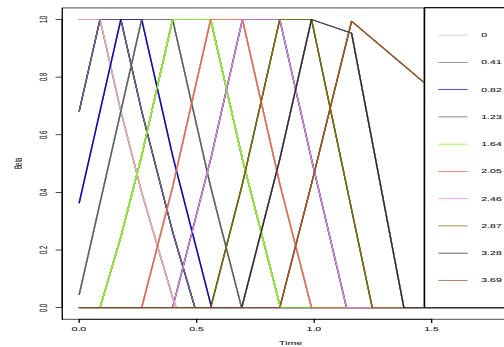
Same situation as at time s_1 . The system is periodic.



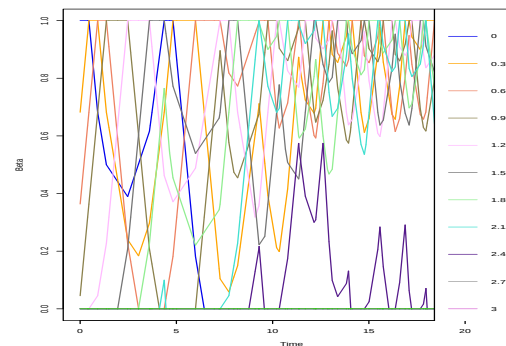
Other situations



$$\delta = 1.1, \alpha = 0.32, \tau = 1.3$$



$$\delta = 0.41, \alpha = 0.32, \tau = 4$$



$$\delta = 0.3, \alpha = 0.32, \tau = 1$$

Main result

Theorem For $i \in \{0, 1, \dots, \lfloor 1/\delta \rfloor\}$,

$$\left(\frac{\log(1 + N_{i\delta}(s \log K))}{\log K}, s \in [0, T] \right) \xrightarrow{K \rightarrow +\infty} (\beta_i(s), s \in [0, T])$$

uniformly on $[0, T]$, in probability,

where β_i is *continuous, piecewise affine and solution of a ODEs system* with $\beta_i(0) = (1 - i\alpha) \vee 0$

and where *changes of slopes* of the exponents $(\beta_0(s), \dots, \beta_{\lfloor 1/\delta \rfloor}(s))$ can occur at times where

- a new exponent reaches 1 $\rightsquigarrow$ *change of resident trait*
 - a new exponent reaches 0 $\rightsquigarrow$ *extinction of the trait*
 - The slope of an exponent which was driven by its fitness becomes driven by its mutations
-
- It seems really difficult to go further with probabilistic tools.
 - Alternative approach: to derive a Hamilton-Jacobi equation and work with analytical tools (cf. Champagnat, M., Mirrahimi, Tran' 23).

Références

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- ⑨ Stochastic analysis of emergence of evolutionary cyclic behavior in population dynamics with transfer. C. Champagnat, S. Méléard, V.C. Tran. Annals of Applied Probability, 31, no. 4, 1820-1867. DOI : <https://doi.org/10.1214/20-AAP1635>.

Adresses utiles

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<http://www.cmap.polytechnique.fr/chaire-mmb/>

Master (M2) Mathématiques pour les sciences du vivant (MSV). (Cours essentiellement en français).

<https://sites.google.com/view/m2-msv/accueil>

<https://www.universite-paris-saclay.fr/formation/master/mathematiques-et-applications/m2-mathematiques-pour-les-sciences-du-vivant>

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"After years, I have deeply regretted that I did not proceed far enough at least to understand something of the great leading principles of mathematics: for men thus endowed seem to have an extra-sense".

Charles Darwin, *Autobiography*.

Charles DARWIN, *Uses and abuses of Mathematics in Biology*.

Merci pour votre attention!

