

Limites d'échelle de modèles individu-centrés en dynamique adaptative et extinction locale de populations

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Adaptive dynamics

Adaptive dynamics: Darwinian evolution

- **Heredity:** transmission of phenotypes
- **Mutation:** modification of phenotypes
- **Selection:** consequence of ecological interactions

Adaptive dynamics

Adaptive dynamics: Darwinian evolution **with focus on**

- **Heredity**: transmission of phenotypes \rightsquigarrow **simplified (asexual)**
- **Mutation**: modification of phenotypes
- **Selection**: consequence of ecological interactions \rightsquigarrow **focus on the interplay between ecology and evolution**

Main question: characterize long-term evolution under assumptions of

- large populations
- small mutations
- rare mutations

Goal of this talk: build macroscopic models from several combinations of these 3 hypotheses satisfying key biological features.

An individual-based (toy) model

Asexual birth and death process with logistic competition and mutation

- Evolution of a quantitative **phenotypic trait**
- Trait space $\mathcal{X} = \mathbb{R}$
- A population composed of $N(t)$ individuals with traits $x_1, \dots, x_{N(t)} \in \mathbb{R}$ is represented by

$$\nu_t = \sum_{i=1}^{N(t)} \delta_{x_i}$$

- Measure-value pure jump Markov process

Population dynamics

For an individual with trait $x \in \mathbb{R}$ in the population $\nu_t = \sum_{i=1}^{N(t)} \delta_{x_i}$:

- clonal reproduction at rate $b(x)$
- reproduction with mutation at rate $p(x)$, mutant trait $x + z$ with $z \sim \mathcal{N}(0, 1)$
- death with rate $d(x) + \sum_{i=1}^{N(t)} c(x, x_i) = d(x) + \int_{\mathbb{R}} c(x, y) \nu_t(dy)$

Population dynamics

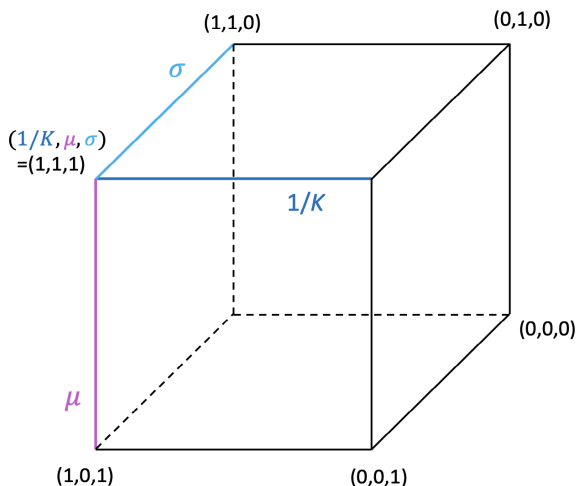
For an individual with trait $x \in \mathbb{R}$ in the population $\nu_t^K = \frac{1}{K} \sum_{i=1}^{N(t)} \delta_{x_i}$:

- clonal reproduction at rate $b(x)$
- reproduction with mutation at rate $\mu p(x)$, mutant trait $x + z$ with $z \sim \mathcal{N}(0, \sigma^2)$
- death with rate $d(x) + \frac{1}{K} \sum_{i=1}^{N(t)} c(x, x_i) = d(x) + \int_{\mathbb{R}} c(x, y) \nu_t^K(dy)$

3 scaling parameters:

- large population: $K \rightarrow +\infty$
- rare mutations: $\mu \rightarrow 0$
- small mutations: $\sigma \rightarrow 0$

The cube of scaling parameters

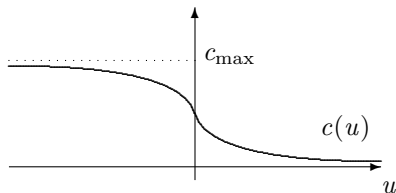


Simulations: evolutionary arms race with asymmetric competition

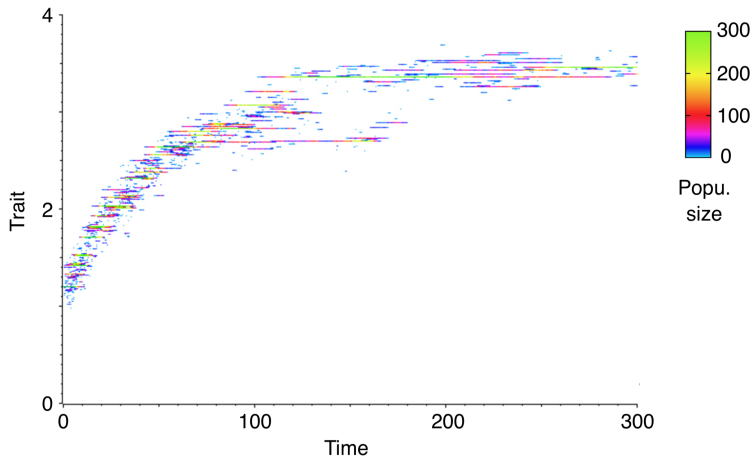
Trait space $\mathcal{X} = [0, 4]$, $d(x) \equiv 0$,

mutation law $\mathcal{N}(0, \sigma^2)$ (conditioned on $x + h \in \mathcal{X}$)

$b(x) = 4 - x$, $p(x) = 1$, $c(x, y) = c(x - y)$ with



Simulation



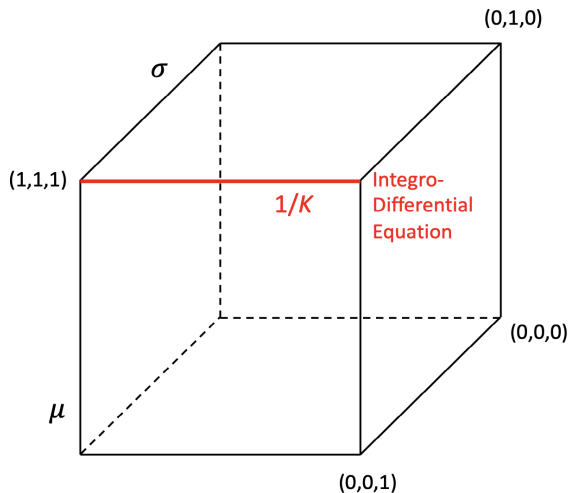
$$K = 100, \quad \mu = 0.03, \quad \sigma = 0.1$$

Limit $K \rightarrow +\infty$ alone

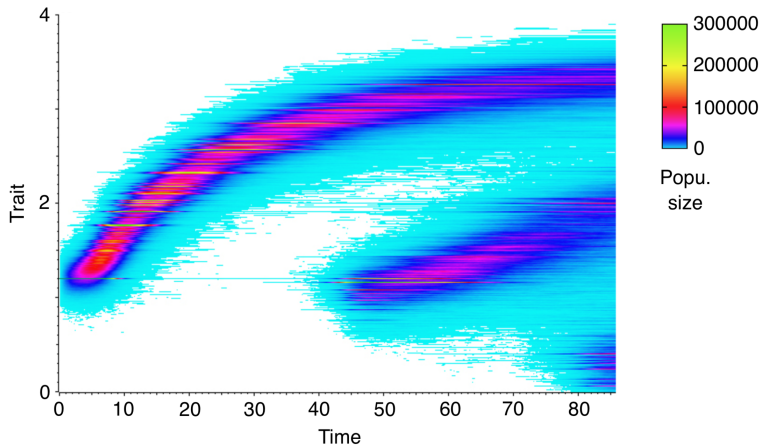
Theorem

Under general assumptions on the parameters and the initial condition, assuming μ and σ constant, ν^K converges in $\mathbb{D}(\mathbb{R}_+, M_F(\mathbb{R}))$ as $K \rightarrow +\infty$ to the unique (weak, measure) solution of

$$\begin{aligned} \partial_t u(t, x) = & \left(b(x) - d(x) - \int_{\mathbb{R}} c(x, y) u(t, y) dy \right) u(t, x) \\ & + \int_{\mathbb{R}} \frac{1}{\sigma} G\left(\frac{x-y}{\sigma}\right) \mu p(y) u(t, y) dy. \end{aligned}$$

Limit $K \rightarrow +\infty$ 

Simulation



$$K = 100000, \quad \mu = 0.03, \quad \sigma = 0.1$$

Small mutations and long time: concentration limit

$$\begin{aligned} \partial_t u_\sigma(t, x) = & \frac{1}{\sigma} \left(b(x) - d(x) - \int_{\mathbb{R}} c(x, y) u_\sigma(t, y) dy \right. \\ & \left. + \mu \int_{\mathbb{R}} p(x - \sigma h) G(h) dh \right) u_\sigma(t, x) \\ & + \frac{\mu}{\sigma} \int_{\mathbb{R}} p(x - \sigma h) (u_\sigma(t, x - \sigma h) - u_\sigma(t, x)) G(h) dh. \end{aligned}$$

Hopf-Cole transformation:

$$u_\sigma(t, x) = \exp\left(\frac{\beta_\sigma(t, x)}{\sigma}\right), \quad \text{or} \quad \beta_\sigma(t, x) = \sigma \ln u_\sigma(t, x)$$

gives

$$\begin{aligned} \partial_t \beta_\sigma(t, x) = & b(x) - d(x) - \int_{\mathbb{R}} c(x, y) u_\sigma(t, y) dy + \mu \int_{\mathbb{R}} p(x - \sigma h) G(h) dh \\ & + \mu \int_{\mathbb{R}} p(x - \sigma h) \left[\exp\left(\frac{\beta_\sigma(t, x - \sigma h) - \beta_\sigma(t, x)}{\sigma}\right) - 1 \right] G(h) dh. \end{aligned}$$

Hamilton-Jacobi equation

We expect $\beta_\sigma \rightarrow \beta$ solution to the Hamilton-Jacobi equation

$$\begin{aligned} \partial_t \beta(t, x) = & b(x) - d(x) - \int_{\mathbb{R}} c(x, y) \mu_t(dy) + \mu p(x) \\ & + \mu p(x) \int_{\mathbb{R}} \left(e^{-\partial_x \beta(t, x) h} - 1 \right) G(h) dh, \end{aligned}$$

where μ_t is the limit of $u_\sigma(t, \cdot)$.

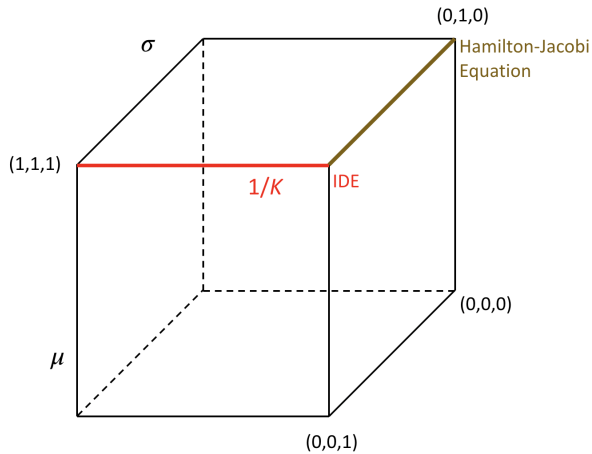
- $b - d > 0 \rightsquigarrow$ non-explosion and non-extinction of the population:

$$\limsup_{\sigma \rightarrow 0} \max_x \beta_\sigma(t, x) = 0.$$

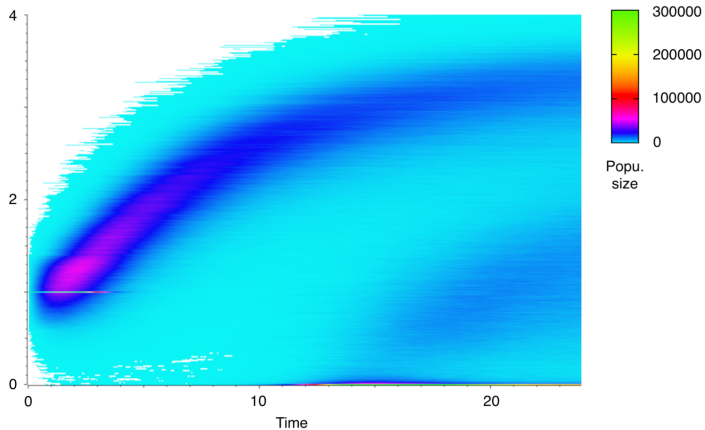
- How to characterize μ_t ? difficult problem in general!
 - μ_t only charges $\{\beta(t, \cdot) = 0\}$.
 - if $\{\beta(t, \cdot) = 0\} = \{\bar{x}(t)\}$, then $\partial_t \beta(t, \bar{x}(t)) = 0$ gives

$$\mu_t = \frac{b(\bar{x}(t)) + \mu p(\bar{x}(t)) - d(\bar{x}(t))}{c(\bar{x}(t), \bar{x}(t))} \delta_{\bar{x}(t)}$$

Hamilton-Jacobi limit

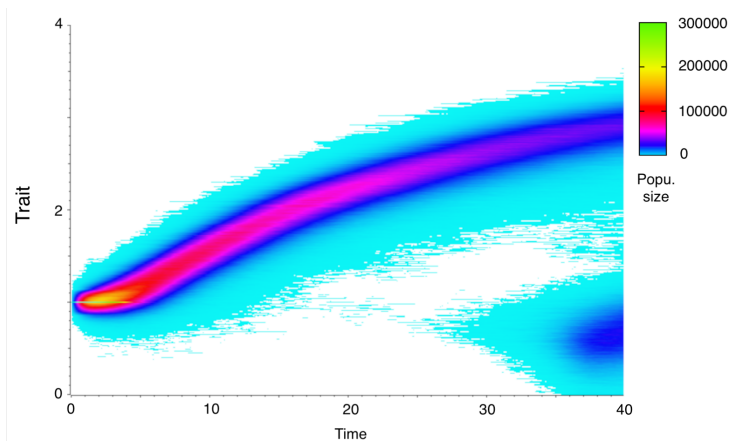


Simulation



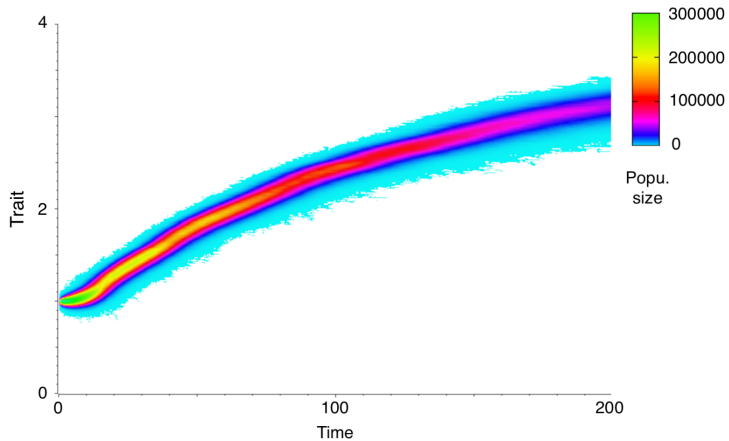
$$K = 100000, \quad \mu = 0.3, \quad \sigma = 0.03$$

Simulation



$$K = 100000, \quad \mu = 0.3, \quad \sigma = 0.01$$

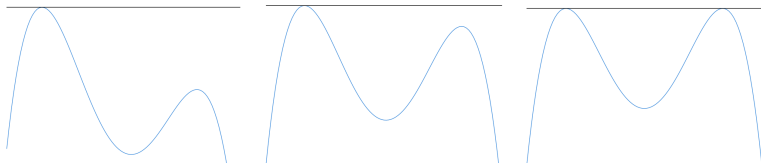
Simulation



$$K = 100000, \quad \mu = 0.3, \quad \sigma = 0.003$$

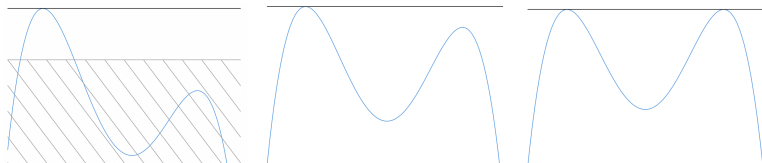
The tail problem

Example of dynamics of the function $\beta(t, x)$:



The tail problem

Example of dynamics of the function $\beta(t, x)$:



- The dynamics is strongly influenced by exponentially small initial population densities in favorable regions far away from the initial population
- Positive population densities everywhere \rightsquigarrow no local extinction
- Evolutionary time-scale is too fast (t/σ)

(Very) rare mutations

The selection process has sufficient time between two mutations to eliminate disadvantaged traits (**time scale separation**):

- succession of phases of **mutant invasion**, and **competition** between traits
- the outcome of competition is given by the **deterministic** population dynamics obtained above

Time scales:

- of individual mutations: $\frac{1}{\mu}$
- of mutations at the populations level: $\frac{1}{K\mu}$
- of competition: **1**
- of mutant invasion: **$\log K$** (time for a super-critical branching process to reach K)

(Very) rare mutations: $K \rightarrow +\infty$ and $\mu \rightarrow 0$

Theorem

Assume that $\nu_0^K \rightarrow n_0 \delta_x$ with $n_0 > 0$. If

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

then $(\nu_{t/K\mu}^K, t \geq 0)$ converges for f.d.d. to a pure jump Markov process $(\Lambda_t, t \geq 0)$ with values in the set of positive measures on \mathbb{R} with finite support.

Under assumptions preventing coexistence of several traits,

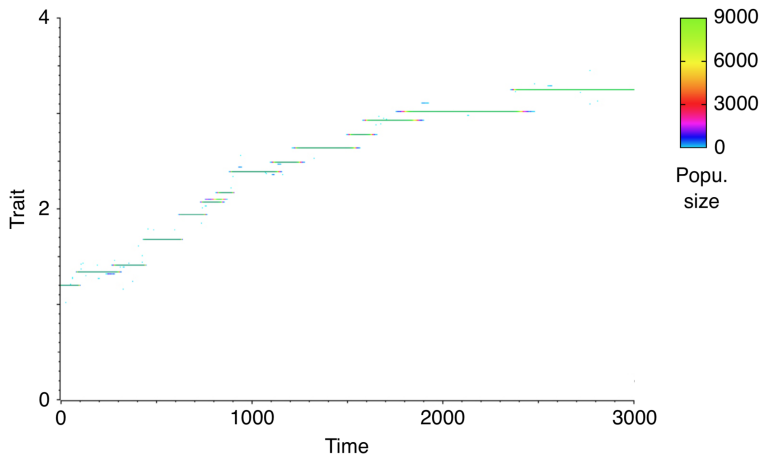
$$\Lambda_t = \bar{n}(X_t) \delta_{X_t},$$

where $\bar{n}(x) = \frac{b(x)-d(x)}{c(x,x)}$ and $(X_t)_{t \geq 0}$ is Markov with generator

$$L\varphi(x) = \int_{\mathbb{R}} (\varphi(x + \sigma h) - \varphi(x)) p(x) \bar{n}(x) \frac{[f(x + \sigma h, x)]^+}{b(x + \sigma h)} G(h) dh,$$

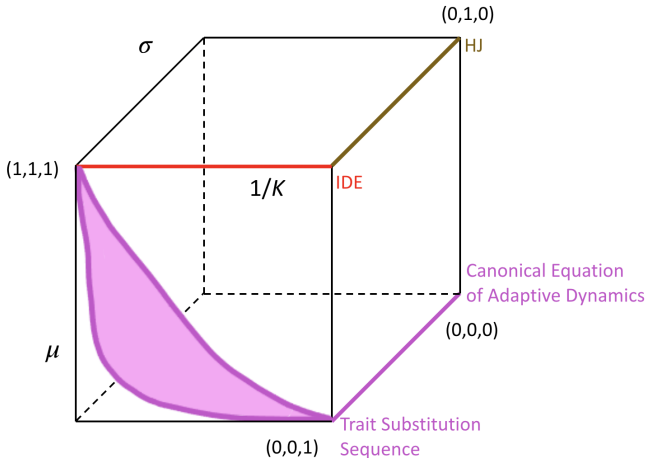
where $f(y, x) = b(y) - d(y) - c(y, x) \bar{n}(x)$ is the fitness function.

Simulation: trait substitution sequence (TSS)



$$K = 1000, \quad \mu = 0.00001, \quad \sigma = 0.1$$

Convergence to the TSS



Biological criticism: too rare mutations

The scaling limit leading to the TSS has been also criticized by biologists:

- strictly monomorphic populations are unrealistic
- time scale of evolution is **too long** ($\frac{t}{K\mu}$)
- mutations are too rare

Intermediate approach: less rare mutations

- allowing to take into account non-extinct but negligible populations may have a strong influence on long term evolution
- allowing for local extinction

A discretized model

- Discretized state space $\mathcal{X} = \{i\delta, 0 \leq i \leq 1/\delta\}$ with step δ
- Population state $(N_0^K(t), \dots, N_{1/\delta}^K(t))$
- Symmetric mutations to the closest trait

We define

$$\beta_i^K(t) = \frac{\log(1 + N_i^K(t \log K))}{\log K}, \quad \text{i.e.} \quad N_i^K(t \log K) = K^{\beta_i^K(t)} - 1.$$

- $\beta_i^K(t) = 0$: the population with trait $i\delta$ is extinct
- $\beta_i^K(t) \in (0, 1)$: the population with trait $i\delta$ is non-extinct but negligible w.r.t. the dominant population (of the order of K).

A scaling with (less) rare mutations

Define the relative fitness function $S(i; \ell) = r(i\delta) - r(\ell\delta)$ with $r(x) = b(x) - d(x)$.

Theorem

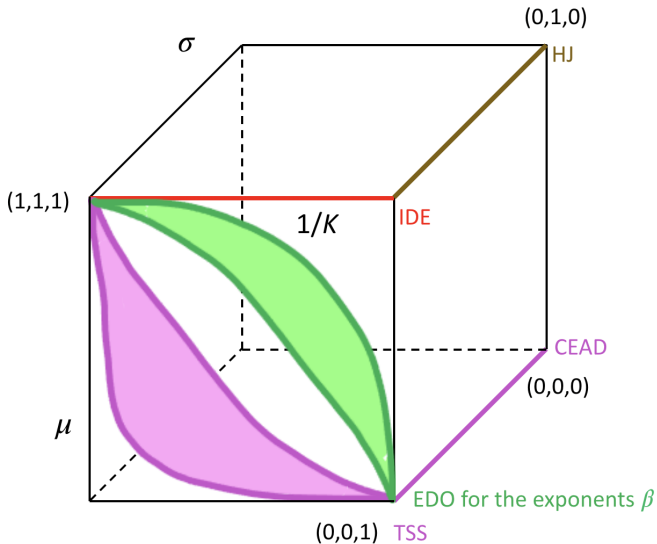
Assume $\mu = K^{-\alpha}$ with $\alpha \in (0, 1)$ and that $N_i^K(0) = \lfloor K^{\beta_i(0)} \rfloor$ with $\max_i \beta_i(0) = \beta_{i_0}(0) = 1$ for a unique i_0 .

Then $(\beta_i^K)_{0 \leq i \leq 1/\delta}$ converges in probability in $L_{loc}^\infty(\mathbb{R}_+^*)$ to a piecewise affine function $(\beta_i)_{0 \leq i \leq 1/\delta}$ such that

$$\dot{\beta}_\ell(t) = \begin{cases} 0 & \text{if } \ell = \ell^*(t), \\ \max\{S(i; \ell^*(t)), i: \beta_j(t) = \beta_\ell(t) + |j - \ell|\alpha, \forall \ell \wedge i \leq j \leq \ell \vee i\} & \text{if } \beta_\ell(t) > 0, \\ \max\{S(i; \ell^*(t)), i \neq \ell: \beta_j(t) = \beta_\ell(t) + |j - \ell|\alpha, \forall \ell \wedge i \leq j \leq \ell \vee i\} & \text{if } \beta_\ell(t) = 0, \end{cases}$$

where $\ell^*(t) \in \{0, \dots, 1/\delta\}$ is such that $\ell^*(0) = i_0$ and $\ell^*(t) = j$ for all j and t such that $j \neq \ell^*(t-)$ and $\beta_j(t-) = 1$.

Another scaling limit



Intuition

Follow small populations of size K^β on the timescale $\log K$.

Lemma (without mutation)

Consider a linear birth-death (branching) process $(Z_t)_{t \geq 0}$ with birth rate b and death rate d , such that $Z_0 = \lfloor K^\beta \rfloor$. Then, in probability in $L^\infty([0, T])$,

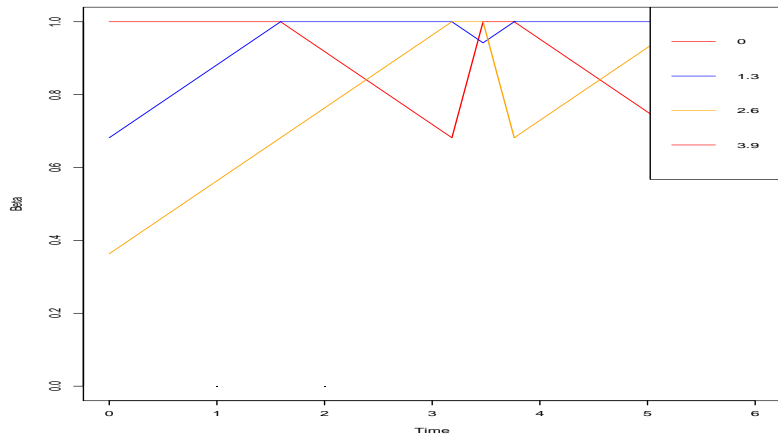
$$\left(\frac{\log(1 + Z_s^K)}{\log K}, s \geq 0 \right) \xrightarrow{K \rightarrow +\infty} ((\beta + s(b - d)) \vee 0, s \geq 0).$$

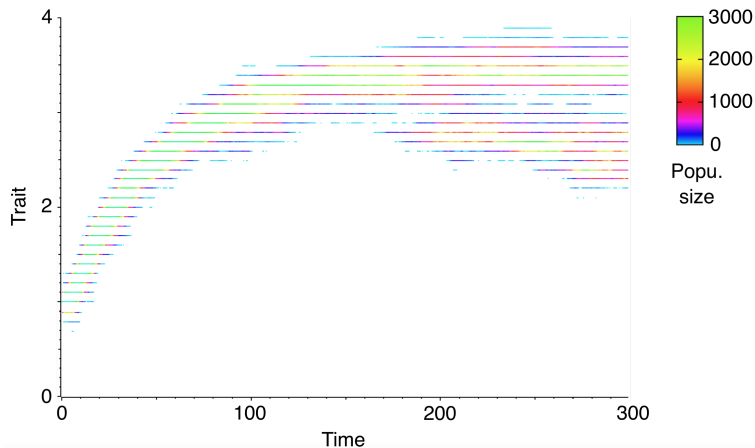
Lemma (with mutation)

Consider the same process as above with additional *immigration* at rate $K^c e^{as}$, for $a, c \in \mathbb{R}$. Then, in probability in $L^\infty([0, T])$,

$$\left(\frac{\log(1 + Z_s^K)}{\log K}, s \geq 0 \right) \xrightarrow{K \rightarrow +\infty} ((\beta + s(b - d)) \vee (c + as), s \geq 0).$$

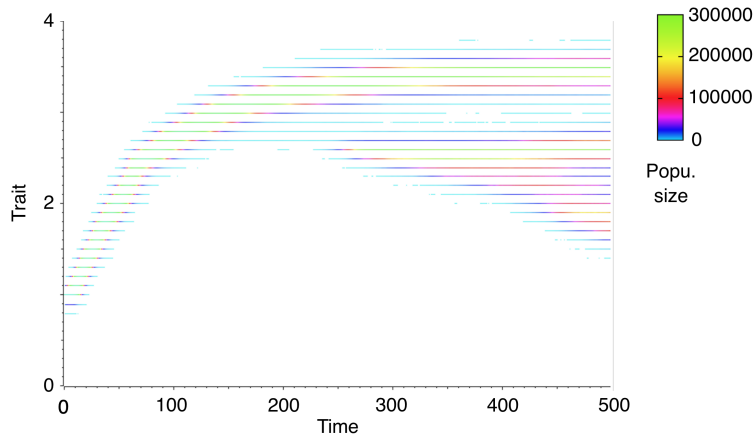
Example of dynamics of $\beta_\ell(t)$



Simulation with $\alpha = 0.5$ 

$$K = 1000, \quad \mu = 0.03 \propto 1/\sqrt{K}, \quad \delta = 0.1$$

Simulation with $\alpha = 0.5$



$$K = 100\,000, \quad \mu = 0.003 \propto 1/\sqrt{K}, \quad \delta = 0.1$$

Perspectives: small mutations and vanishing grid mesh

Complex limit dynamic: the Hamilton-Jacobi approach suggests that a scaling with small mutations instead of rare mutations should give simpler dynamics \rightsquigarrow **vanishing grid mesh**

Only preliminary results: assume

- no competition: $c(x, y) \equiv 0$
- no extinction: supercritical case and large initial population
- trait space $[0, 1]$ with **periodic boundary conditions**
- grid mesh δ_K , such that $h_K = \delta_K \log K \rightarrow 0$
- grid $\mathcal{X}_K = \{i\delta_K : 0 \leq i \leq 1/\delta_K - 1\}$
- an individual with trait $\ell\delta_K$ gives birth to a mutant individual with trait $j\delta_K$ at rate $p(\ell\delta_K)h_K G(h_K(j - \ell))$
 - \rightsquigarrow **total mutation rate** of the order of $p(\ell\delta_K)$
 - \rightsquigarrow **mutation size** of the order of $1/\log K$

Convergence theorem

For all x, t , let i_K be the integer such that $x \in [i_K \delta_K, (i_K + 1) \delta_K)$ and define the affine interpolation function

$$\tilde{\beta}^K(t, x) = \beta_{i_K}^K(t) \left(1 - \frac{x}{\delta_K} + i_K \right) + \beta_{i_K+1}^K(t) \left(\frac{x}{\delta_K} - i_K \right).$$

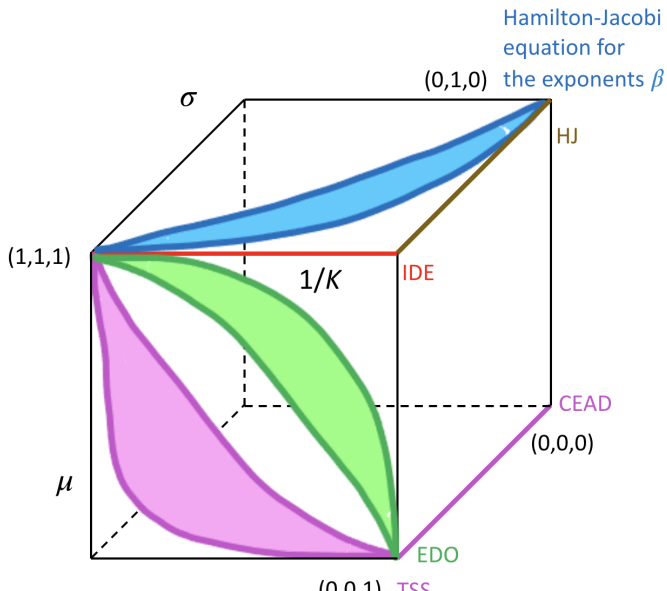
Theorem

Assume $\tilde{\beta}^K(0, \cdot)$ is uniformly Lipschitz and converges in L^∞ to β_0 .
Then $\tilde{\beta}^K$ converges to the unique viscosity solution of the
Hamilton-Jacobi equation

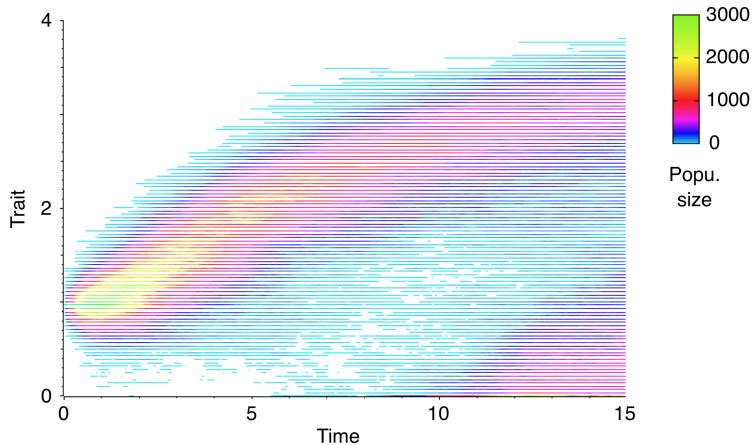
$$\partial_t \beta(t, x) = b(x) + \mu p(x) - d(x) + \mu p(x) \int_{\mathbb{R}} \left(e^{-z \cdot \nabla \beta(t, x)} - 1 \right) G(z) dz$$

such that $\beta(0, x) = \beta_0(x)$, in $\mathbb{D}(\mathbb{R}_+, C(\mathbb{R}, \mathbb{R}))$.

A fourth scaling limit

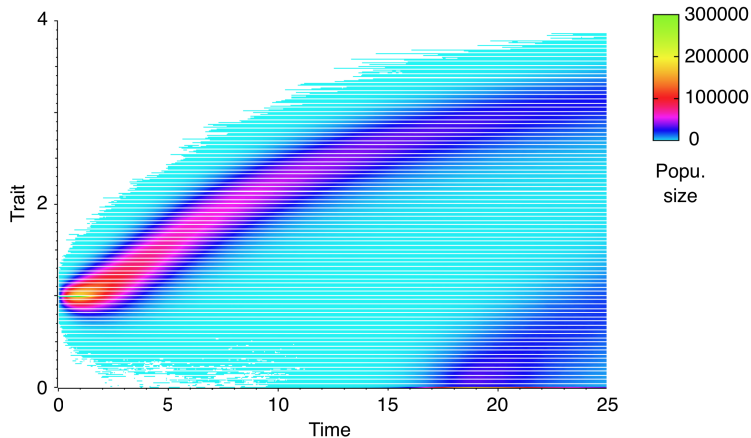


Simulation



$$K = 1000, \quad \mu = 1, \quad \sigma = 0.067, \quad \delta_K = 0.036$$

Simulation

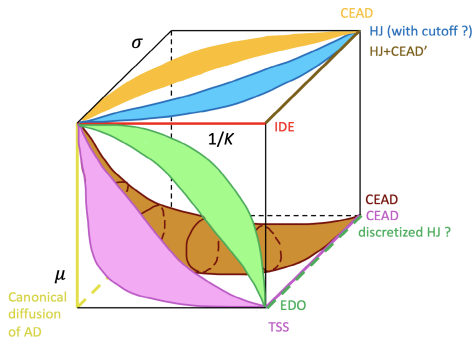


$$K = 100\,000, \quad \mu = 1, \quad \sigma = 0.04, \quad \delta_K = 0.0128$$

Conclusion

- Great variety of dynamics starting from the same individual-based model
- All are concentration limits, with very different evolutionary time-scales and macroscopic behaviors
- Parameter scalings motivated by discussions in the biological literature and interactions with biologists
- Mathematics can help to shed light on the biological debate
- Also great richness of mathematical tools
- And this is not the end of the story...

Filling in the cube...



Fournier, Méléard, AAP 2004

Diekmann *et al.* TPB 2005; Barles *et al.* MAA 2009

C. SPA 2006; C., Méléard, PTRF 2011

C., Lambert, AAP 2007

Baar, Bovier, C., AAP 2017

Durrett, Mayberry 2011; C., Méléard, Tran 2021

C., Méléard, Mirrahimi, Tran, 2022+

C., Hass, in prep.