Limites d'échelle de modèles individu-centrés en dynamique adaptative

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Funded by the European Union
European Research Council
Established by the European Commission

Journée de la chaire MMB, siège de Véolia Environnement, 9 octobre 2024

Evolutionary and diversity scales

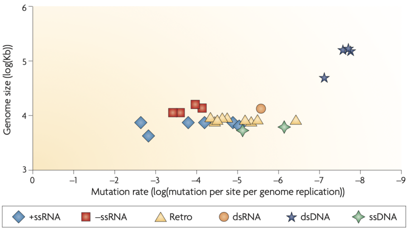


Figure 1 | **Average rates of spontaneous mutation in viruses, adjusted to the rate per genome replication.** Positive-sense single-stranded (ss) RNA viruses (+ssRNA; RNA phage Qβ, poliovirus[10] and Tobacco mosaic virus[103]), negative-sense ssRNA viruses (-ssRNA; vesicular stomatitis virus, influenza A virus[10] and measles virus[23]), the retrotranscribing viruses (Retro; spleen necrosis virus, murine leukaemia virus, Rous sarcoma virus[10], human immunodeficiency virus type-1 and bovine leukaemia virus[2]) and the double-stranded (ds) RNA virus (dsRNA; bacteriophage ϕ6 (REF. 30)) have RNA-dependent polymerases without any proofreading capabilities. Large dsDNA viruses (dsDNA; bacteriophages λ, T2 and T4 (REF. 65), and herpes simplex virus type 1 (REF. 11)) encode their own DNA polymerases. The two ssDNA viruses (ssDNA; bacteriophages M13 (REF. 65) and ϕX174 (REF. 12)) use the DNA polymerase of their host, *Escherichia coli*. There are multiple independent estimates for several of these viruses and all were included in this figure.

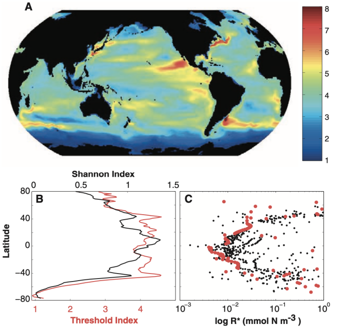
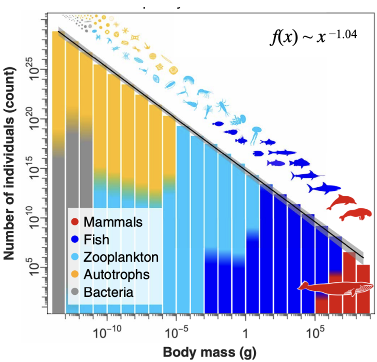


Fig. 1. **(A)** Diversity of modeled phytoplankton types in the uppermost 260 m, averaged annually across 10 ensemble members. Diversity is defined as the number of phytoplankton types comprising greater than 0.1% of the total biomass. **(B)** Zonal mean diversity, as well as the Shannon Index (*10*), for the map shown in (A). **(C)** Annual mean R^* (small black dots) of all phytoplankton types with a concentration above 10^{-12} mmol N m^{-3} along a meridional transect through the Atlantic Ocean at 20°W in an idealized global model with a single limiting nutrient (*12*). The large red dots show the R^* for only the most abundant type in each latitude.

Duffy *et al.* Nature Reviews 2008

Barton *et al.* Science 2010

Evolutionary and population scales



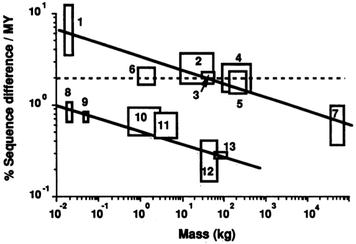


FIG. 2. Relationship between rate of mtDNA sequence divergence (% change per million years) and body size (in kg) for various vertebrates. Data are from Table 2. 1, Mice; 2, dogs; 3, human–chimpanzee; 4, horses; 5, bears; 6, geese; 7, whales; 8, newts; 9, frogs; 10, tortoise; 11, salmon; 12, sea turtles; 13, sharks. Boxes represent the range of rates and body sizes for a given taxon. Solid lines are drawn to pass through the boxes. Dashed line represents the hypothesis of rate constancy.

Hatton *et al.* Sci. Adv. 2021

Martin, Palumbi, PNAS 1993

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.

Metz *et al.* 1996; Dieckmann and Law 1996, Geritz *et al.* 1997, 1998

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 $x_1, \ldots, x_{N(t)} \in \mathbb{R}$ 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 $\nu_t^K = \frac{1}{K}\sum_{i=1}^{N(t)} \delta_{x_i}$:

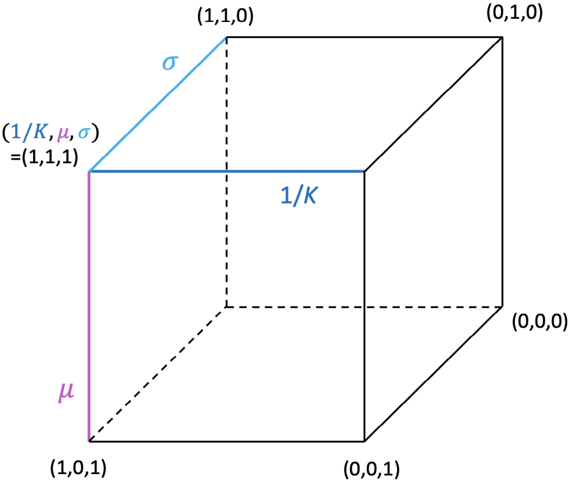
- clonal reproduction at rate $b(x)$
- reproduction with mutation at rate $\mu p(x)$, mutant trait $x+z$ with $z \sim \mathcal{N}(0,\sigma^2)$
- death with rate $d(x) + \frac{1}{K}\sum_{i=1}^{N(t)} c(x,x_i) = d(x) + \int_{\mathbb{R}} c(x,y)\nu_t^K(dy)$

3 scaling parameters:

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

`Metz` *`et al.`* `1996; Bolker and Pacala 1997, DeAngelis and Mooij 2005`

The cube of scaling parameters

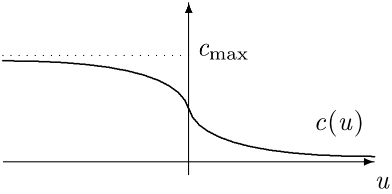


Simulations: evolutionary arms race with asymetric competition

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

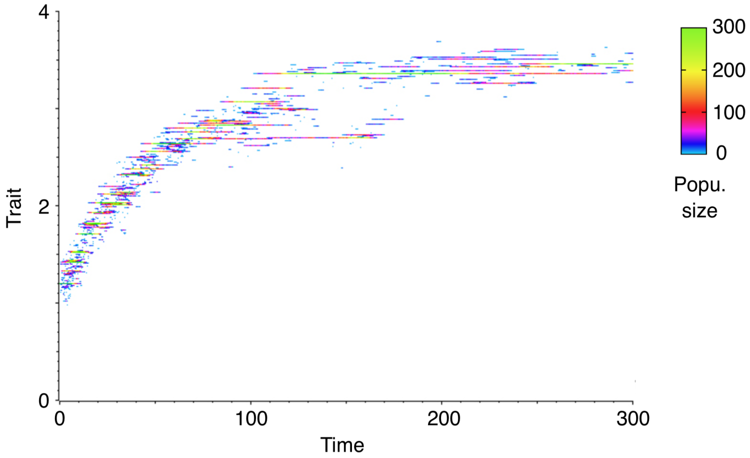
$$\text{mutation law } \mathcal{N}(0, \sigma^2) \text{ (conditioned on } x + h \in \mathcal{X})$$

$$b(x) = 4 - x, \quad p(x) = 1, \quad c(x,y) = c(x-y) \text{ with}$$



Kisdi, JTB 1999; C., Ferrière, Méléard, TPB 2006

Simulation



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

Limit $K \to +\infty$ alone

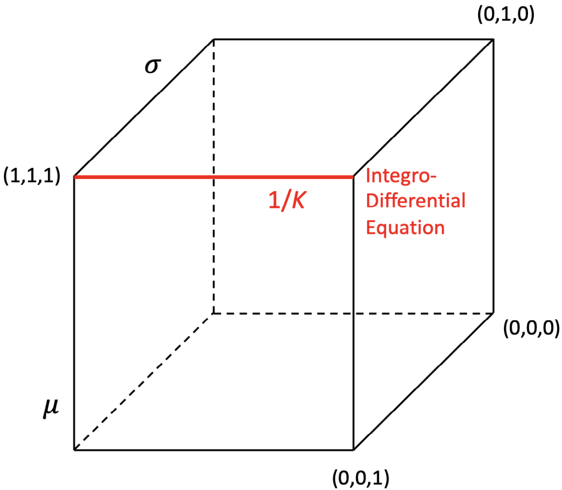
Theorem

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 $K \to +\infty$ to the unique (weak, measure) solution of

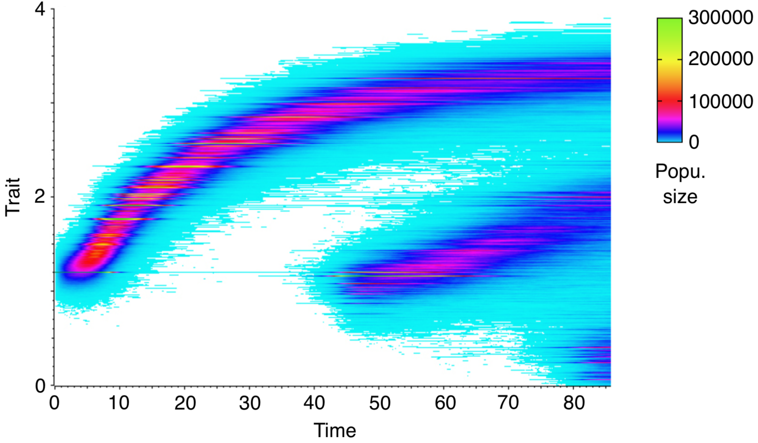
$$\partial_t u(t,x) = \left(b(x) - d(x) - \int_{\mathbb{R}} c(x,y) u(t,y) \mathrm{d}y \right) u(t,x) + \int_{\mathbb{R}} \frac{1}{\sigma} G\left(\frac{x-y}{\sigma} \right) \mu p(y) u(t,y) \mathrm{d}y.$$

Fournier, Méléard, AAP 2004, C., Ferrière, Méléard, TPB 2006

Limit $K \to +\infty$



Simulation



$$K = 100\,000, \qquad \mu = 0.03, \qquad \sigma = 0.1$$

Small mutations and long time: concentration limit

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

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

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

Hamilton-Jacobi equation

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

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

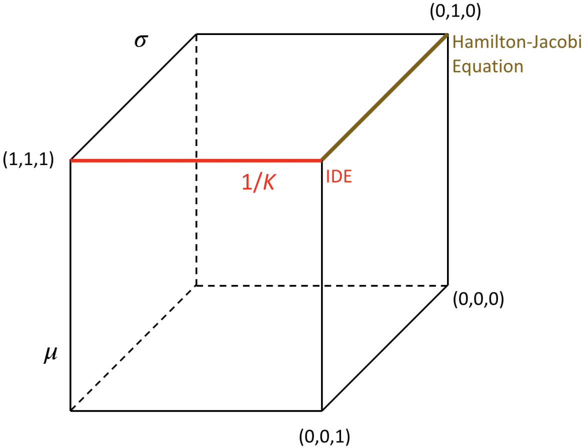
where μ_t is the limit of $u_\sigma(t,\cdot)$, with the constraint

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

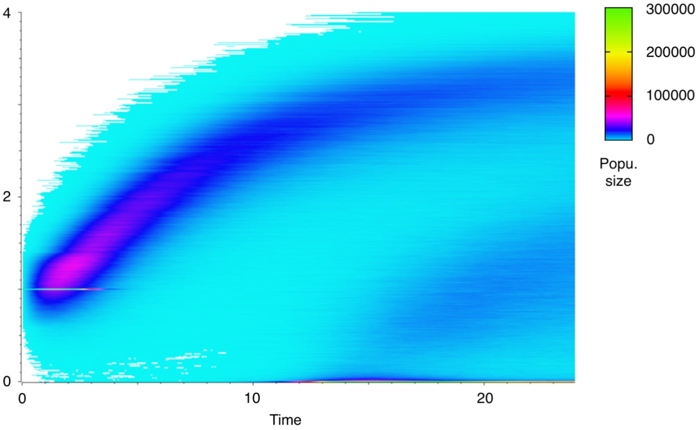
`Diekmann` *`et al.`* `2005; Barles, Perthame 2008;`

`Mirrahimi` *`et al.`* `2009; Mirrahimi, Roquejoffre, 2018`

Hamilton-Jacobi limit

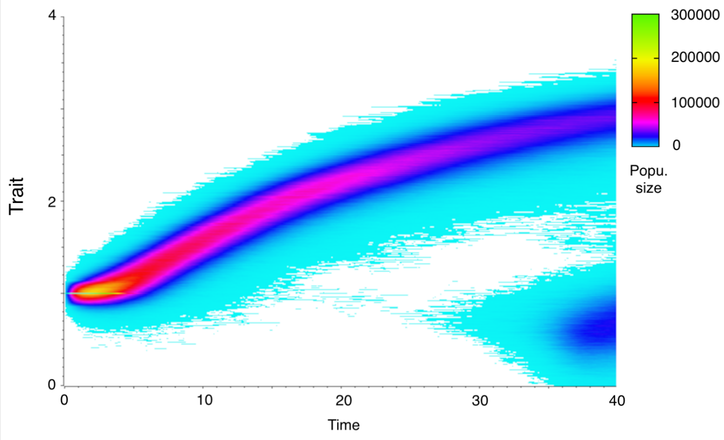


Simulation



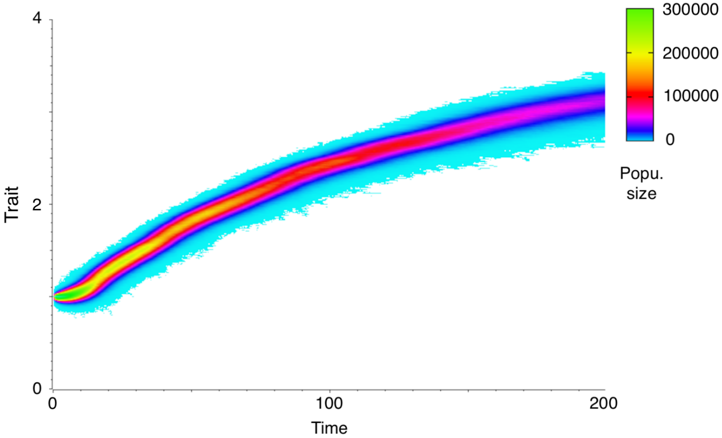
$$K = 100\,000, \qquad \mu = 0.3, \qquad \sigma = 0.03$$

Simulation



$K = 100\,000, \quad \mu = 0.3, \quad \sigma = 0.01$

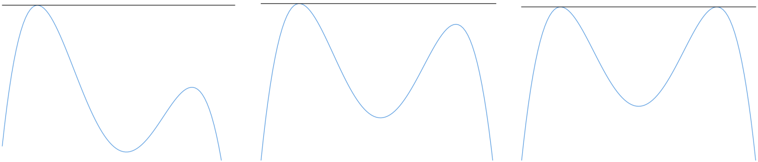
Simulation



$$K = 100\,000, \quad \mu = 0.3, \quad \sigma = 0.003$$

The "tail problem"

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



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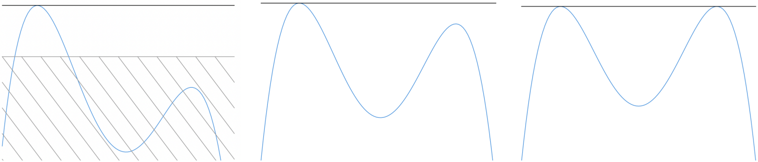
Example of dynamics of the function $\beta(t, x)$:



- 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)

`Perthame and Gauduchon, MMB 2010, Mirrahimi et al., SIAM JMA 2012`

(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 ecology (changes in the population densities): 1
- of mutant invasion: $\log K$ (time for a super-critical branching process to reach K)

`Metz` *`et al.`* `1996, C. SPA 2006`

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

Theorem

Assume that $\nu_0^K \to n_0\,\delta_x$ *with* $n_0 > 0$. *If*

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

then $(\nu^K_{t/K\mu}, t \geq 0)$ *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,

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

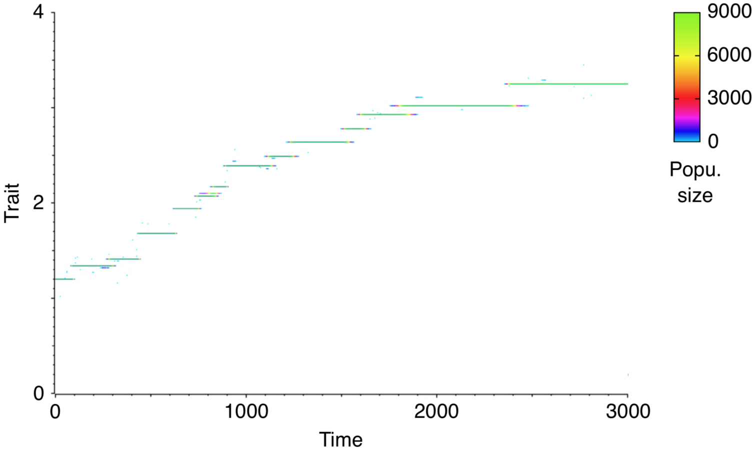
where $\bar{n}(x) = \frac{b(x)-d(x)}{c(x,x)}$ *and* $(X_t)_{t\geq 0}$ *is Markov with generator*

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

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

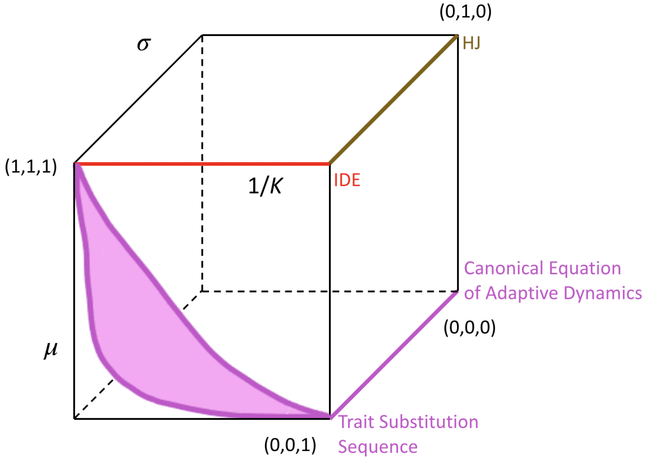
`C. SPA 2006; C., Méléard, PTRF 2011; C., Jabin, Méléard JMPA 2014`

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

Waxman, Gavrilets, JEB 2005

A discretized model

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

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

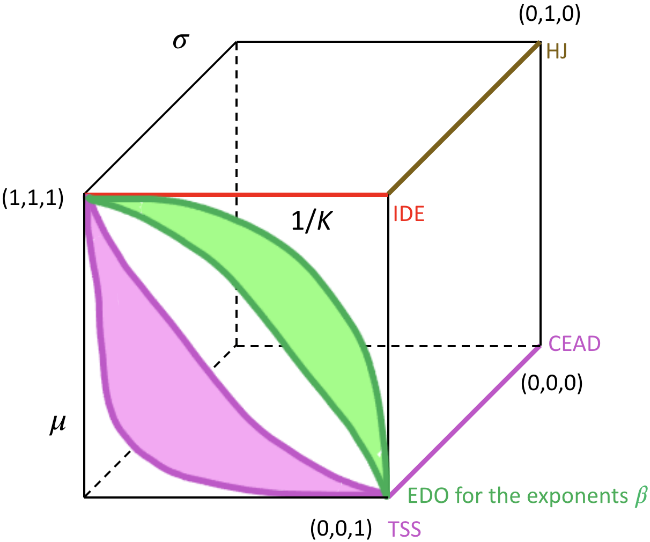
Assume $\mu = K^{-\alpha}$ *with* $\alpha \in (0,1)$ *and that* $N_i^K(0) = \lfloor K^{\beta_i(0)} \rfloor$ *with* $\max_i \beta_i(0) = \beta_{i_0}(0) = 1$ *for a unique* i_0.
Then $(\beta_i^K)_{0\leq i\leq 1/\delta}$ *converges in probability in* $L^\infty_{loc}(\mathbb{R}_+^*)$ *to a piecewise affine function* $(\beta_i)_{0\leq i\leq 1/\delta}$ *such that*

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

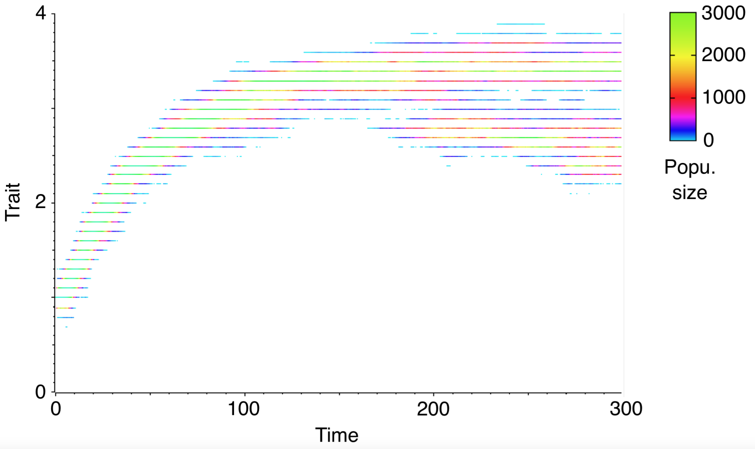
where $\ell^*(t) \in \{0,\dots,1/\delta\}$ *is such that* $\ell^*(0) = i_0$ *and* $\ell^*(t) = j$ *for all* j *and* t *such that* $j \neq \ell^*(t-)$ *and* $\beta_j(t-) = 1$*; otherwise,* ℓ^* *is constant.*

`Durrett, Mayberry, AAP 2011; Bovier, Coquille, Smadi, AAP 2019;`
`C., Méléard, Tran, AAP 2021; Coquille, Kraut, Smadi, EJP 2021`

Scaling with less rare mutations

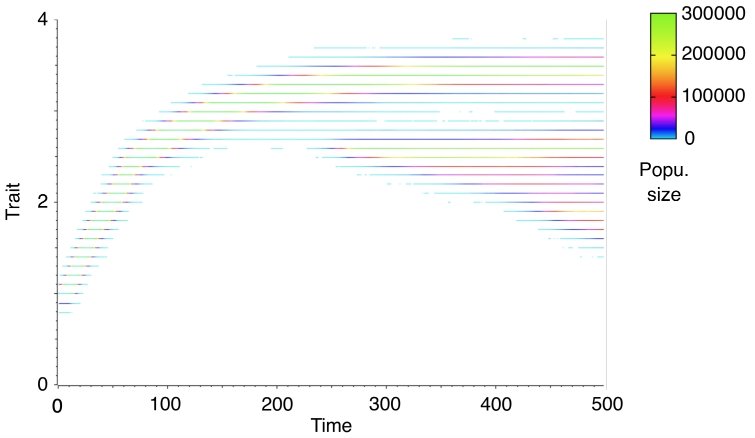


Simulation with $\alpha = 0.5$



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

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

We assume

- grid mesh δ_K, such that $h_K = \delta_K \log K \to 0$
- 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 $1/\log K$

Expected convergence

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 piecewise affine interpolation function

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

Conjecture (informal)

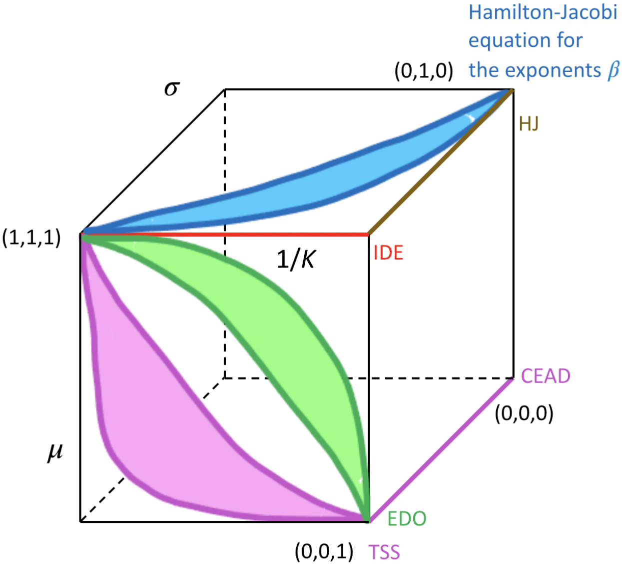
Assume $\widetilde{\beta}^K(0,\cdot)$ *converges in* L^∞ *to* $\beta_0 > 0$. *Then* $\widetilde{\beta}^K$ *converges to the solution of the Hamilton-Jacobi equation with constraint and cutoff*

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

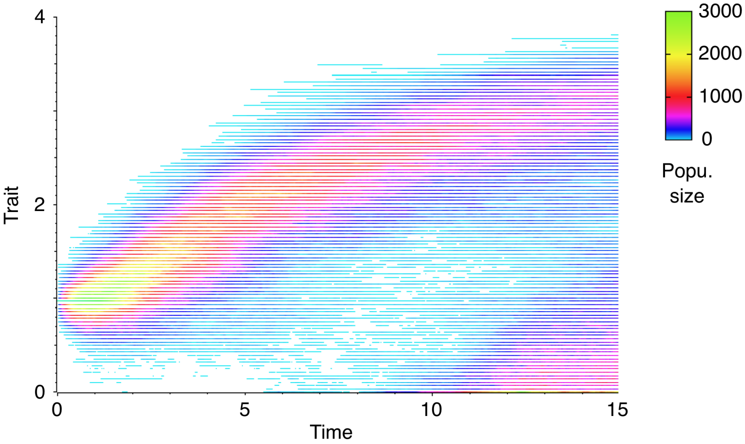
such that $\beta(0,x) = \beta_0(x)$ *with cutoff corresponding to extinction.*

`First results in: C., Méléard, Mirrahimi, Tran, JEP 2023; PhD A. Jeddi`

A scaling with vanishing grid mesh

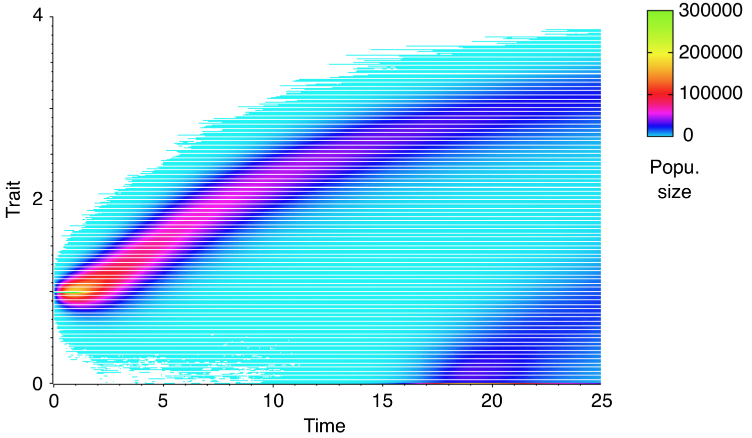


Simulation



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

Simulation

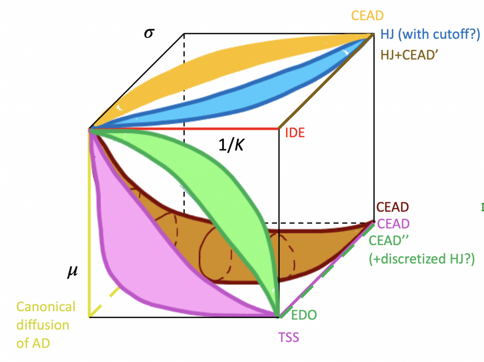


$$K = 100\,000, \quad \mu = 1, \quad \sigma = 0.04, \quad \delta_K = 0.0128$$

Conclusion

- General approach: design macroscopic models allowing to describe the evolutionary dynamics in a simpler (?) way
- Great variety of dynamics starting from the same individual-based model
- All are concentration limits (to evolving Dirac masses), but with very different levels of diversity, evolutionary time-scales and macroscopic behaviors
  $\rightsquigarrow$ provides a large range of modeling tools, but prediction from these models must be done carefully!
- Parameter scalings motivated by discussions in the biological literature and interactions with biologists
  $\rightsquigarrow$ Mathematics can help shed light on the biological debate
- Great diversity of mathematical tools, and several open problems
- ... 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, Mayberrry 2011; C., Méléard, Tran 2021
Coquille, Kraut, Smadi, EJP 2021
dashed line: T. Paul, 2024+

C., Méléard, Mirrahimi, Tran, JEP 2023

C., Hass, AAP 2024