Adaptation en présence d’un optimum phénotypique mobile

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Introduction

Modelling evolutionary dynamics in *asexuals*

- **General objectives:**

  - To **predict** the evolution of asexual organisms such as viruses, bacteria, some insect and fungi species, or cancer lineages in response to a treatment

  - To **understand** complex interplay of selection, mutation and environmental changes in asexuals

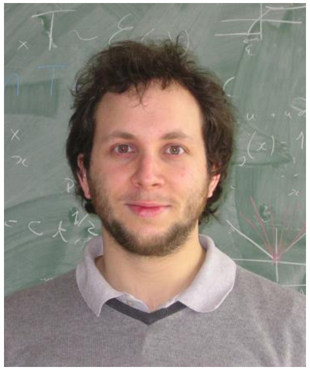
- **Challenge:** Better management strategies of resistance emergence,

  World Health Organization describes antibiotic resistance as one of the biggest threats to global health, food security, and development today.

Modelling evolutionary dynamics in asexuals

- **ANR Project RESISTE:** *Evolutionary rescue, stochastic effects and interactions with environmental stress.* **Partnership** with Montpellier Institute of Evolutionary Sciences (experimental evolution of bacteria, theoretical models)



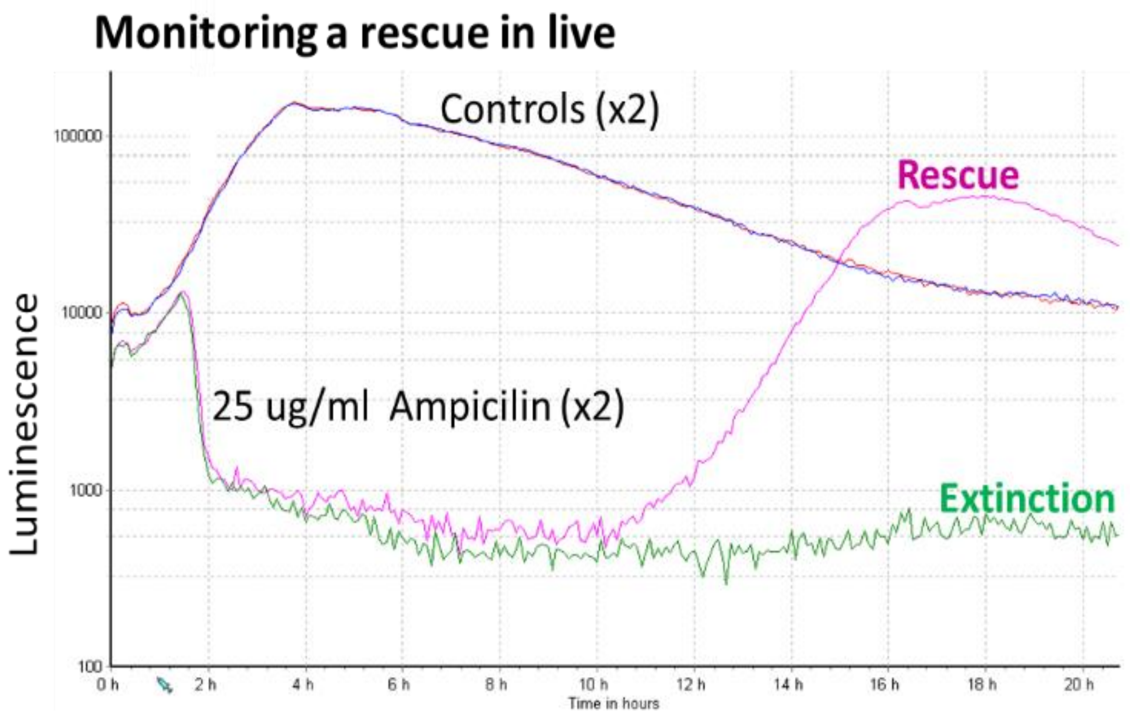



Agence Nationale de la Recherche ANR

isem Institut des Sciences de l'Evolution-Montpellier

Evolutionary rescue

When a population that initially declines because of exposure to an environment outside of its ecological niche can avoid extinction, via genetic adaptation. [Lynch and Lande 1993, Gomulkiewicz and Holt 1995]

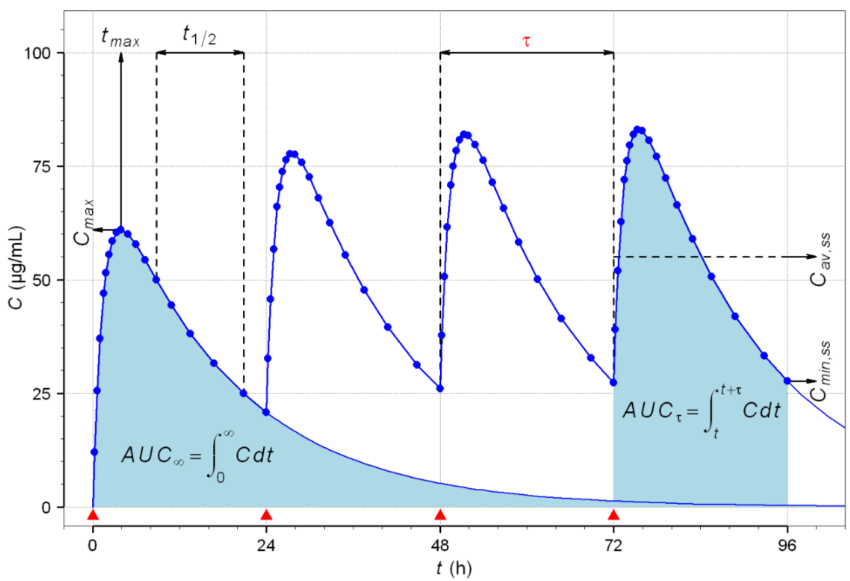


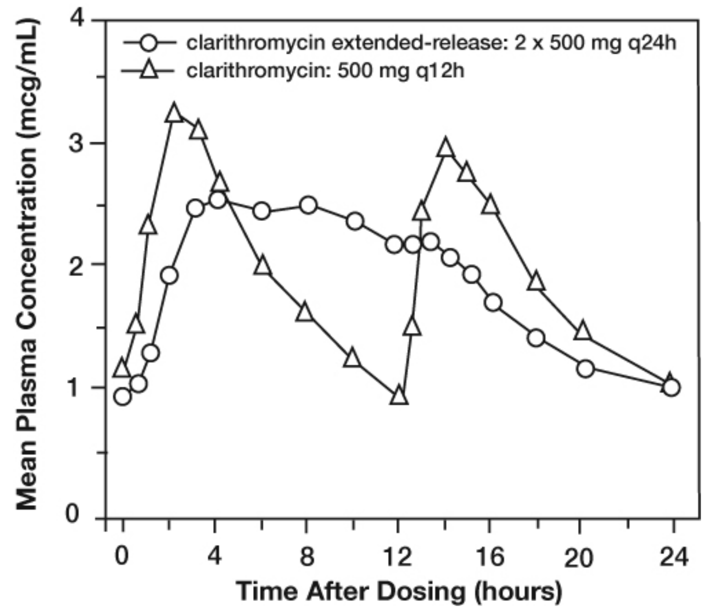
Experimental illustration: four pops of E. coli were monitored over time (hours) with either no antibiotics or 25ug/ml ampicillin

Experiment by G Martin

Environmental changes (from the point of view of the pathogen):

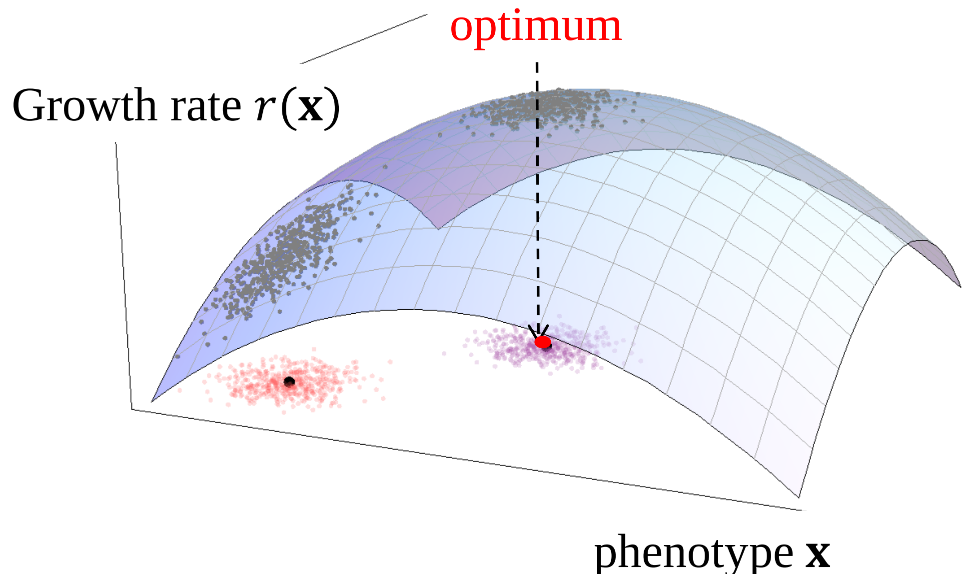
- **May be abrupt:** host shift in a pathogen, antibiotic treatment (*in vitro*), …
- **May also be more progressive:** temperature change, increase in salinity …
- **May have more or less periodic trajectories:** time course of drug plasma concentrations





Modelling the phenotype-fitness relationship: Isotropic Fisher's Geometrical Model with 1 optimum

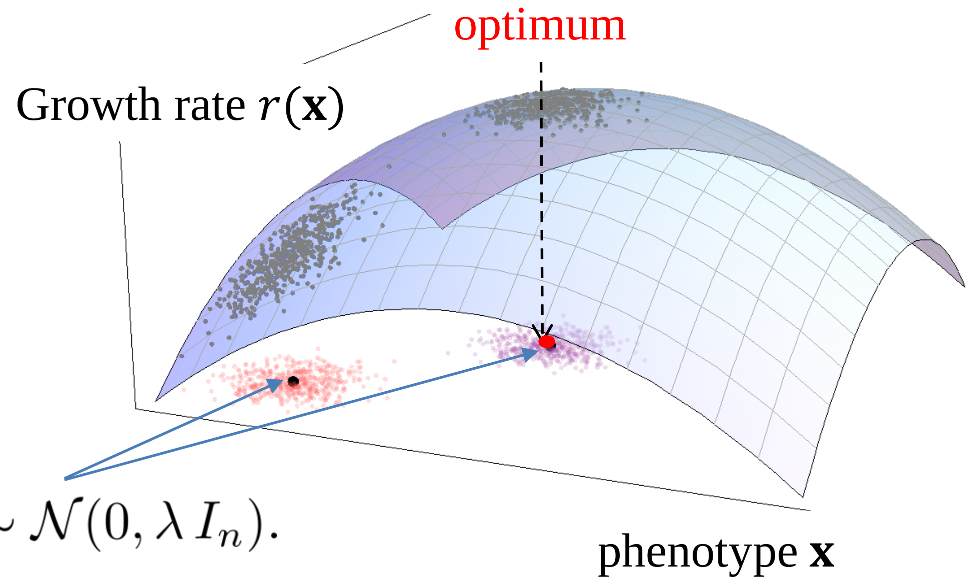
Phenotype $\mathbf{x} \in \mathbb{R}^n$ at n traits. Unique fitness optimum $\mathcal{O}$.



Growth rate r (= fitness) of genotype $\mathbf{x}$:

$$\boxed{r(\mathbf{x}) = r_{max} - \frac{\|\mathbf{x} - \mathcal{O}\|^2}{2}.}$$

Modelling the phenotype-fitness relationship: Isotropic Fisher's Geometrical Model with 1 optimum



Gaussian FGM: mutation $d\mathbf{x} \sim \mathcal{N}(0, \lambda\, I_n)$.

Mutation rate U

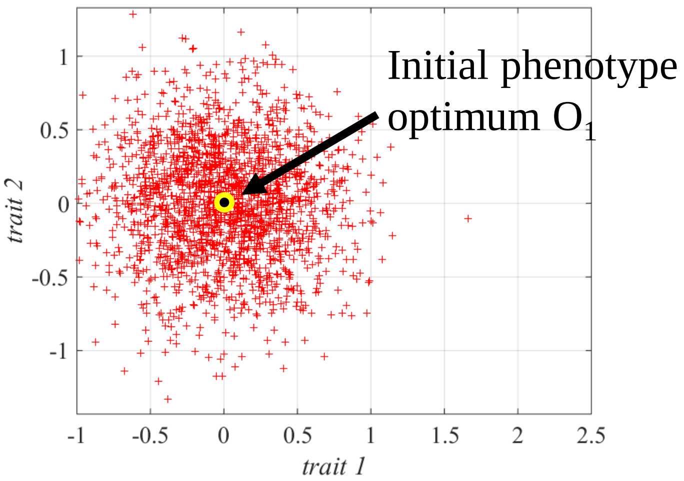
$$r(\mathbf{x}) = r_{max} - \frac{\|\mathbf{x} - \mathcal{O}\|^2}{2}.$$

Induces epistasis: the distribution of fitness effects of mutations depends on the current phenotype

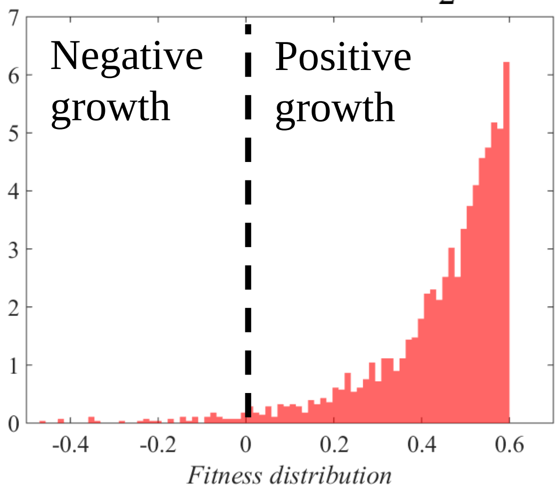
Consistent with various empirical patterns of mutation fitness effects in fungus, bacteria and viruses *[Martin and Lenormand 2006, Schoustra and Hwang 2016]*

Abrupt environmental change

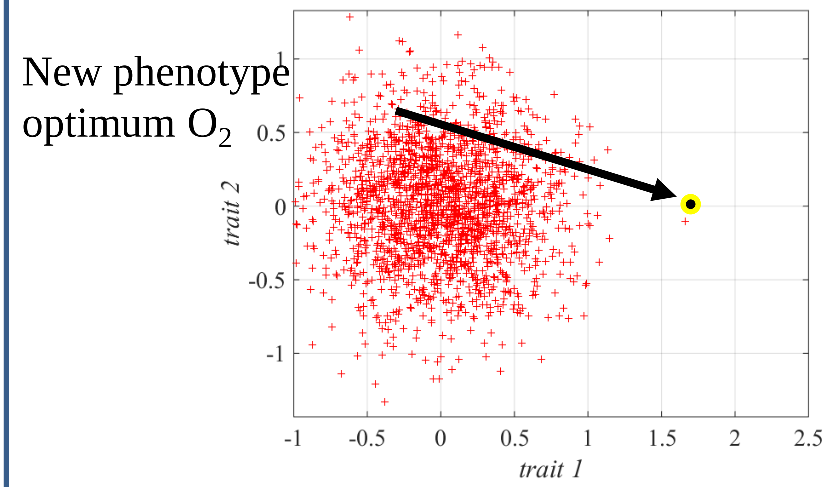
BEFORE



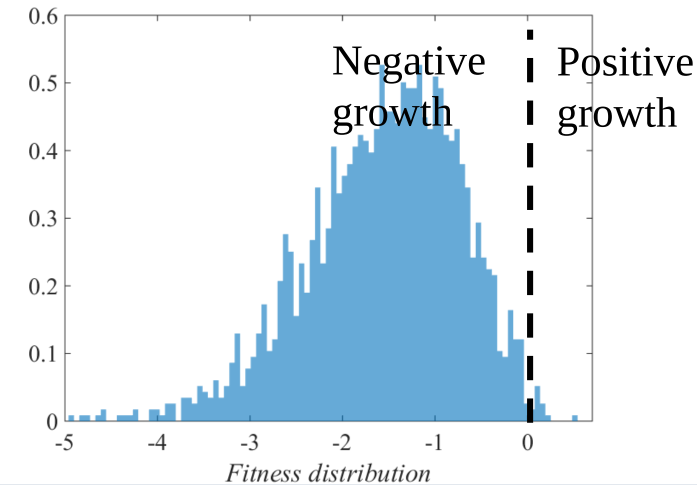
$$\text{Fitness: } r_{max} - \frac{\|x - O_1\|^2}{2}$$



AFTER



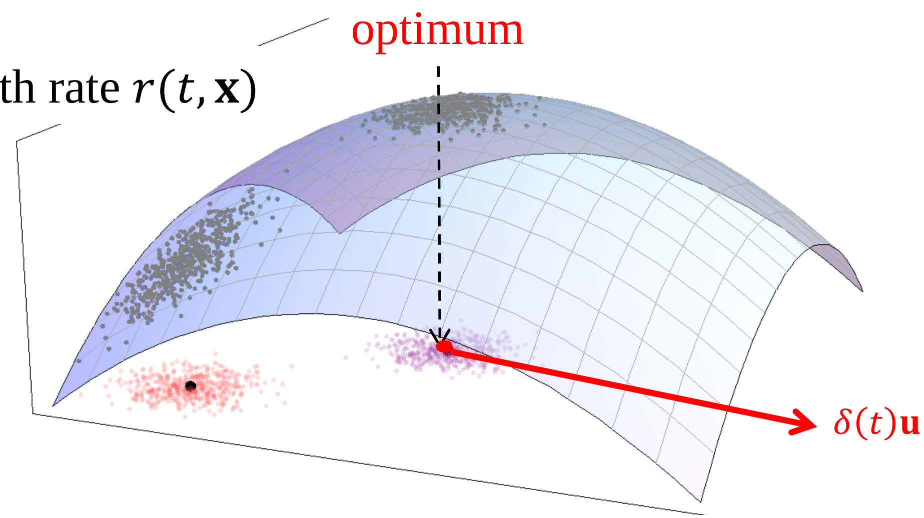
$$\text{Fitness: } r_{max} - \frac{\|x - O_2\|^2}{2}$$



Arbitrarily moving optimum

Moving optimum $\mathcal{O}(t) = \mathcal{O}_0 + \delta(t)\,\mathbf{u}$

$\delta(t)$ arbitrary function with $\delta(0) = 0$
$\mathbf{u}$: unit vector in $\mathbb{R}^n$



Growth rate $r(t, \mathbf{x})$ (= fitness) of phenotype $\mathbf{x}$:

$$\boxed{r(t, \mathbf{x}) = r_{max} - \frac{\|\mathbf{x} - \mathcal{O}(t)\|^2}{2}.}$$

FGM + Wright-Fisher IBM with constant population size

Generation t

N individuals

Phenotypes: $\boldsymbol{x_i} \in \mathbb{R}^n$
Fitnesses r_t^i:

$$r_{max} - \frac{\|\mathbf{x}_i - \mathcal{O}(t)\|^2}{2}.$$

Fitness of the indiv. :
$\mathbf{r}_t = (r_t^1, \ldots, r_t^N)$

Reproduction/selection

N individuals are sampled with replacement in the previous generation

Nb offspring:
$\sim \mathrm{Multi}(N, \exp(\mathbf{r}_t))$

+

Mutation

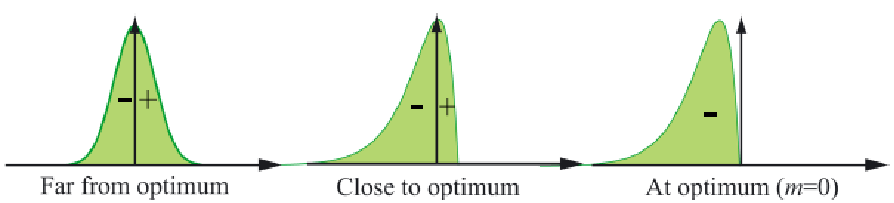
Nb mutations/indiv. :
$k \sim \mathcal{P}(\varepsilon\, U)$

Mutation effect on phenotype:
$\boldsymbol{x_i} \to \boldsymbol{x_i} + \boldsymbol{dx_i}$
$\boldsymbol{dx_i} \sim \mathcal{N}(0, \lambda\, \boldsymbol{I_n})$

Mutation effect on fitness: $r_i \longrightarrow r_i + s$

Generation t+ε

Context-dependent mutation kernel



Convergence towards an integro-differential equation

$q_t^N = \frac{1}{N}\sum_{i=1}^N \delta_{\mathbf{x}_i}$: phenotype distribution of the population at time t.

Lemma (Forien, R, 2020) Fix $T > 0$. Assume that $\varepsilon_N \to 0$ and $\varepsilon_N^2 N \to +\infty$ as $N \to \infty$. The process $(q_t^N, t \in [0,T])$ converges in distribution to the solution of the deterministic equation:

$$\partial_t q(t,\mathbf{x}) = U\ (J \star q - q) + q(t,\mathbf{x})\,(r(t,\mathbf{x}) - \overline{r}(t)),\ t \in (0,T),\ \mathbf{x} \in \mathbb{R}^n,$$

with

$$\overline{r}(t) = \int_{\mathbb{R}^n} r(t,\mathbf{x})\, q(t,\mathbf{x})\, d\mathbf{x},$$

and J the isotropic Gaussian kernel with variance λ.

Can be obtained by simple adaptations of *[Fournier, Méléard, 2004; Champagnat, Ferrière, Méléard, 2006]*, to take into account discrete time - fixed population size.

Existing results

- Fixed optimum (= abrupt change) *[Martin and Roques 2016]* isotropic FGM dimension n, *[Alfaro and Carles 2017, Alfaro and Veruete 2019]*: 1D diffusion approximation, full trajectory; *[Gil, Hamel, Martin, Roques]* Dynamics of fitness distribution w/o diffusion approximation; *[Hamel, Lavigne, Martin, Roques 2019]* Anisotropic mutations effects, diffusive case

- Optimum with constant speed in geographical space, w/o adaptation (local competition term, KPP eqs) : *[Berestycki, Diekmann et al. 2009, Berestycki and Rossi 2008]*.

- Phenotype optimum with constant speed: *[Alfaro, Berestycki, Raoul 2017]:* diffusion, n-D, optimum moving at constant speed, asymptotic analysis

- Periodically fluctuating: *[Lorenzi, Chisholm, Desvillettes, and Hughe, 2015]* Gaussian periodic (stationary) solution 1D case; *[Carrère, Nadin 2020]* principal eigenfunction analysis in bounded domains, study of the mean limit population; *[Figueroa Iglesias and Mirrahimi, 2018, 2019]*: method of constrained Hamilton-Jacobi equations: large time-small mutation regime.

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Large-time dynamics

- Optimum with constant speed in geographical space, w/o adaptation (local competition term, KPP eqs) : *[Berestycki, Diekmann et al. 2009, Berestycki and Rossi 2008]*.
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Here

- Description of the full dynamics (not only the asymptotics in time): of critical importance for the study of rescue events

- Do not need a small mutation regime assumption (but a diffusion approximation ~ weak selection-strong mutation regime)

- We consider a general form of moving optimum (+ general time-dependent strength of selection)

$$r(t, \mathbf{x}) = r_{max} - \frac{\|\mathbf{x} - \mathcal{O}(t)\|^2}{2\,\sigma(t)^2}.$$

Distribution of phenotype

We focus on the dynamics of the deterministic phenotype distribution $q(t,\mathbf{x})$ under a diffusion approximation:

$$\boxed{\begin{aligned}&\partial_t q(t,\mathbf{x}) = \frac{\lambda U}{2}\Delta q + q(t,\mathbf{x})\left(m(t,\mathbf{x}) - \overline{m}(t)\right),\ t>0,\ \mathbf{x}\in\mathbb{R}^n\\ &\text{with } m(t,\mathbf{x}) = r(t,\mathbf{x}) - r_{max} = -\frac{\|\mathbf{x}-\mathcal{O}(t)\|^2}{2}.\end{aligned}}$$

Equivalent to the study of eqs of the form:

$$\partial_t n(t,\mathbf{x}) = \frac{\mu^2}{2}\Delta n + n(t,\mathbf{x})\left(r(t,\mathbf{x}) - \rho(t)\right),\ t>0,\ \mathbf{x}\in\mathbb{R}^n,$$

with $n(t,\mathbf{x})$ the total population density and $\rho(t)$ its integral over $\mathbb{R}^n$, as in *[Lorenzi, Chisholm, Desvillettes, and Hughe, 2015; Alfaro, Berestycki, Raoul 2017; Figueroa Iglesias and Mirrahimi, 2018, 2019; Carrère, Nadin 2020]* . Simply set

$$q(t,\mathbf{x}) = n(t,\mathbf{x})/\rho(t).$$

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$$q(t,\mathbf{x}) = n(t,\mathbf{x})/\rho(t).$$

Strategy that we had developed in previous works (fixed optimum)

1. Derive a 1D equation satisfied by the distribution of fitness $p(t,m)$

$$\partial_t p(t,m) = U\left(J_y \circledast p - p\right)(t,m) + p(t,m)\left(m - \overline{m}(t)\right), \; t \geq 0, \; m \in \mathbb{R},$$

$$\text{with } (J_y \circledast p - p)(t,m) = \int_{\mathbb{R}} J_y(m-y)\, p(t,y)\, dy - p(t,m).$$

2. Diffusive approximation

$$\partial_t p(t,m) = -\mu^2 m\, \partial_{mm} p(t,m) + \mu^2 \left(\frac{n}{2} - 2\right) \partial_m p(t,m) + \left(m - \overline{m}(t)\right) p(t,m),$$

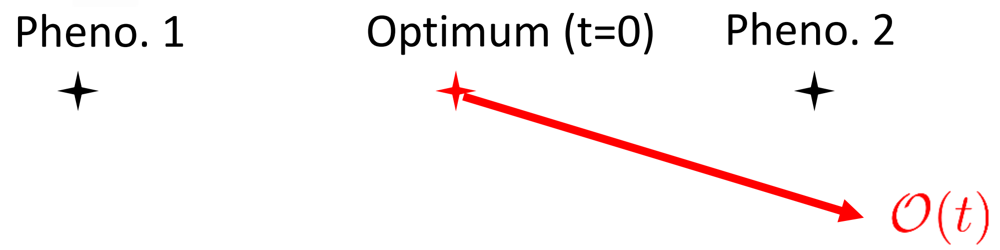
3. Define the cumulant generating function

$$C(t,z) = \ln\left(\int_{\mathbb{R}} p(t,s)\, e^{s\,z}\, ds\right)$$

4. Solve (explicitly) the equation satisfied by the CGF.

$$C(t,z) = (1 - \mu^2 z^2)\partial_z C(t,z) - \frac{n}{2}\mu^2 z - \overline{m}(t), \; t \geq 0, \; z \in \mathbb{R}_+$$

Why this cannot work here



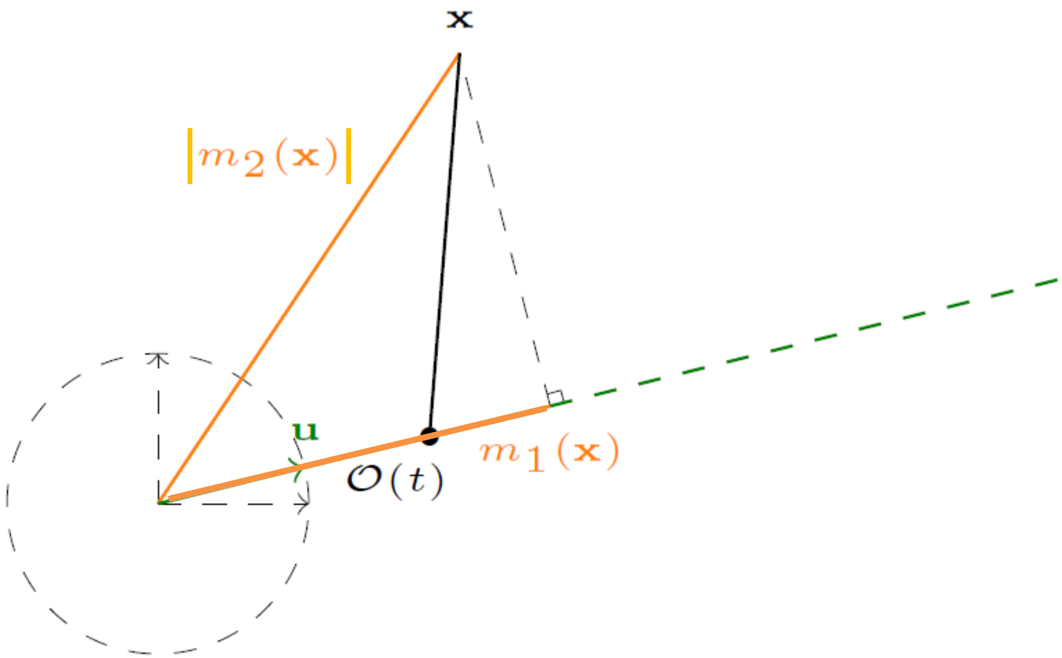
Pheno. 1 and 2 have the same fitness at $t = 0$.

Pheno. 2 has a better fitness at larger times.

Contrarily to the « fixed optimum » case, the distribution of fitness does not fully determine its own evolution

Definition of 2D fitness components

Two time-independent ‘components’:



$$\begin{cases} m_1(\mathbf{x}) &= \mathbf{u}\cdot\mathbf{x}, \\ m_2(\mathbf{x}) &= -\dfrac{\|\mathbf{x}\|^2}{2}. \end{cases}$$

At any time,

$$\boxed{m(t,\mathbf{x}) = -\frac{\|\mathbf{x}-\mathcal{O}(t)\|^2}{2} = \delta(t)\, m_1(\mathbf{x}) + m_2(\mathbf{x}) - \frac{\delta(t)^2}{2}.}$$

Distribution of the fitness components

$p(t, m_1, m_2)$: bivariate distribution of the components (m_1, m_2)

Defined by:

Theorem (Bonnefon, Martin, Patout, Roques, 2020) There exists a unique nonnegative density function $p \in C^1(\mathbb{R}_+, L^2(\mathbb{R} \times \mathbb{R}_-))$ that satisfies the following relationship

$$\int_{\mathbb{R}^n} q(t, \mathbf{x}) \phi(m_1(\mathbf{x}), m_2(\mathbf{x})) d\mathbf{x} = \int_{\mathbb{R}\times\mathbb{R}_-} p(t, m_1, m_2) \phi(m_1, m_2) dm_1 dm_2,$$

for every test functions $\phi \in L^2(\mathbb{R} \times \mathbb{R}_-)$ and all $t \geq 0$.

2D cumulant generating function

Define the CGF of the components m_1, m_2: for all $(z_1, z_2) \in \mathbb{R} \times \mathbb{R}_+$

$$C(t, z_1, z_2) := \ln\left(\int_{\mathbb{R}\times\mathbb{R}_-} p(t, m_1, m_2)\, e^{m_1\, z_1 + m_2\, z_2}\, dm_1\, dm_2\right).$$

Simple characterizations of the central moments of the fitness distribution:

$$\overline{m}(t) = \delta(t)\,\partial_1 C(t,0,0) + \partial_2 C(t,0,0) - \frac{\delta(t)^2}{2},$$
$$V_m(t) = \delta(t)^2 \partial_{11} C(t,0,0) + \partial_{22} C(t,0,0) + 2\delta(t)\partial_{12} C(t,0,0).$$

2D cumulant generating function

$$C(t,z_1,z_2) := \ln\left(\int_{\mathbb{R}\times\mathbb{R}_-} p(t,m_1,m_2)\, e^{m_1\, z_1 + m_2\, z_2}\, dm_1\, dm_2\right).$$

Theorem (Bonnefon, Martin, Patout, R. 2020) The CGF satisfies, for $t \geq 0$ and $(z_1, z_2) \in \mathbb{R}\times\mathbb{R}_+$:

$$\partial_t C(t,z_1,z_2) = \mathbf{a}(t)\cdot(\nabla C(t,z_1,z_2) - \nabla C(t,0,0)) + \mathbf{k}(z_1,z_2)\cdot\nabla C(t,z_1,z_2)$$

where $\mathbf{a}(t) = (\delta(t),1) \in \mathbb{R}^2$ and $\begin{cases} \mathbf{k}(z_1,z_2) = -\mu^2(z_1\, z_2, z_2^2), \\ \gamma(z_1,z_2) = \mu^2\,(z_1^2/2 - n\, z_2/2). \end{cases}$

Solving the CGF equation

Define a change of variable $\phi_t : \mathbb{R}_+^2 \to \mathbb{R} \times \mathbb{R}_+$, such that

$$Q(t, z, \tilde{z}) := C(t, \phi_t(z, \tilde{z}))$$

solves a simpler equation:

$$\partial_t Q(t, z, \tilde{z}) = (1, 1) \cdot (\nabla Q(t, z, \tilde{z}) - \nabla Q(t, 0, 0)) + \beta(t, z, \tilde{z}),$$

for $(t, z, \tilde{z}) \in \mathbb{R}_+^3$.

Proposition (Bonnefon, Martin, Patout, R., 2020) Q is given by the expression:

$$Q(t, z, \tilde{z}) = \int_0^t \beta(t - s, z + s, \tilde{z} + s) - \beta(t - s, s, s)\, ds + Q_0(z + t, \tilde{z} + t) - Q_0(t, t).$$

Solving the CGF equation

Define the change of variable $\phi_t : \mathbb{R}_+^2 \to \mathbb{R} \times \mathbb{R}_+$, by

$$\phi_t(z, \tilde{z}) = (y_1(t, z, \tilde{z}), y_2(z))$$

with

$$\begin{cases} y_1(t, z, \tilde{z}) := & \displaystyle\int_0^z \delta(z + t - s) \frac{\cosh(\mu\, s)}{\cosh(\mu\, z)}\, ds + (z - \tilde{z}) \frac{\cosh(\mu(z + t))}{\cosh(\mu\, z)}, \\ y_2(z) := & \displaystyle\frac{\tanh(\mu\, z)}{\mu}. \end{cases}$$

Note: surjectivity is not needed

Main theorem (Bonnefon, Martin, Patout, Roques, 2020)
For all $t \geq 0$ and $(z, \tilde{z}) \in \mathbb{R}_+^2$, the CGF satisfies:

$$C(t, \phi_t(z, \tilde{z})) = Q(t, z, \tilde{z}).$$

Cumulant generating function: explicit solution

Main theorem (Bonnefon, Martin, Patout, Roques, 2020)
For all $t \geq 0$ and $(z, \tilde{z}) \in \mathbb{R}_+^2$, the CGF satisfies:

$$C(t, \phi_t(z, \tilde{z})) = Q(t, z, \tilde{z}).$$

Corollary

$$\overline{m}(t) = -\mu \, \frac{n}{2} \, \tanh(\mu \, t) - \frac{1}{2} \left(H_\delta(t) - \delta(t)\right)^2 + R_0'(t)$$

with $H_\delta(t) := \mu \displaystyle\int_0^t \delta(u) \, \frac{\sinh(\mu \, u)}{\cosh(\mu \, t)} \, du$ and

$$R_0'(t) = \frac{1}{\cosh(\mu \, t)} \left(\delta(t) - H_\delta(t)\right) \partial_1 C_0(\phi_0(t,t)) + \left(1 - \tanh^2(\mu \, t)\right) \partial_2 C_0(\phi_0(t,t)).$$

Cumulant generating function: explicit solution

Clonal case ($\mathcal{O}(0) = 0$)

$$\overline{m}(t) = \boxed{-\mu \frac{n}{2} \tanh(\mu\, t)} - \boxed{\frac{1}{2} \left(H_\delta(t) - \delta(t)\right)^2}$$

with $H_\delta(t) := \mu \displaystyle\int_0^t \delta(u) \frac{\sinh(\mu\, u)}{\cosh(\mu\, t)}\, du$

$\overline{m}(t)$ with a steady optimum ($\delta \equiv 0$),

Squared distance between $\mathcal{O}(t)$, and a 'weighted history' of $\mathcal{O}(s)$ for $s \in (0, t)$.

Example 1. Optimum shifting with a constant speed

Standard assumption in theoretical papers *[e.g., Alfaro, Berestycki, Raoul 2017; Figueroa Iglesias and Mirrahimi, 2019]*

But, linear environmental change does not necessarily mean linear shift of the optimum

Proposition (Bonnefon, Martin, Patout, R, 2020)

Assume that $\delta(t) = c\,t$ for some $c \in \mathbb{R}$ and clonal initial population at $\mathcal{O}(0)$. Then,

$$\overline{m}(t) = \boxed{-\mu\,\frac{n}{2}\,\tanh(\mu\,t)} - \boxed{\frac{c^2}{2\,\mu^2}\,\tanh^2(\mu\,t)}$$

$\overline{m}(t)$ with a steady optimum $(\delta \equiv 0)$,

Effect of the speed c.

Shifting and fluctuating environments, as those considered in [*Figueroa Iglesias and Mirrahimi, 2019]*, could be treated as well, by taking:

$$r(t, \mathbf{x}) = r_{max} - \frac{\|\mathbf{x} - \mathcal{O}(t)\|^2}{2\,\sigma(t)^2}.$$

Example 1. Optimum shifting with a constant speed

At large times ($t \to \infty$),

$$\overline{m}(\infty) = \boxed{-\mu \frac{n}{2}} - \boxed{\frac{c^2}{2\,\mu^2}},$$

independently of the initial phenotype distribution.

Mutation load Lag load

- μ tends to increase the mutation load and to decrease the lag load
  $\to$ optimum value $\mu^* = (2\,c^2/n)^{1/3}$.
- critical speed c^* for persistence ($r(t,\mathbf{x}) = r_{max} + m(t,\mathbf{x})$):

$$c^* = \mu \sqrt{2\,r_{max} - \mu\,n}.$$

Consistent with *[Alfaro, Berestycki, Raoul 2017]*

Example 1. Optimum shifting with a constant speed

At large times ($t \to \infty$),

$$\boxed{V_m(\infty) = \mu^2 \frac{n}{2} + \frac{c^2}{\mu}}$$

- increases with the speed c
- nonmonotonic function of μ. Critical value reached at $\mu = (c^2/n)^{1/3}$

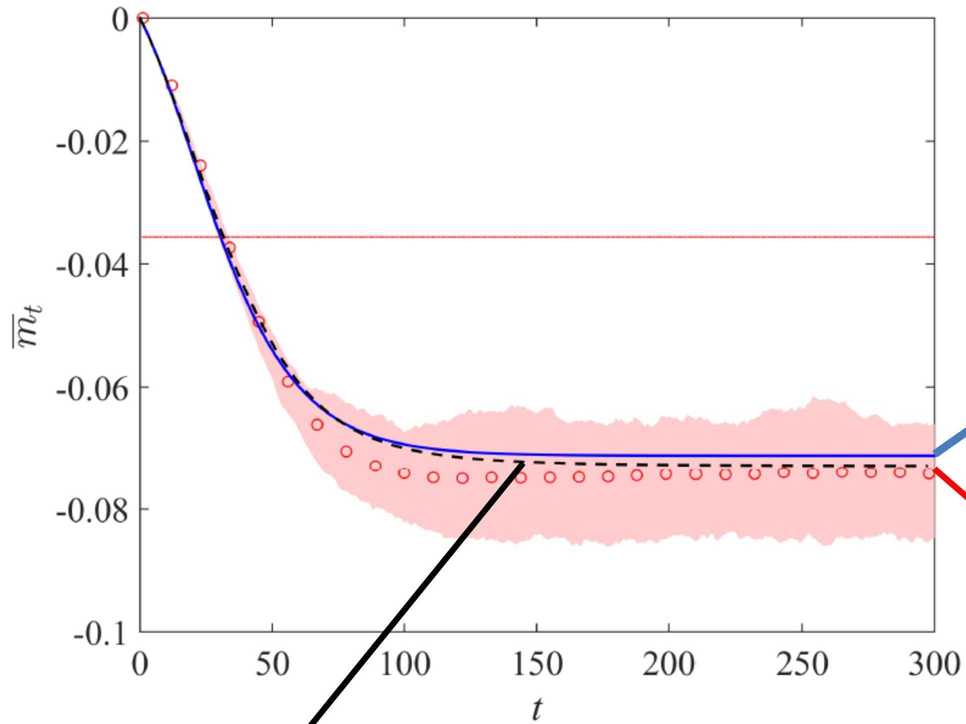
Skewness

$$\boxed{\mathrm{Skew}_m(\infty) = -\frac{\mu^3\, n + 3\, c^2}{V_m(t)^{3/2}}}$$

- negative skewness: distribution is asymmetrical, with a longer left tail.
- c is increased: reinforces the asymmetry of the distribution.

Example 1. Optimum shifting with a constant speed
Comparison with individual-based simulations

Speed c s.t. equilibrium= 2 (mut. load)



Explicit solution

circles: IBM simulations (mean value)

Numerical solution of:

$$\partial_t q(t,\mathbf{x}) = U\ (J \star q - q) + q(t,\mathbf{x})\,(r(t,\mathbf{x}) - \overline{r}(t))$$

Parameters: $N = 10^4$ invid, $n = 3$, $\lambda = 0.005$ $U = 10\,U_c$ $(U_c := n^2\,\lambda/4)$

Example 2. Sub- and superlinear cases

Proposition (Bonnefon, Martin, Patout, R, 2020)
Assume that $\delta(t) = c\, t^\alpha$ for some $c \in \mathbb{R}^*$ and $\alpha > 0$.

(i) If $\alpha < 1$, then $\overline{m}(t) \to -\mu\, n/2$ and $V_m(t) \to \mu^2\, n/2$, as $t \to +\infty$.

(ii) If $\alpha > 1$, then $\overline{m}(t) \to -\infty$ and $V_m(t) \to +\infty$, as $t \to +\infty$.

Example 3. Periodically varying optimum

Proposition (Bonnefon, Martin, Patout, R, 2020)
Assume that $\delta(t) = \delta_{max}\, \sin(\omega\, t)$. Then:

$$\overline{m}(t) = -\mu\, \frac{n}{2}\, \tanh(\mu\, t) - \frac{1}{2} \left(\frac{\delta_{max}\, \omega}{\omega^2 + \mu^2} \right)^2 (\omega\, \sin(\omega\, t) + \mu\, \cos(\omega\, t) \tanh(\mu\, t))^2$$

In *[Figueroa Iglesias and Mirrahimi, 2018]* same example (with $n = 1$). Asymptotics at large time, small mutation regime:

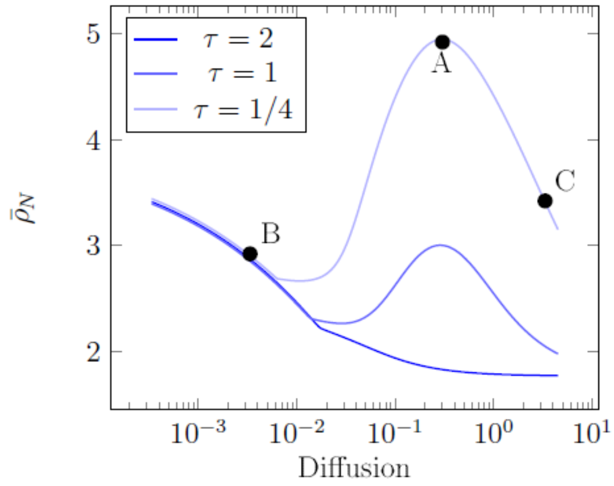
$$\overline{m}(t) \approx -\frac{\mu}{2} - \frac{1}{2} \left(\frac{\delta_{max}}{\omega} \right)^2 (\omega\, \sin(\omega\, t) + \mu\, \cos(\omega\, t))^2.$$

Example 3. Periodically varying optimum

At large times, average value over one period:

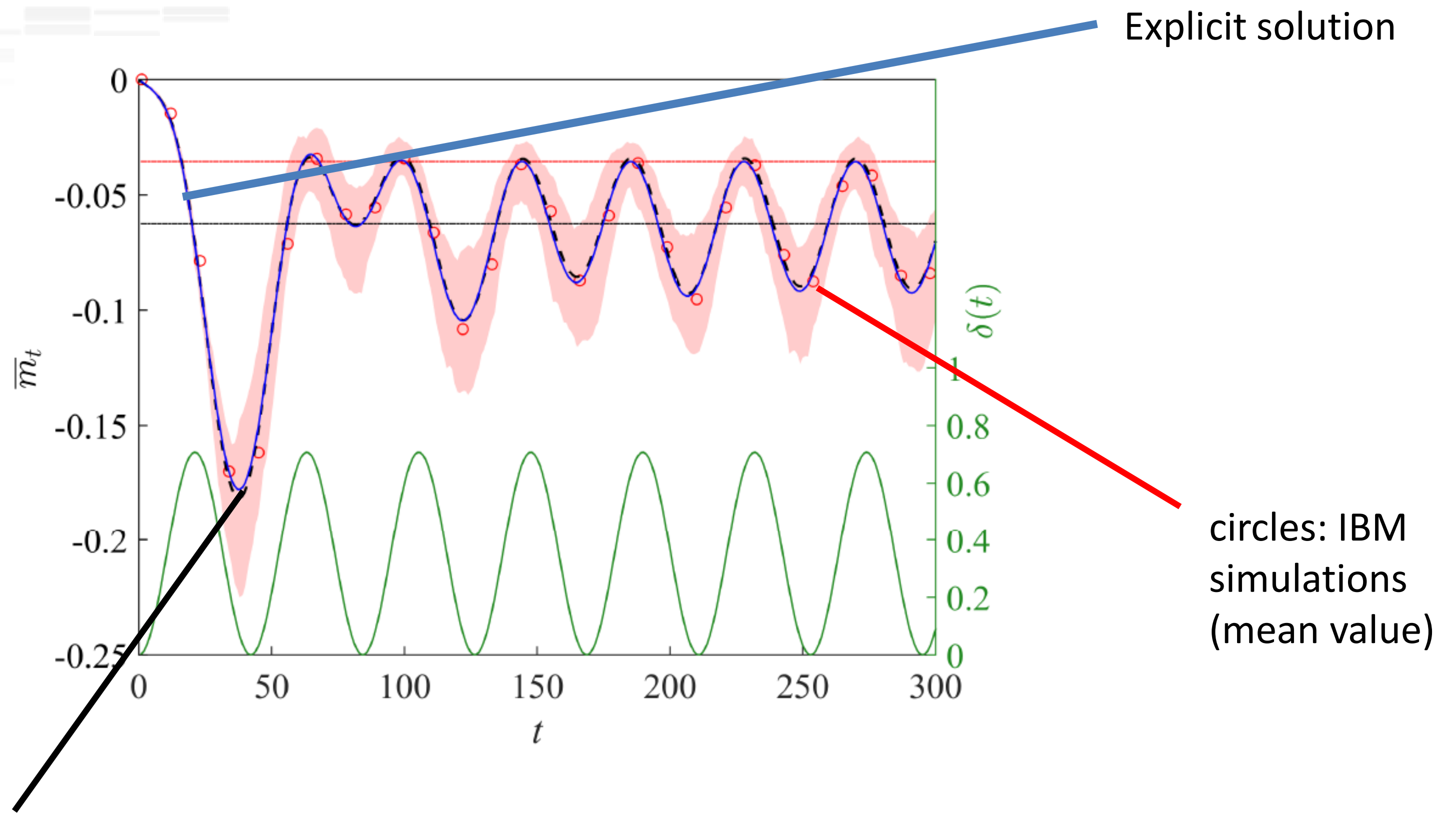
$$\langle \overline{m}_\infty \rangle := \lim_{t\to+\infty} \frac{\omega}{\pi} \int_t^{t+\pi/\omega} \overline{m}(s)\, ds = -\mu\, \frac{n}{2} - \frac{\delta_{max}^2\, \omega^2}{2\omega^2 + 2\mu^2}.$$

- higher frequencies tend to impede adaptation
- as $\omega \to +\infty$, the average lag load converges to $-\delta_{max}^2/2$
- reaches a maximum for some other value of $\mu = K\,\omega$, with $K > \omega/\sqrt{3}$ the root of $-n/2 + \delta_{max}^2 K/[\omega^2(K^2+1)]^2 = 0$.



Numerical simulations in *[Carrère, Nadin 2020]*

Example 3. Periodically varying optimum
Comparison with individual-based simulations

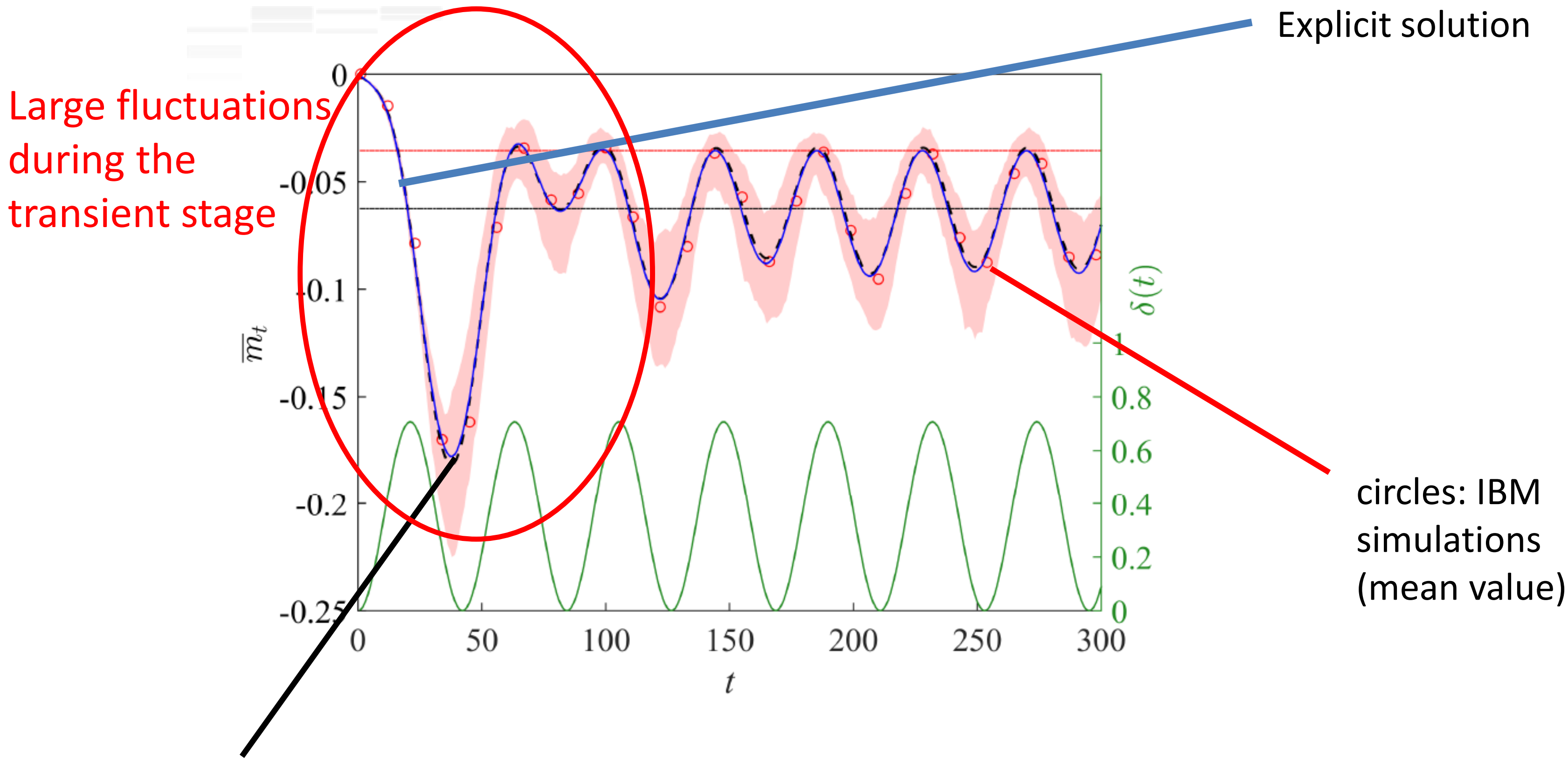


Numerical solution of:

$$\partial_t q(t, \mathbf{x}) = U \, (J \star q - q) + q(t, \mathbf{x}) \, (r(t, \mathbf{x}) - \overline{r}(t))$$

$$\text{Parameters: } N = 10^3 \text{ invid, } n = 3, \, \lambda = 0.005 \; U = 10 \, U_c \; (U_c := n^2 \, \lambda / 4)$$

Example 3. Periodically varying optimum
Comparison with individual-based simulations



Numerical solution of:

$$\partial_t q(t,\mathbf{x}) = U\ (J \star q - q) + q(t,\mathbf{x})\,(r(t,\mathbf{x}) - \overline{r}(t))$$

$$\text{Parameters: } N = 10^3 \text{ invid}, \; n = 3, \; \lambda = 0.005 \; U = 10\, U_c \; (U_c := n^2\, \lambda/4)$$

Example 4. Stochastic position of the optimum.

$\delta(t)$ is an Ornstein-Uhlenbeck process:

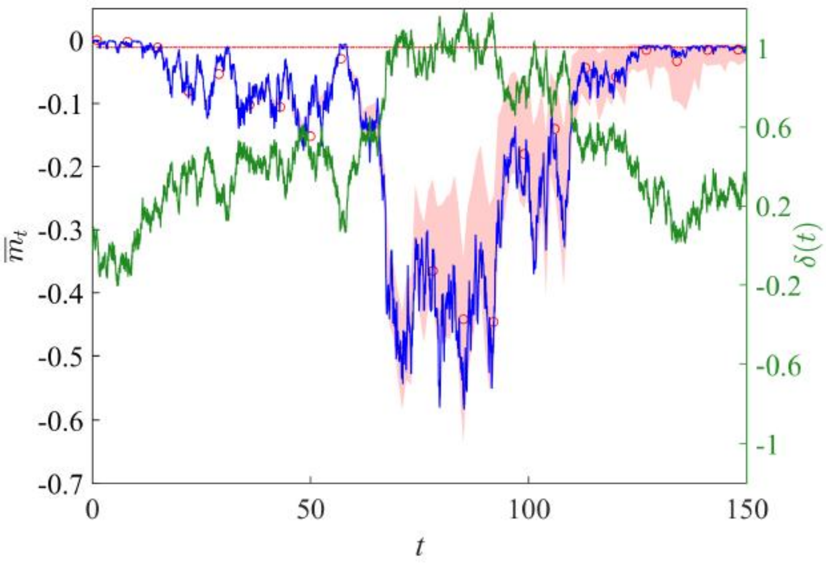
$$d\delta(t) = -\nu\delta(t)\,dt + \beta\,dW_t,$$

We use the general formula (initially clonal population):

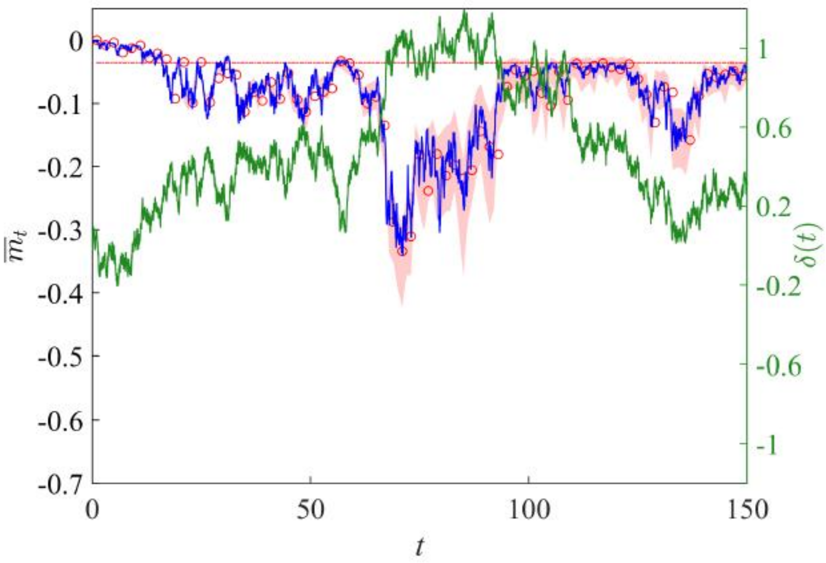
$$\overline{m}(t) = -\mu\,\frac{n}{2}\,\tanh(\mu\,t) - \frac{1}{2}\,(H_\delta(t) - \delta(t))^2$$

with $H_\delta(t) := \mu \displaystyle\int_0^t \delta(u)\,\frac{\sinh(\mu\,u)}{\cosh(\mu\,t)}\,du.$

Example 4. Stochastic position of the optimum.



(a) $U = U_c$



(b) $U = 10\, U_c$

- dynamics of the mean fitness simulated by the IBM are well-described by our theory
- complex interplay between the environment and the mutation rate: the same environment leads to very different dynamics of adaptation

What next

Theoretical problems:

- Coupling with Feller diffusion SDEs (birth-death process) to describe the population dynamics, and compute the probability of rescue depending on the strategy. As in *[Anciaux, Lambert, Ronce, Roques, Martin, 2019]*.

- Consider an optimum moving along a curve

Forthcoming experiments (ISEM):

- In vitro adaptation of *E. coli* to a saline solution. Various $\delta(t)$ functions will be imposed by different regimes of salinity increase. Mean fitness over time (growth rate) will be followed by fluoroluminometric measures.

Thank you!

Preprint: Adaptation in general temporally changing environments, Arxiv:2002.09542