Modèles de génétique quantitative dans un régime de faible variance

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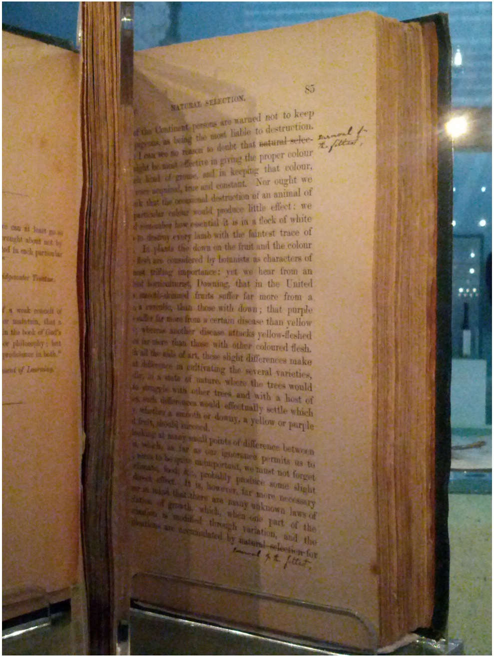
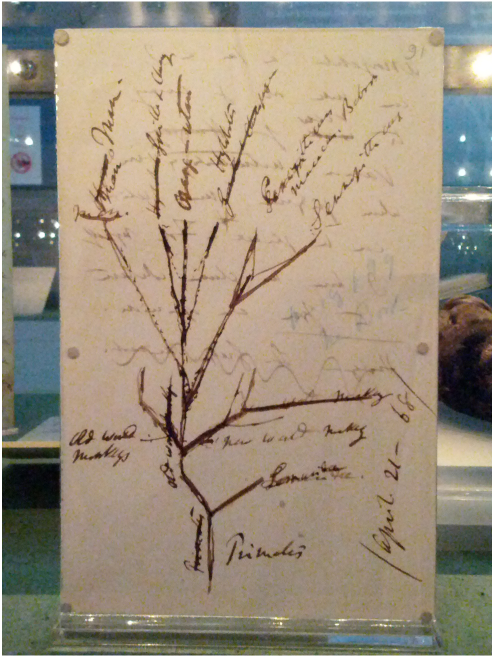
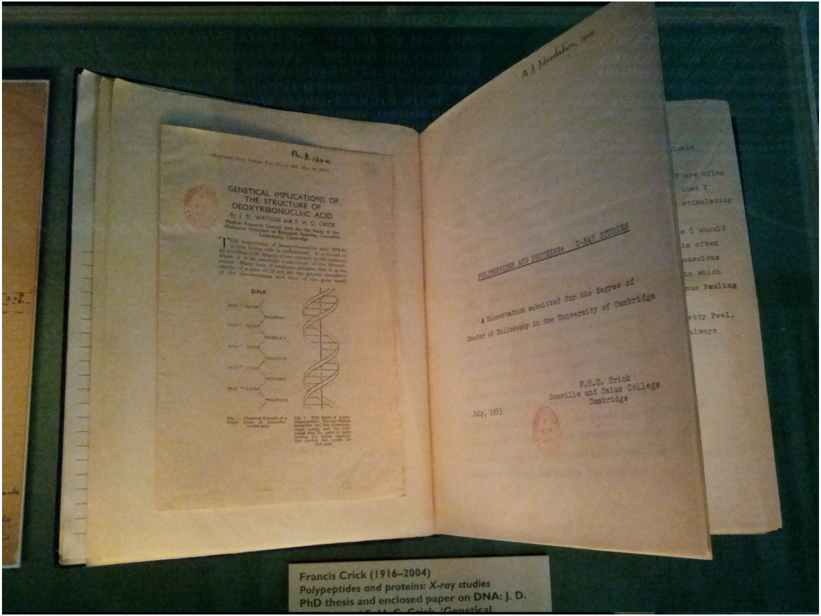


Darwin's *On the origin of species by means of natural selection*, personal copy of A.R. Wallace, 1859 (Cambridge Library).

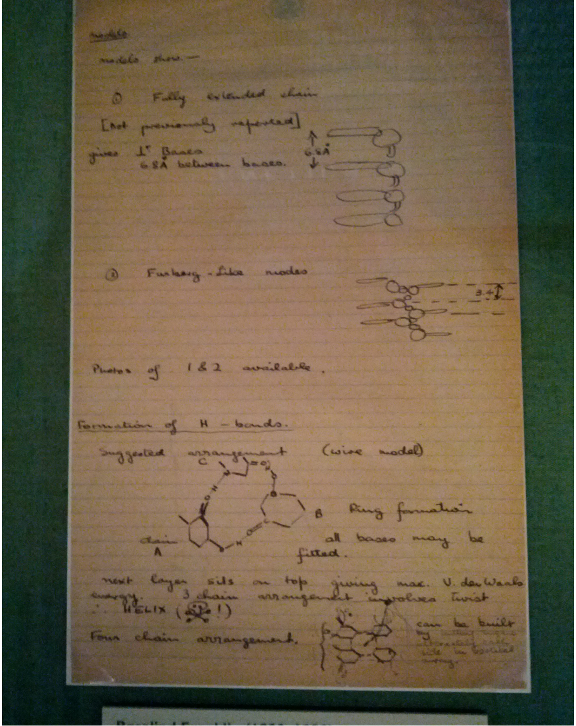


Darwin's *original drawing*, 1868
(Cambridge Library).

Ramon y Cajal
circa 1900
(Museo Cajal).



Francis Crick's PhD thesis, 1953 (Cambridge Library).



models

models show —

(1) Fully extended chain

[Not previously reported]

gives ⊥r Bases
6.8 Å between bases.

(2) Furberg-like modes

Photos of 1 & 2 available.

Formation of H-bonds.

Suggested arrangement (wire model)

B Ring formation

all bases may be fitted.

next layer sits on top giving max. V. der Waals energy. 3 chain arrangement involves twist
∴ HELIX (☠ !)

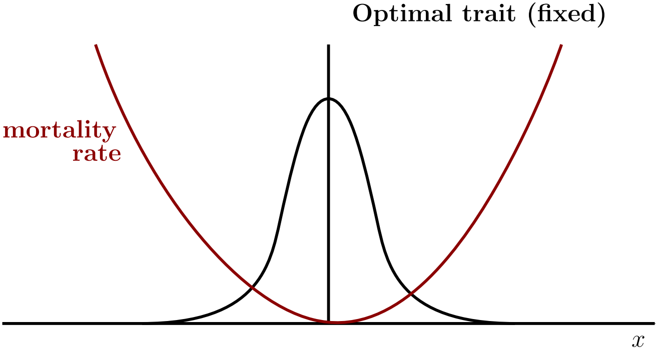
Four chain arrangement.

can be built [illegible]

Rosalind Franklin's working notes, circa 1950 (Churchill College Archive).

Selection-mutation equilibria

In quantitative genetics models, natural selection and generation of diversity are balanced to shape selection-mutation equilibria.



Equilibrium in a fixed environment

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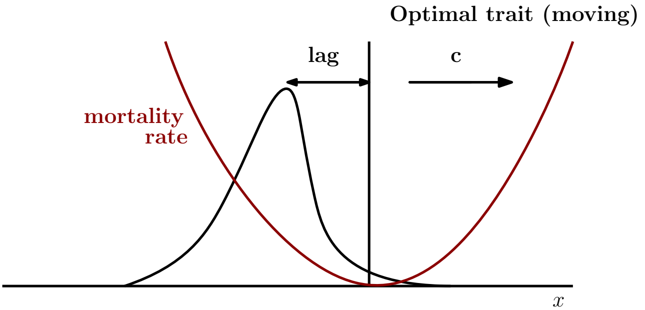
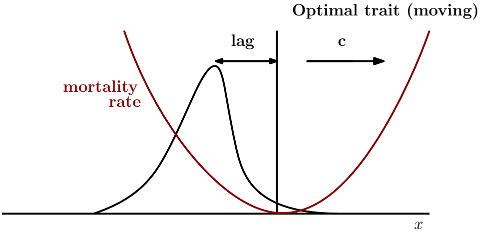


Equilibrium in a changing environment



Equation for the distribution $F(z)$:

$$\rho F(z) - c_\varepsilon \partial_z F(z) + m(z)F(z) = \mathcal{B}_\varepsilon(F)(z)\,.$$

Two modes of reproduction:

$$\begin{cases} Z = Z' + \varepsilon Y & \text{(asexual)} \\ Z = \dfrac{1}{2}(Z_1' + Z_2') + \varepsilon Y & \text{(sexual)} \end{cases}$$

The corresponding integro-differential operators are:

$$\mathcal{B}(F)(z) = \begin{cases} \dfrac{1}{\varepsilon} \displaystyle\int_{\mathbb{R}} K\left(\frac{z - z'}{\varepsilon}\right) F(z')\, dz' \\ \dfrac{1}{\varepsilon\sqrt{\pi}} \displaystyle\iint_{\mathbb{R}^2} \exp\left(-\frac{1}{\varepsilon^2}\left(z - \frac{z_1 + z_2}{2}\right)^2\right) F(z_1) \frac{F(z_2)}{\int_{\mathbb{R}} F(z_2')\, dz_2'}\, dz_1 dz_2 \end{cases}$$

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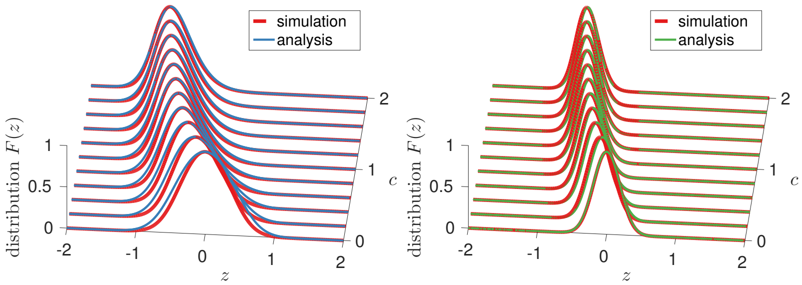
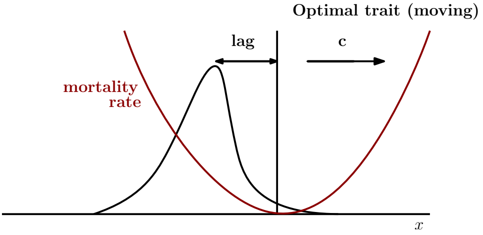


Equilibrium distribution: Asexual case

Equilibrium distribution: Sexual case



Equation for the distribution $F(z)$:

$$\rho F(z) - c_\varepsilon \partial_z F(z) + m(z)F(z) = \mathcal{B}_\varepsilon(F)(z)\,.$$

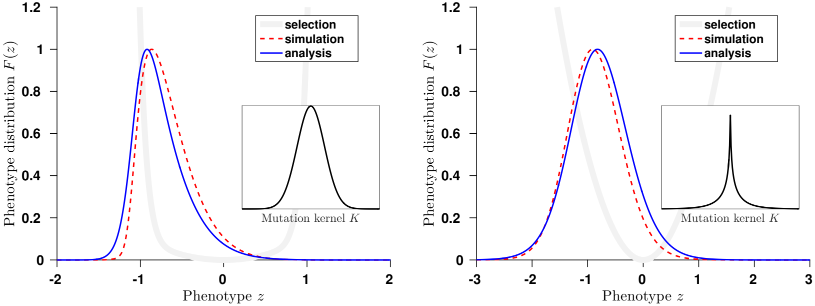
A pair of useful relationships:

$$\begin{cases} \rho \approx 1 - m(z^*) \\ \mathrm{Var}(F) \approx -\dfrac{c_\varepsilon}{\partial_z m(z^*)} \end{cases}$$

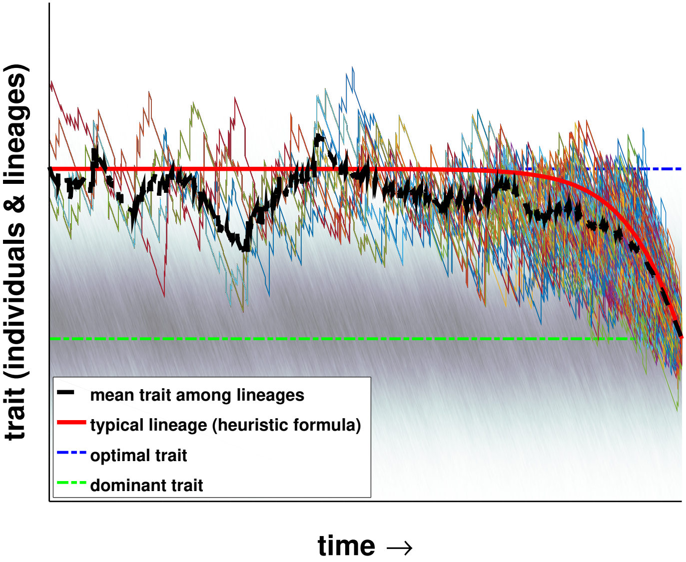
Asexual model

Population size	$\boldsymbol{\rho} \approx \boldsymbol{\beta} - \mathbf{m}(0) - \boldsymbol{\beta} L\left(\frac{\mathbf{c}}{\boldsymbol{\sigma\beta}}\right) - \frac{1}{2}\left(\frac{\boldsymbol{\sigma}^2\boldsymbol{\beta}\,\mathbf{m}''(0)}{L''\left(\frac{\mathbf{c}}{\boldsymbol{\sigma\beta}}\right)}\right)^{1/2}$
Mean phenotypic lag	$\mathbf{m}(\mathbf{z}^*) - \mathbf{m}(0) \approx \boldsymbol{\beta} L\left(\frac{\mathbf{c}}{\boldsymbol{\sigma\beta}}\right)$
Phenotypic variance	$\mathrm{Var}(\mathbf{F}) \approx -\frac{\mathbf{c}}{\mathbf{m}'(\mathbf{z}^*)}$

Comparison of the distributions (simu vs. analysis)



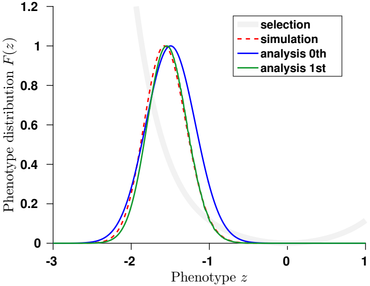
Lineages in the asexual case

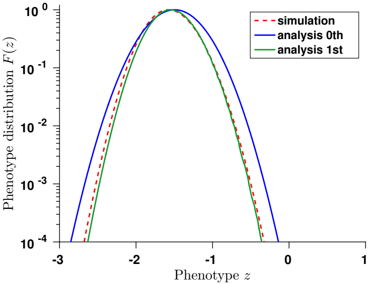


Sexual Infinitesimal model

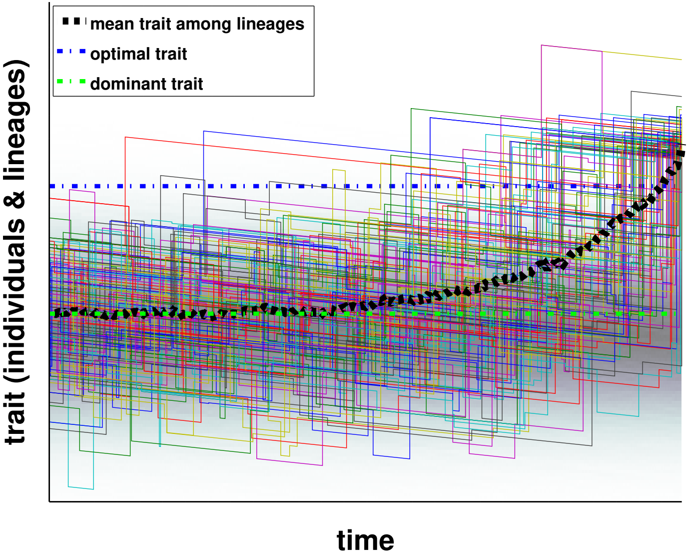
Mean phenotypic lag	$\mathbf{z}^* \approx \mathbf{z}_0^* - \boldsymbol{\sigma}^2 \frac{\mathbf{m}'''(\mathbf{z}_0^*)}{2\mathbf{m}''(\mathbf{z}_0^*)} - 2\frac{\mathbf{c}}{\boldsymbol{\beta}}$
Population size	$\rho \approx \boldsymbol{\beta} - \boldsymbol{\mu}_0 - \mathbf{m}(\mathbf{z}_0^*) - \left(\frac{2\mathbf{c}^2}{\boldsymbol{\sigma}^2\boldsymbol{\beta}} + \mathbf{c}\frac{\mathbf{m}'''(\mathbf{z}_0^*)}{2\mathbf{m}''(\mathbf{z}_0^*)} + \frac{\boldsymbol{\sigma}^2\mathbf{m}''(\mathbf{z}_0^*)}{2} \right)$
Phenotypic variance	$\mathrm{Var}(\mathbf{F}) \approx \frac{\boldsymbol{\sigma}^2}{1+2\frac{\boldsymbol{\sigma}^2}{\boldsymbol{\beta}}\mathbf{m}''(\mathbf{z}_0^*)}$

Comparison of the distributions (simu vs. analysis)

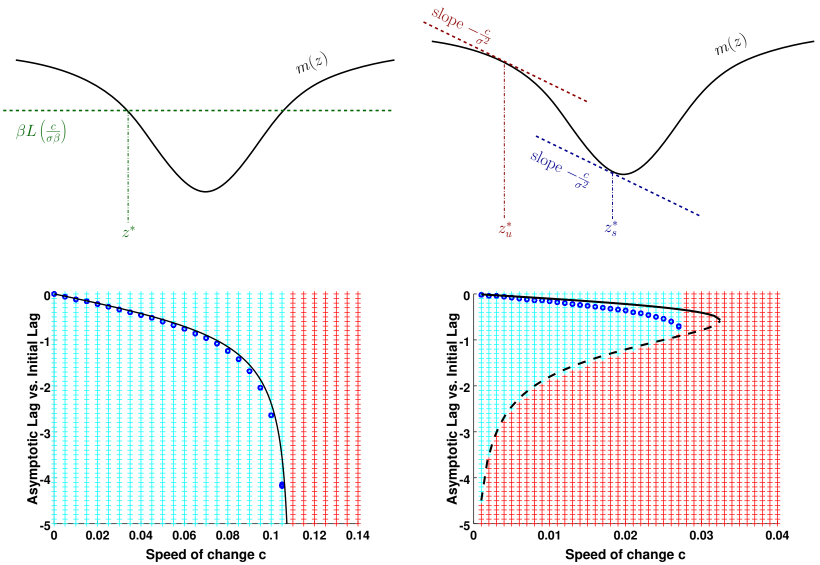




Lineages in the sexual case



Comparison (qualitative)



Maladaptation in age-structured populations

Evolution of aging

Maladaptation in age-structured populations

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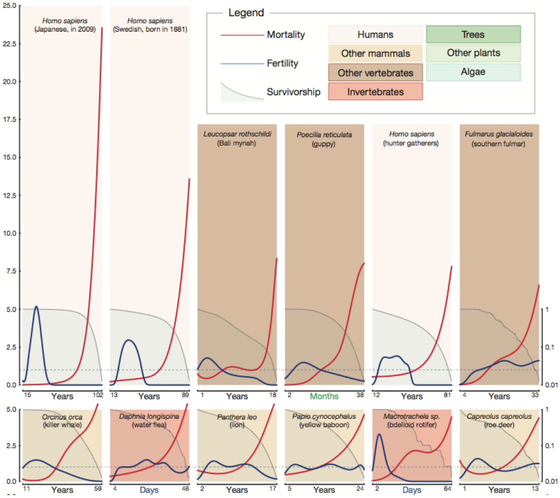
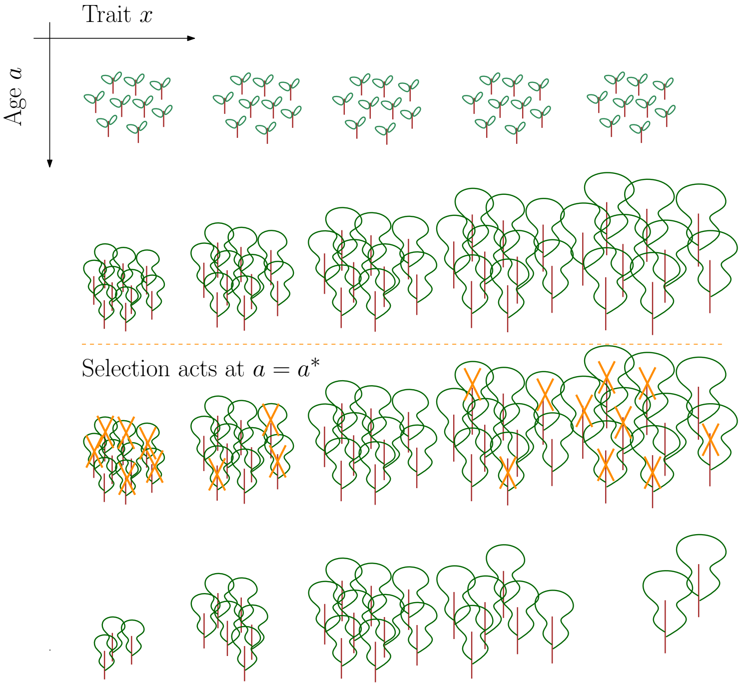


Patterns of mortality and fertility rates accross species, Jones et al, Nature 2014

Age-dependent selection

Suppose selection acts at a given age (or after some age threshold)

Hamilton (1966); Charlesworth (1994, 2001).


Trait x
Age a
Selection acts at $a = a^*$

MALADAPTATION AS A SOURCE OF SENESCENCE IN HABITATS VARIABLE IN SPACE AND TIME

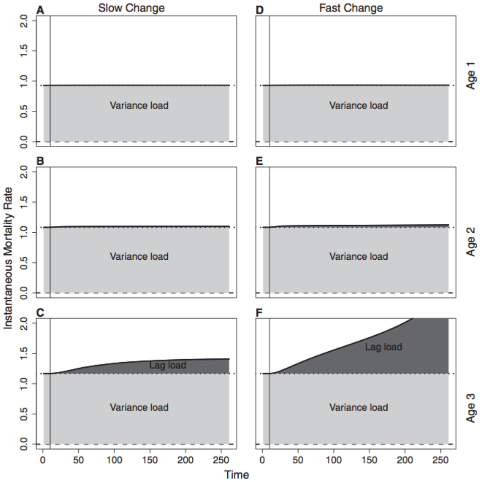
Olivier Cotto[1] and Ophélie Ronce[1,2]

In this study, we use a quantitative genetics model of structured populations to investigate the evolution of senescence in a variable environment. Adaptation to local environments depends on phenotypic traits whose optimal values vary with age and

– a changing environment can have a different impact on different age classes. –

results highlight the need to study age-specific adaptation, as a changing environment can have a different impact on different age classes.

A changing environment can have a different impact on different age classes



Cotto and Ronce, Evolution 2014

A quantitative genetics model of aging populations

(adapted from Cotto and Ronce 2014 to a continous setting)

$$\begin{cases} \partial_t f(t,a,z) + \partial_a f(t,a,z) + (\mu(a,m(z)) + \rho(t))\, f(t,a,z) = 0 \\ f(t,0,z) = \int_{\mathbb{R}} K(z-z') \left(\int_0^\infty \beta(a) f(t,a,z')\, da \right) dz' \,. \end{cases}$$

Ex. $\mu(a,m) = \mu(a) + m\delta_{a=a*}$, $m(z) = \alpha|z|^2$.

Rk. Here, asexual reproduction, but similar framework in the case of sexual reproduction.

Goal: Investigate the mutation/selection balance as a function of the age class $a*$.

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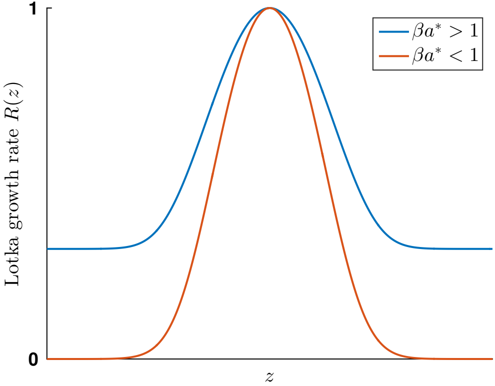
Goal: Investigate the mutation/selection balance as a function of the age class $a*$ in a changing environment.



Shape of the eigenvalue $r(m(z))$ (effective fitness)

(Severe) maladaptation (asexual)

In the age-free model, the lag z_0 increases gradually with c.

It can be more singular in the age-structured model. It can even diverge for some critical speed $c**$:

$$\lim_{c \to c**} z_0(c) = \infty$$

It means that the population in the age classes $a > a^*$ goes extinct if $c** < c < c*$ (the critical speed for population extinction)

More precisely, we find,

$$z_0 = \left(-\frac{1}{\alpha} \log \left(1 - \frac{L(c) e^{-L(c) a^*}}{\beta e^{-\beta a^*}} \right) \right)^{1/2}$$

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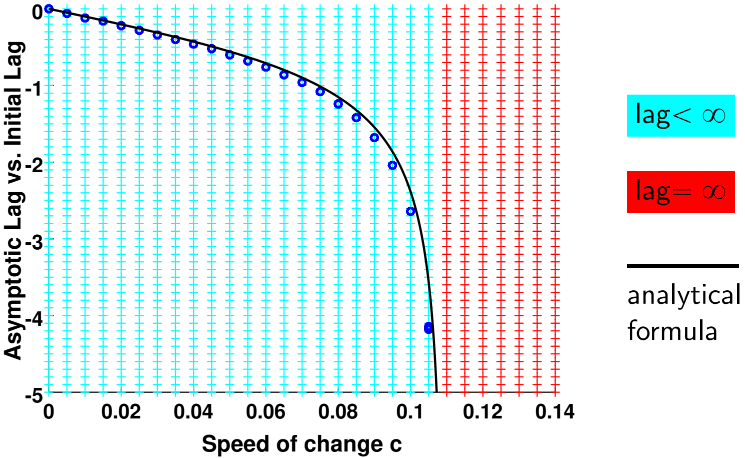
Numerical vs. analytical results (asexual mode)

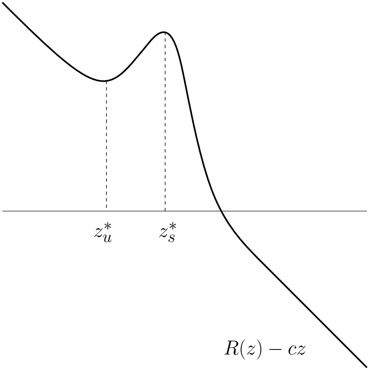


Severe maladaptation (sexual)

Similar analysis in the case of sexual reproduction.

In this case, the lag is given by the simple formula:

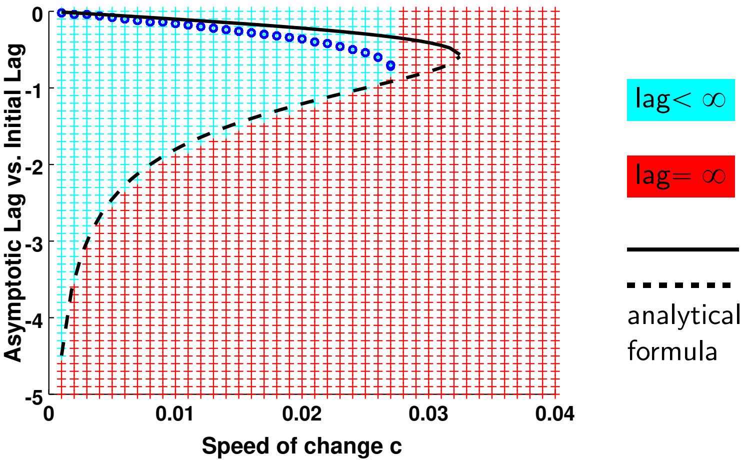
$$\frac{d}{dz} r(m(z)) = c$$

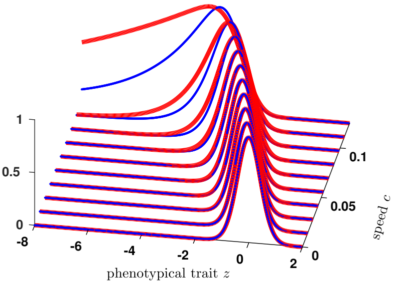


$\iff$ critical point for the modified fitness $r(m(z)) - cz$

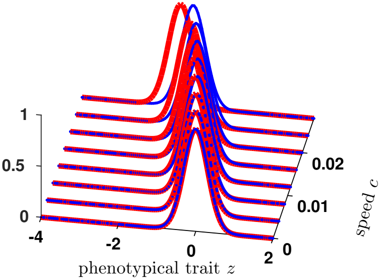
$\implies$ **Bistability**!

Numerical vs. analytical results (sexual mode)





Equilibrium distribution:
Asexual case



Equilibrium distribution:
Sexual case

Some conclusions

- Mathematical toolbox to handle some quantitative genetics models in the regime of small variance.
- Indirect informations on the history of adaptation within the population (lineages). Direct methods are needed! (stochastic processes)
- For migration between patches (cf. D. Roze), see Mirrahimi, Gandon-Mirrahimi, and on-going work by Calvez-Dekens-Mirrahimi.
- Extension to other rules of reproduction under study (finite number of loci + recombination)