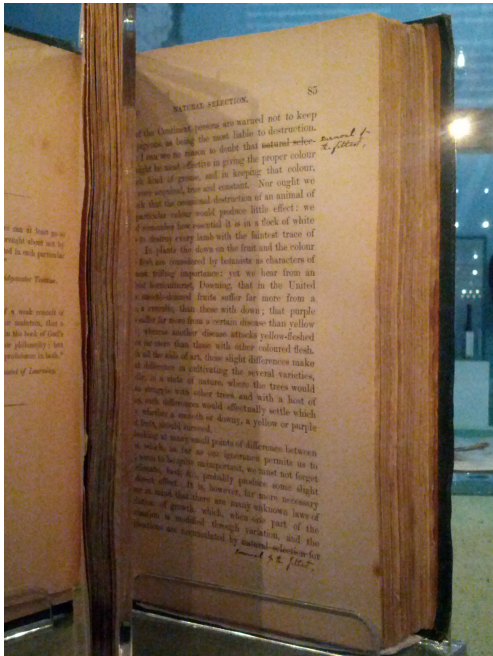


Modèles de génétique quantitative dans un régime de faible variance

Vincent Calvez

Institut Camille Jordan, CNRS & Université de Lyon

Ecole de recherche de la chaire MMB, Aussois, Mai 2019



NATURAL SELECTION.

of the Continent, peacocks are warned not to keep
progress in being the most liable to destruction.
I can see no reason to doubt that natural selection
might be most effective in giving the proper colour
to the kind of grass, and in keeping that colour,
year after year, true and constant. Nor ought we
to think that the occasional destruction of an animal of
particular colour would produce little effect; we
frequently lose poultry if it is a flock of white
or almost every lamb with the faintest trace of
black spots on the feet and the colour.

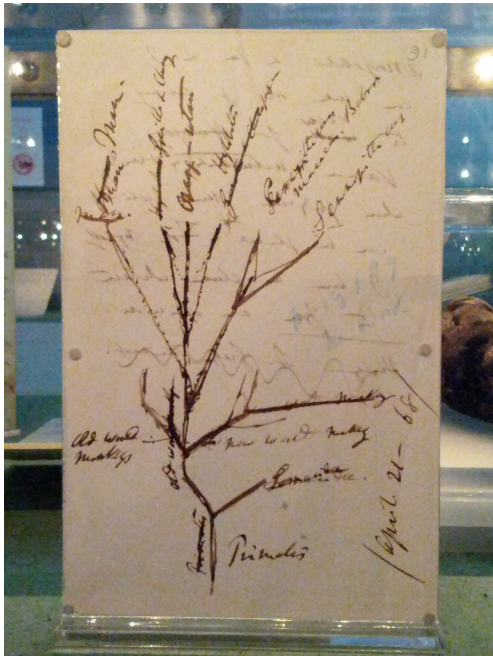
*examined
A. R. Wallace*

In plants the same is characters of
and being important; yet we hear from an
old horticulturist, Downing, that in the United
States, almost all fruits suffer far more from a
disease, than those with down; that purple
suffer far more from a certain disease than yellow
or those another disease attacks yellow-fleshed
or more than those with other coloured flesh.
In all the arts, these slight differences make
a difference in cultivating the several varieties,
as in a state of nature when the trees would
struggle with other trees and with a host of
insects, differences would ultimately settle which
variety a peach or cherry, a yellow or purple
of bark, should succeed.

Looking at many small points of difference between
a variety as far as our ignorance permits us to
know to be quite unimportant, we must not forget
sometimes, that it probably produces some slight
direct effect. It is however, far more necessary
not to insist that there are many unknown laws of
nature of growth which, when one part of the
organism is modified through variation, and the
whole is annihilated by natural selection for
the sake of a single part.

examined A. R. Wallace

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).

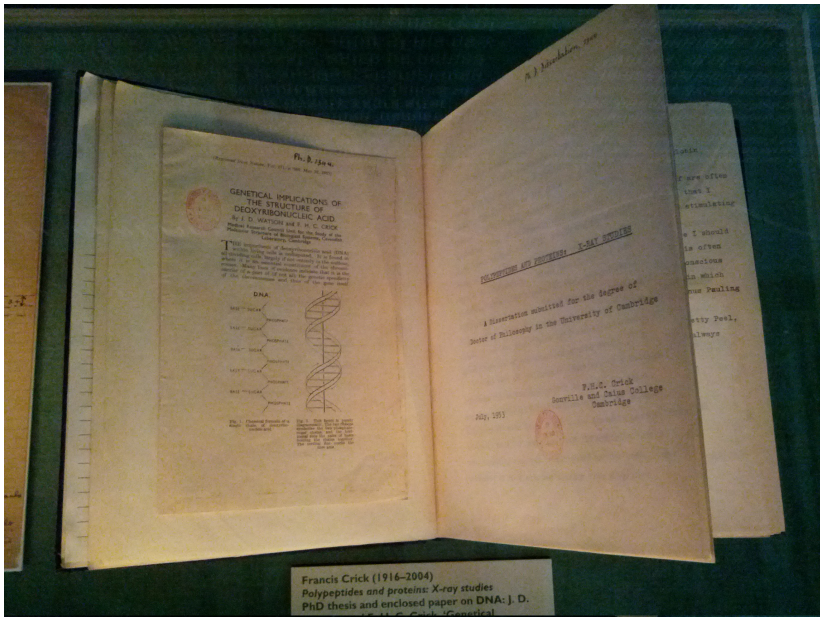


Ramon y Cajal
 circa 1900
 (Museo Cajal).

diminuido en una 3a parte $\frac{2}{3}$



16338



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

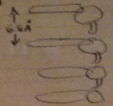
models

models show -

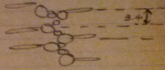
① Fully extended chain

[Not previously reported]

gives 1st bases
GSA between bases.



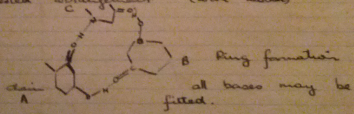
② Furberg-like nodes



Photos of 1 & 2 available.

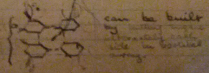
Formation of H-bonds.

Suggested arrangement (wire model)



next layer sits on top giving max. V. der Waals energy.
3 chain arrangement involves twist
HELIX (2.5 x 1)

Four chain arrangement.

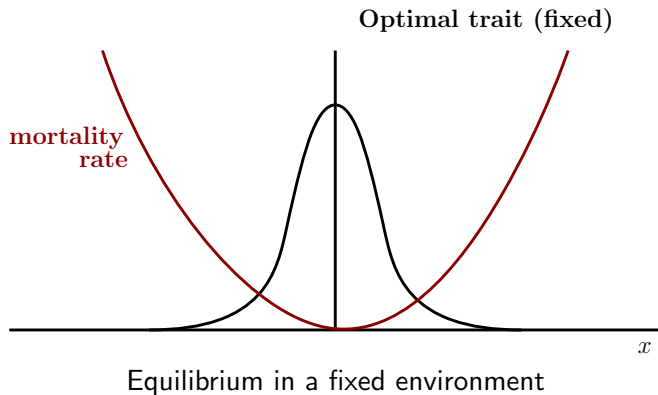


can be built by... side in twisted way.

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

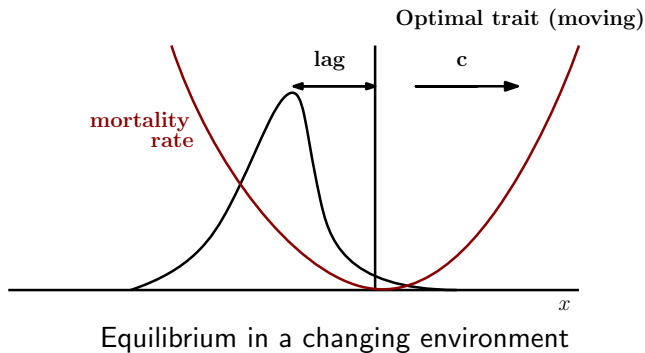
Selection-mutation equilibria

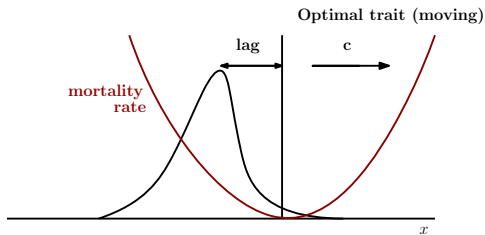
In quantitative genetics models, natural selection and generation of diversity are balanced to shape selection-mutation equilibria.



Selection-mutation equilibria

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





Equation for the distribution $F(z)$:

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

Two modes of reproduction:

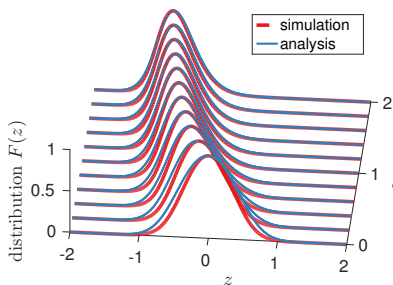
$$\begin{cases} Z = Z' + \varepsilon Y & \text{(asexual)} \\ Z = \frac{1}{2}(Z'_1 + Z'_2) + \varepsilon Y & \text{(sexual)} \end{cases}$$

The corresponding integro-differential operators are:

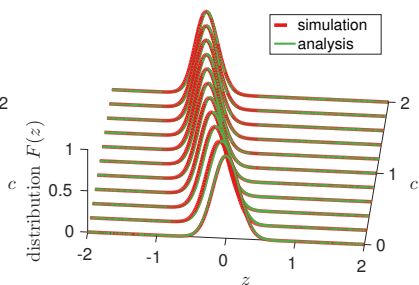
$$\mathcal{B}(F)(z) = \begin{cases} \frac{1}{\varepsilon} \int_{\mathbb{R}} K\left(\frac{z - z'}{\varepsilon}\right) F(z') dz' \\ \frac{1}{\varepsilon\sqrt{\pi}} \iint_{\mathbb{R}^2} \exp\left(-\frac{1}{\varepsilon^2} \left(z - \frac{z_1 + z_2}{2}\right)^2\right) F(z_1) \frac{F(z_2)}{\int_{\mathbb{R}} F(z'_2) dz'_2} dz_1 dz_2 \end{cases}$$

Equation for the distribution $F(z)$:

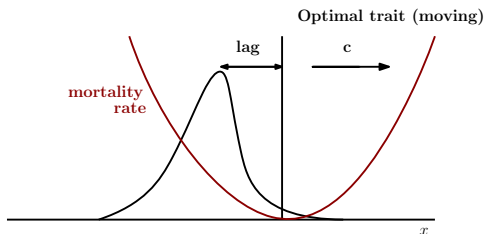
$$\rho F(z) - c_\varepsilon \partial_z F(z) + m(z)F(z) = \mathcal{B}_\varepsilon(F)(z).$$



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:

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

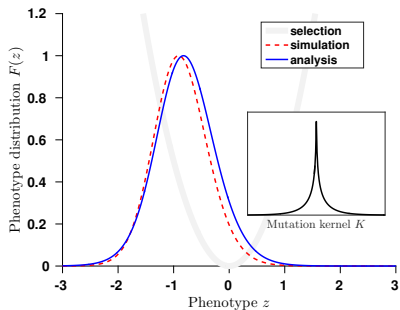
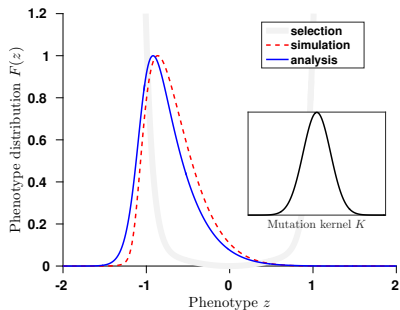
Asexual model

Population size $\rho \approx \beta - \mathbf{m}(0) - \beta L \left(\frac{\mathbf{c}}{\sigma\beta} \right) - \frac{1}{2} \left(\frac{\sigma^2 \beta \mathbf{m}''(0)}{L'' \left(\frac{\mathbf{c}}{\sigma\beta} \right)} \right)^{1/2}$

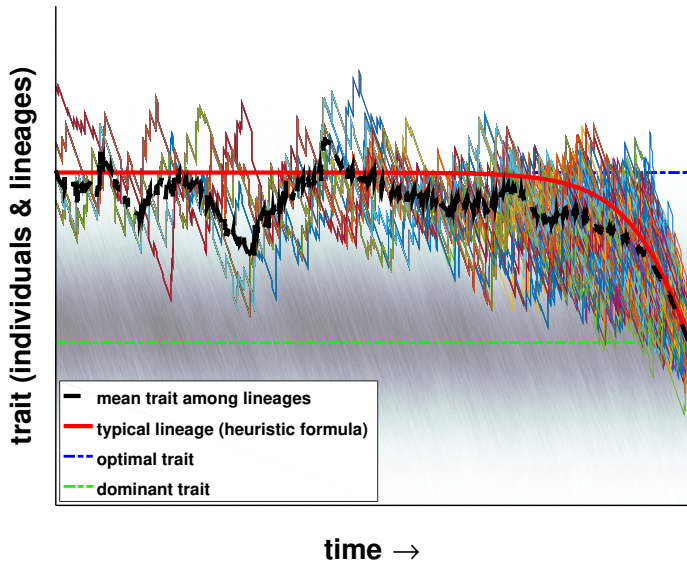
Mean phenotypic lag $\mathbf{m}(\mathbf{z}^*) - \mathbf{m}(0) \approx \beta L \left(\frac{\mathbf{c}}{\sigma\beta} \right)$

Phenotypic variance $\text{Var}(\mathbf{F}) \approx -\frac{\mathbf{c}}{\mathbf{m}'(\mathbf{z}^*)}$

Comparison of the distributions (simu vs. analysis)



Lineages in the asexual case



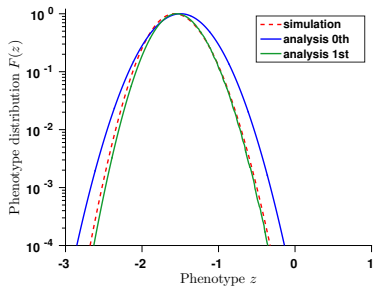
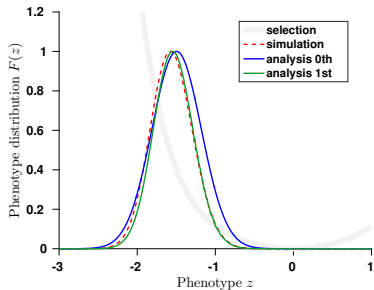
Sexual Infinitesimal model

Mean phenotypic lag $\mathbf{z}^* \approx \mathbf{z}_0^* - \sigma^2 \frac{\mathbf{m}'''(\mathbf{z}_0^*)}{2\mathbf{m}''(\mathbf{z}_0^*)} - 2\frac{\mathbf{c}}{\beta}$

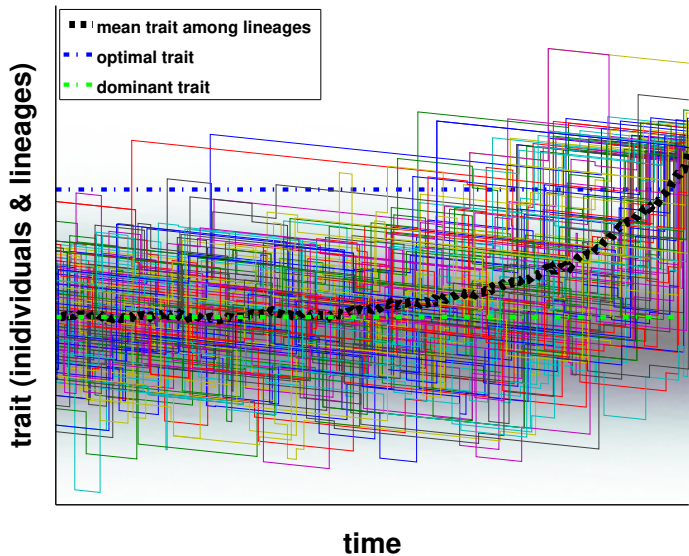
Population size $\rho \approx \beta - \mu_0 - \mathbf{m}(\mathbf{z}_0^*) - \left(\frac{2\mathbf{c}^2}{\sigma^2\beta} + \mathbf{c} \frac{\mathbf{m}'''(\mathbf{z}_0^*)}{2\mathbf{m}''(\mathbf{z}_0^*)} + \frac{\sigma^2 \mathbf{m}''(\mathbf{z}_0^*)}{2} \right)$

Phenotypic variance $\text{Var}(\mathbf{F}) \approx \frac{\sigma^2}{1 + 2\frac{\sigma^2}{\beta} \mathbf{m}''(\mathbf{z}_0^*)}$

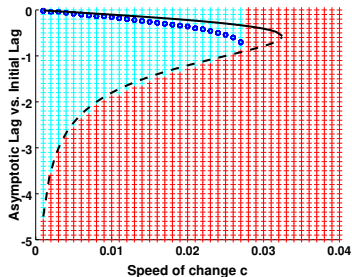
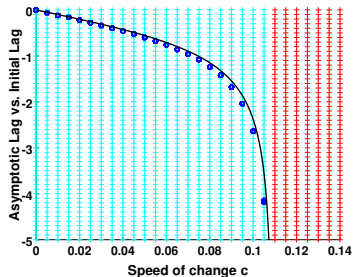
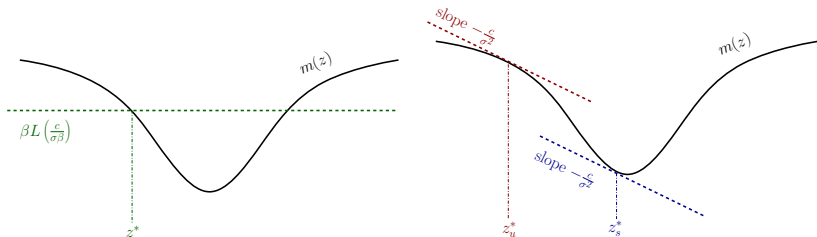
Comparison of the distributions (simu vs. analysis)



Lineages in the sexual case



Comparison (qualitative)



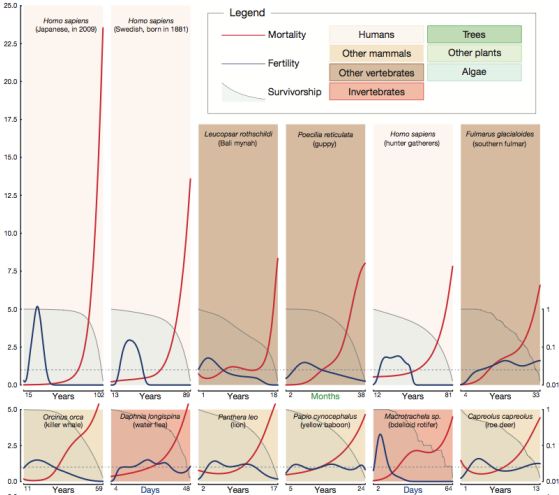
Maladaptation in age-structured populations

Evolution of aging



Maladaptation in age-structured populations

Evolution of aging

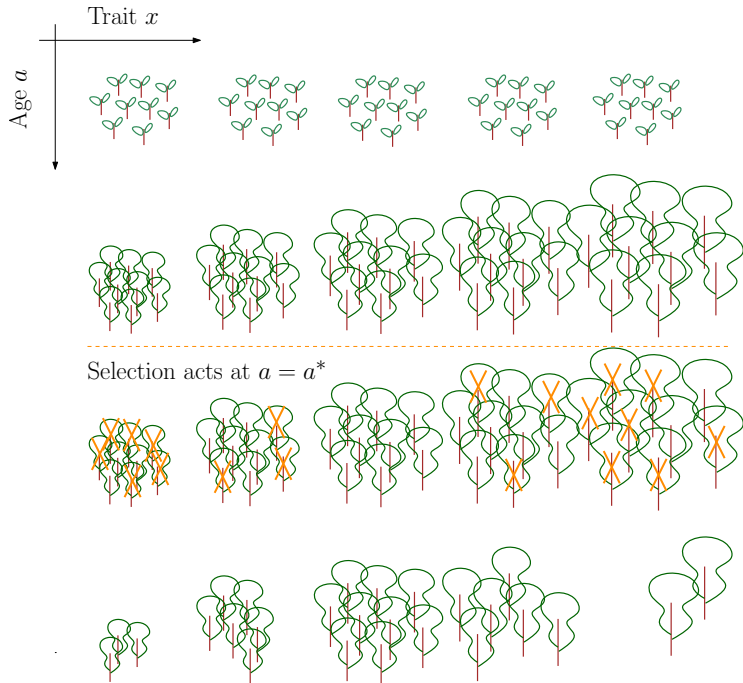


Patterns of mortality and fertility rates across species, Jones et al, Nature 2014

Age-dependent selection

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

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





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

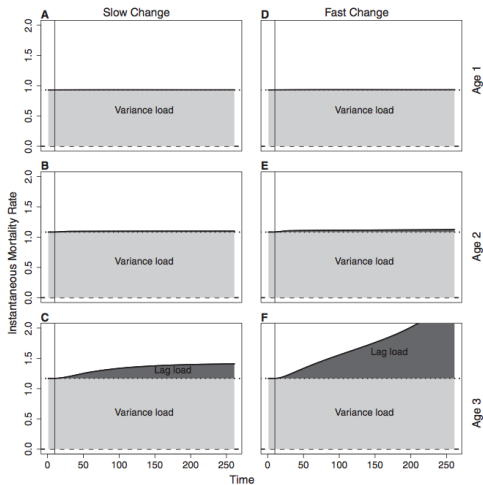
Olivier Cotto¹ and Ophélie Ronce^{1,2}

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



A quantitative genetics model of aging populations

(adapted from Cotto and Ronce 2014 to a continuous 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^*** .

A quantitative genetics model of aging populations

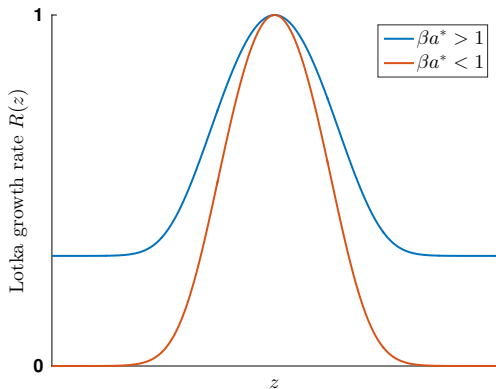
(adapted from Cotto and Ronce 2014 to a continuous setting)

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

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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^{**} :

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

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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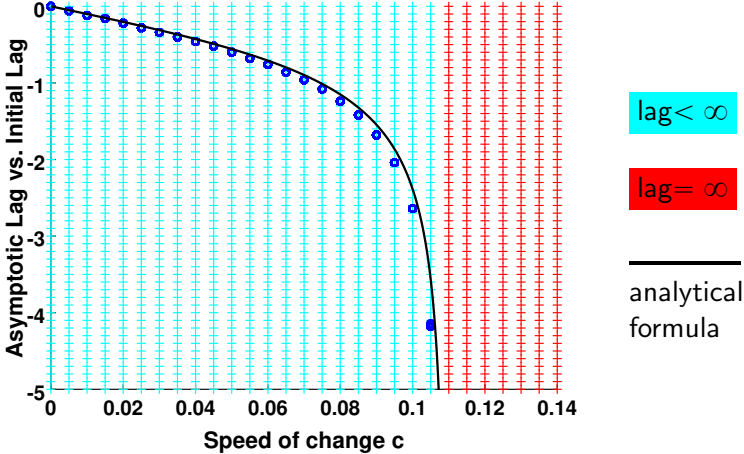
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Numerical vs. analytical results (asexual mode)

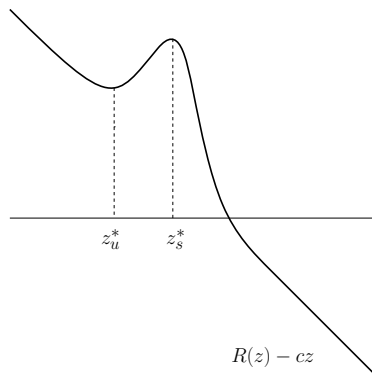


Severe maladaptation (sexual)

Similar analysis in the case of sexual reproduction.

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

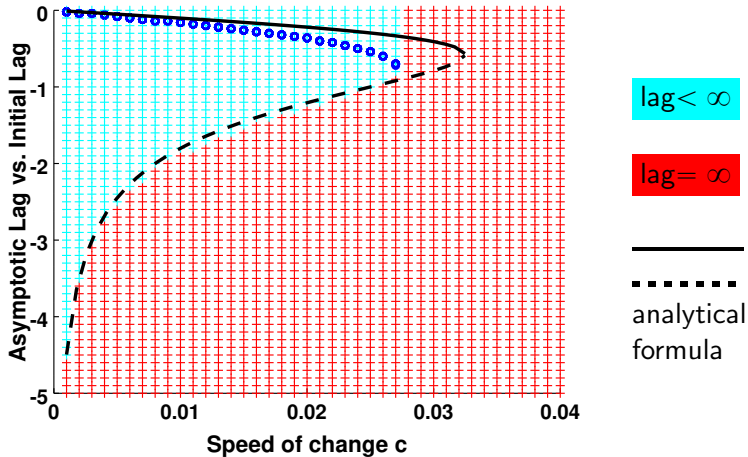
$$\frac{d}{dz}r(m(z)) = c$$

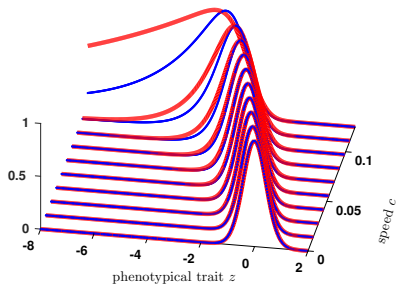


\iff critical point for the
modified fitness $r(m(z)) - cz$

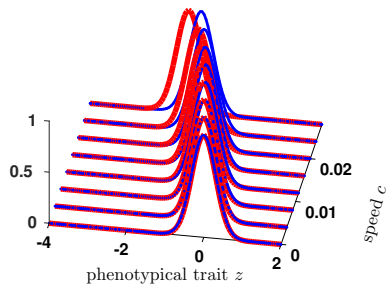
\implies **Bistability!**

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)