

Fisher's adaptive landscape across environments

Evolutionary rescue and resistance in asexual populations

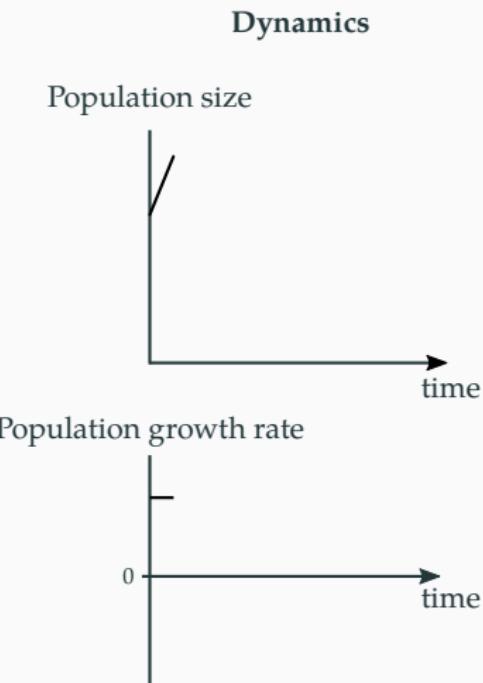
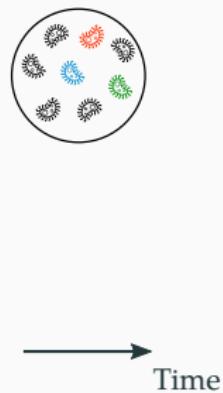
Yoann Anciaux

October 29, 2018

Bioinformatic research center Aarhus, Danemark.

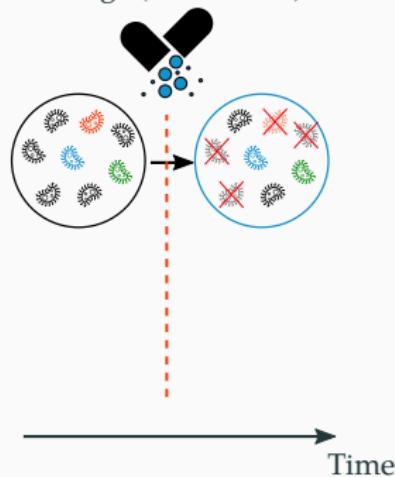


Eco-evolutionary dynamics



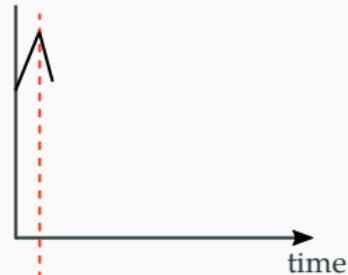
Eco-evolutionary dynamics

Stressing environmental change (Antibiotics)

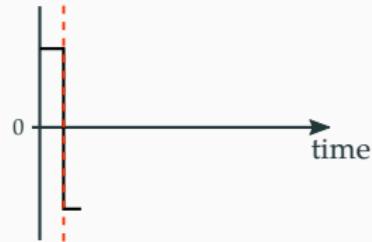


Dynamics

Population size



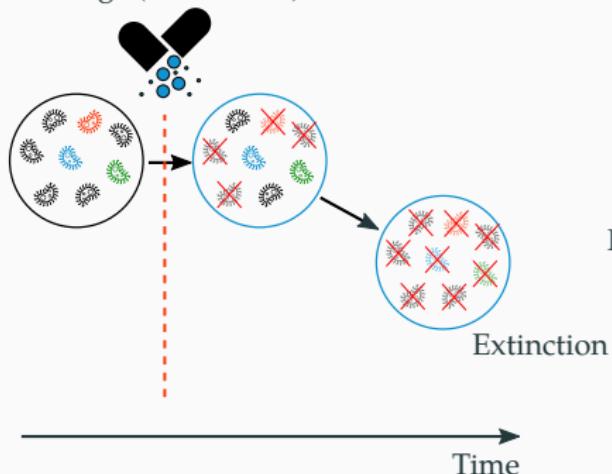
Population growth rate



Environmental change

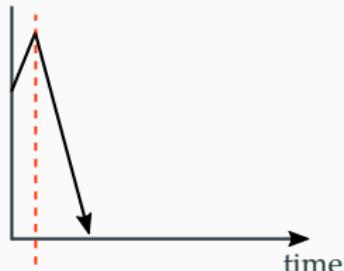
Eco-evolutionary dynamics

Stressing environmental change (Antibiotics)



Dynamics

Population size

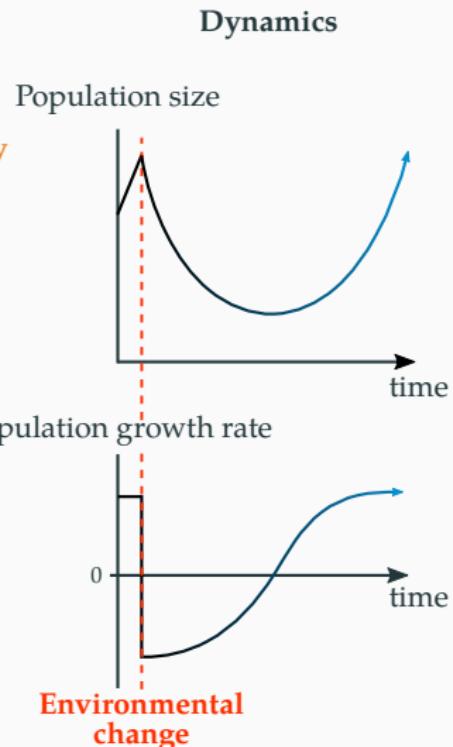
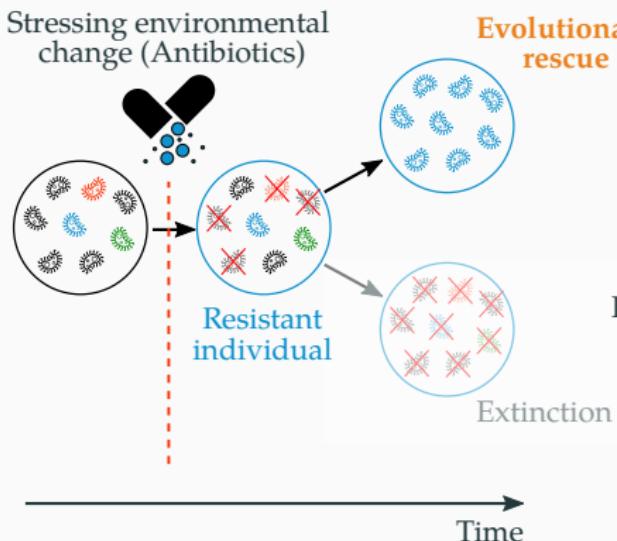


Population growth rate

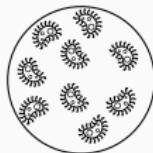


Environmental
change

Eco-evolutionary dynamics



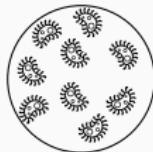
Genetic basis of evolutionary rescue



Genetic basis of
Evolutionary rescue

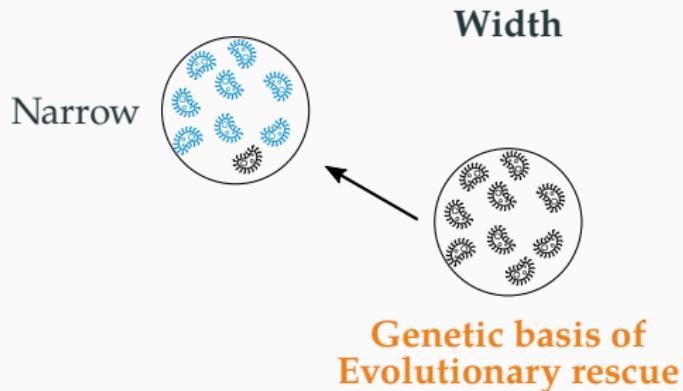
Genetic basis of evolutionary rescue

Width

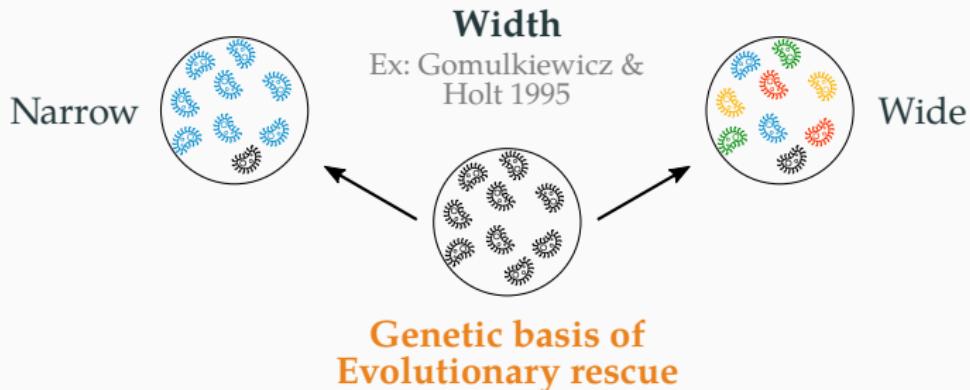


Genetic basis of
Evolutionary rescue

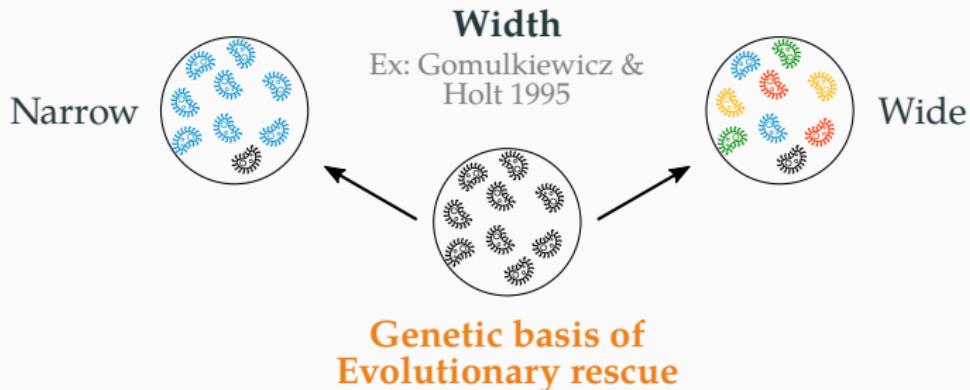
Genetic basis of evolutionary rescue



Genetic basis of evolutionary rescue

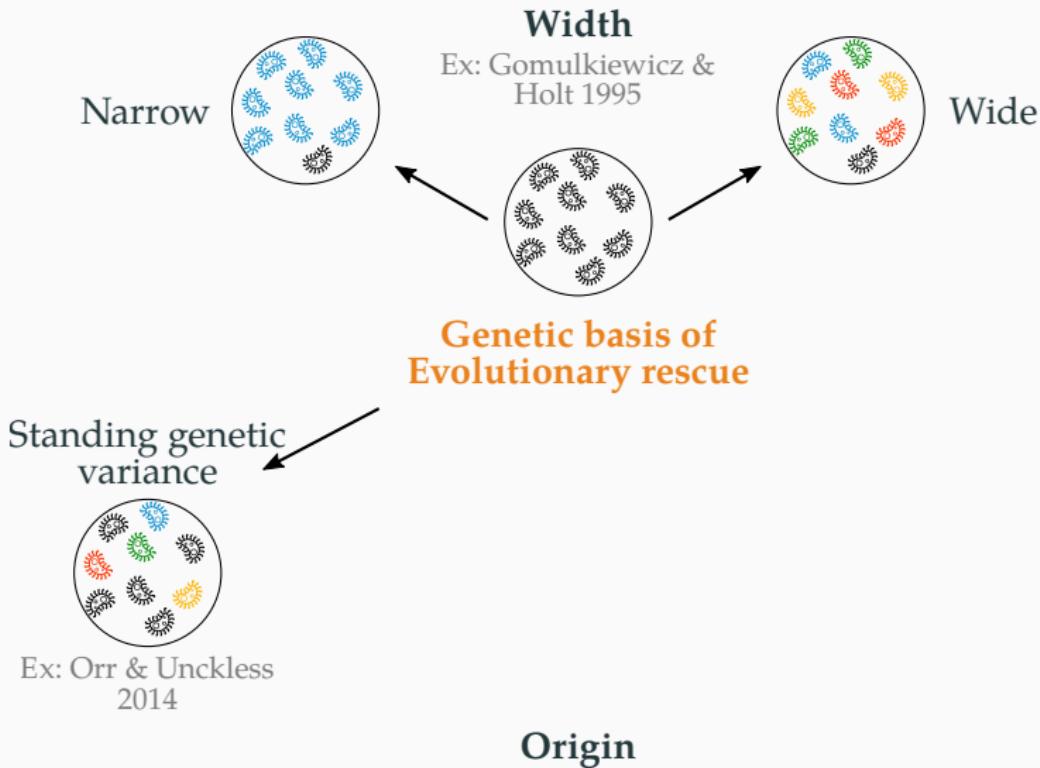


Genetic basis of evolutionary rescue

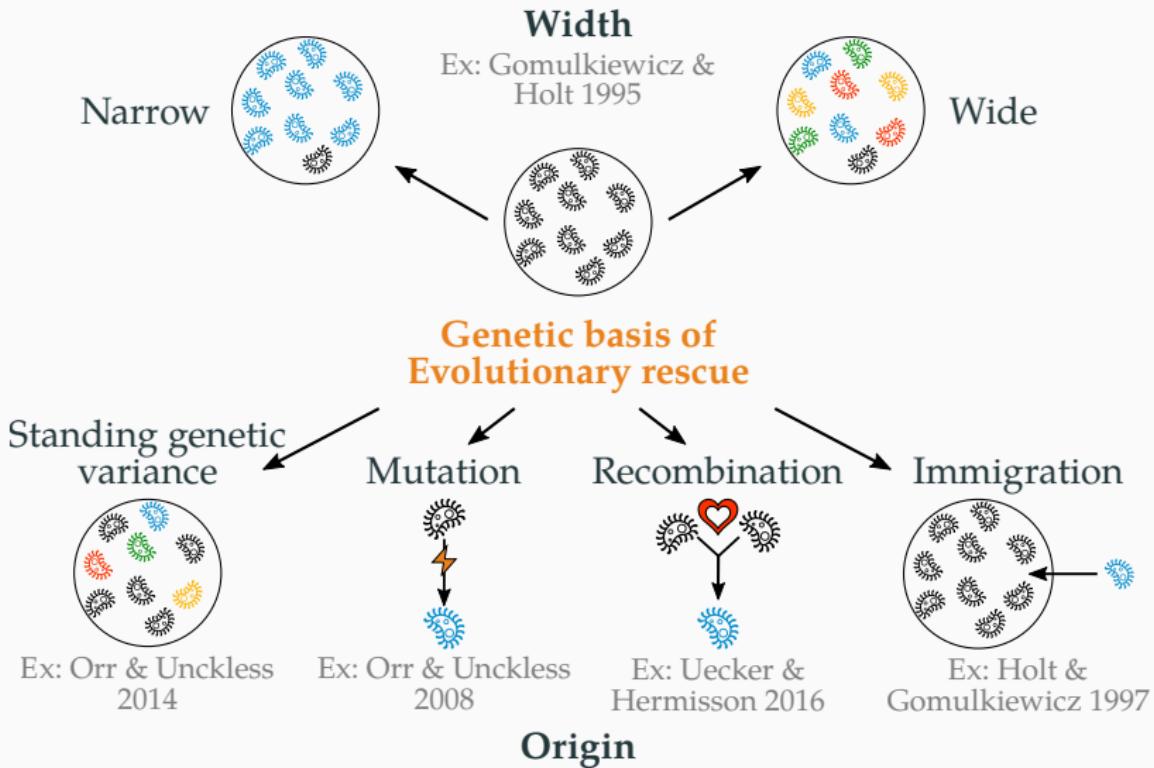


Origin

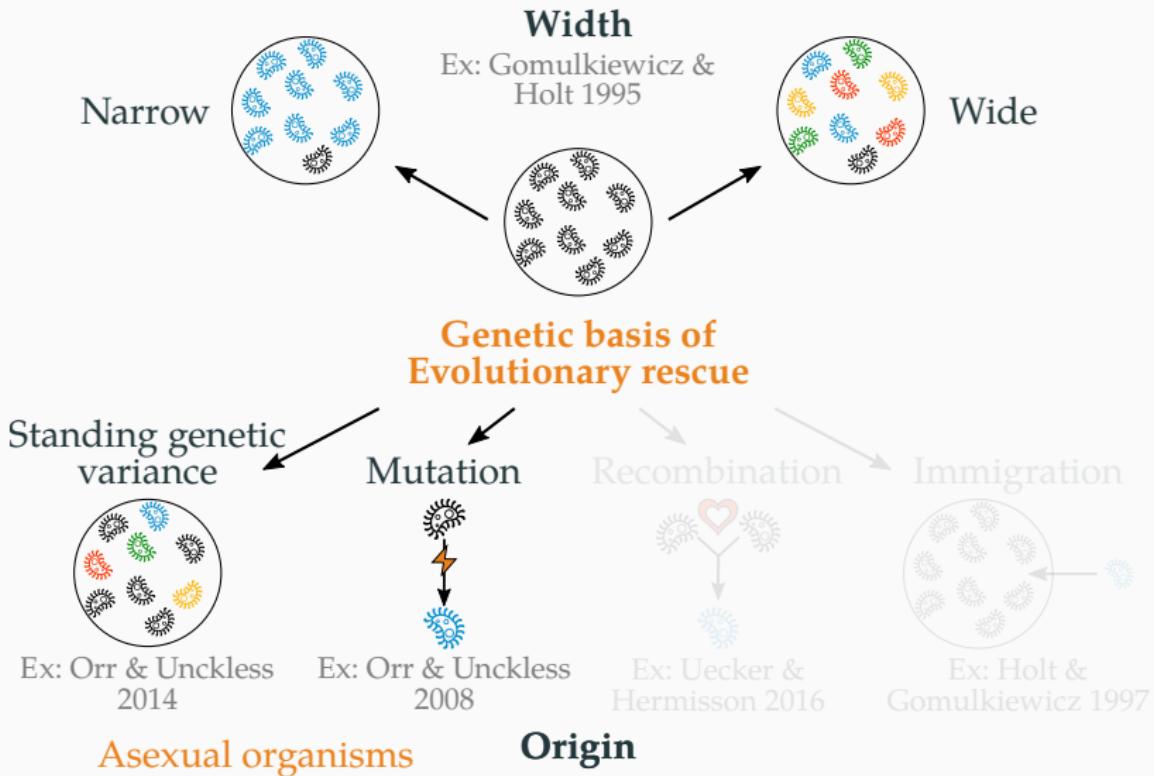
Genetic basis of evolutionary rescue



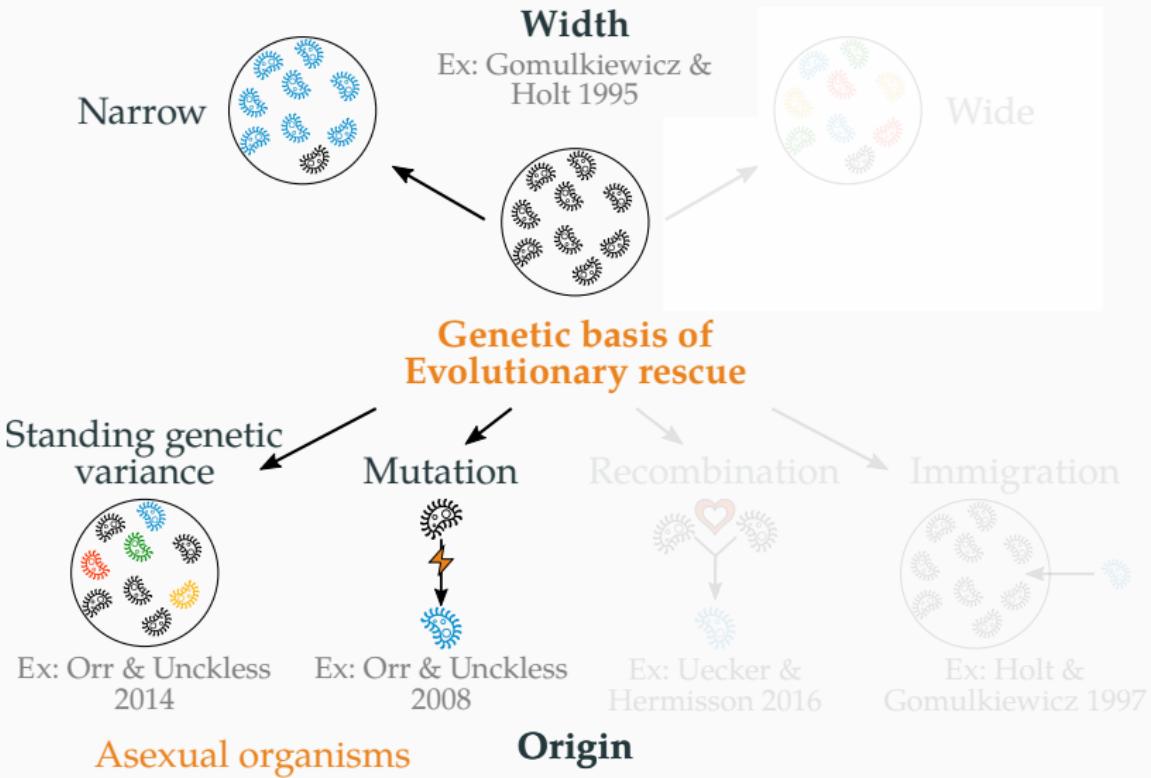
Genetic basis of evolutionary rescue



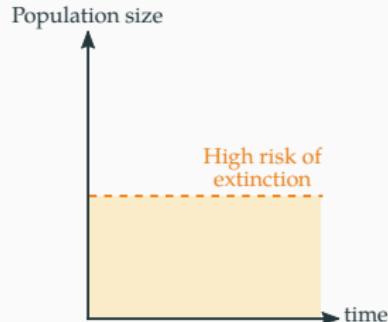
Genetic basis of evolutionary rescue



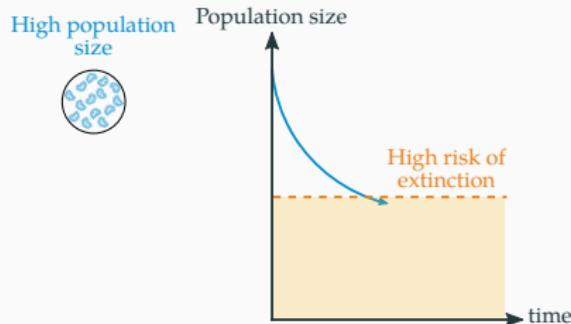
Genetic basis of evolutionary rescue



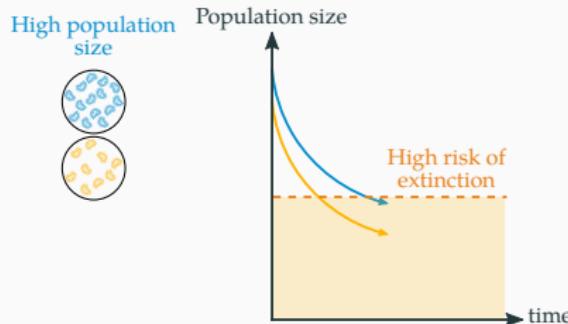
Model of evolutionary rescue from mutation



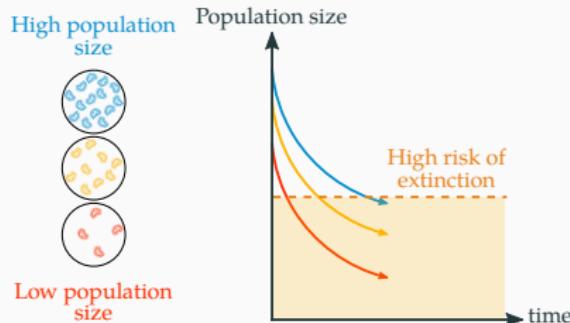
Model of evolutionary rescue from mutation



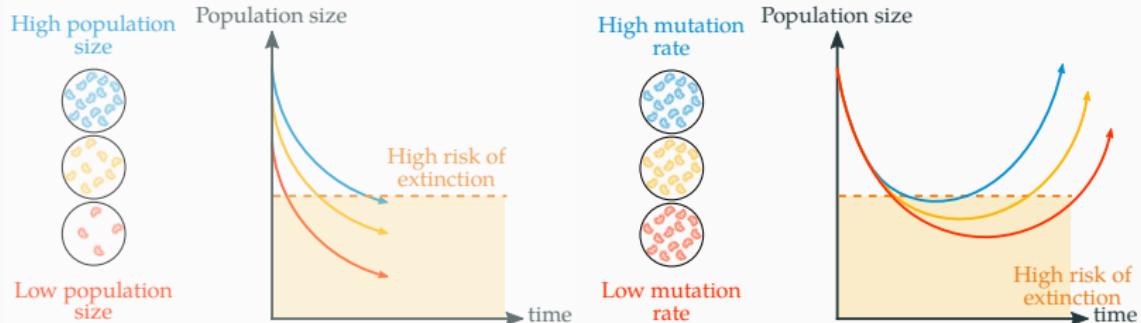
Model of evolutionary rescue from mutation



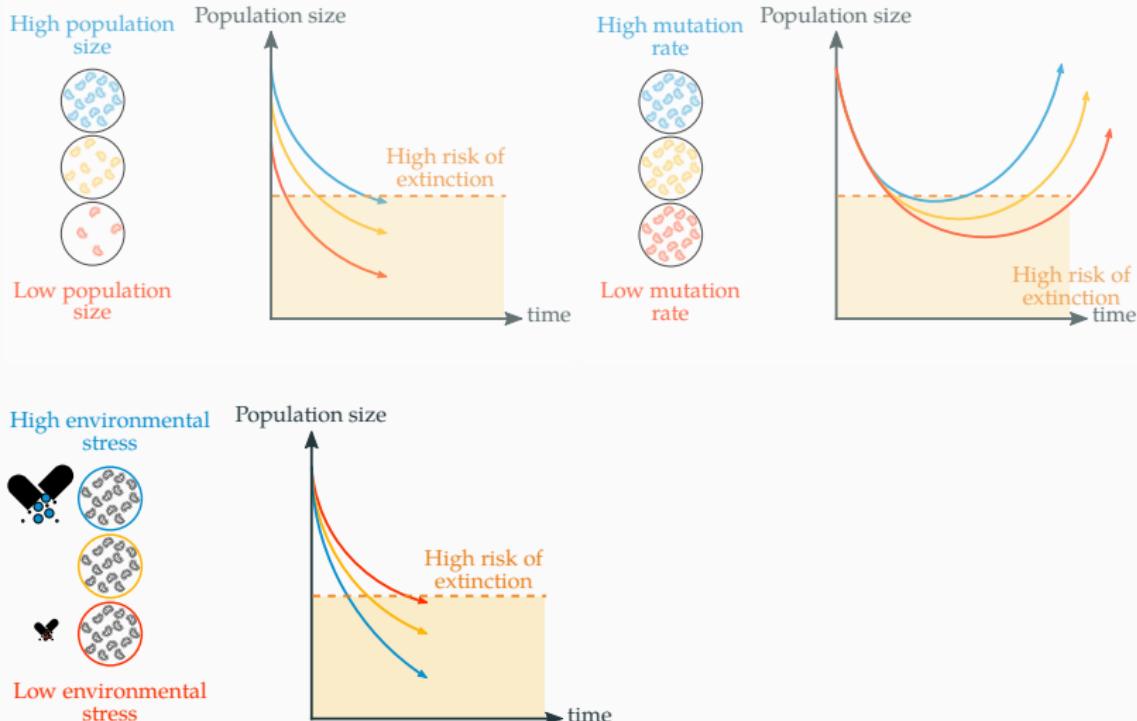
Model of evolutionary rescue from mutation



Model of evolutionary rescue from mutation



Model of evolutionary rescue from mutation



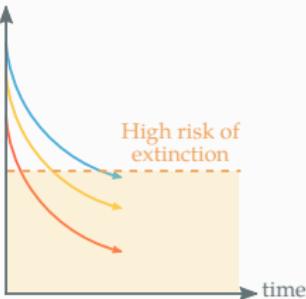
Model of evolutionary rescue from mutation

High population size



Low population size

Population size

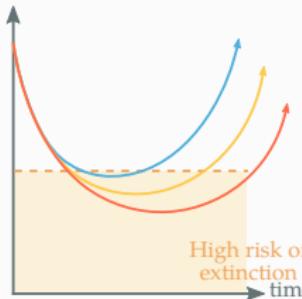


High mutation rate

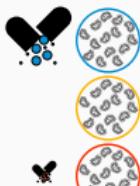


Low mutation rate

Population size

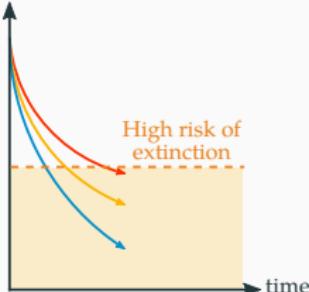


High environmental stress



Low environmental stress

Population size



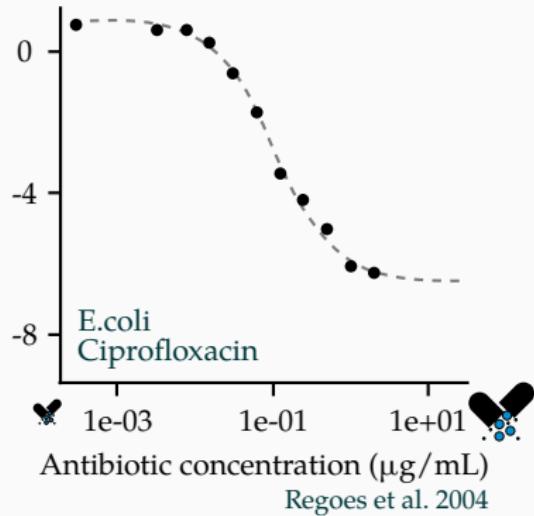
Effect of environmental change on demography

BUT

Fixed probability
of apparition of resistant mutations
across environments

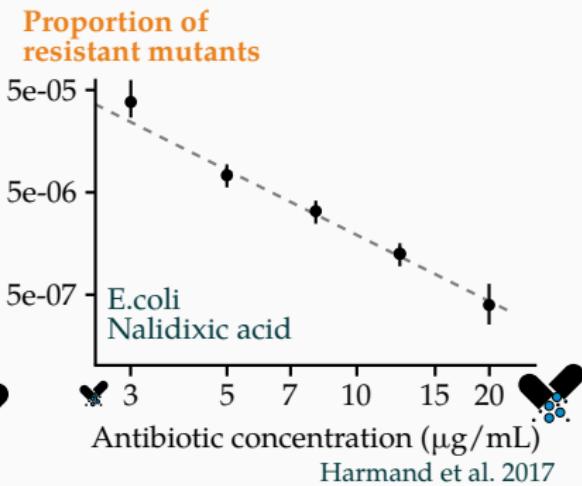
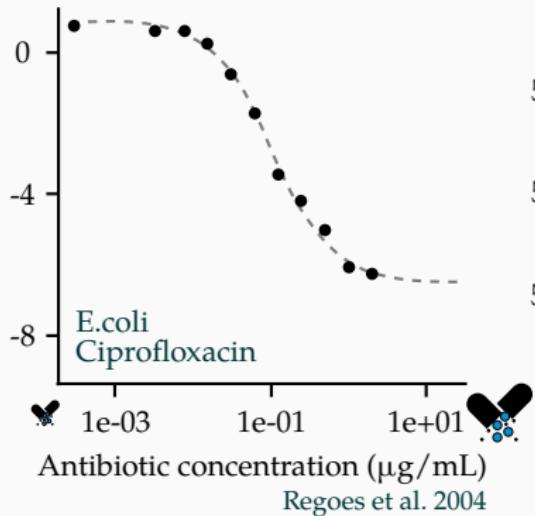
Model of evolutionary rescue from mutation

Maladaptation of the ancestor
= level of **environmental stress**



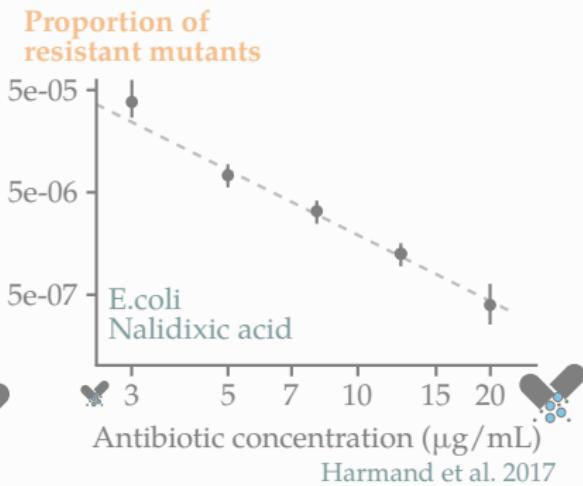
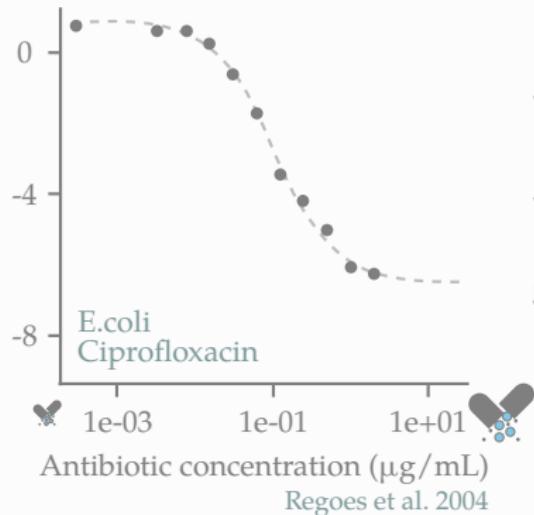
Model of evolutionary rescue from mutation

Maladaptation of the ancestor
= level of **environmental stress**



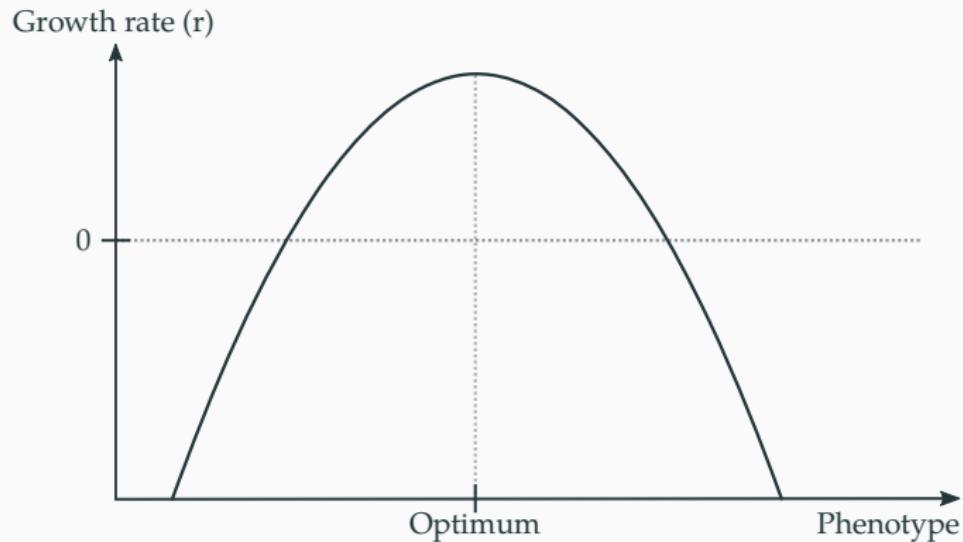
Model of evolutionary rescue from mutation

Maladaptation of the ancestor
= level of **environmental stress**



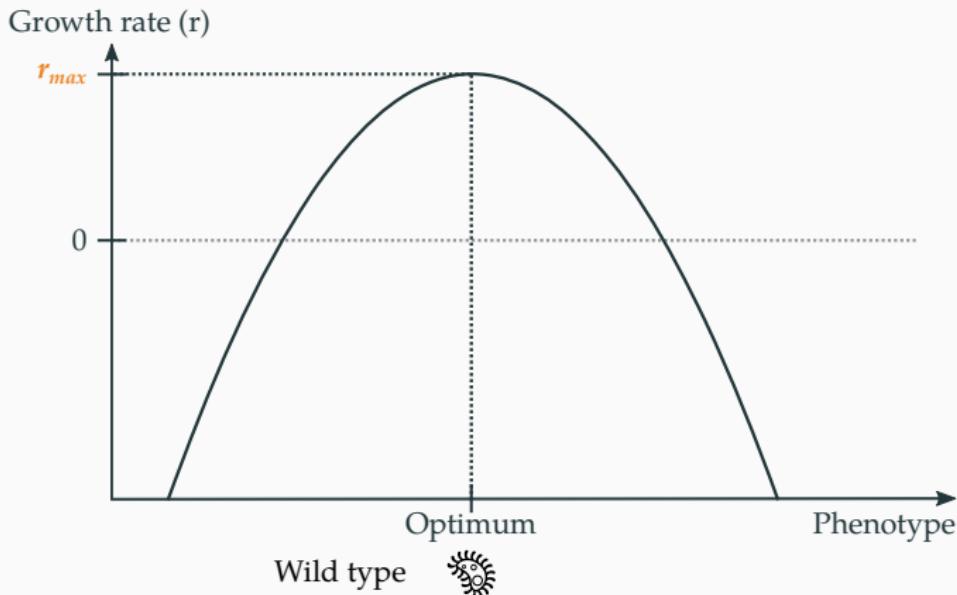
Derive ER models for asexual organisms integrating a **dependence between the environmental and the genetic contexts**

Fisher's Geometric Model



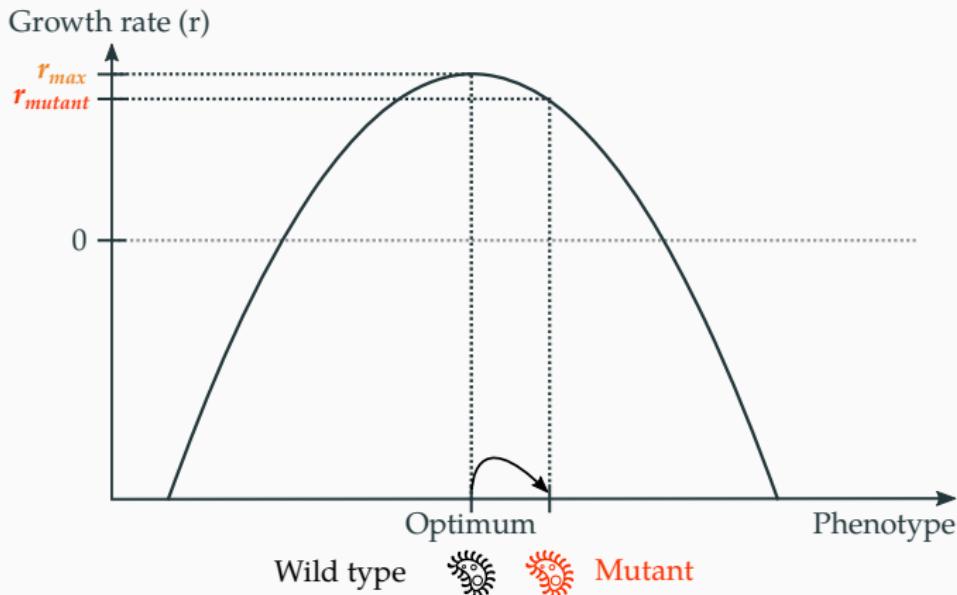
Fisher's Geometric Model

r_{max} : Maximal growth rate reachable in an environment.



Fisher's Geometric Model

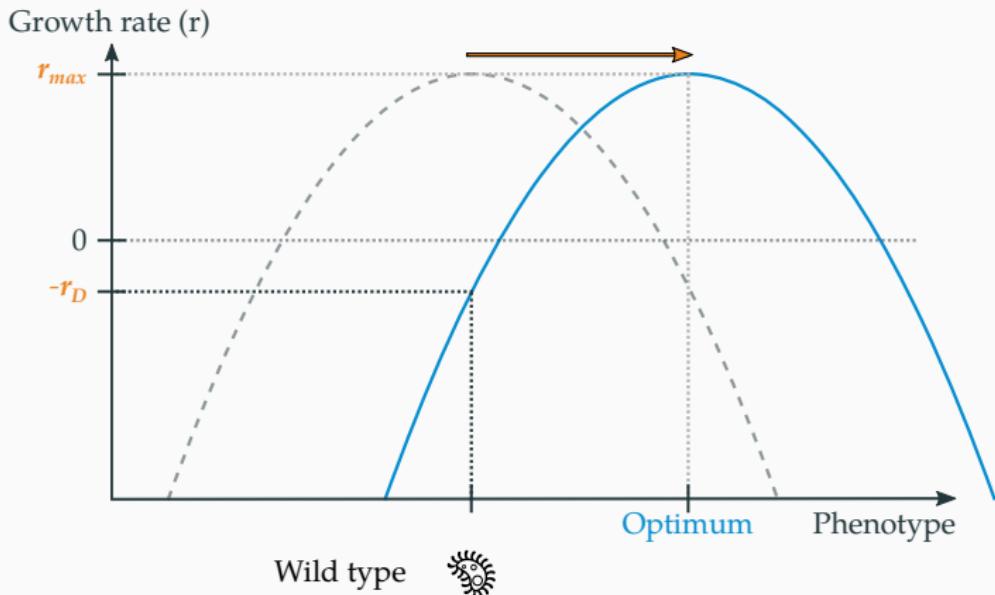
r_{max} : Maximal growth rate reachable in an environment.



Fisher's Geometric Model

r_{max} : Maximal growth rate reachable in an environment.

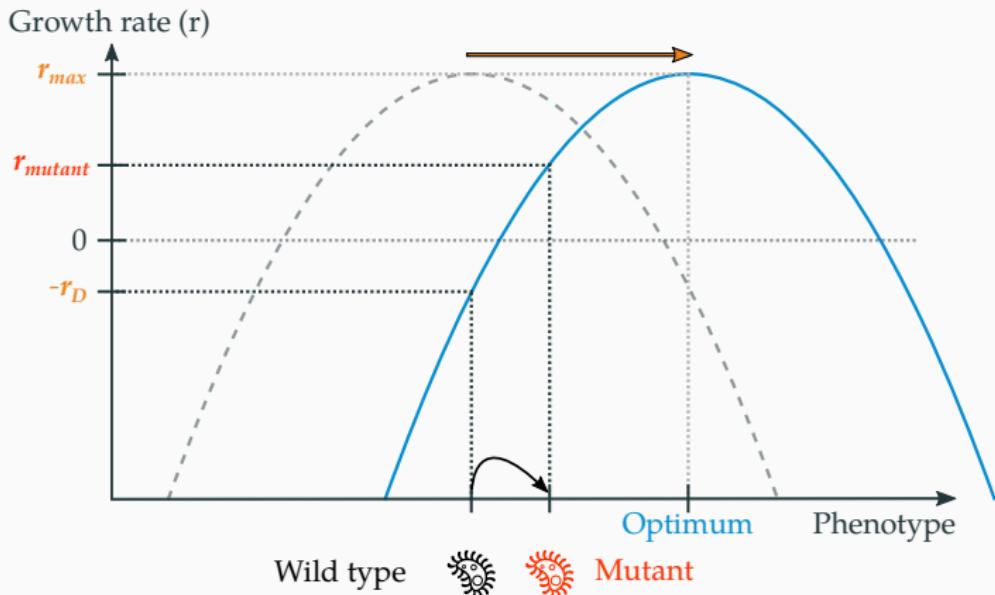
r_D : Decay rate of the wild type in the stressing environment.



Fisher's Geometric Model

r_{max} : Maximal growth rate reachable in an environment.

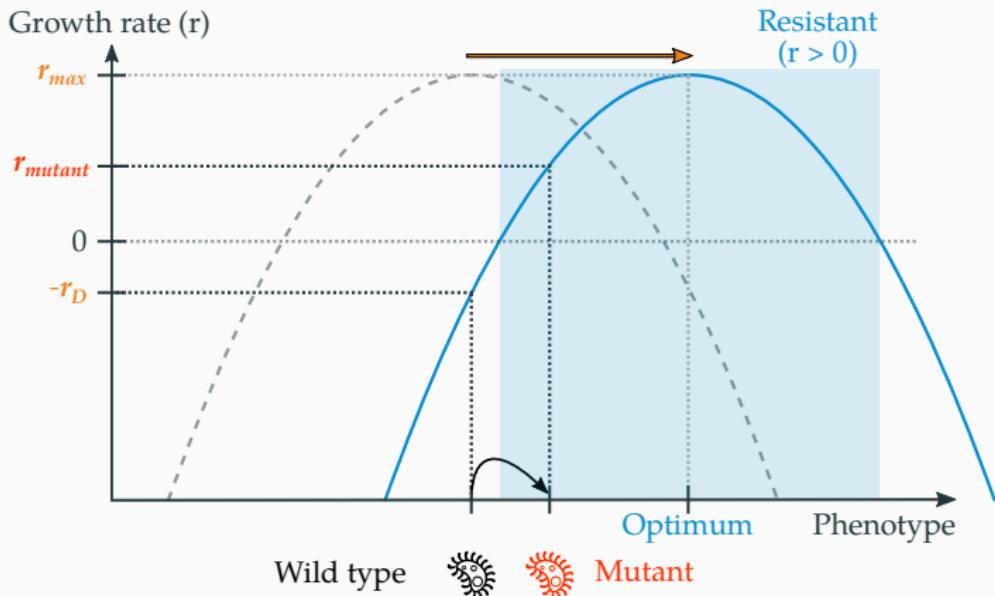
r_D : Decay rate of the wild type in the stressing environment.



Fisher's Geometric Model

r_{max} : Maximal growth rate reachable in an environment.

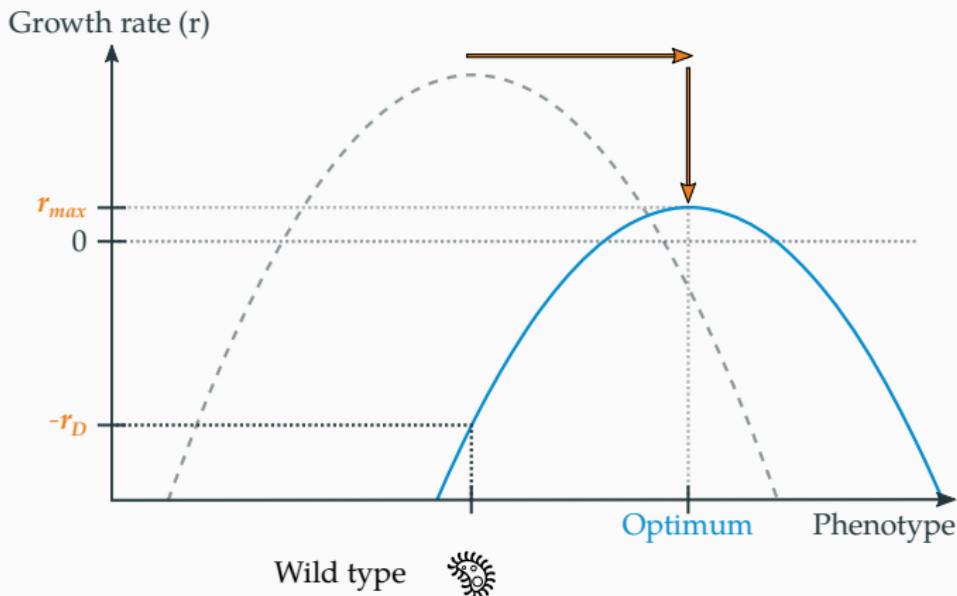
r_D : Decay rate of the wild type in the stressing environment.



Fisher's Geometric Model

r_{max} : Maximal growth rate reachable in an environment.

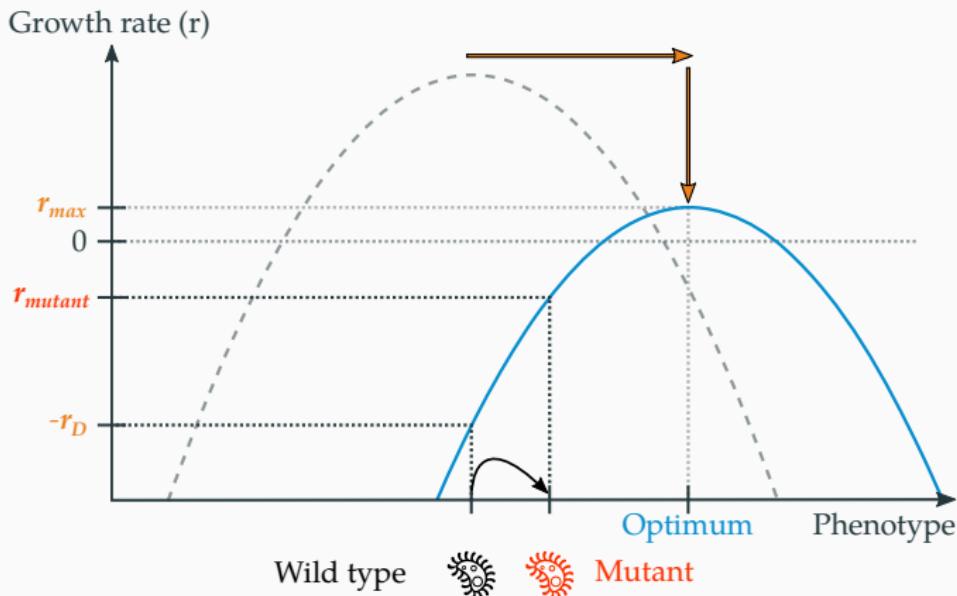
r_D : Decay rate of the wild type in the stressing environment.



Fisher's Geometric Model

r_{max} : Maximal growth rate reachable in an environment.

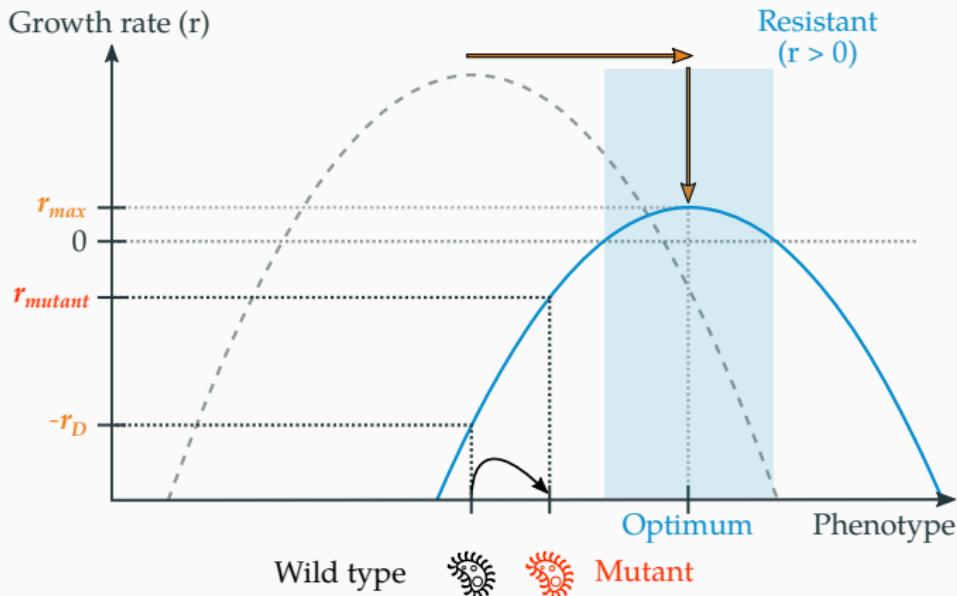
r_D : Decay rate of the wild type in the stressing environment.



Fisher's Geometric Model

r_{max} : Maximal growth rate reachable in an environment.

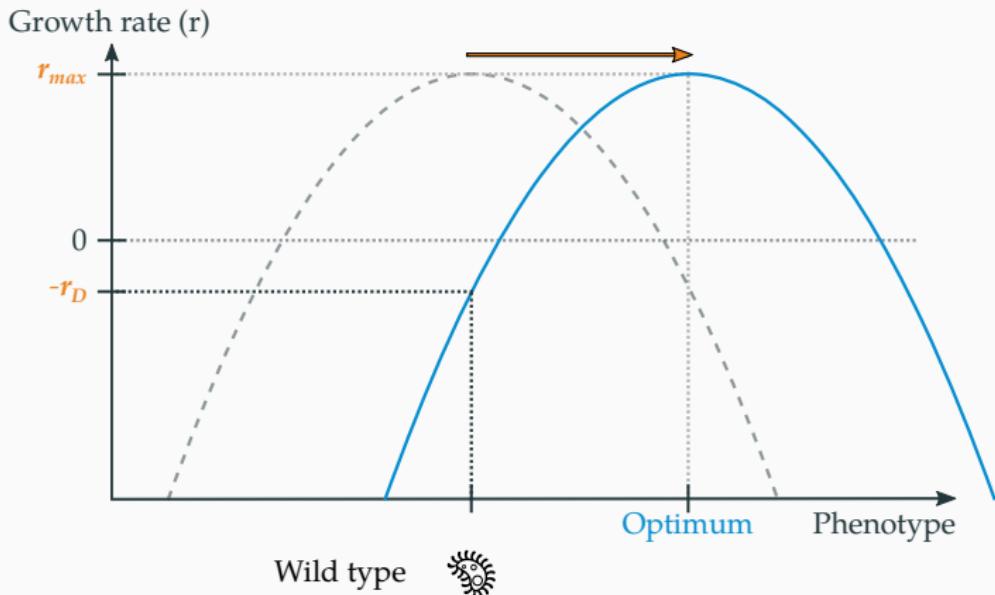
r_D : Decay rate of the wild type in the stressing environment.



Fisher's Geometric Model

r_{max} : Maximal growth rate reachable in an environment.

r_D : Decay rate of the wild type in the stressing environment.

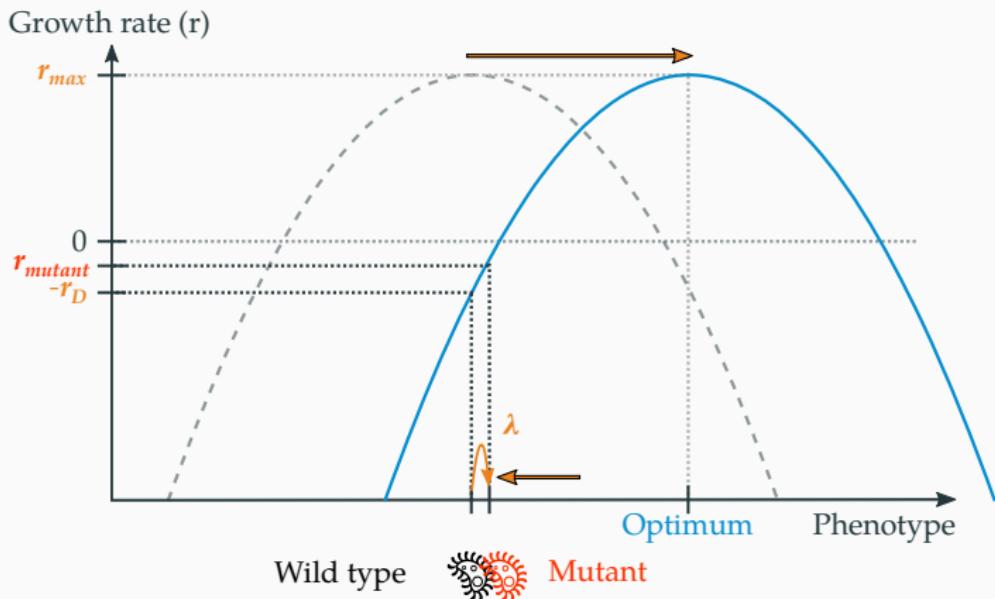


Fisher's Geometric Model

r_{max} : Maximal growth rate reachable in an environment.

r_D : Decay rate of the wild type in the stressing environment.

λ : Variance of mutation effects on phenotype

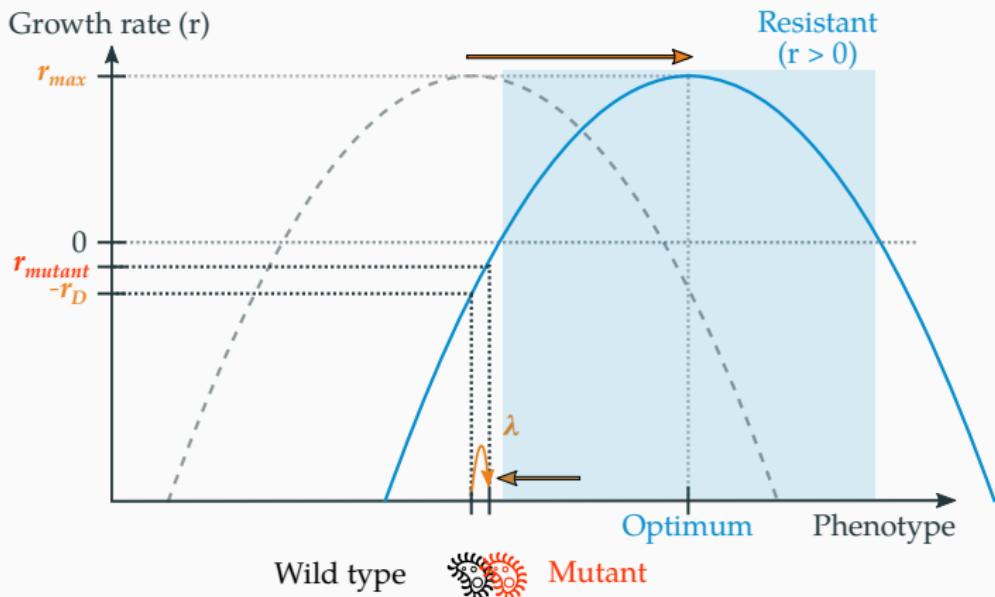


Fisher's Geometric Model

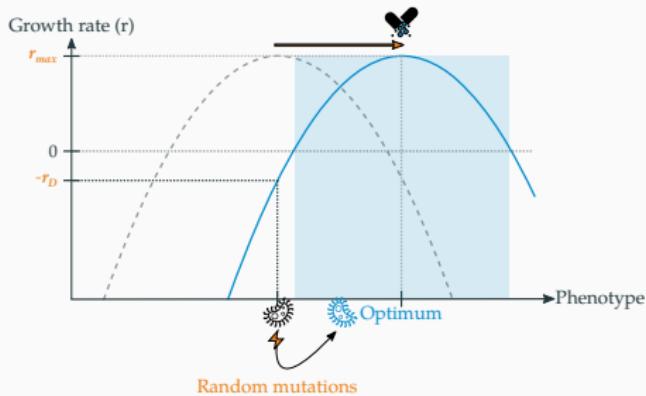
r_{max} : Maximal growth rate reachable in an environment.

r_D : Decay rate of the wild type in the stressing environment.

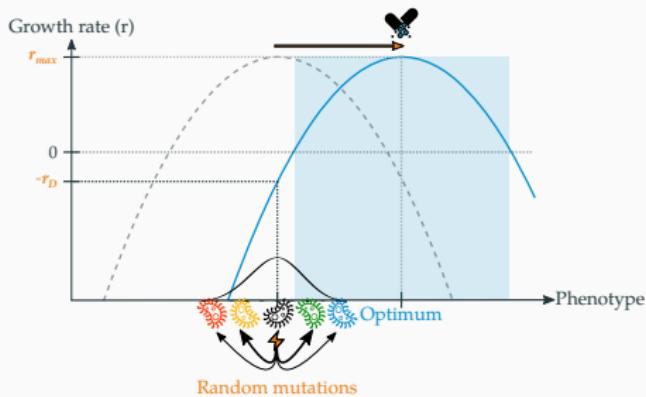
λ : Variance of mutation effects on phenotype



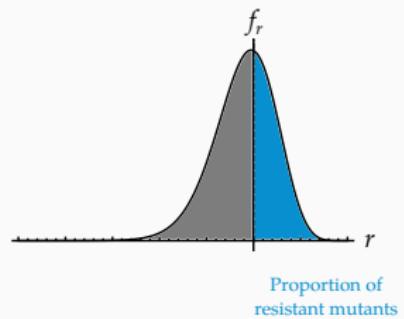
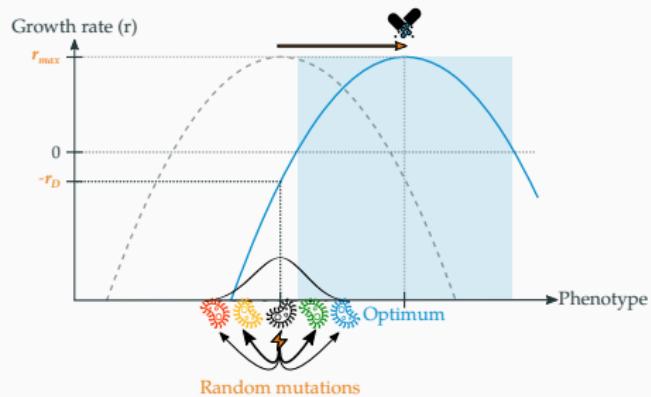
Fisher's Geometric Model



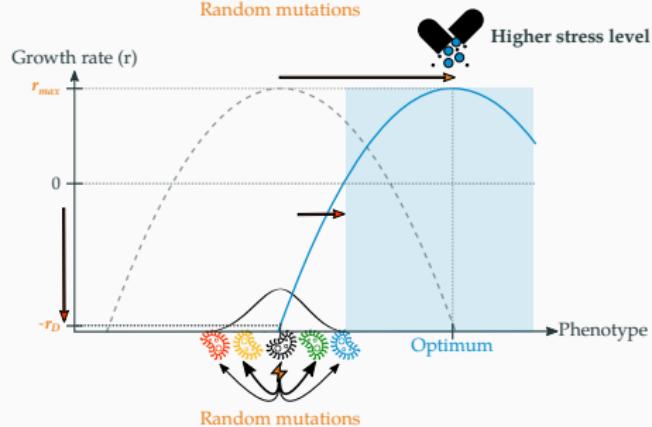
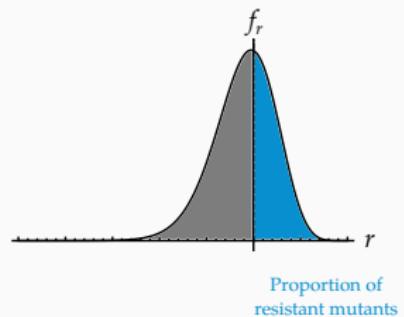
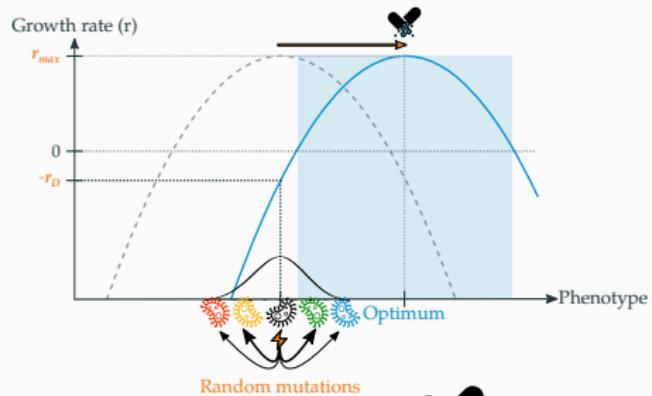
Fisher's Geometric Model



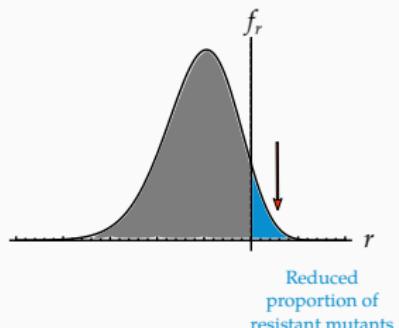
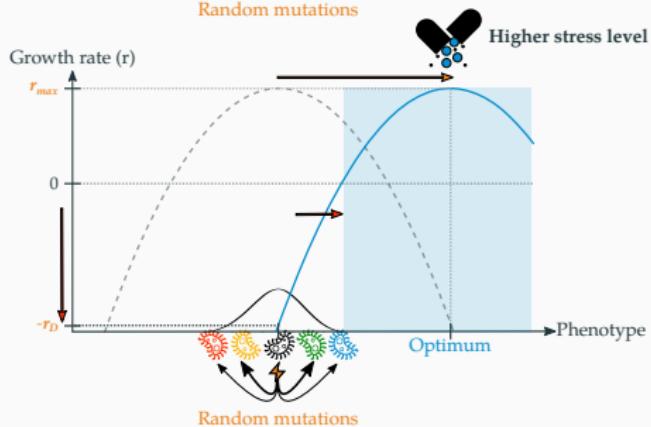
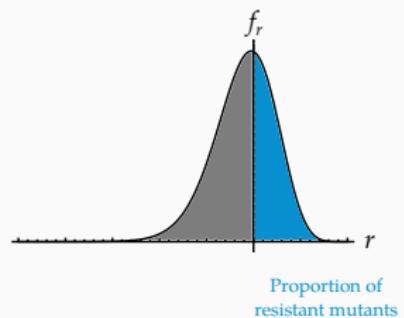
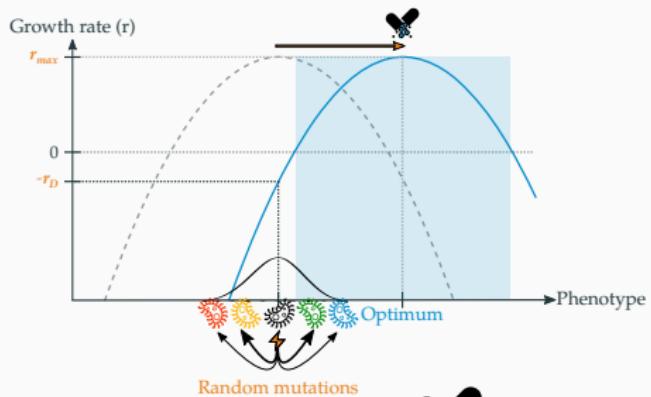
Fisher's Geometric Model



Fisher's Geometric Model

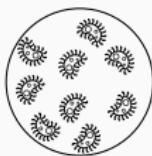


Fisher's Geometric Model



Mutation regimes

Rescue from a
narrow genetic
basis



Mutation regimes

Rescue from a
narrow genetic
basis



Mutation regimes

Rescue from a
narrow genetic
basis



Low mutation rate regime

Stochastic demography

Stochastic evolution

Prediction of evolutionary rescue probabilities

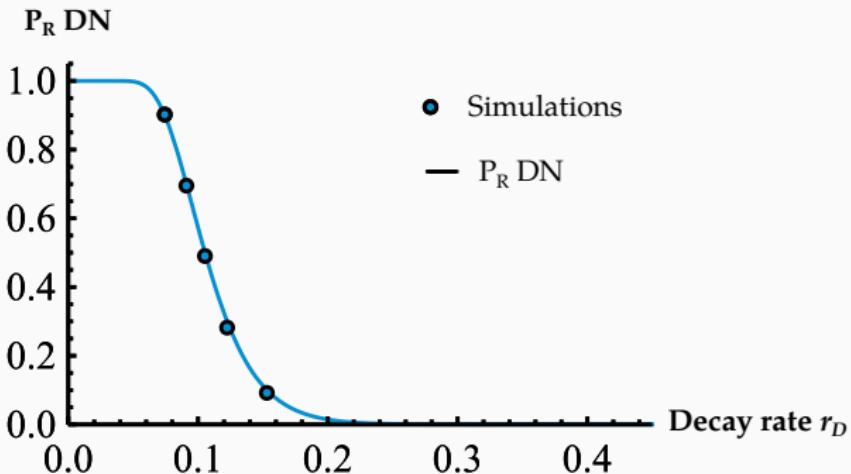
Probability of evolutionary rescue against stress

Exact numeric
solve

Probability of evolutionary rescue against stress

Exact numeric
solve

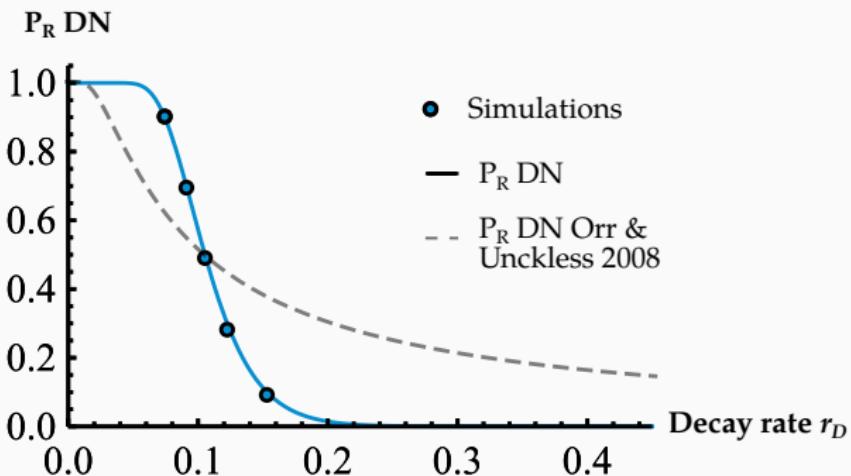
$$P_R \text{ DN} = f(U, r_D, r_{max}, \lambda, n)$$



Probability of evolutionary rescue against stress

Exact numeric
solve

$$P_R \text{ DN} = f(U, r_D, r_{max}, \lambda, n)$$



Probability of evolutionary rescue against stress

Exact numeric
solve

Weak mutations effects
approximation

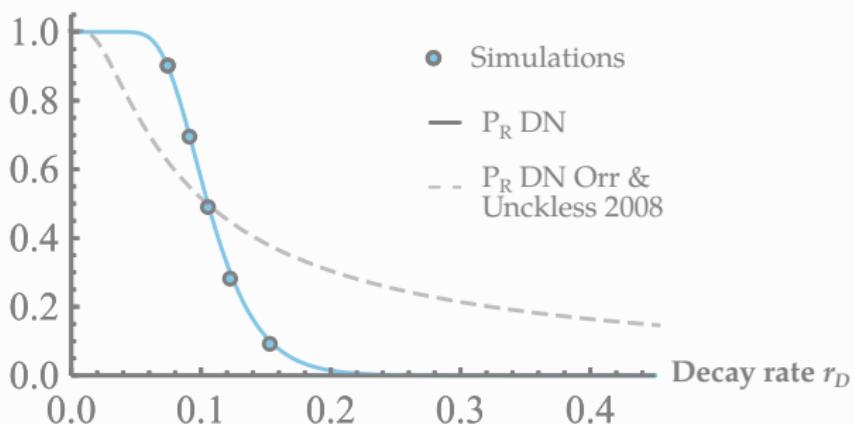
$$\lambda \ll r_{max}$$

$$P_R \text{ DN} = f(U, r_D, r_{max}, \lambda, n)$$



effects of dimension n
vanish

$P_R \text{ DN}$



Probability of evolutionary rescue against stress

Exact numeric
solve

Approximated analytical
closed form

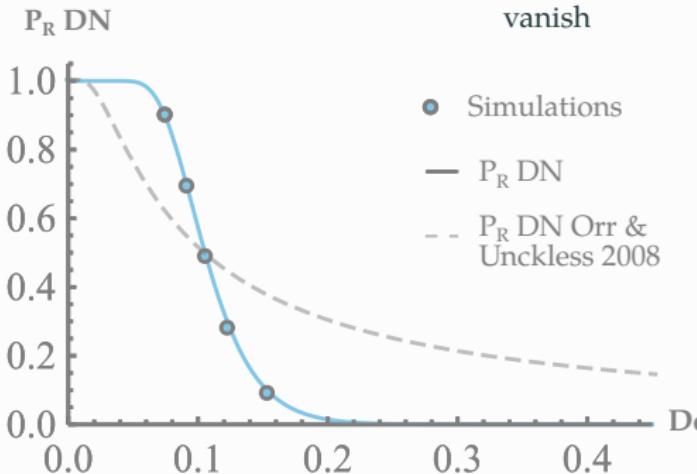
Weak mutations effects
approximation

$$\lambda \ll r_{max}$$

$$P_R \text{ DN} = f(U, r_D, r_{max}, \lambda, n)$$

$$P_R \text{ DN} = f(U, \alpha)$$

effects of dimension n
vanish



$$\alpha \approx \frac{r_D^2}{4 r_{max} \lambda}$$

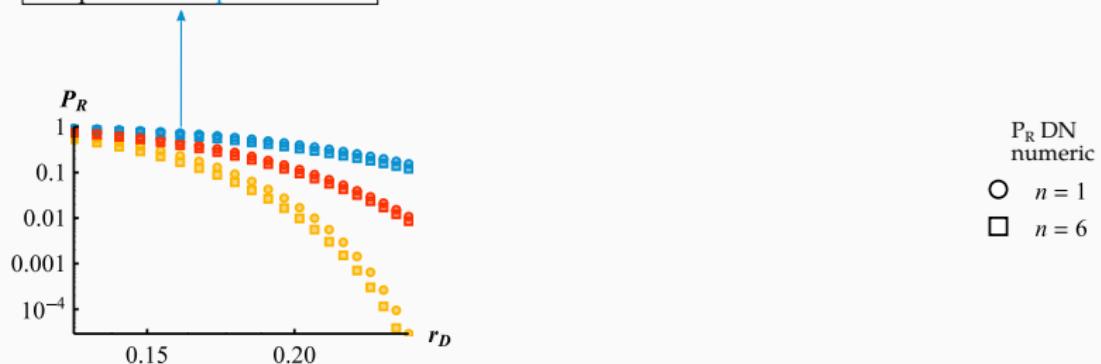
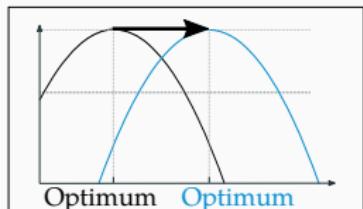
The effective stress level

The effective stress level (α)



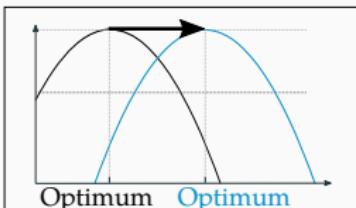
The effective stress level (α)

Change in r_D

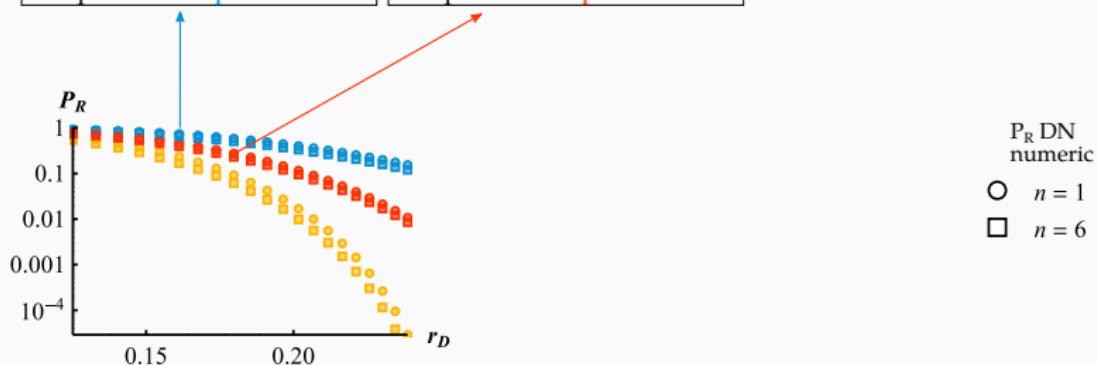
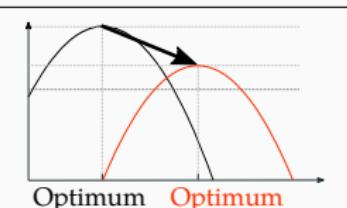


The effective stress level (α)

Change in r_D

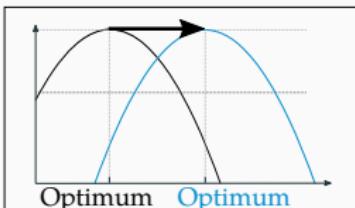


Change in r_D & r_{max}

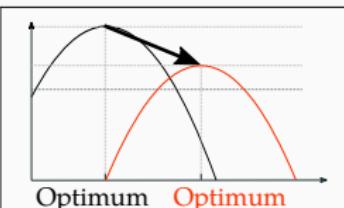


The effective stress level (α)

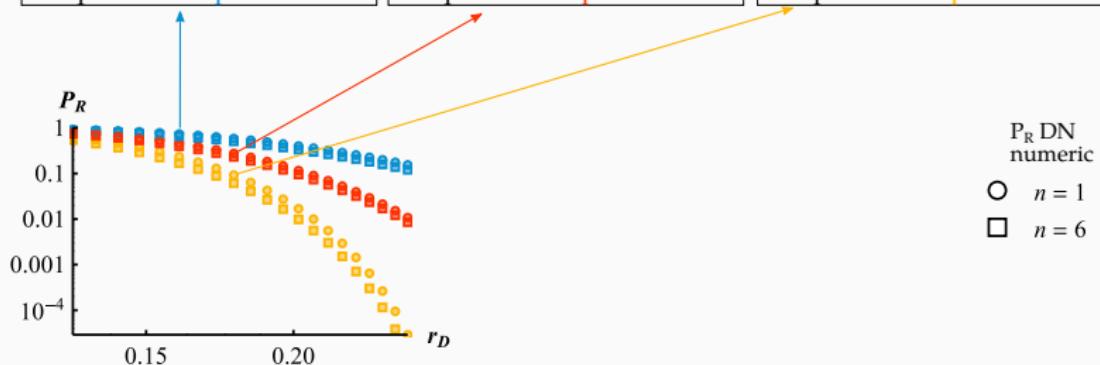
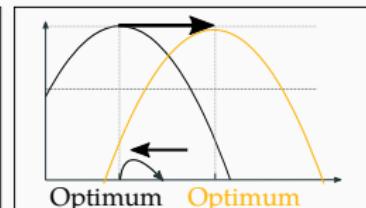
Change in r_D



Change in r_D & r_{max}

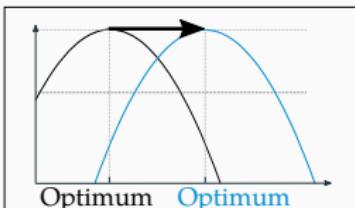


Change in r_D and λ

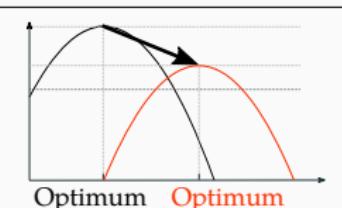


The effective stress level (α)

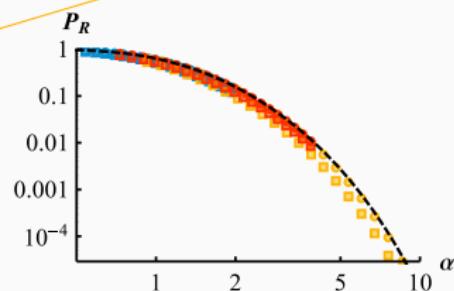
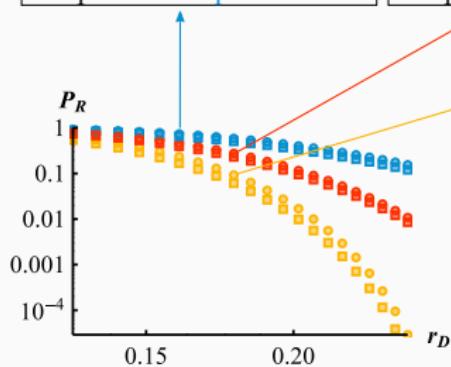
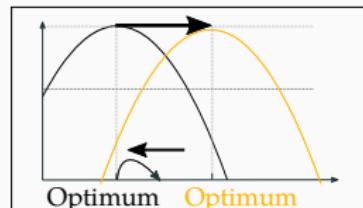
Change in r_D



Change in r_D & r_{max}



Change in r_D and λ

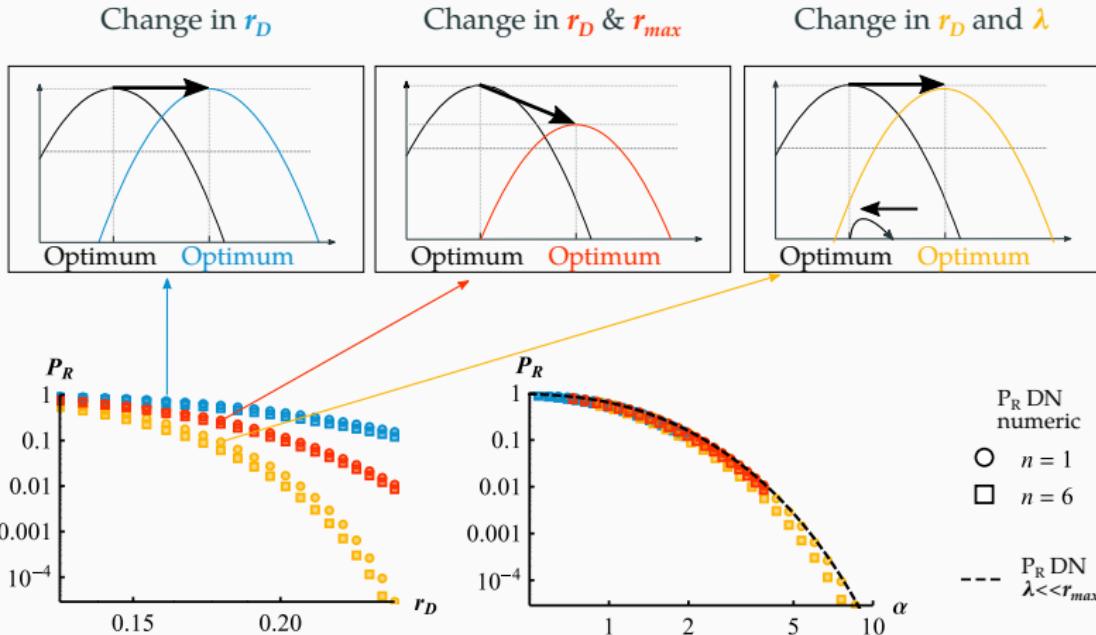


P_R DN
numeric

○ $n = 1$
□ $n = 6$

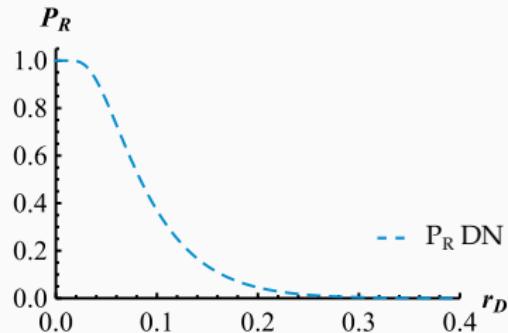
--- P_R DN
 $\lambda \ll r_{max}$

The effective stress level (α)

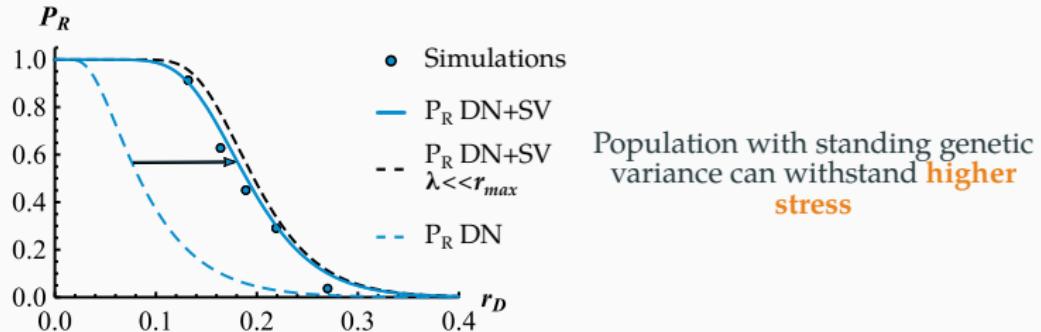


α summarizes the effect on the ER probability of **all the different scenarios** of stressing environmental change

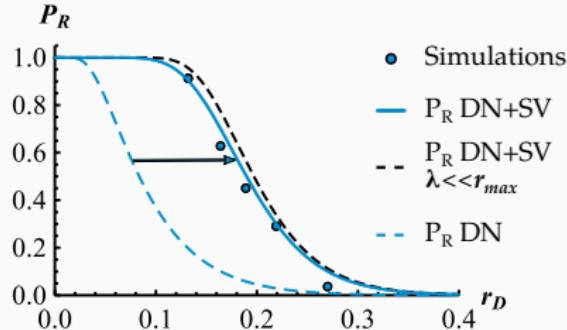
Proportion of ER from standing variance



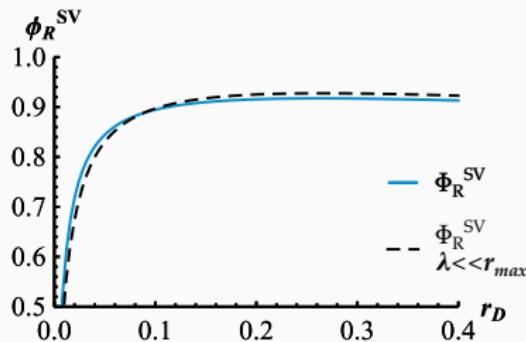
Proportion of ER from standing variance



Proportion of ER from standing variance

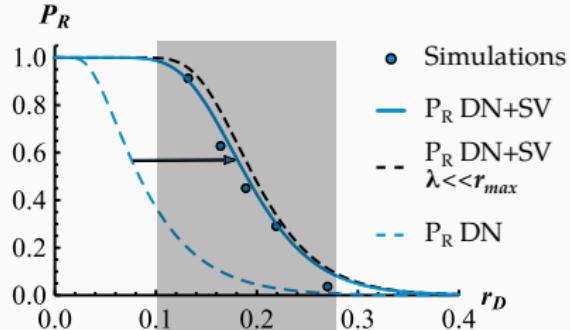


Population with standing genetic variance can withstand **higher stress**

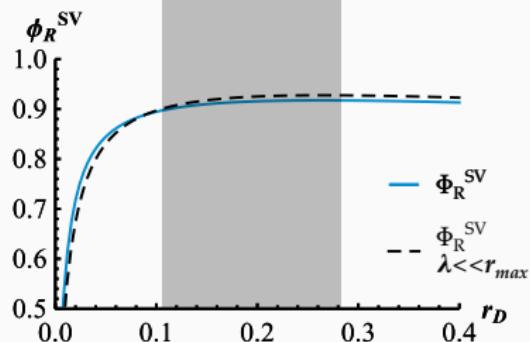


ER is **more likely** from SV than from DN mutations

Proportion of ER from standing variance



Population with standing genetic variance can withstand **higher stress**



ER is **more likely** from SV than from DN mutations

The **proportion of ER from standing variance** is roughly constant with r_D

Summary

Sharper drop of ER probability with **context-dependence**

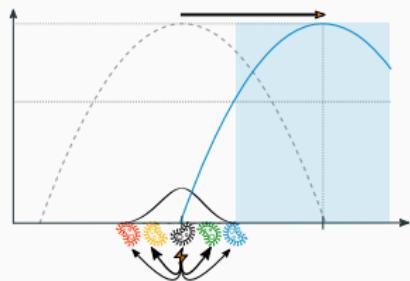
Multiple stress effects from the context dependence can be
summarized in α

Proportion of rescue from standing variance always **higher** than
from de novo mutations and **roughly stable with r_D**

Fitness accross environments and genotypes

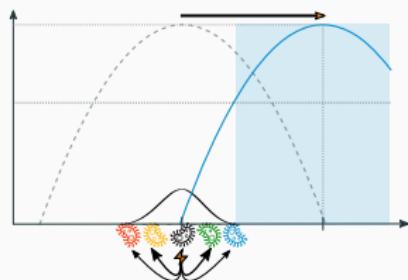
Landscape parametrization

Parametrized fitness landscape

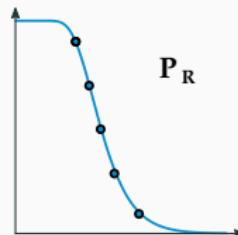


Landscape parametrization

Parametrized fitness landscape

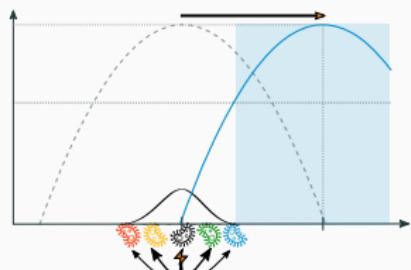


Quantitative predictions
on eco-evolutionary dynamics
across environments

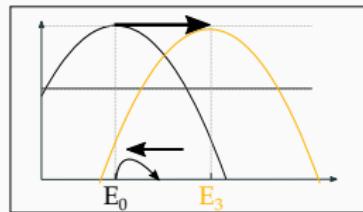
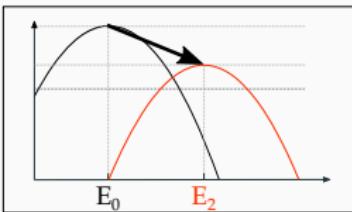
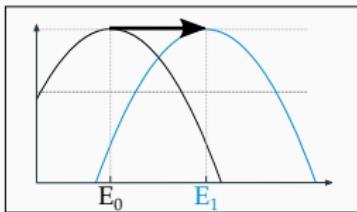
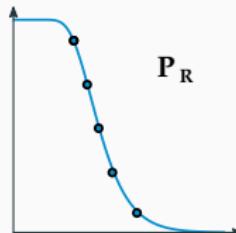


Landscape parametrization

Parametrized fitness landscape

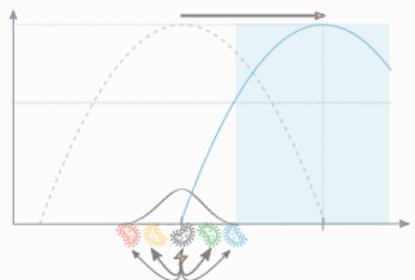


Quantitative predictions
on eco-evolutionary dynamics
across environments

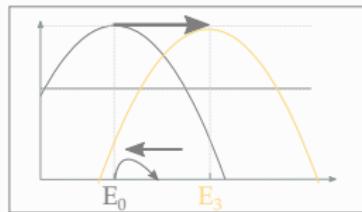
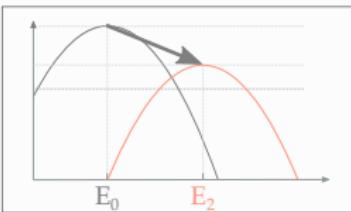
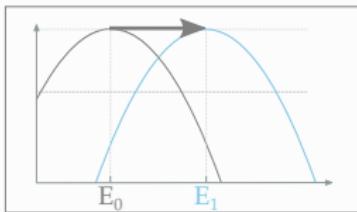
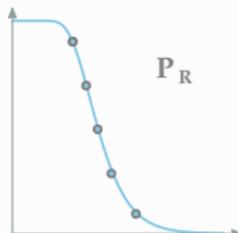


Landscape parametrization

Parametrized fitness landscape

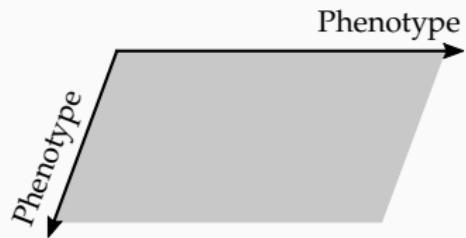


Quantitative predictions
on eco-evolutionary dynamics
across environments

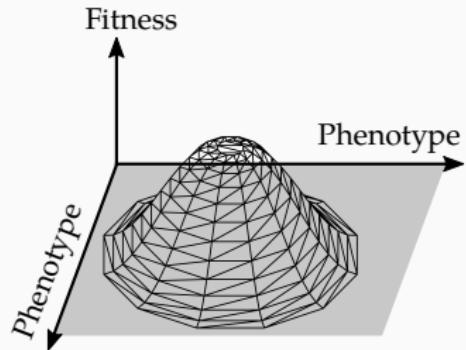


How to **parametrize** the landscape across environments ?
How to **predict fitness changes** across environments ?

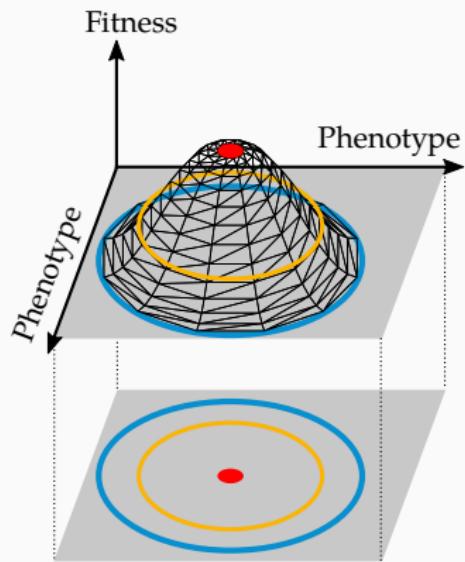
Landscape parametrization



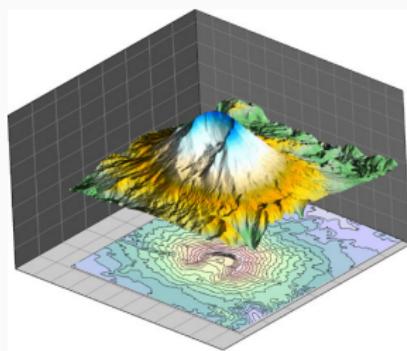
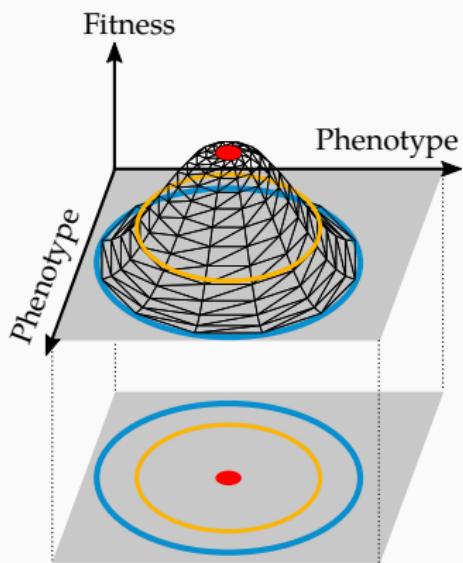
Landscape parametrization



Landscape parametrization



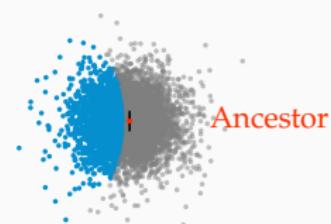
Landscape parametrization



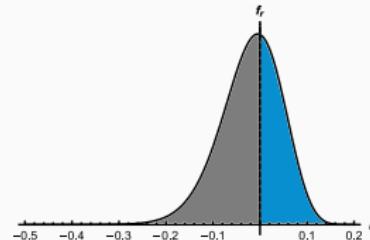
Landscape parametrization



Landscape parametrization

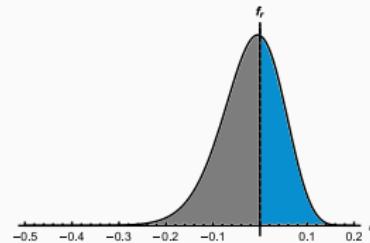
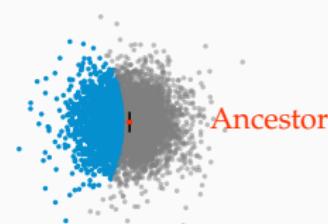


Ancestor



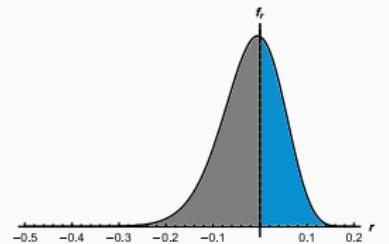
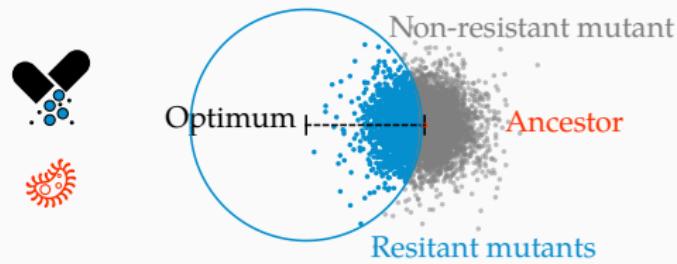
Distribution of fitness effects
(DFE)

Landscape parametrization

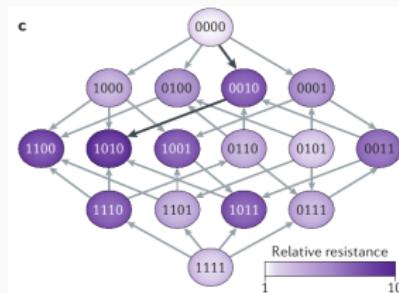
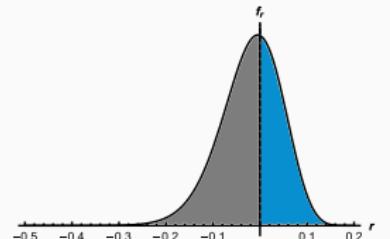
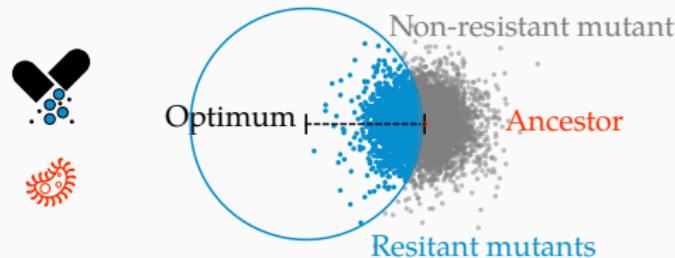


Distribution of fitness effects
(DFE)

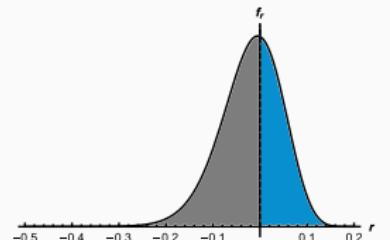
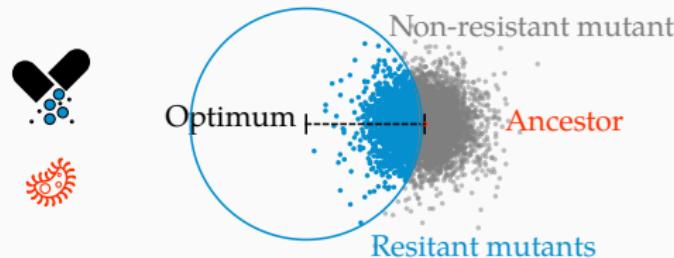
Landscape parametrization



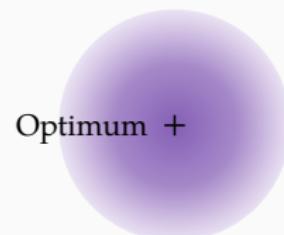
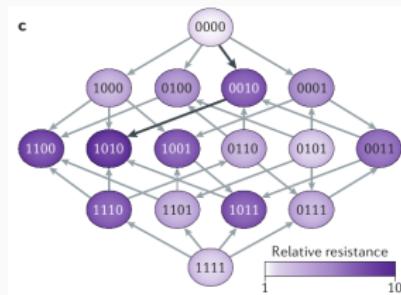
Landscape parametrization



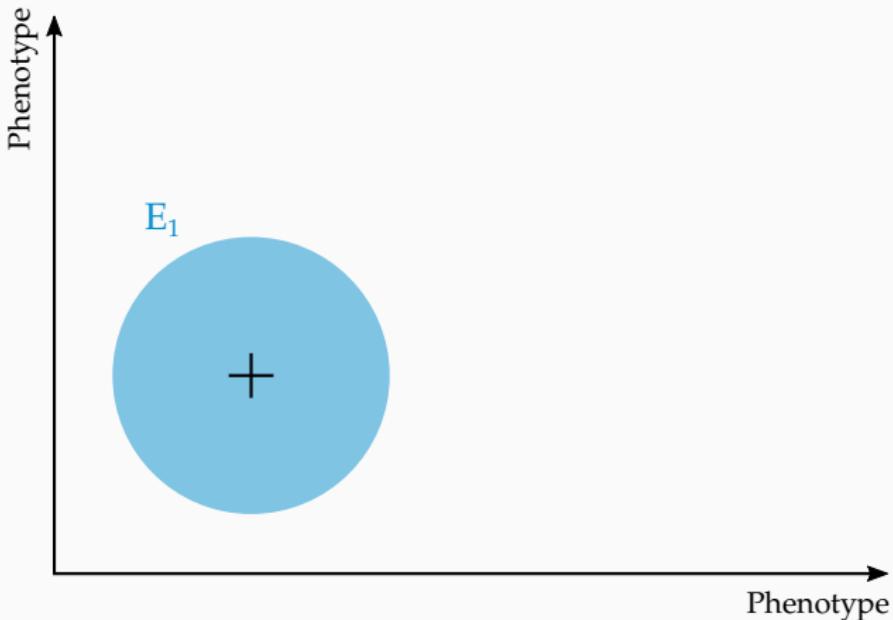
Landscape parametrization



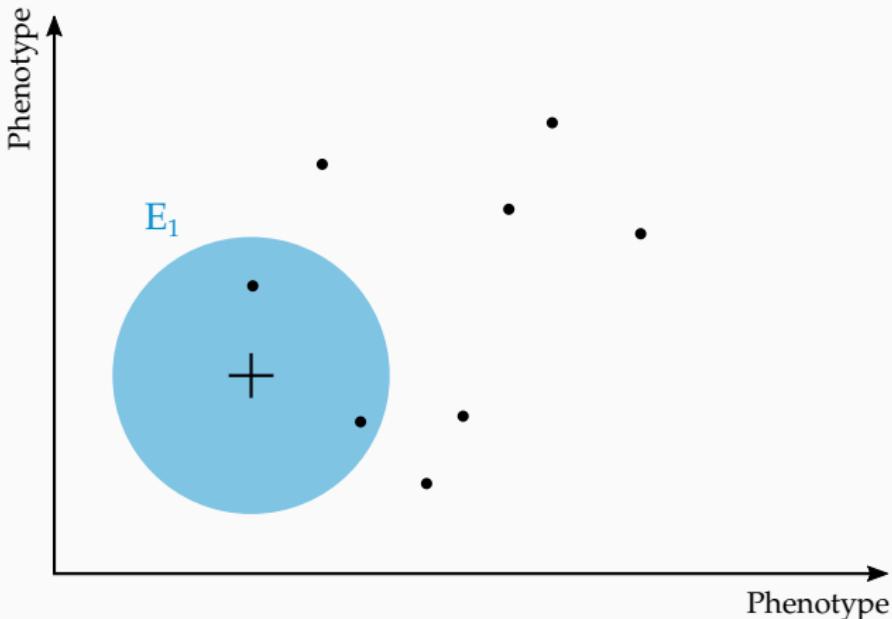
Distribution of fitness effects
(DFE)



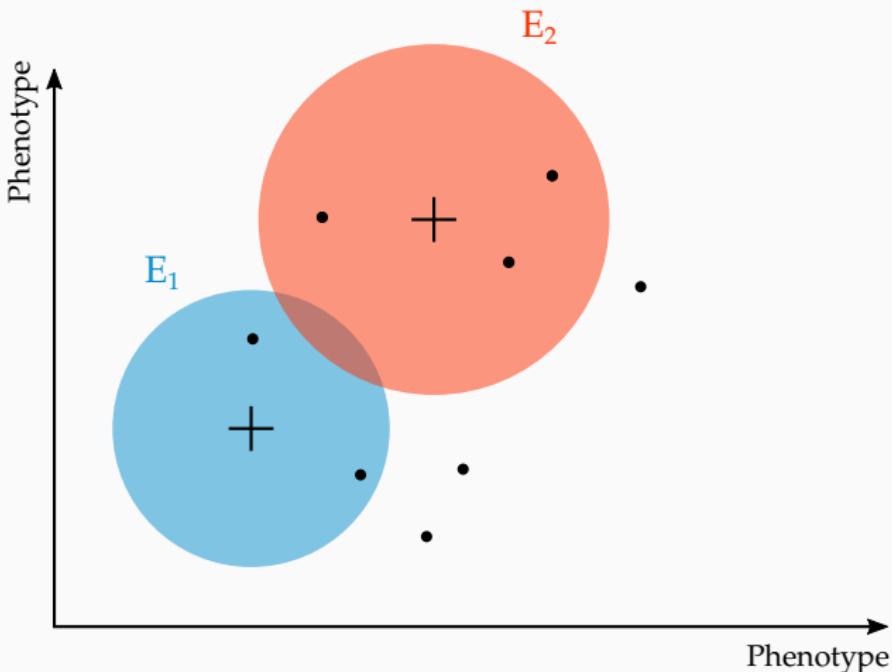
Mapping across environments and genotypes



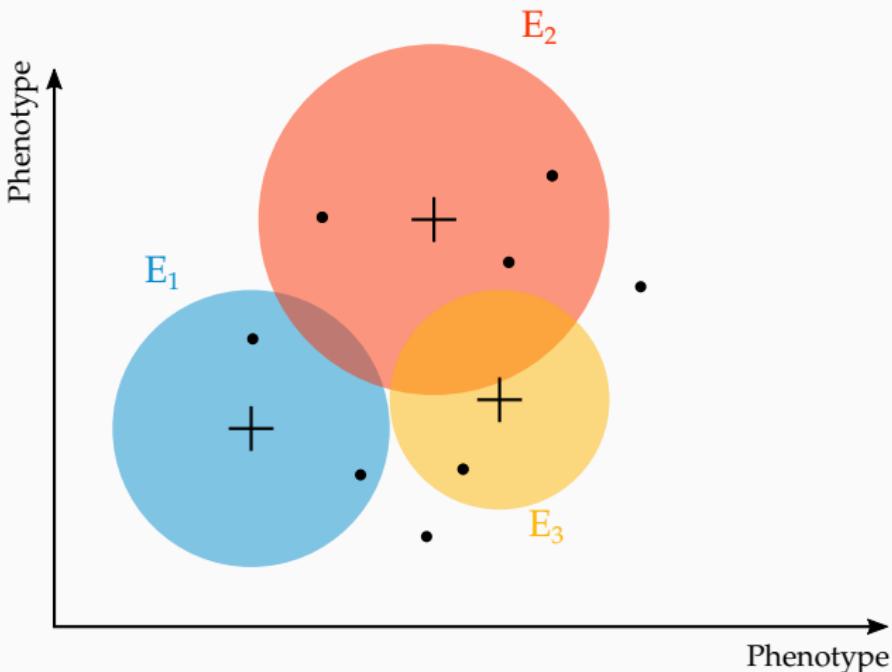
Mapping across environments and genotypes



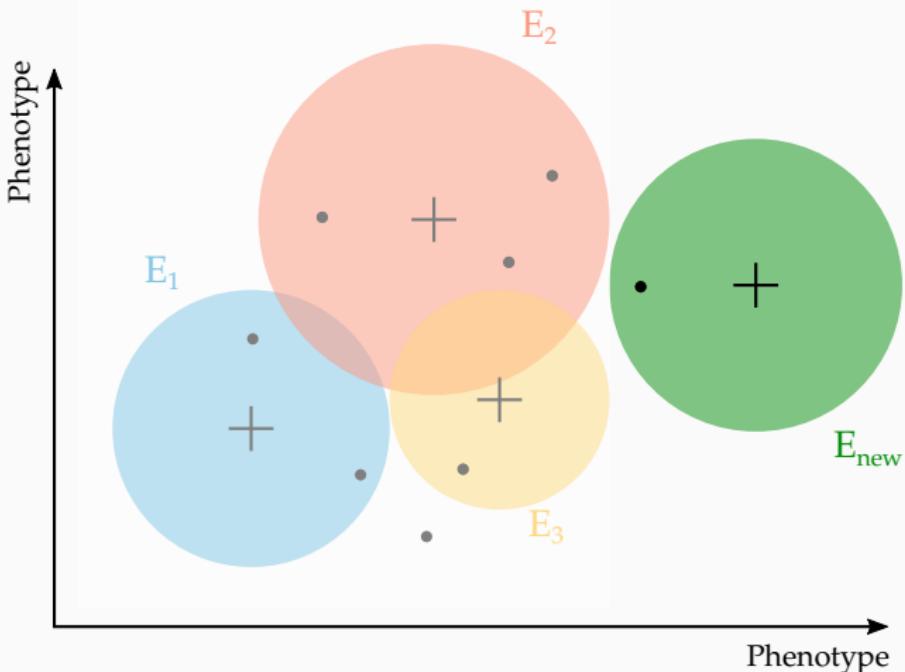
Mapping across environments and genotypes



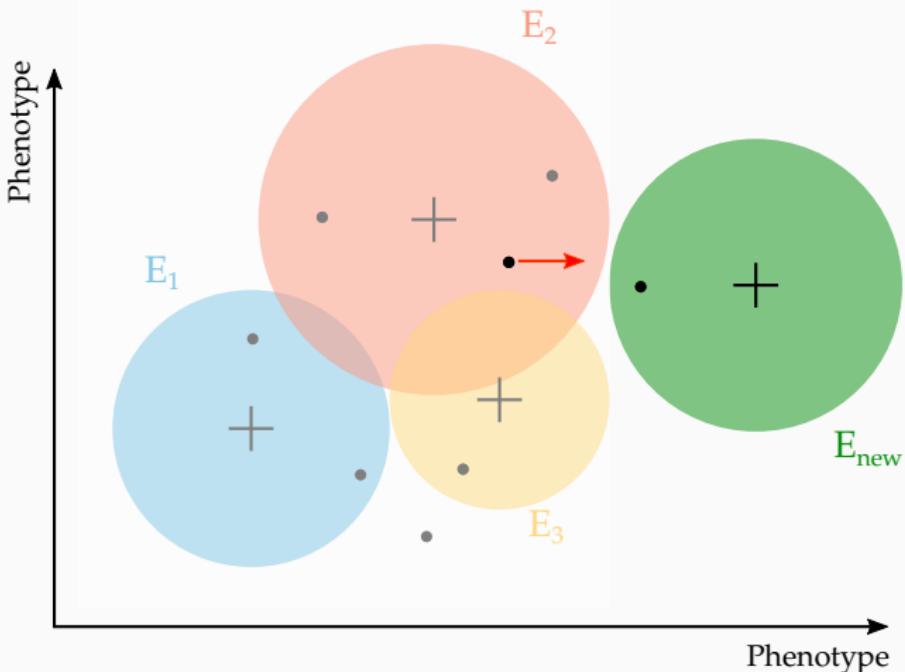
Mapping across environments and genotypes



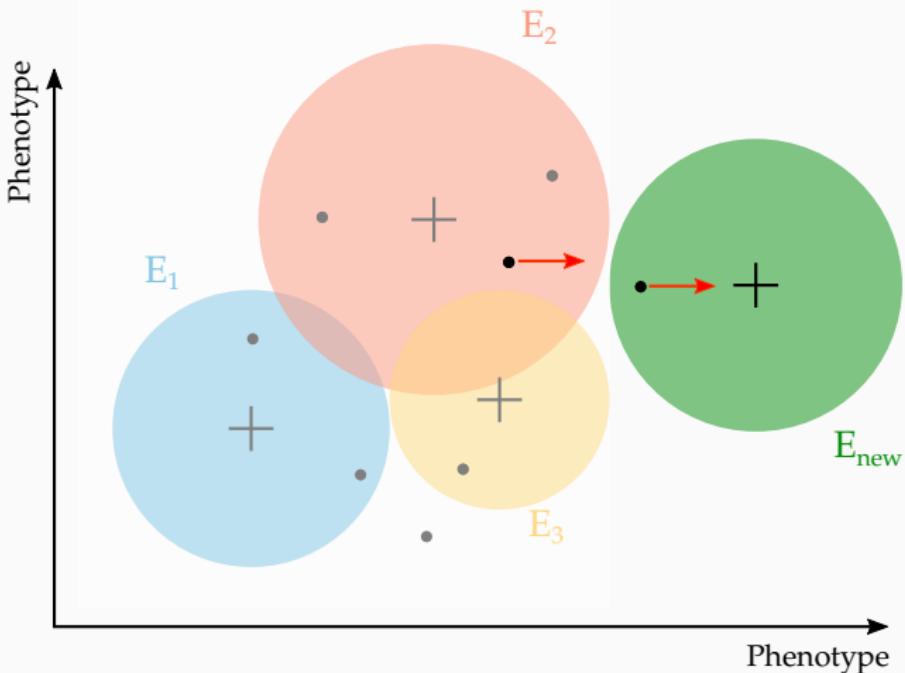
Mapping across environments and genotypes



Mapping across environments and genotypes

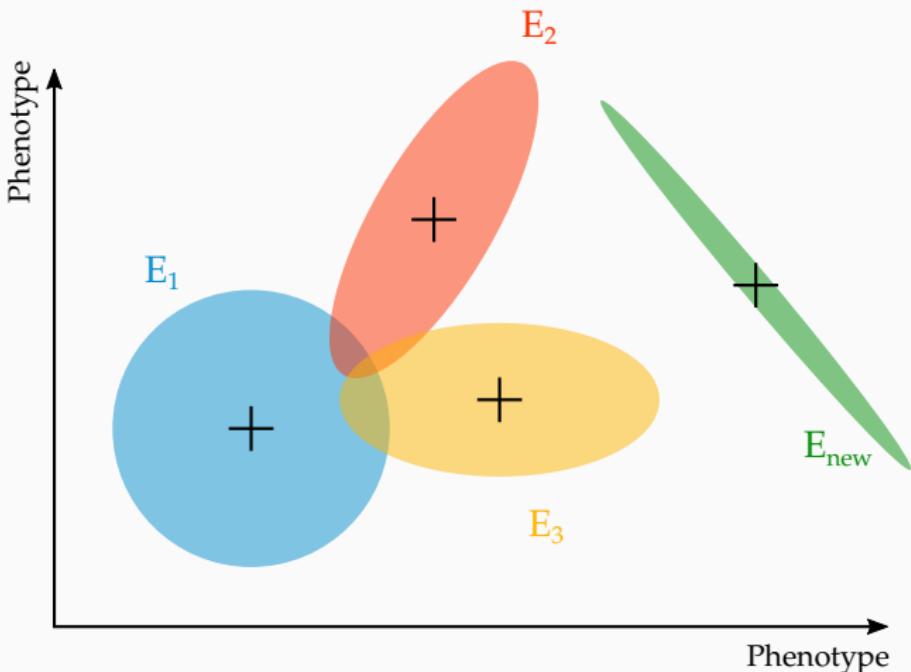


Mapping across environments and genotypes

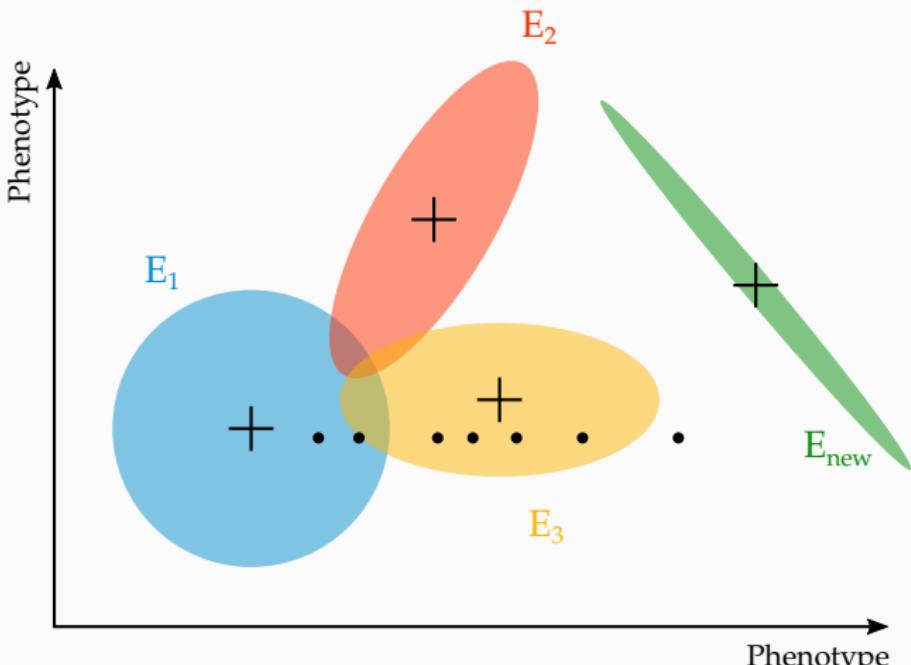


Prediction of fitness **across environments**
and **genotypes**

Mapping across environments and genotypes



Mapping across environments and genotypes

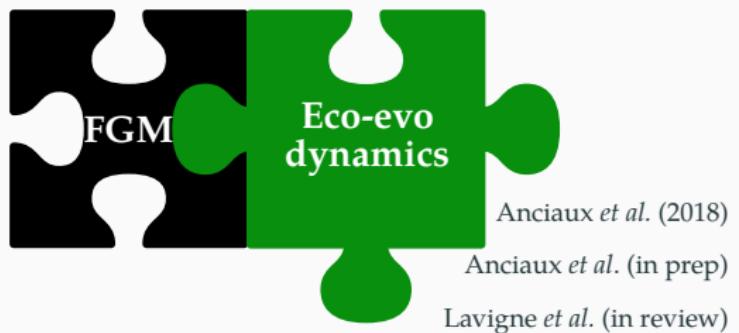


Anisotropy and partial pleiotropy

Conclusions and Perspectives



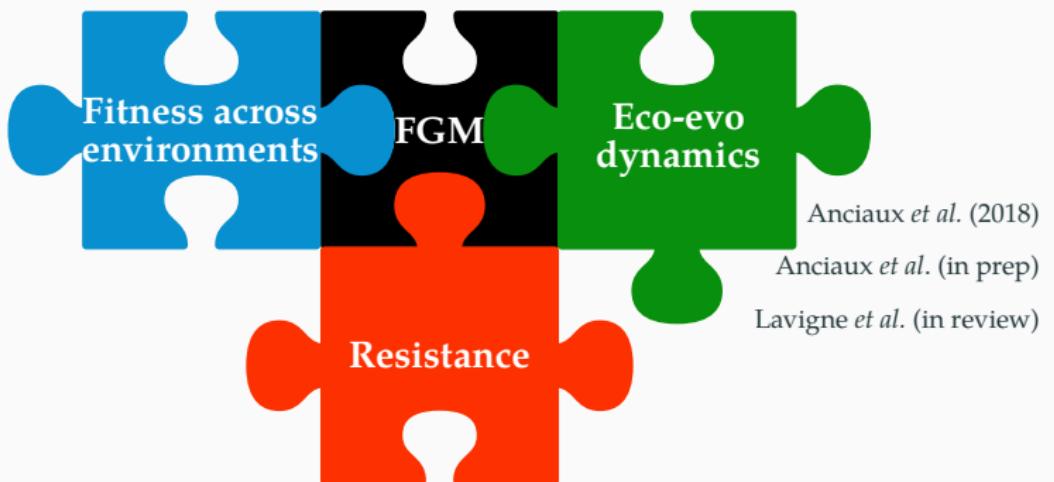
Conclusions and Perspectives



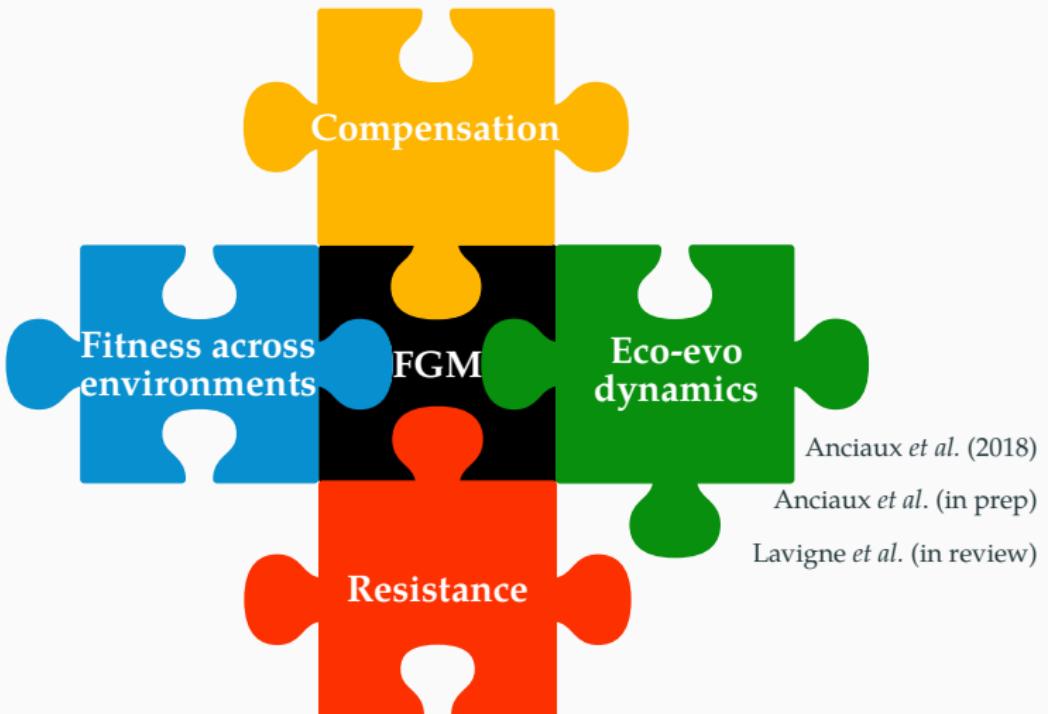
Conclusions and Perspectives



Conclusions and Perspectives



Conclusions and Perspectives



Thanks

THANK YOU !

Rescue project

Resistance across environment
project

Guillaume Martin

Ophélie Ronce

Lionel Roques

Amaury Lambert

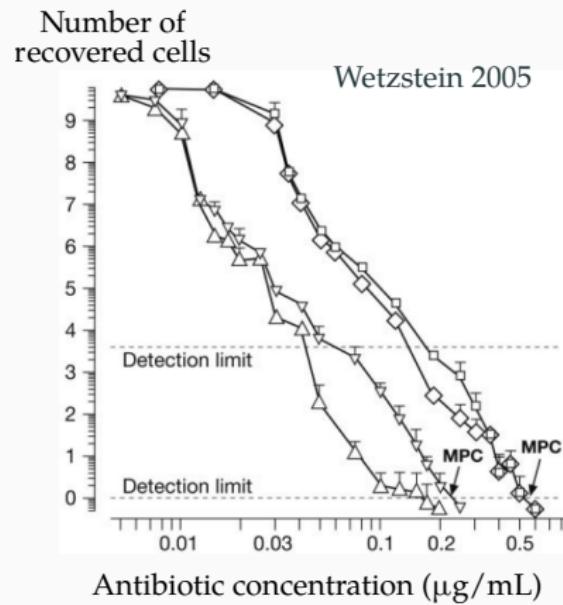
Luis-Miguel Chevin

Thomas Bataillon

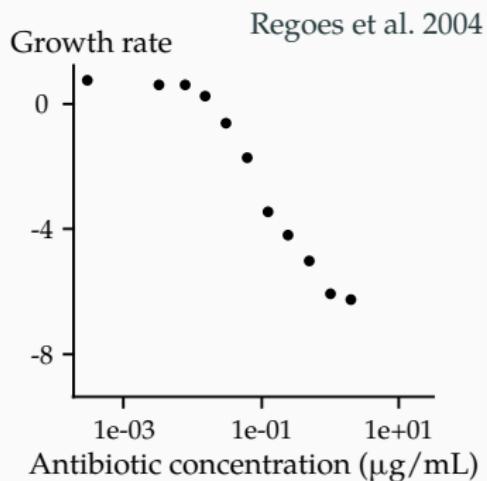
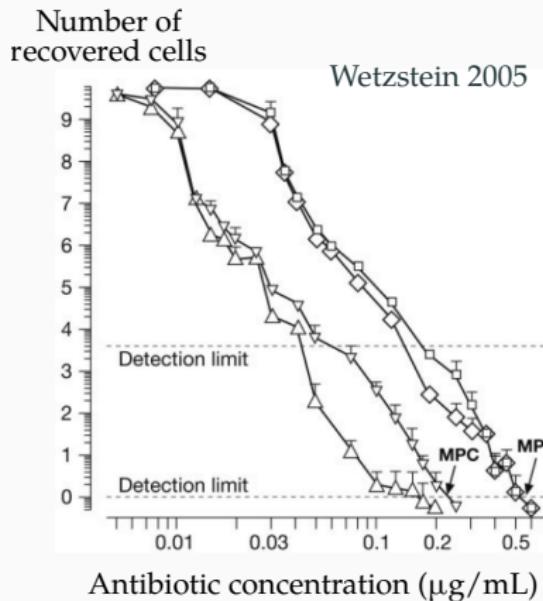
Claudia Bank

Appendix

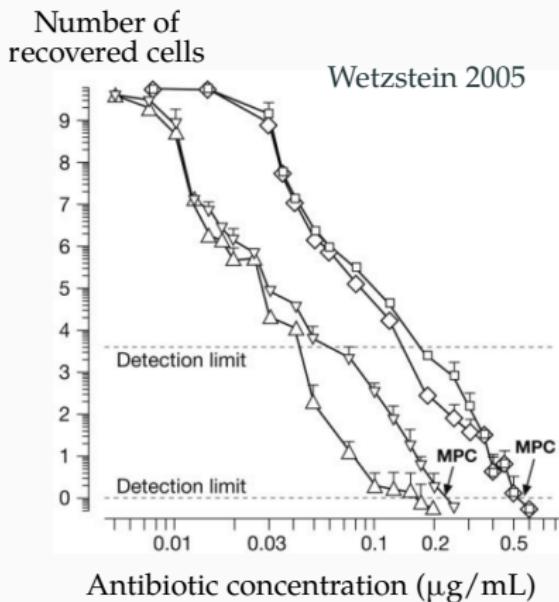
Available data



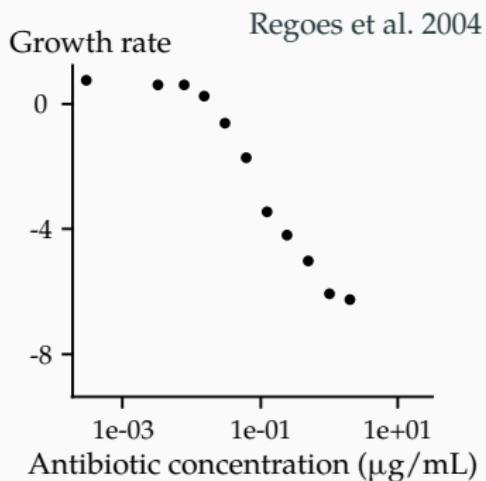
Available data



Available data

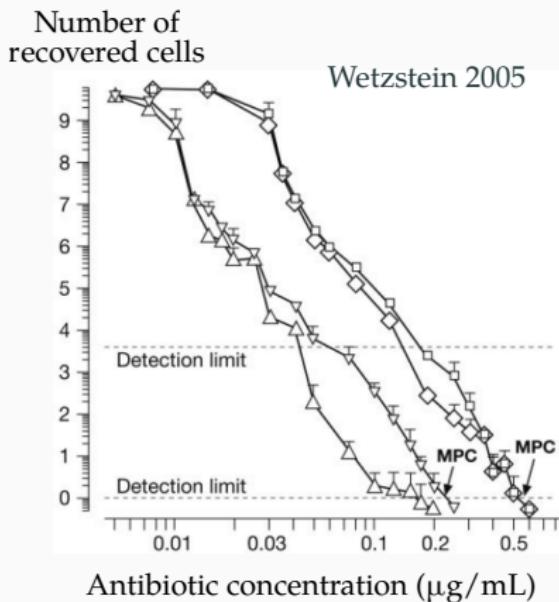


E. coli ATCC8739
Pradofloxacin
Medium USP



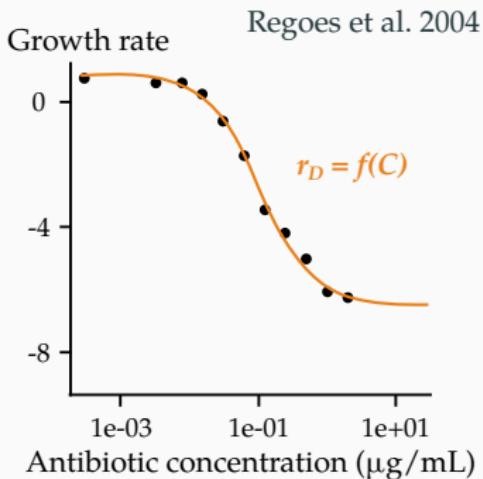
E. coli CAB1
Ciprofloxacin
Medium LB

Available data



E. coli ATCC8739
Pradofloxacin
Medium USP

Relationship between antibiotic concentration C and decay rates r_D



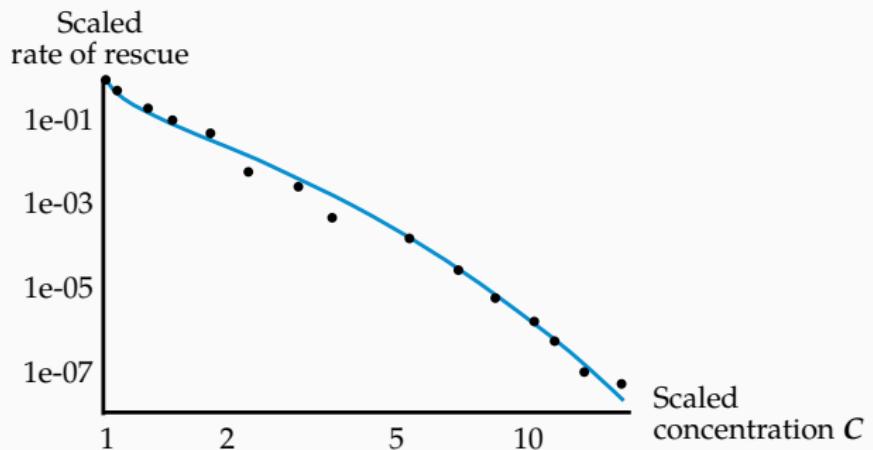
E. coli CAB1
Ciprofloxacin
Medium LB

Available data

Model "Weak U" $r_D = f(C)$

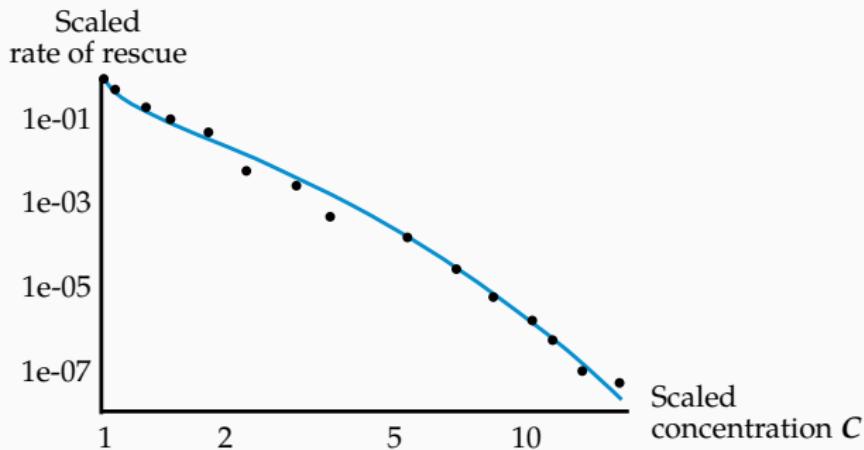
Available data

Model "Weak U" $r_D = f(C)$



Available data

Model "Weak U" $r_D = f(C)$



The model combining the "Weak U" model and the function $r_D = f(C)$ has too many parameters.

The model gives a better visual fit than a model without context-dependence