Adaptation at the levels of fitness and traits

Bridging population and quantitative genetics

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What is adaptation?

The word **adaptation** might refer to

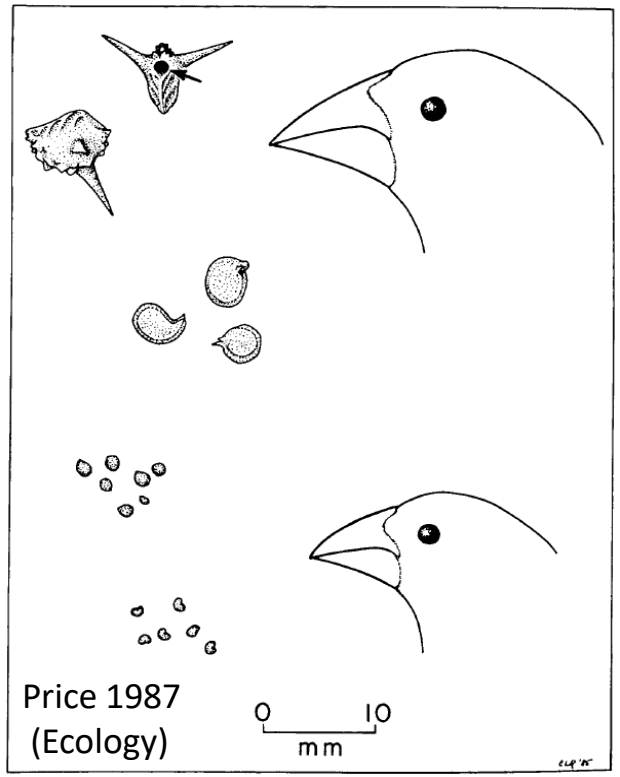
- A state = being adapted/fit: Match between phenotype and environment
- A trait: lungs are “adaptations” to terrestrial life.
- A **process = adaptive evolution**:
  Increase of fitness through **natural selection** causing the **genetic evolution** of **traits that match the requirements set by the environment**.

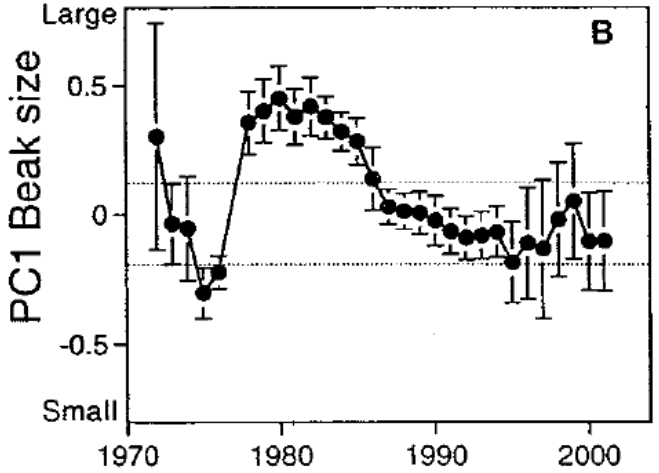
Other processes occurring within individuals or genotypes (acclimation, physiological adjustments, phenotypic plasticity) are sometimes described as adaptation, but not our focus here.

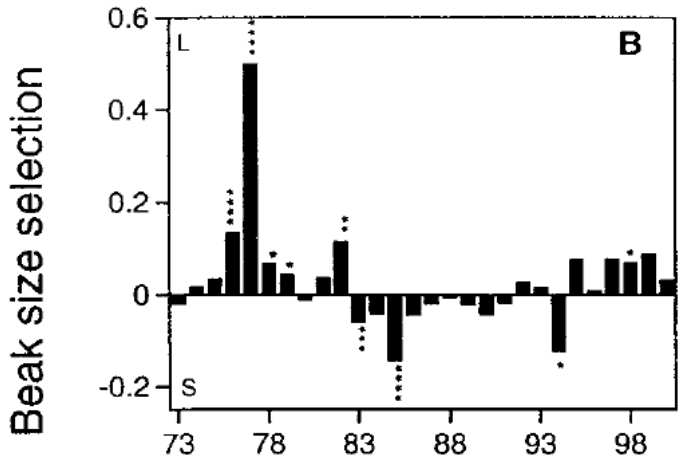
Some examples of adaptation

- **Resource specialization**

Medium ground finch *Geospiza fortis*



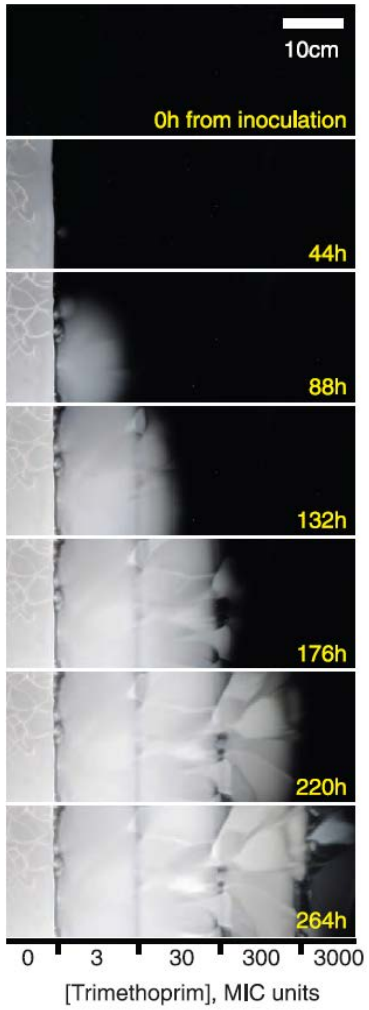


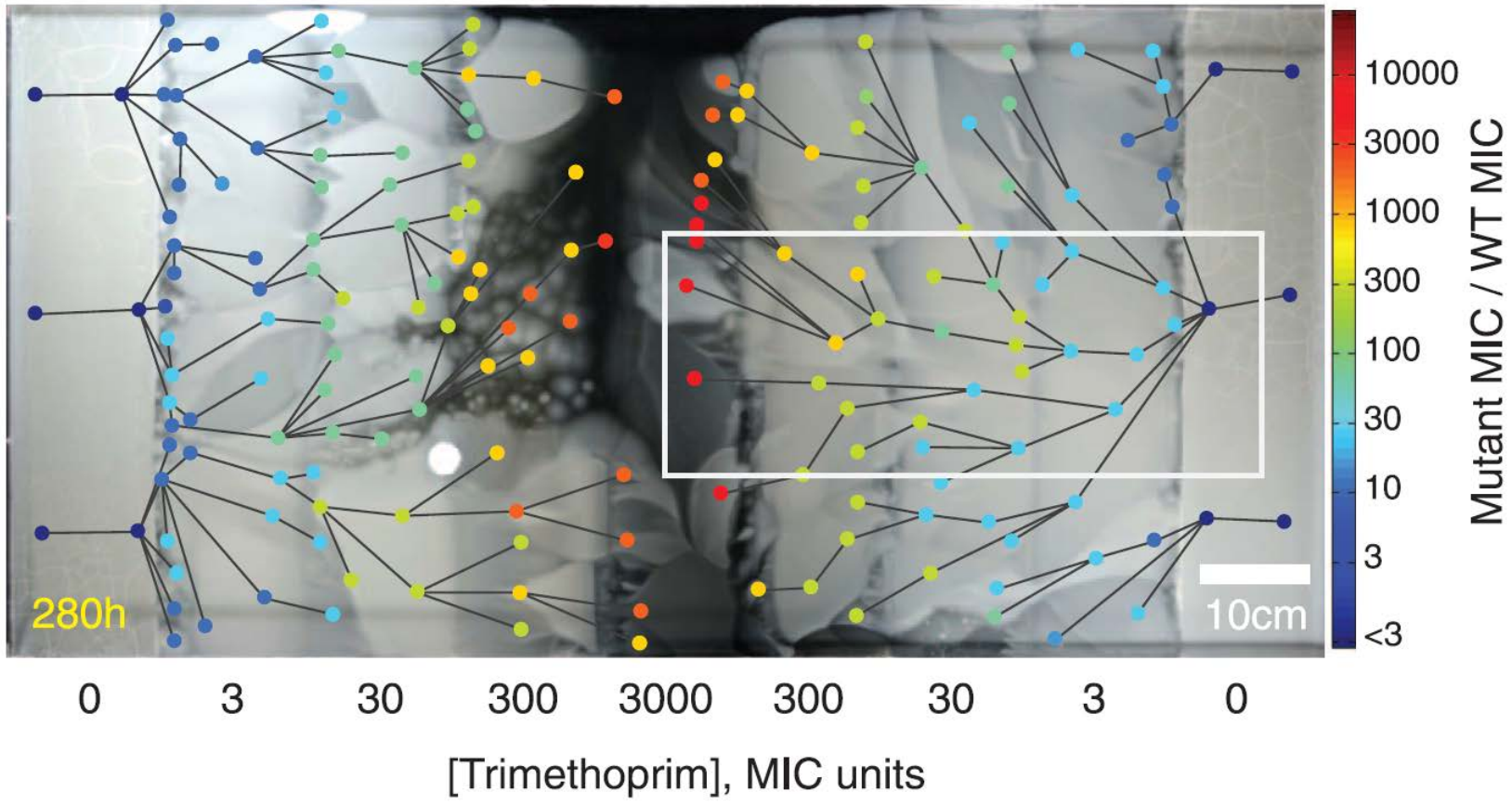


Grant et Grant (2002 Science, 2014 PUP)

Some examples of adaptation

- **Antibiotic resistance**



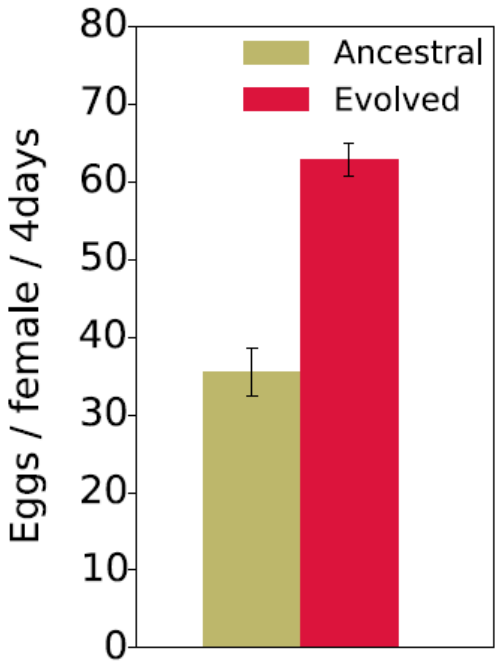


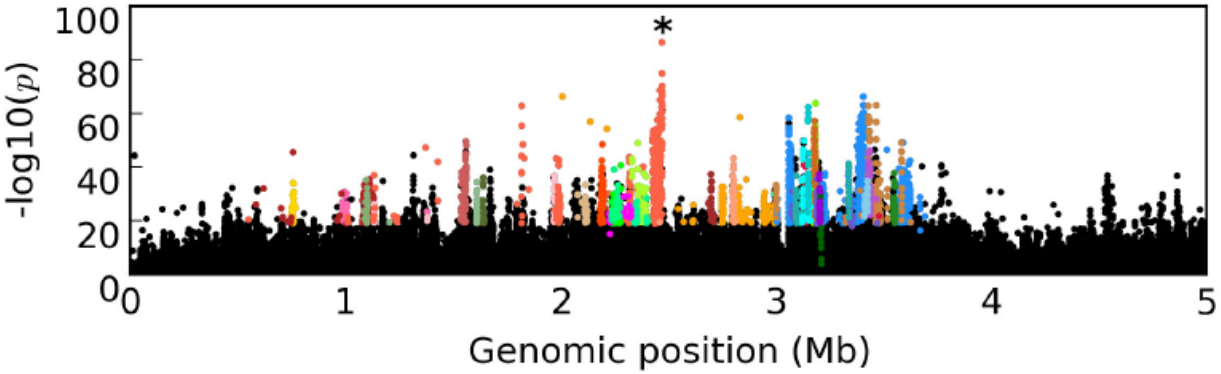
Baym et al (2016 Science)

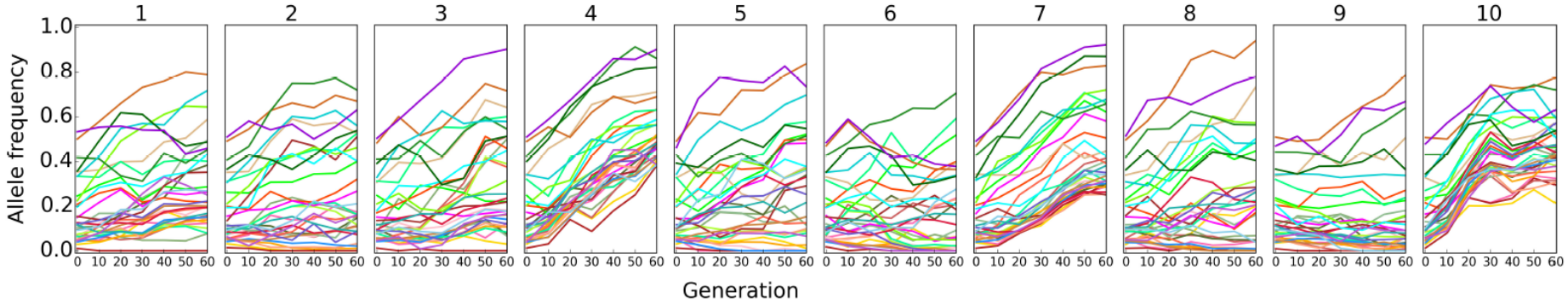
Some examples of adaptation

- **Thermal adaptation**

  Daily cycles between 18 and 28˚C







Barghi et al (2019 PLoS Biol)

How to study the process of adaptation?

- Most comprehensive approach:

1. Find **which phenotypes are favored in the relevant environent**, **for all traits** under selection
2. Decipher the **genotype-phenotype map**, to propagate selection on traits to their underlying genetic basis
3. Derive **population genetic changes** caused by natural selection + other forces (mutation, recombination, drift, migration).
4. Infer **evolutionary changes in traits** (response to selection) **and fitness** (rate of adaptation)

- But most population genetics work by-passes the steps involving phenotype (and environment), instead just focusing on effects on fitness

Goal and overview of the lecture

How can we understand and predict the dynamics of adaptation?

1. Approaches that focus only on fitness
    i. Adaptation by sequential fixations
    ii. Adaptation in polymorphic population
    iii. Distribution of fitness effects (DFE)
2. Approaches that account for the phenotype
    i. DFE emerging from selection on traits
    ii. Models of phenotypic evolution

Adaptation at the level of fitness

By-passing the phenotype

What is fitness?

- Central evolutionary concept: the “engine” of selection.
  Measures genetic contributions to the next generation(s)
- Evolutionists focus on **relative fitness** (competition between genotypes/phenotypes), but estimating it often requires to measure **absolute fitness** (pop growth rate).
- Simple in non-overlapping generations: **survival x fecundity** over a complete life cycle (e.g. number of zygotes produced per zygote).

1: Fisher (1930);
Lande (1982); Charlesworth (1994)

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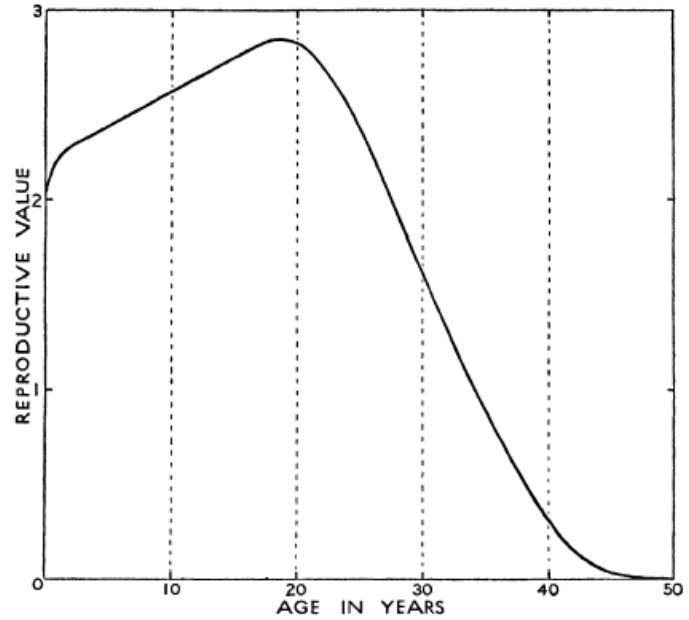
- Simple in non-overlapping generations: **survival x fecundity** over a complete life cycle (e.g. number of zygotes produced per zygote).
- More complex in overlapping generations/continuous time[1], where there’s a benefit to reproducing earlier

by the analogy of compound interest the present value of the future offspring of persons aged x is easily seen to be

$$v_x = \frac{e^{mx}}{l_x}\int_x^\infty e^{-mt} l_t b_t dt.$$

l_x proba to survive to age x
b_x fertility in age x
m Malthusian pop growth parameter



1: Fisher (1930);
Lande (1982); Charlesworth (1994)

What is fitness?

Other conceptual and practical difficulties in true populations:

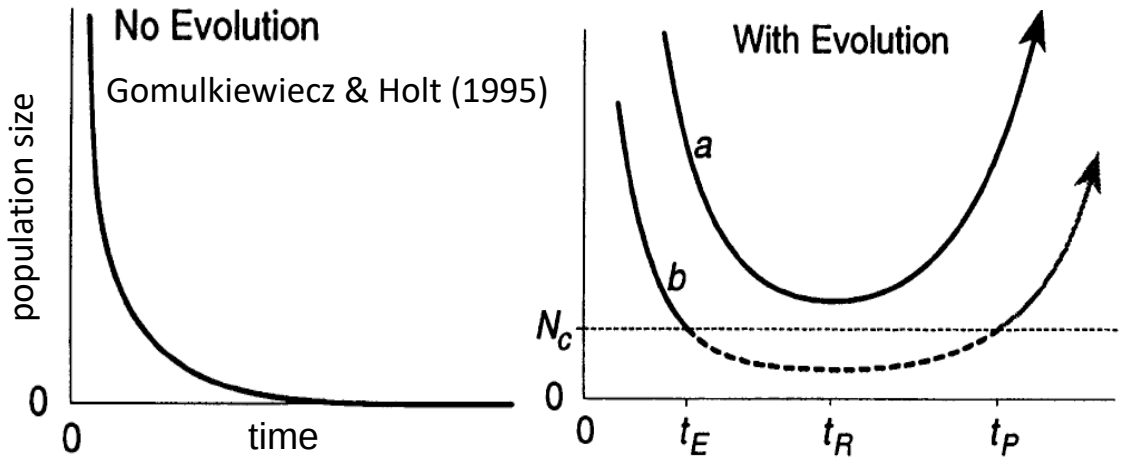
- Fitness is a **propensity**[1] of a genotype /phenotype (expectation of random variable)
  → not directly measurable in an individual, needs to be averaged.
  Otherwise includes a component of demographic stochasticity (genetic drift)
- Relative fitnesses may **change with population size** (density-dependent selection)[2]
  Eg rapid colonizers favored at low density (r strategists),
  versus good competitions at high density (K-strategists)
- Relative fitnesses may depend not just on intrinsic performance,
  but on **interaction among genotypes** (frequency-dependence)[3]
- Here focus on simplest case of density- and frequency-independent adaptation

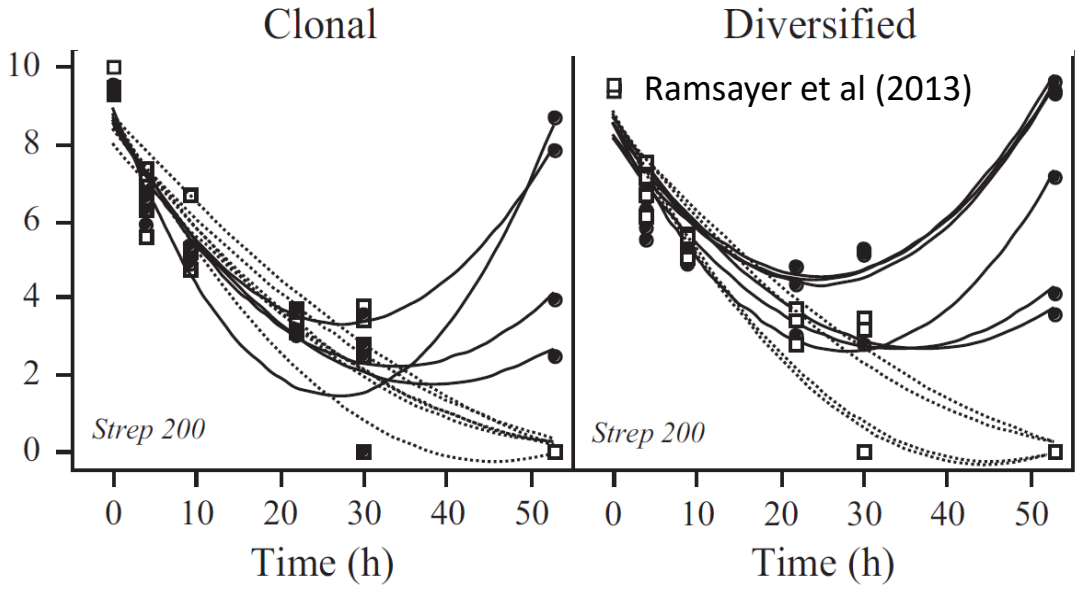
1: Mills & Beatty (1979)
2: MacArthur (1962); Saether et al (2016
3: Lewontin (1958), Ayala & Campbel (1974)

Adaptation as change in mean fitness

Why is **evolution of fitness** relevant?

- Sets **upper bound for evolvability** of other traits[1], selected through their covariance with fitness[2].
- Rate of change in (absolute) fitness is critical for persistence in new or changing environment (climate, pollutant, antibiotics…) → Evolutionary rescue[3]



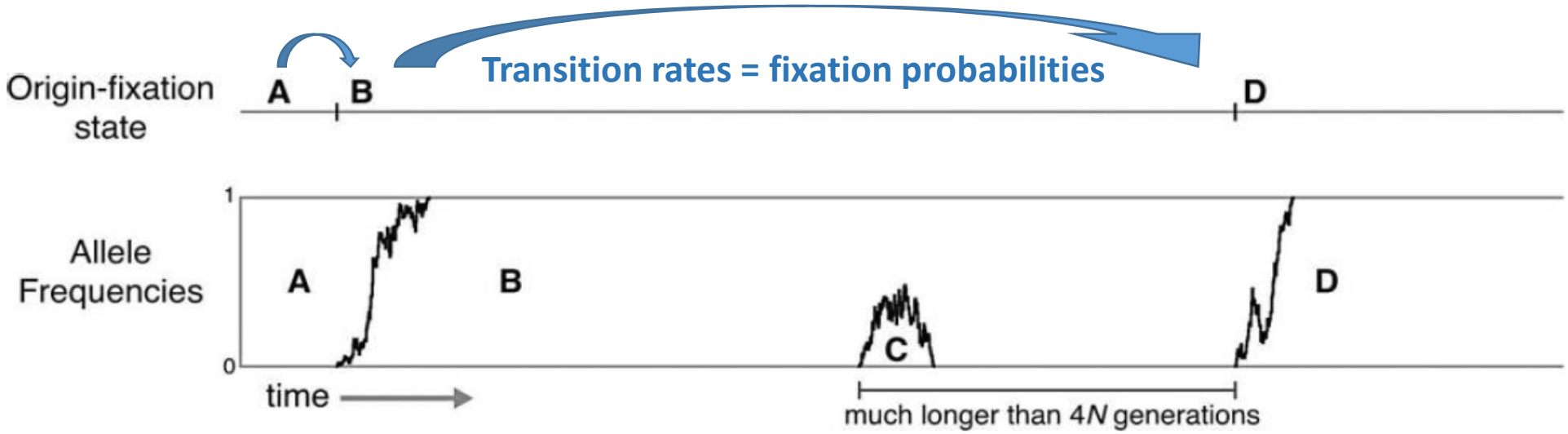


1: Houle (1992 Genetics); Burt (1995 Evolution);Bonnet et al (2022 Science)
2: Price (1970)
3: Lynch & Lande (1993); Gomulkiewicz & Holt (1995)

Rate of adaptation by sequential substitutions

Low mutation limit:

- Each **mutation fixes sequentially** in an otherwise monomorphic populations.
  → Adaptation may involve multiple genes, but is **not polygenic** as each mutation segregates alone in the population
- Strong selection weak mutation (SSWM) approximation[1] or "origin-fixation models" [2] → Adaptation can be treated of a Markov chain between fixed states



1: Gillespie (1983)
2: McCandlish & Stolzfus (2014)

Rate of adaptation by sequential substitutions

Low mutation limit:

- Assuming only beneficial mutations can fix, the rate of adaptation (in haploids) is[1]

$$\Delta\bar{W} = NU_b \int_0^\infty \pi(s) s f_b(s) ds$$

Origination
- N: Population size
- U_b: Genomic rate of beneficial mutations

Selection
- s: Selection coefficient of mutation (fitnesses $= 1, 1+s$)
- $f_b(s)$: Distribution of fitness effects of benefical mutations
- $\pi(s)$: Fixation probability of mutations with fitness effect s

- For small positive s, we have[2] $\pi(s) \approx 2s$, so $\Delta\bar{W} \approx 2NU_b \int_0^\infty s^2 f_b(s) ds$

→ Selection effect on the rate of adaptation summarized by 2nd moment of distribution $f_b(s)$ of beneficial fitness effects

1: Orr (2000)
2: Haldane (1927)

Rate of adaptation in polymorphic population

High mutation limit:

- No need to wait for mutation to introduce new adaptive variants, **standing variation** is present in the population when selection starts.
- Fitness changes over time because of **changes in frequencies** of existing alleles.
- Consider multiple biallelic loci, on which haploid selection acts independently (no linkage disequilibrium).
  Beneficial allele at locus i is in frequency p_i (and $q_i = 1 - p_i$).
- Frequency after selection: $p_i' = \frac{p_i\,(1+s_i)}{p_i\,(1+s_i)+q_i} = \frac{p_i\,(1+s_i)}{1+p_i s_i}$
- Changes under selection: $\Delta p_i = \frac{p_i\,(1+s_i)-p_i(1+p_i s_i)}{1+p_i s_i} = \frac{s_i p_i\,q_i}{1+p_i s} \approx sp_i q_i$ (weak selection)

Rate of adaptation in polymorphic population

- Mean fitness is $\bar{W} = 1 + p_i s_i$
- The change in mean fitness per generation is

$$\Delta\bar{W} = \sum_i \Delta p_i \frac{\partial \bar{W}}{\partial p_i} = \sum_i \Delta p_i \, s_i = \sum_i s_i^2 p_i q_i$$

- If fitness at locus *i* is treated as a random variable X_i,
  with $\Pr(X_i = 1 + s_i) = p_i$ and $\Pr(X_i = 1) = q_i$,
  then the contribution of this locus to the genetic variance in fitness is $V_i = s_i^2 p_i q_i$
- Summing across independent loci: $\Delta\bar{W} = \sum_i V_i = V(W)$

Fisher (1930)

We may consequently state the fundamental theorem of Natural Selection in the form:

The rate of increase in fitness of any organism at any time is equal to its genetic variance in fitness at that time.

Rate of adaptation in polymorphic population

- In terms of allelic fitness effects in standing variation:

$$\Delta\bar{W} = \sum_{i=1}^{n_L} s_i^2 p_i q_i = n_L[\mathrm{E}(s^2)\mathrm{E}(pq) + \mathrm{Cov}(s^2, pq)]$$

n_L: Number of loci with segregating alleles contributing to fitness.

$\mathrm{E}(pq)$: Mean polymorphism (expected heterozygosity) at these loci

$\mathrm{E}(s^2)$: Mean squared fitness effect of segregating beneficial alleles

→2nd moment of **distribution $f_{\mathrm{sv}}(s)$ of fitness effects** of alleles segregating in standing variation determines rate of adaptation

→**Distribution of fitness effects** (DFE) is key to predicting adaptation across regimes.

Distribution of fitness effects of mutations

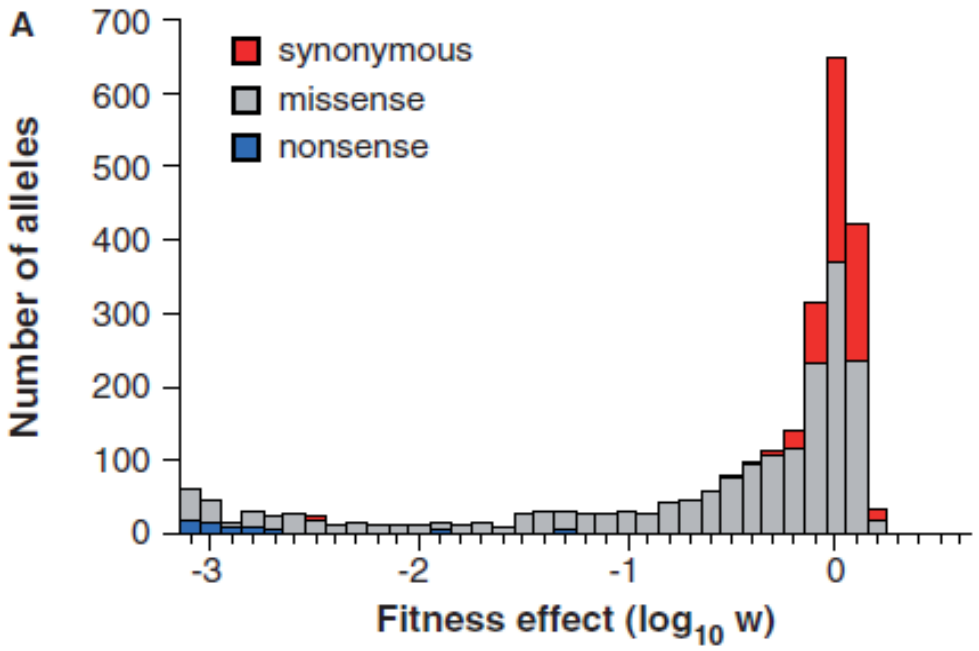
- **Empirical DFE – Measurement**
  - Mutants produced through - accumulation of spontaneous mutations under relaxed selection[1].
    - random mutagenesis
    - target editing of genes (eg CRISPR-cas9[2])
  - Absolute fitness assayed by survival/fecundity each genotype in isolation[3]
  - Relative fitness assayed by pairwise (with wild type) or bulk competition[4]
  - May also be inferred indirectly from patterns of molecular polymorphism and divergence[5].

1: Bataillon (2000 Heredity); Lynch (2007)
2: Shen et al (2022 Nature)
3: Kibota & Lynch (1996 Nature)
4: Hietpas et al (2011 PNAS
5: Keightley & Eyre-Walker (2010 Phil Trans)

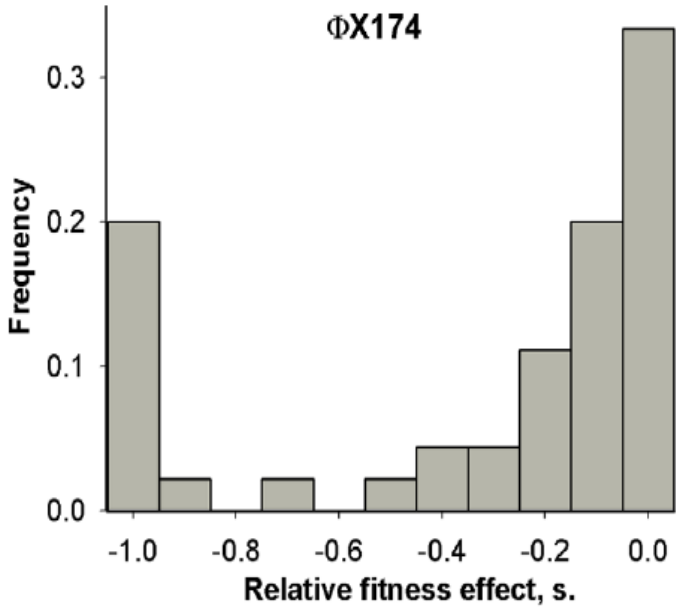
Distribution of fitness effects of mutations

- **Empirical DFE - Typical pattern**

Point and codon mutants of the Escherichia coli TEM-1 b-lactamase gene
(Firnberg et al 2014 MBE)



Mutation-accumulation in phage virus
(Domingo Calap et al 2009 PLoS Gen)



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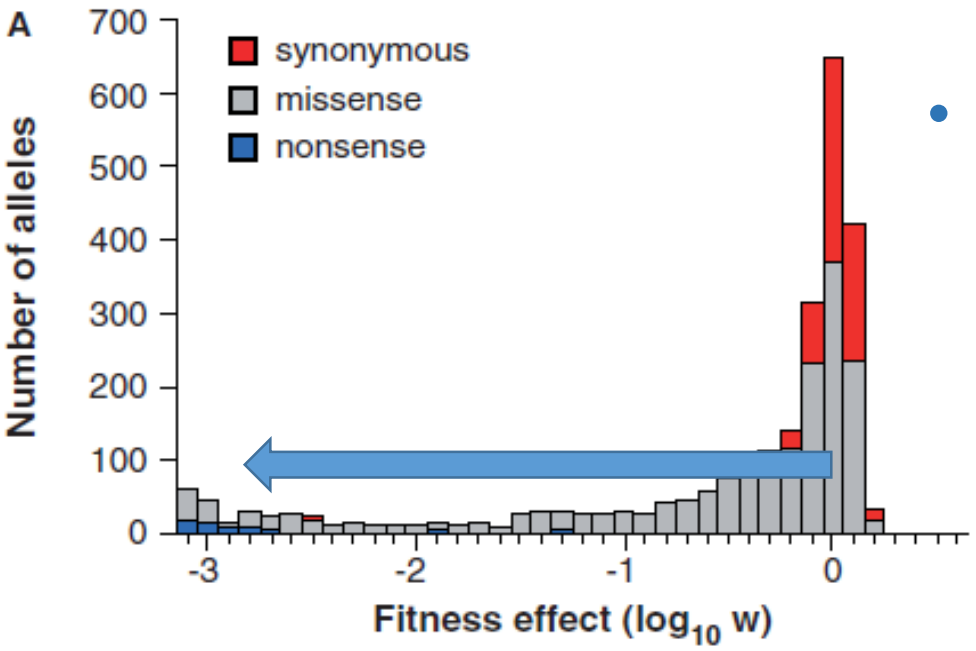

- **Mostly deleterious**

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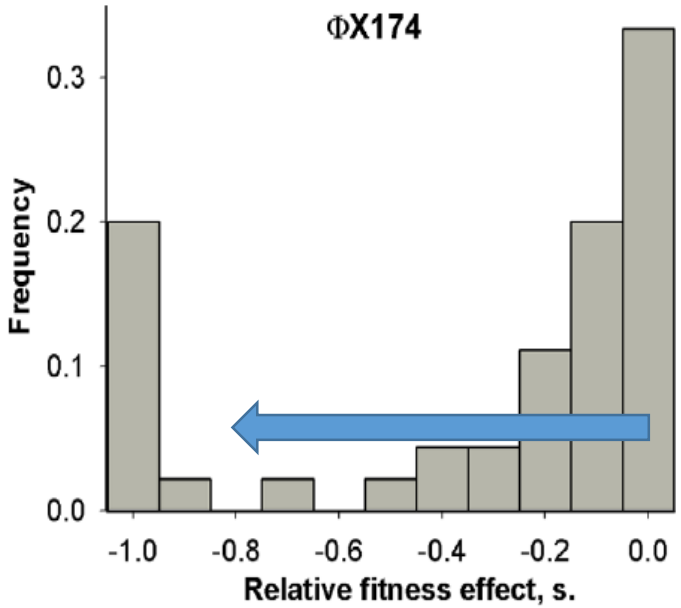

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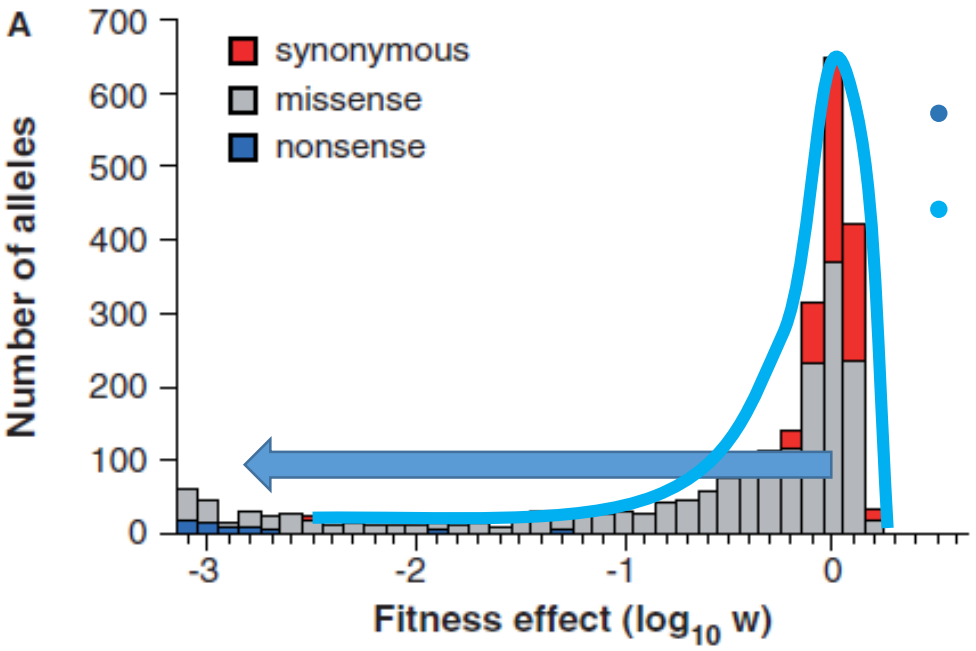

- **Mostly deleterious**
- **Left skewed**

Mutation-accumulation in phage virus
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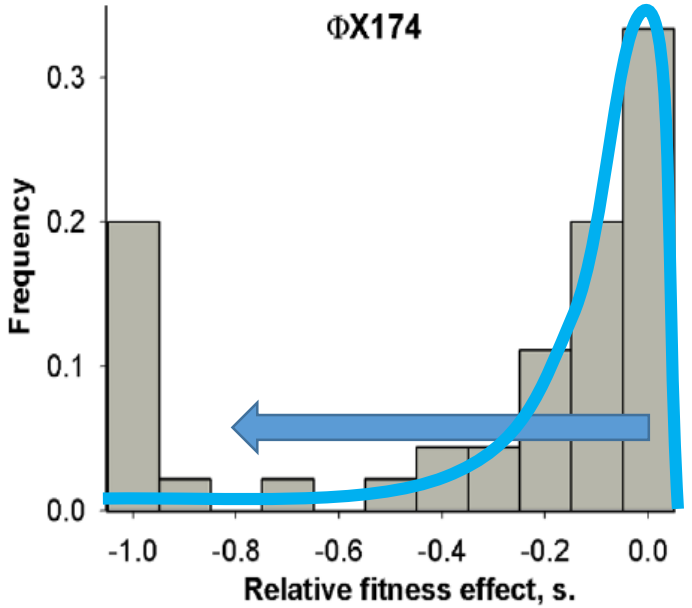

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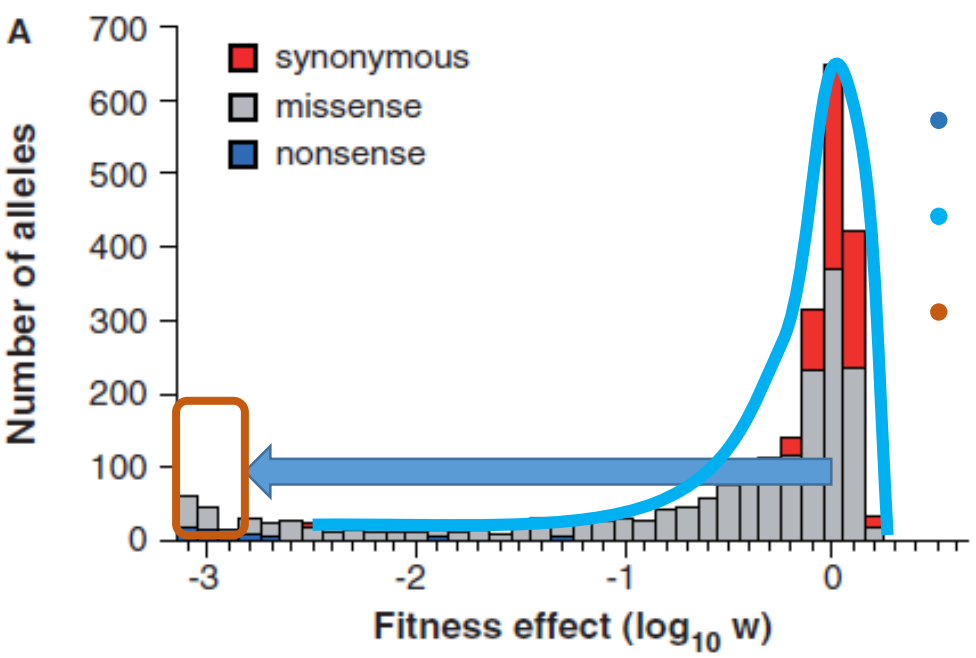

- **Mostly deleterious**
- **Left skewed**
- **Fraction of lethals**

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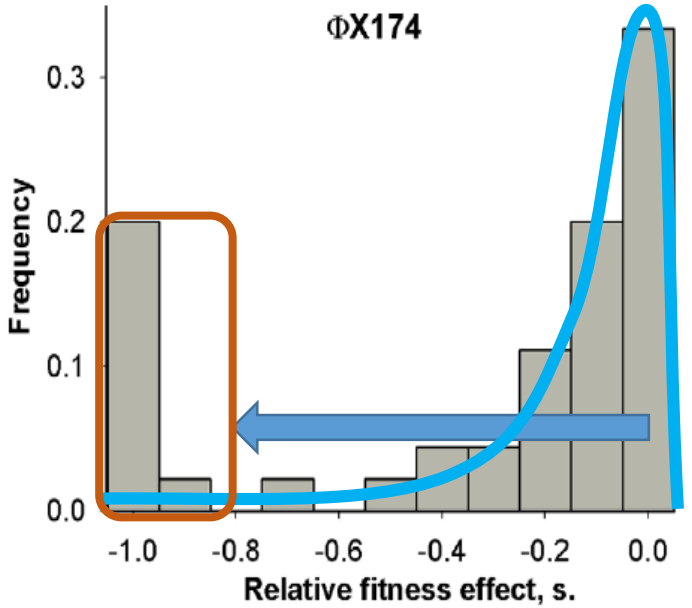

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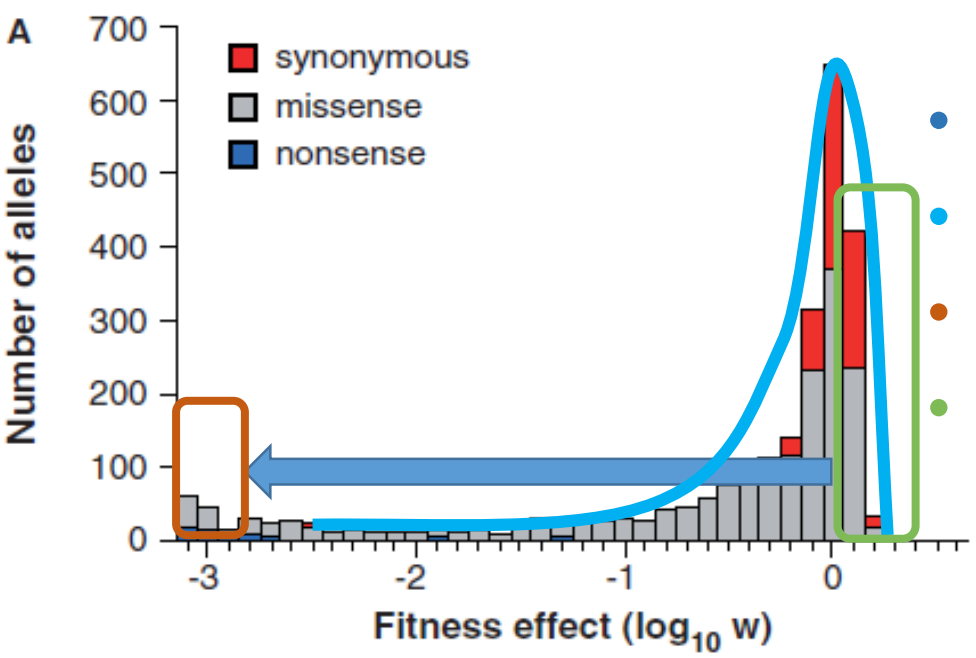
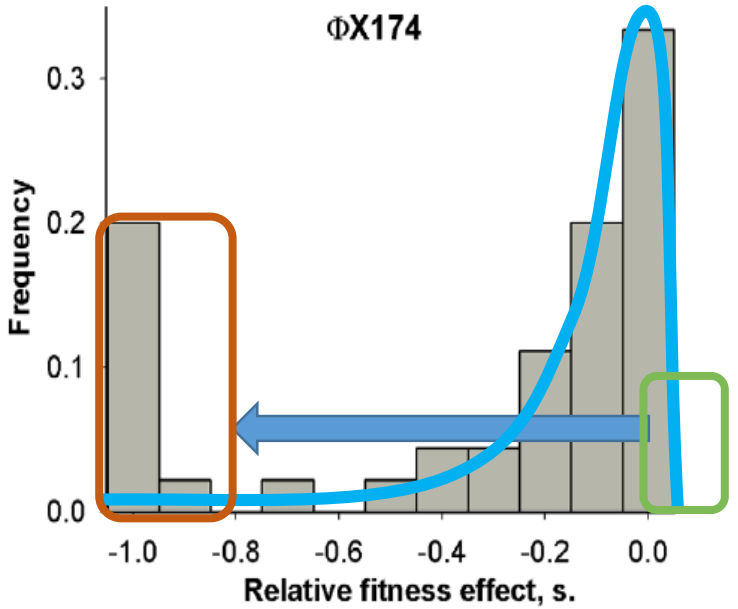


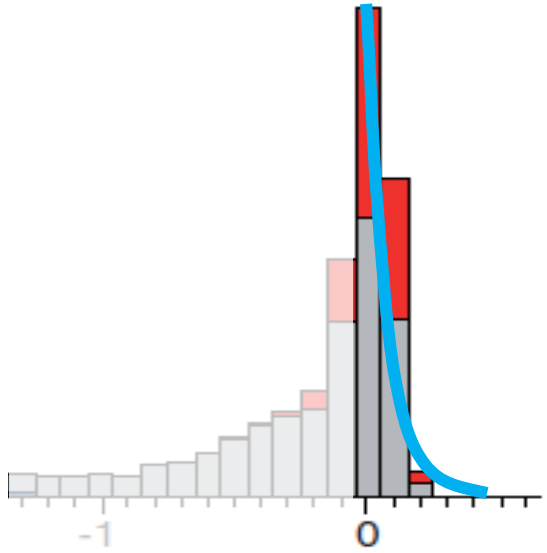
- **Mostly deleterious**
- **Left skewed**
- **Fraction of lethals**
- **Rare beneficials**

Mutation-accumulation in phage virus
(Domingo Calap et al 2009 PLoS Gen)



Distribution of *beneficia* / fitness effects

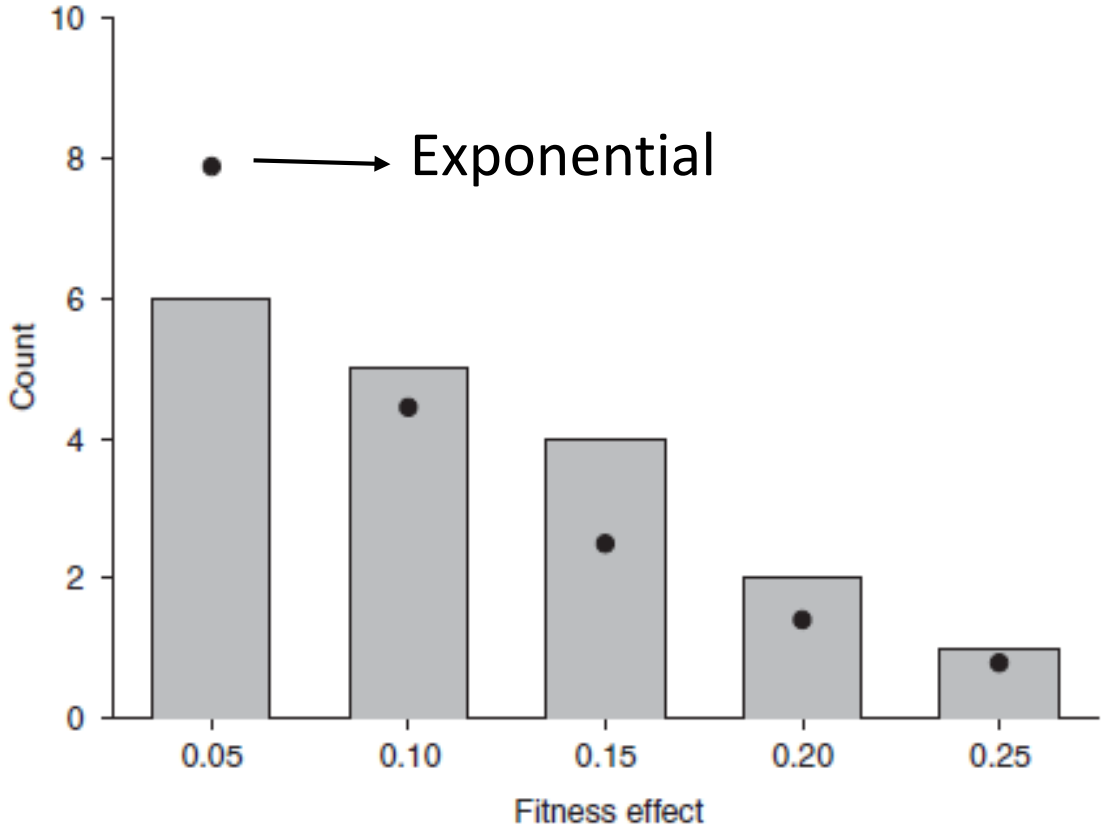
- Beneficials are what matters for adaptation
- Often in right tail of distribution (rare)
  → Extreme value theory (EVT) can be used to analyze them[1]
- Many distributions converge to the same family of distributions in their tails: Generalized Pareto Distribution.
- In particular many unbounded distributions (Gumbel type) converge to the **exponential distribution**.
- This EVT distribution is predicted to not depend on rank or fitness of wild-type, as long as it remains in the right tail



1: Gillespie (1984 Evolution); Orr (2002 Genetics)

Distribution of *beneficia* / fitness effects

- **Empirical measurement:** Single mutants (isolated by fluctuation test with antibiotic) (Kassen & Bataillon 2006 Nat. Genetics)



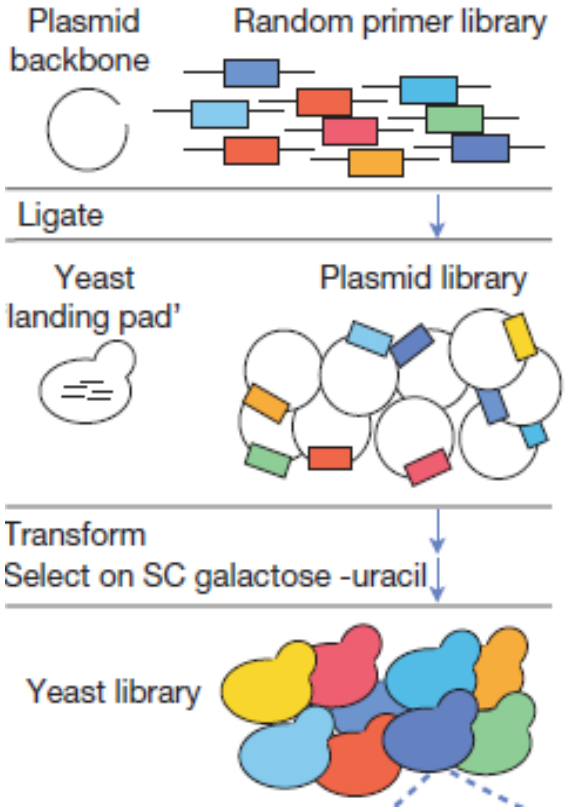
Undistinguishable from exponential

Lack of power?

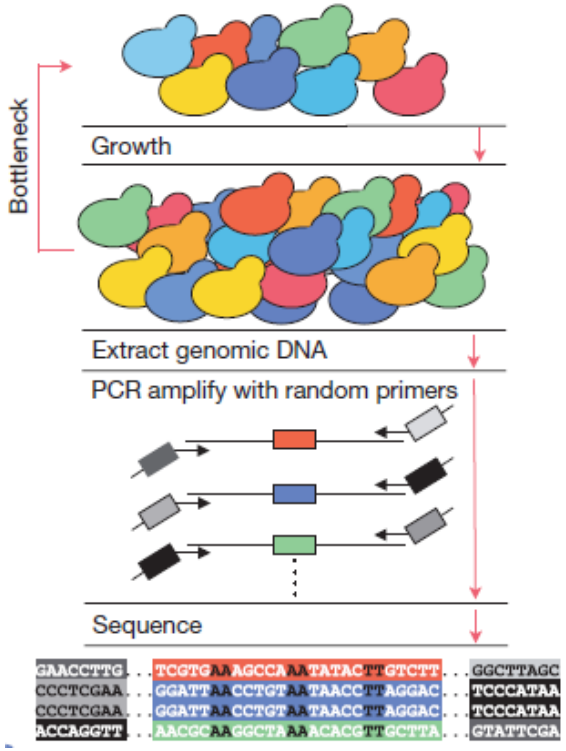
Distribution of *beneficial* fitness effects

- **Empirical measurement:** mutations arising during adaptation (escaping drift and interferences) (Levy et al 2015 Nature)

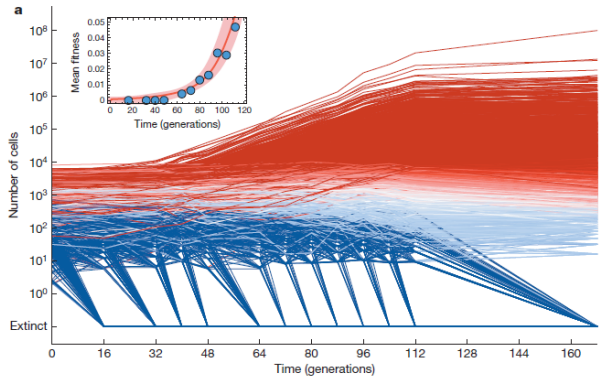
1) Transform with 20 bp barcode → 500 000 genetic markers

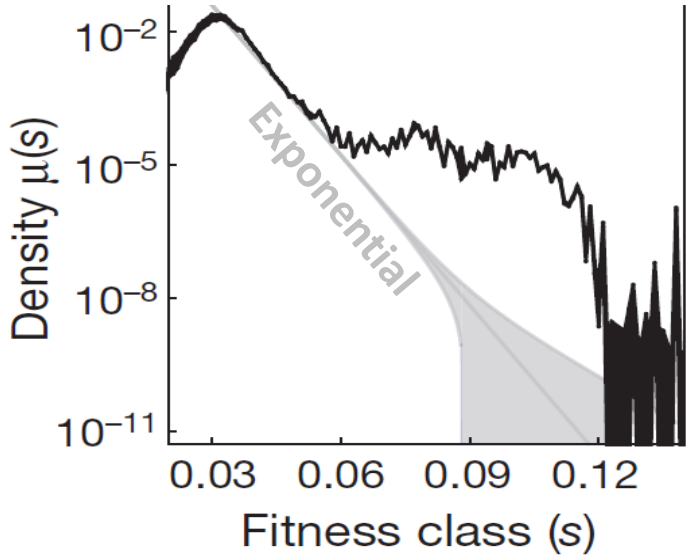


2) Bulk competition & sequence to track frequency



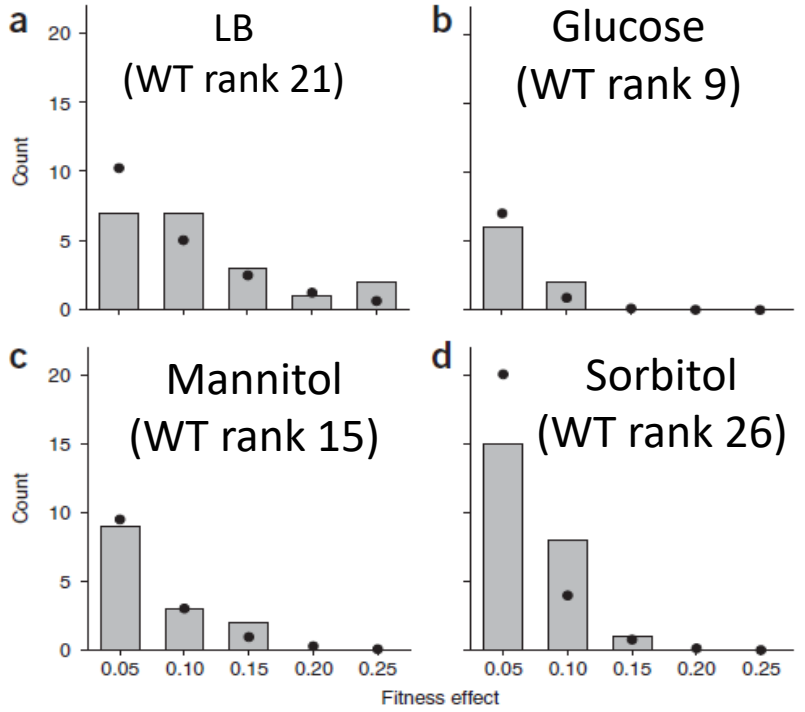
3) Measure *s* of linked beneficial mutations





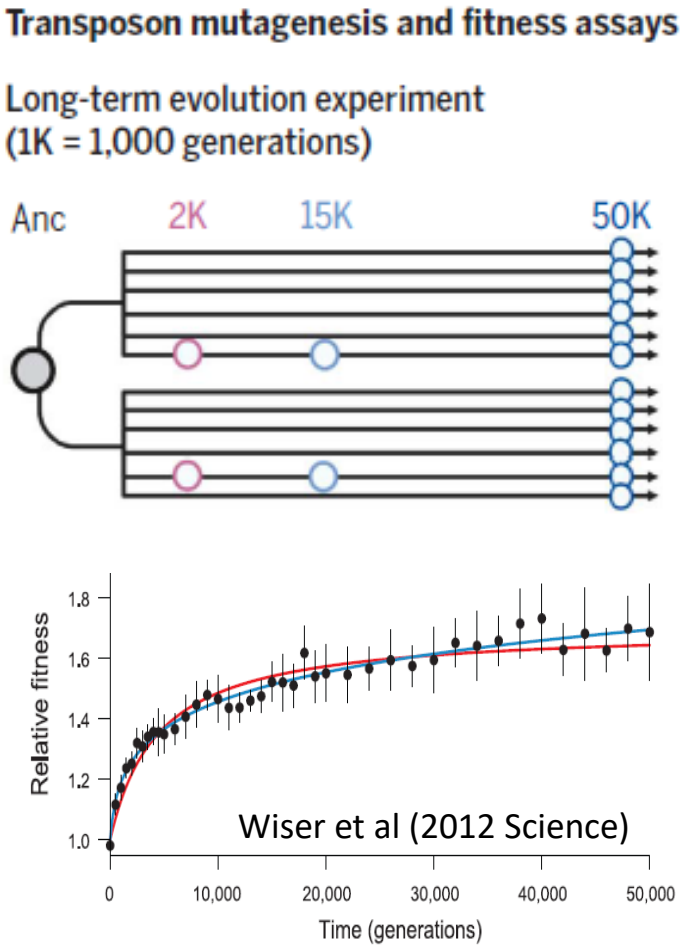
DFE across environments and genotypes

- Important question for predicting adaptive evolution:
  How does the DFE change with environment and background genotype ?
- Background mean fitness changes during adaptation → may modify DFE
- Environmental stress may cause more mutations to become beneficial
- Experiment (Kassen & Bataillon 2006 Nat. Genetics)
  - Different environments affecting fitness and rank of wild type
  - No evidence for change in distribution (exponential with similar mean)
    → consistent with EVT

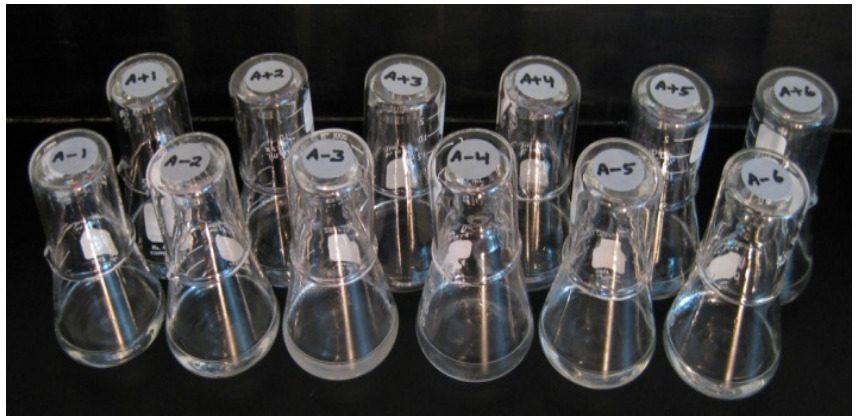


DFE across environments and genotypes

- Change in DFE during adaptation[1]



Wiser et al (2012 Science)



LTEE (Photo: Wikipedia)

1: Couce et al (2024 Science)

DFE across environments and genotypes

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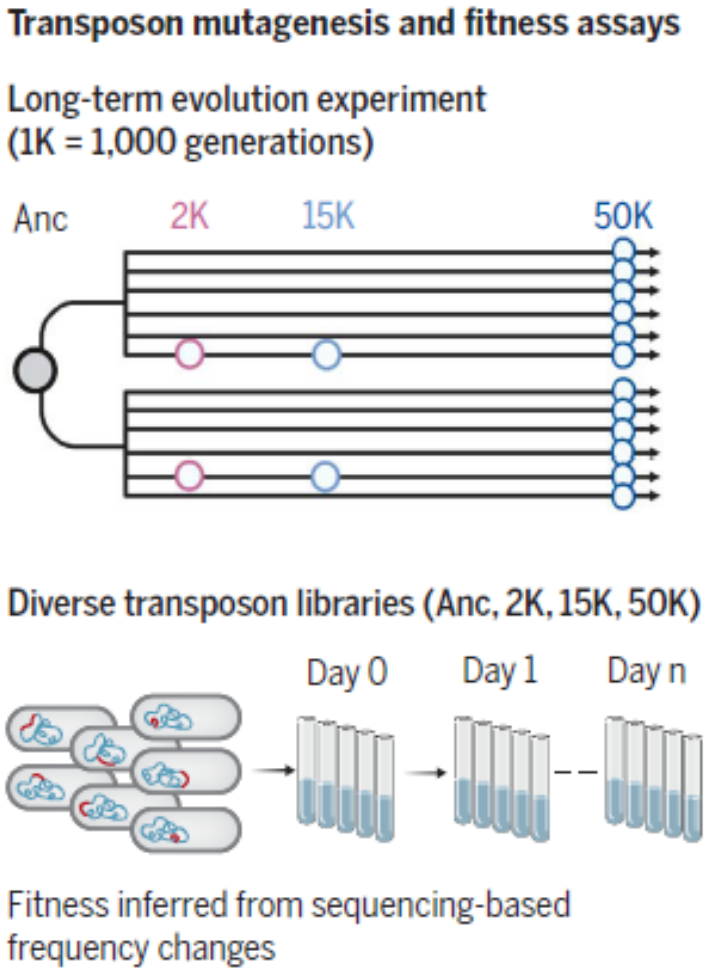
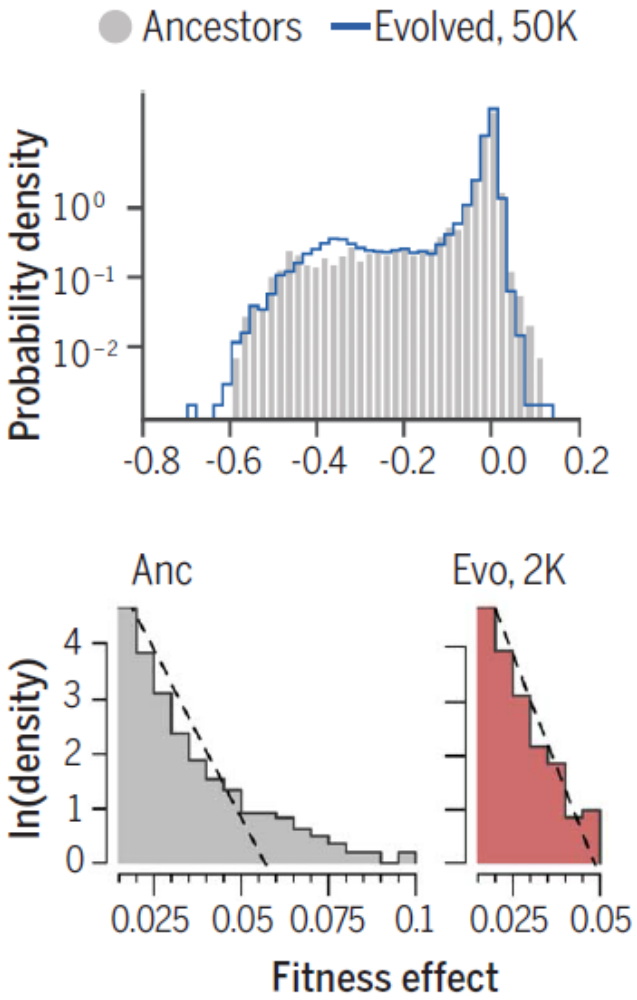




Mostly changes
to the upper tail
(beneficial mutations)

1: Couce et al (2024 Science)

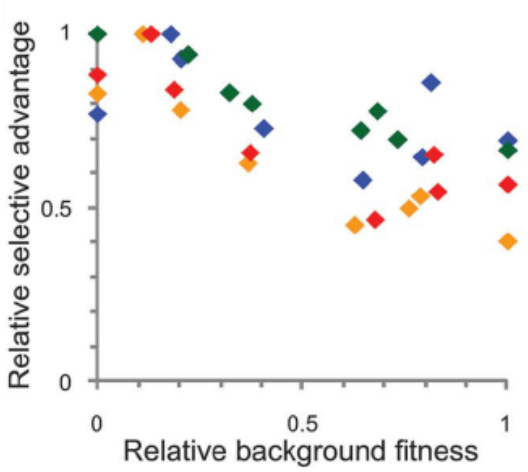
DFE across environments and genotypes

- Diminishing returns: (fixed) beneficial effects are weaker in fitter backgrounds

REPORTS

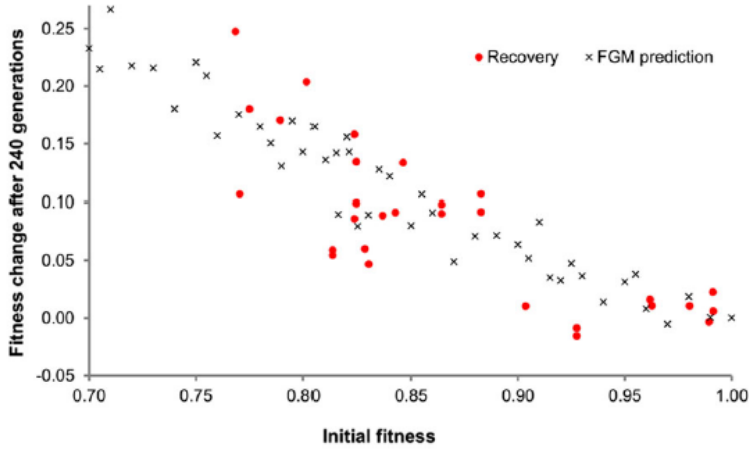
Diminishing Returns Epistasis Among Beneficial Mutations Decelerates Adaptation

Hsin-Hung Chou,[1]* Hsuan-Chao Chiu,[2] Nigel F. Delaney,[1] Daniel Segrè,[2,3] Christopher J. Marx[1,4]†



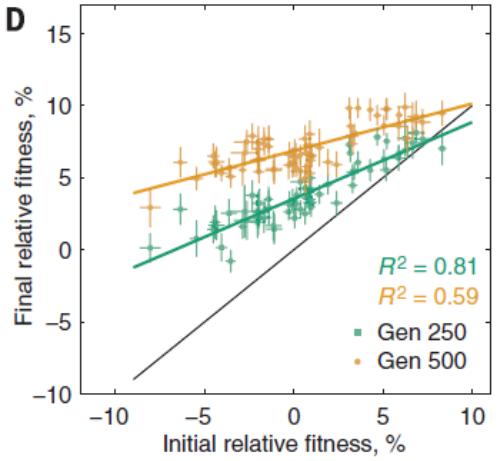
RATES OF FITNESS DECLINE AND REBOUND SUGGEST PERVASIVE EPISTASIS

L. Perfeito,[1,2] A. Sousa,[1,2] T. Bataillon,[3,4] and I. Gordo[1,5]



Global epistasis makes adaptation predictable despite sequence-level stochasticity

Sergey Kryazhimskiy,[1,3]*† Daniel P. Rice,[1,3]* Elizabeth R. Jerison,[2,3] Michael M. Desai[1,2,3]†



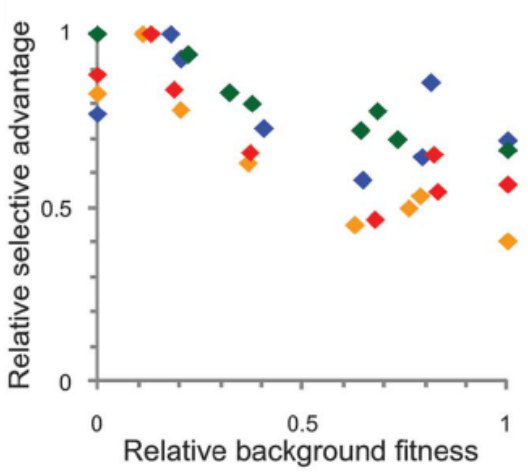
DFE across environments and genotypes

- Diminishing returns: (fixed) beneficial effects are weaker in fitter backgrounds

REPORTS

Diminishing Returns Epistasis Among Beneficial Mutations Decelerates Adaptation

Hsin-Hung Chou,[1]* Hsuan-Chao Chiu,[2] Nigel F. Delaney,[1] Daniel Segrè,[2,3] Christopher J. Marx[1,4]†



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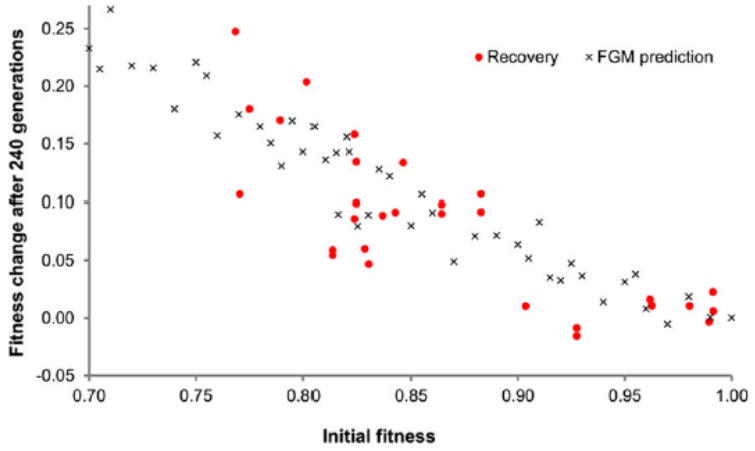

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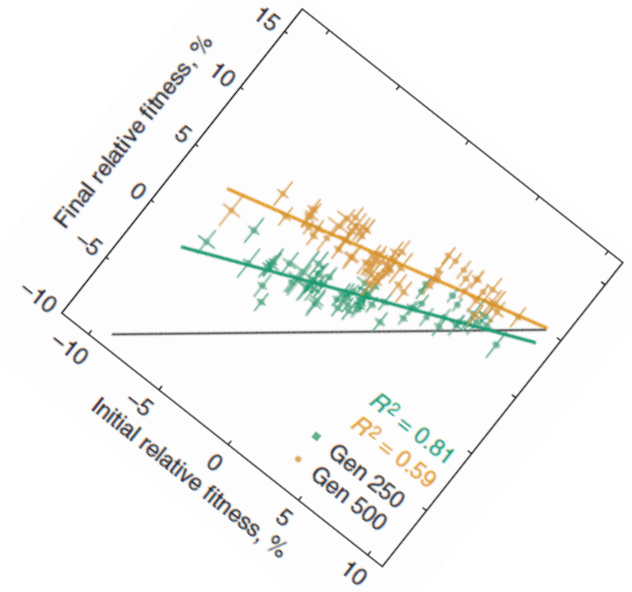


DFE across environments and genotypes

- Diminishing returns: (fixed) beneficial effects are weaker in fitter backgrounds

The rule of declining adaptability in microbial evolution experiments

*Alejandro Couce * and Olivier A. Tenaillon **

- How to **account for these effects to predict rates of adaptation**?

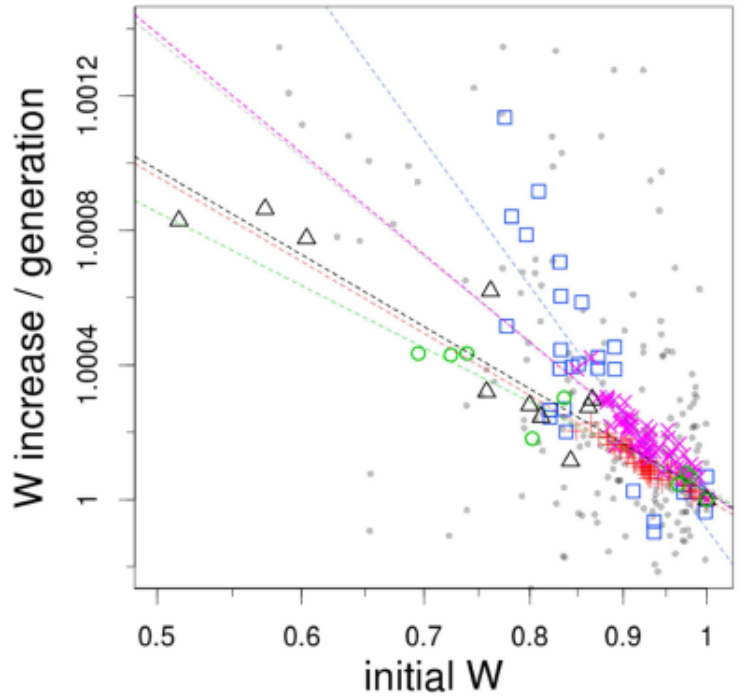


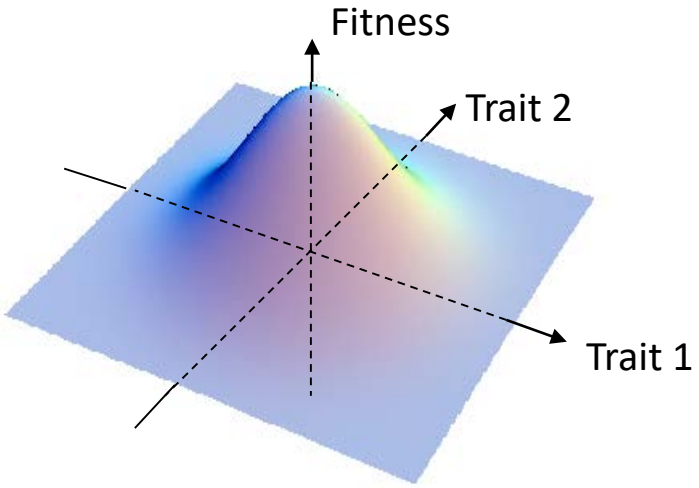
FIGURE 1 | Fitness increase as an inverse function of initial fitness. The datasets used here correspond to evolution experiments with *S. cerevisiae* (BY4741 strain, gray small circles; DBY15108 strain at 250 generations, magenta crosses; at 500 generations, red diagonal crosses), *E. coli* (mutator MG1655 strain, blue squares; wild-type REL606 strain, green circles) and microvirid bacteriophages (black triangles). Dashed lines shows best-fit log-log linear regression model to each dataset (correlation coefficients: gray, 0.33; magenta, 0.80; red, 0.87; blue, 0.67; green, 0.92; black, 0.87; *F*-test, all $P < 10–15$). Note that both axes are on a natural logarithmic scale.

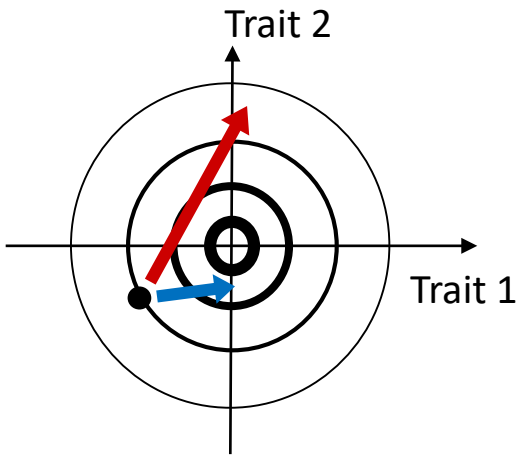
Phenotypic models of adaptation

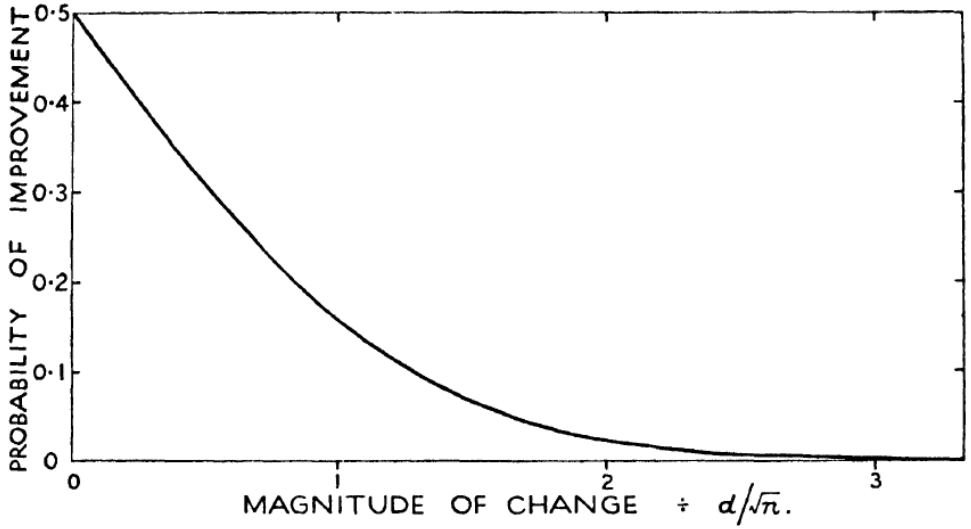
Tracking the genotype- and environment-dependence of selection

Fitness effects arising from effects on traits

- Back to picture of **adaptation as match between phenotypes and their environment** → Fitness landscape with **optimum for multiple traits**
- Fisher's geometrical model[1] (FGM): originally an "engineering" argument about curse of dimensionality, argument for micro-mutationism.







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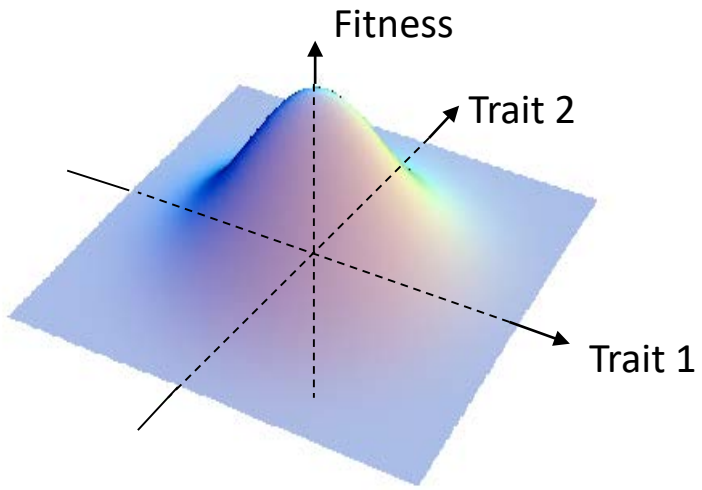


FUNDAMENTAL THEOREM OF NATURAL SELECTION

The nature of adaptation

An organism is regarded as adapted to a particular situation, or to the totality of situations which constitute its environment, only in so far as we can imagine an assemblage of slightly different situations, or environments, to which the animal would on the whole be less well adapted; and equally only in so far as we can imagine an assemblage of slightly different organic forms, which would be less well adapted to that environment.

Equivalence between environment & background genotype as causes for (mal)adaptation

The statistical requirements of the situation, in which one thing is made to conform to another in a large number of different respects, may be illustrated geometrically. The degree of conformity may be represented by the closeness with which a point A approaches a fixed point O.

No explicit fitness function

1: Fisher 1930

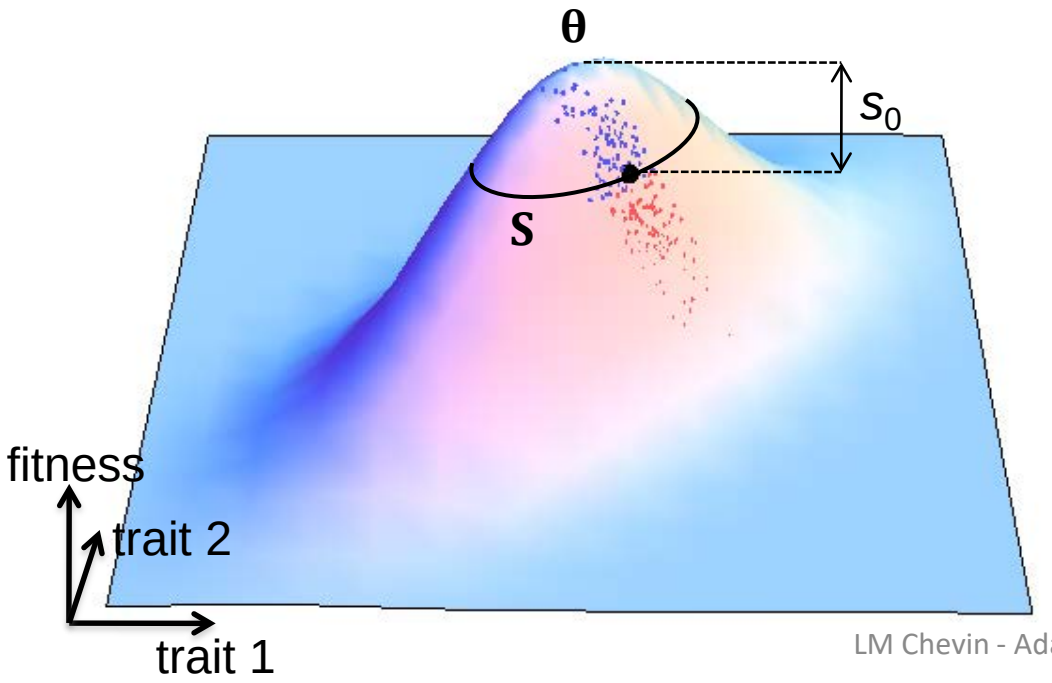
Fitness effects arising from effects on traits

- Back to picture of **adaptation as match between phenotypes and their environment** → Fitness landscape with **optimum for multiple traits**
- Fisher's geometrical model[1] (FGM): originally an "engineering" argument about curse of dimensionality, argument for micro-mutationism.
- Later extended to account for drift[2] and adaptive trajectories towards optimum[3]
- More recently formalized and made more quantitative, to analyze how the distribution of fitness effects of mutations changes across genetic backgrounds and environments[4]

1: Fisher 1930
2: Kimura 1983; Hartl & Taubes (1996);
3: Orr (1998,2000)
4: Tenaillon (2014)

Distribution of fitness effects in FGM

- Generalized multivariate FGM[1]: Gaussian fitness peak
  - Vector $\boldsymbol{\alpha}$: Mutation effects on multiple traits, with covariance matrix $\mathbf{M}$
  - Vector $\boldsymbol{\theta}$: (Environment-dependent) optimum phenotype for multiple traits
  - Matrix $\mathbf{S}$: Strength of stabilizing/correlational selection on (pairs of) traits
- Selection coefficient $s = -\frac{1}{2}\,\boldsymbol{\alpha}^{\mathrm{T}}\mathbf{S}\boldsymbol{\alpha} - \boldsymbol{\alpha}^{\mathrm{T}}\mathbf{S}(\mathbf{z}-\boldsymbol{\theta})$



1: Martin & Lenormand (2006 Evolution)

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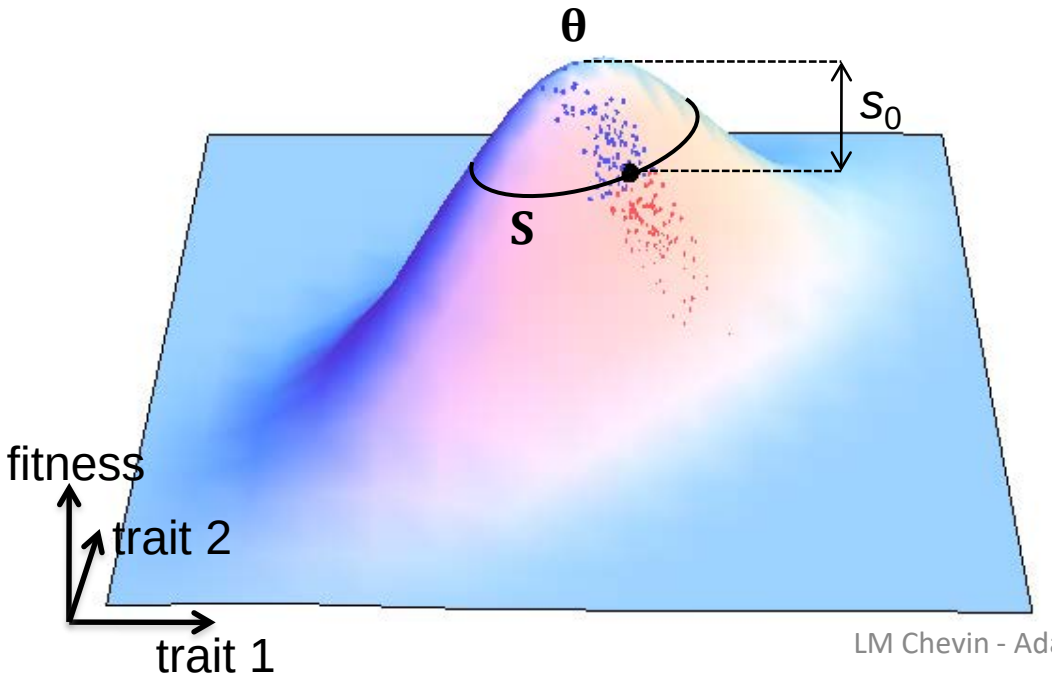
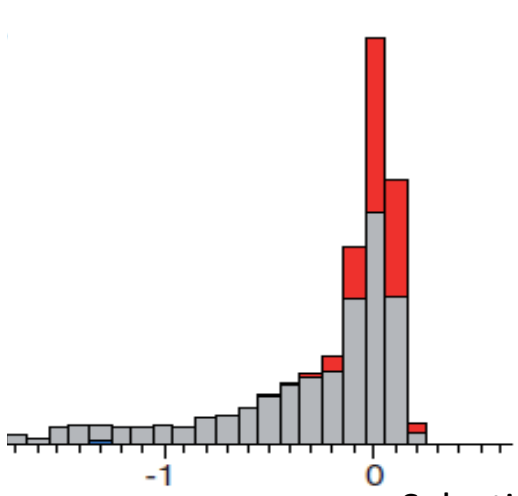
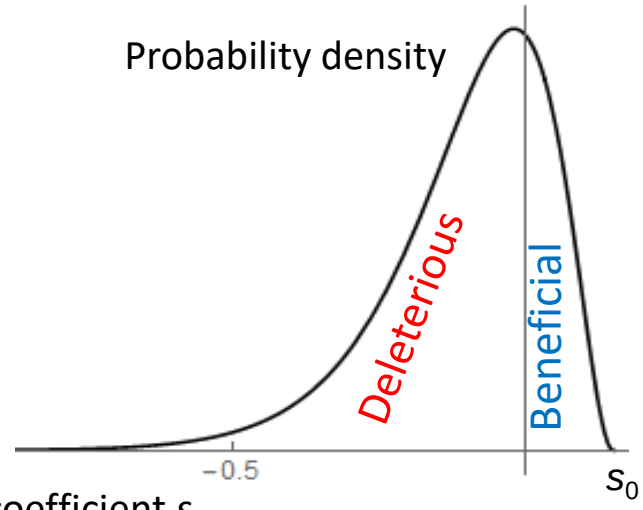
- With Gaussian mutation effects on traits(*), DFE ~reverse gamma[1]/non-central χ^2

→ Left skewed, bounded by optimum







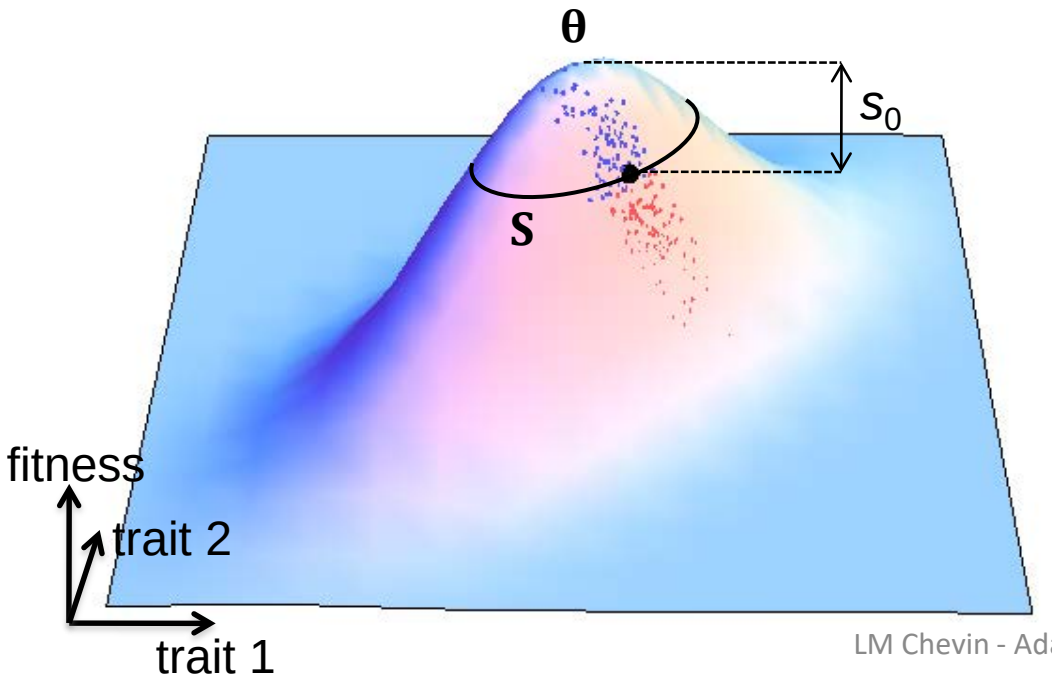
Selection coefficient *s*

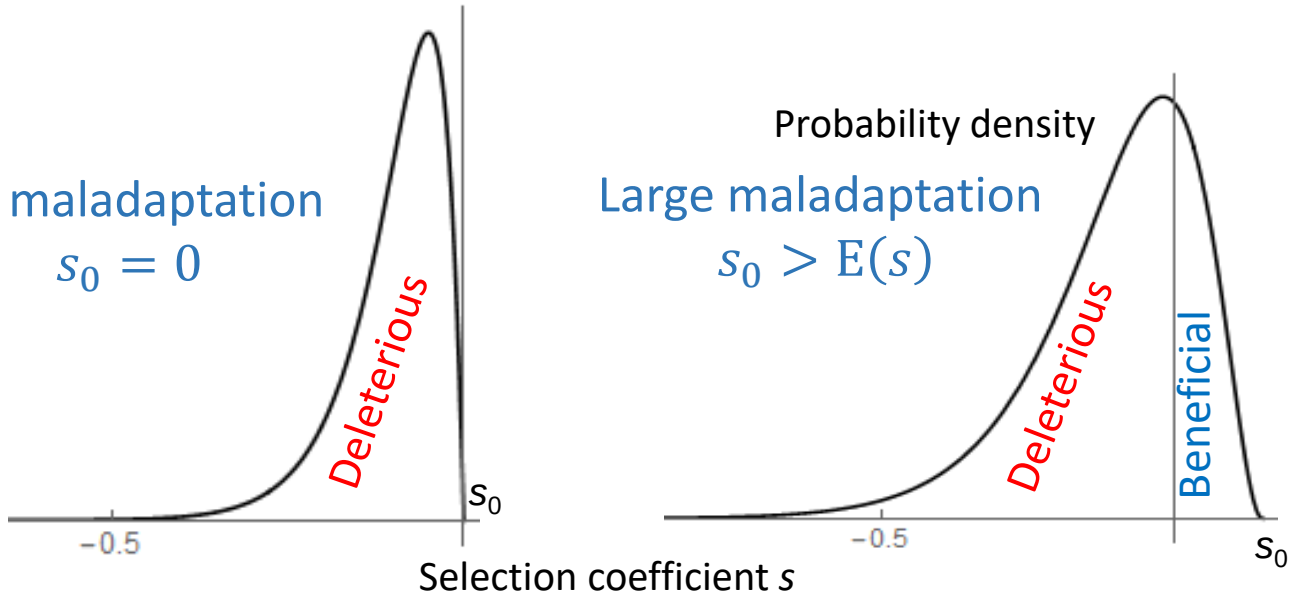
1: Martin & Lenormand (2006 Evolution)

Distribution of fitness effects in FGM

- **Phenotypic maladaptation** $(\mathbf{z}-\boldsymbol{\theta})$, with **fitness cost** $s_0 = -\frac{1}{2}(\mathbf{z}-\boldsymbol{\theta})^{\mathbf{T}}\mathbf{S}(\mathbf{z}-\boldsymbol{\theta})$

  affects: - variance of s
  - proportion of beneficials (more under larger s_0)
  - but not mean $\mathrm{E}(s) = \mathrm{tr}(\mathbf{SM})/2$

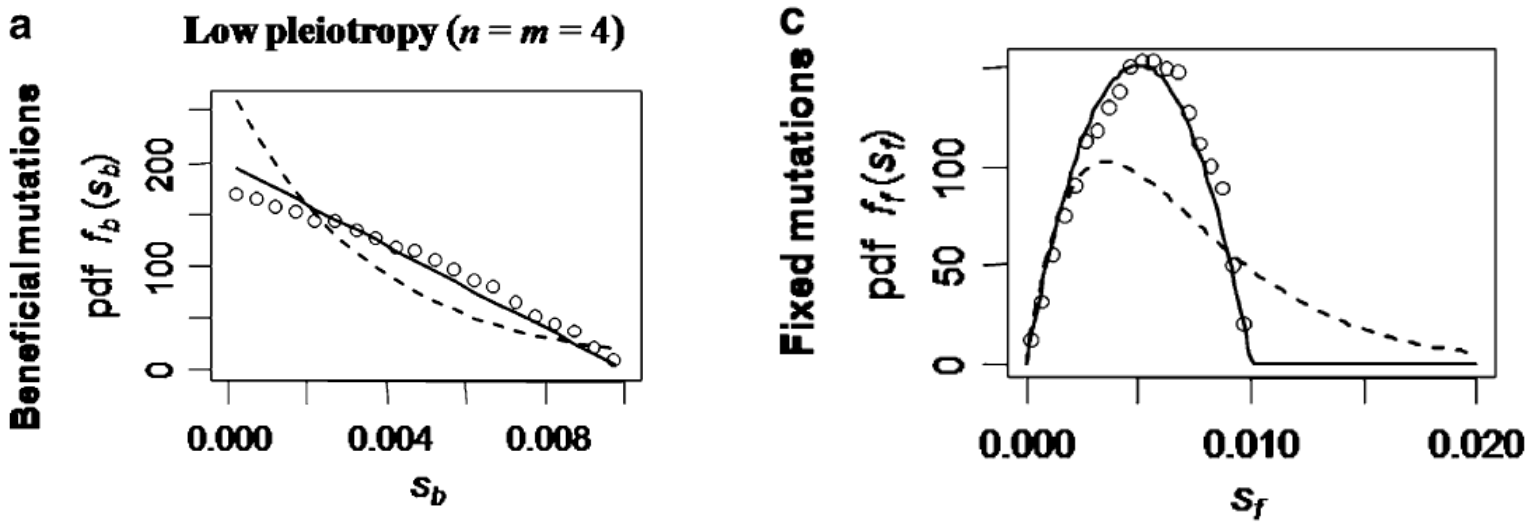




1: Martin & Lenormand (2006 Evolution)

Distribution of beneficial effects in FGM

- Also leads to **predictions more specific to adaptation**: distribution of beneficial and fixed effects, mean fixation probability
- Unless far from optimum: Other extreme value domain than usually assumed: Weibull (bounded by optimum) → beta rather than exponential distribution[1]

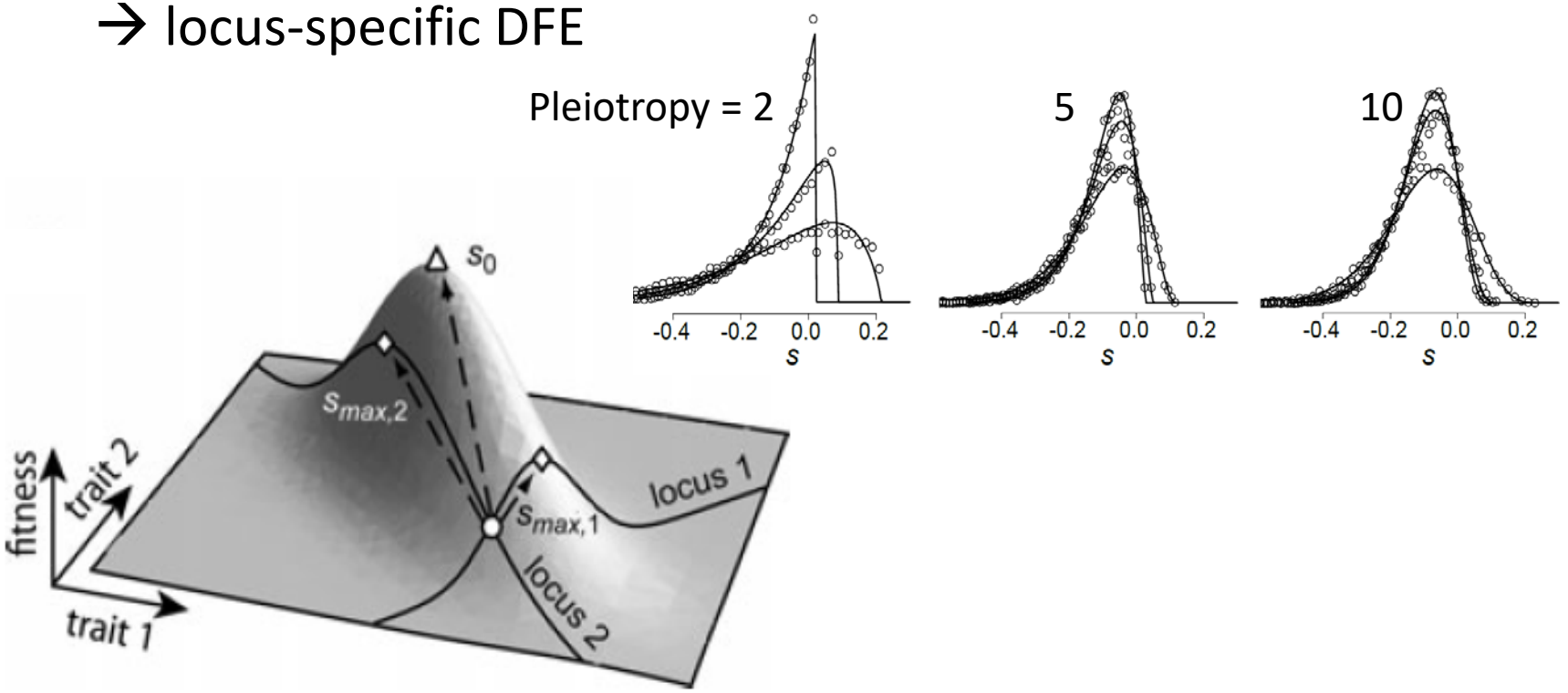


1: Martin & Lenormand (2008 Genetics)

Explicit loci in FGM

- **Genomic context**: Each locus may
  - have a specific distribution of phenotypic effects (mutation heterogeneity)
  - affect a subset of all selected traits (restricted pleiotropy)

→ locus-specific DFE



1: Chevin, Martin & Lenormand (2010 Evolution)

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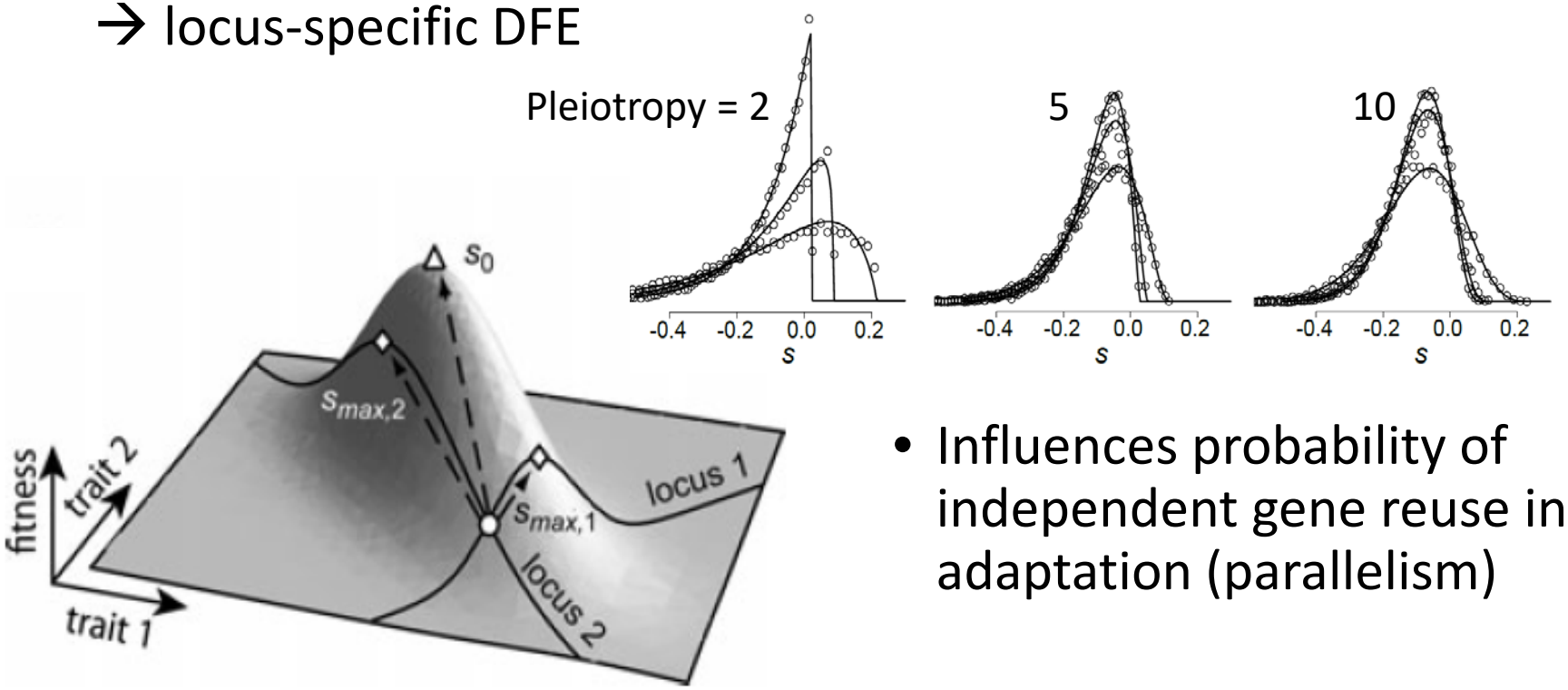
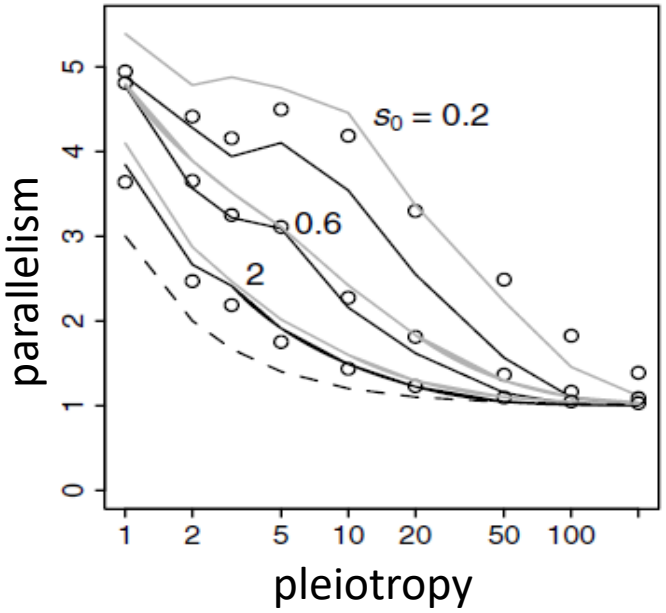


- Influences probability of independent gene reuse in adaptation (parallelism)



1: Chevin, Martin & Lenormand (2010 Evolution)

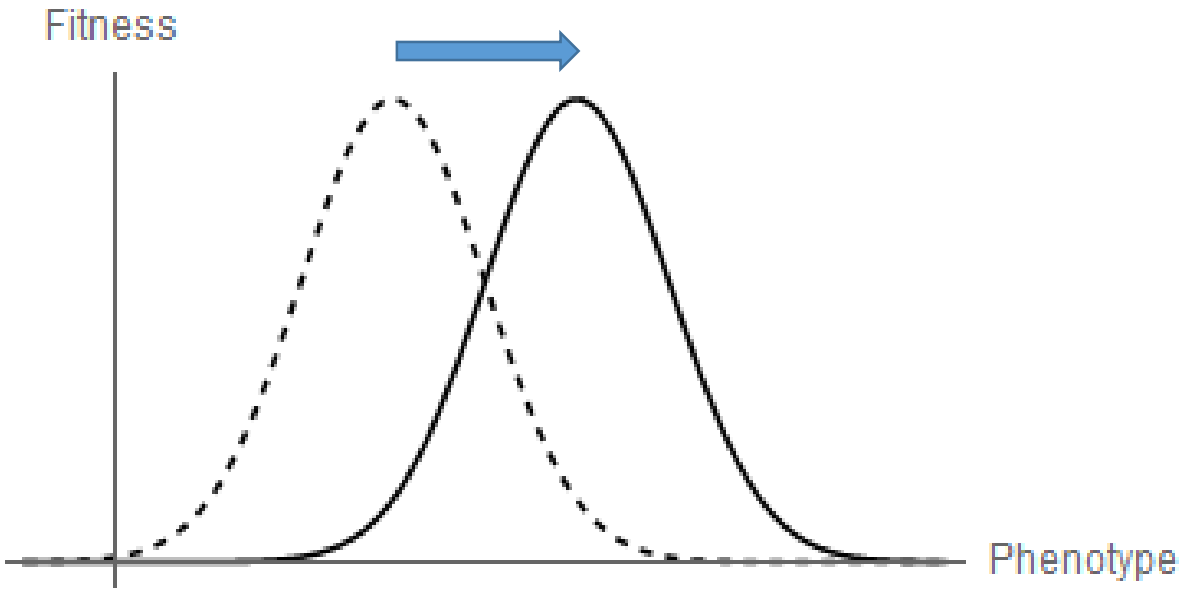
From DFE to adaptation

- FGM captures the **context dependence of mutation DFE**:
  more beneficials under higher stress, diminishing returns, declining adaptability...
- FGM can thus be used to **derive the trajectory of mean fitness** over time by **tracking changes in DFE**, even when traits *per se* are not the focus.
- However predicting future DFEs from maladaptation $s_0 = -\frac{1}{2}\,(\mathbf{z}-\boldsymbol{\theta})^{\mathrm{T}}\mathbf{S}(\mathbf{z}-\boldsymbol{\theta})$ requires tracking the **dynamics of phenotypic traits**
- Furthermore, DFE *per se* best predicts adaptation in sequential (SSWM, origin-fixation) regimes, less so in more polymorphic regimes

→ Focusing on phenotypes (rather than just fitness) can improve prediction and bring more mechanistic insights into adaptation

Dynamics of phenotypic change

- **Phenotypic response to abrupt shift in optimum phenotype**



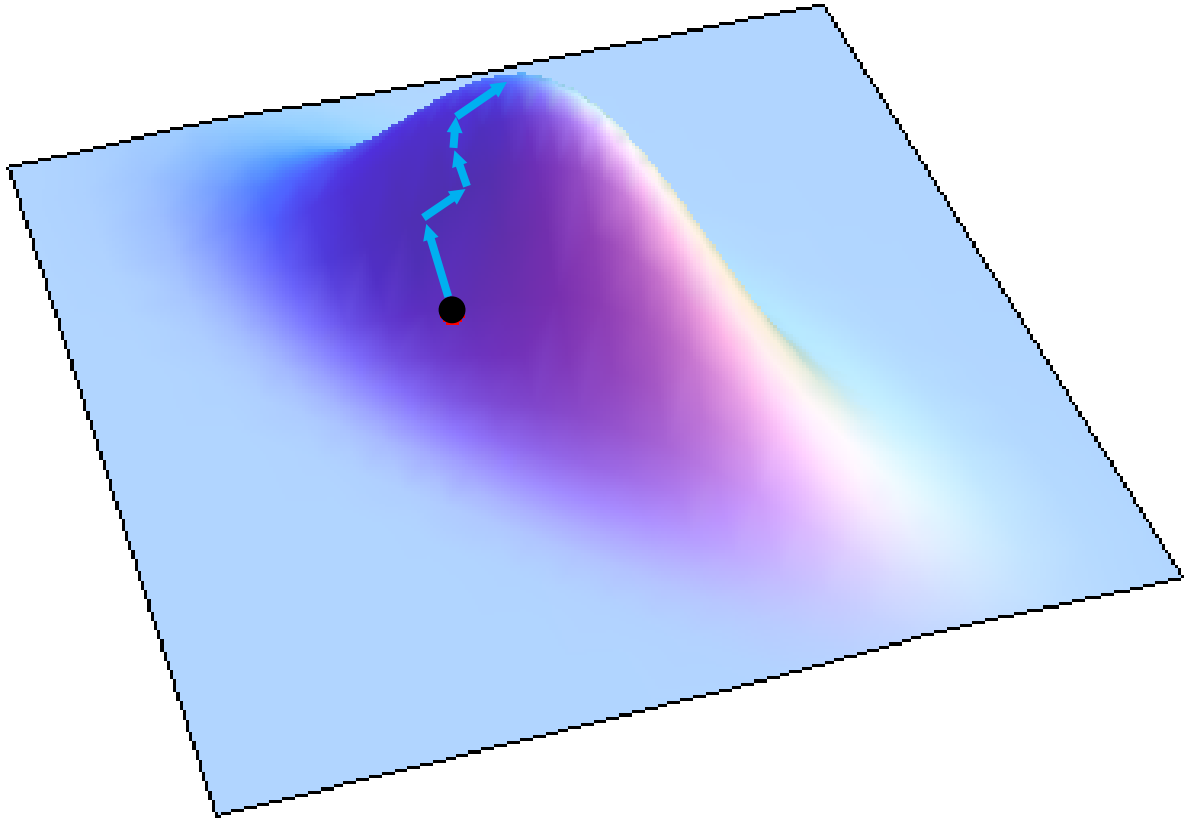
Minimal model of directional selection on a trait.

Relevant for invasion of new habitat, critical transitions in climatic systems, sudden exposure to antibiotic treatment…

Dynamics of phenotypic change

- Low mutation regime -

- **Adaptive walk**: Sequential fixation of mutations approaching optimum (SSWM, origin-fixation)



1: Orr (1998 Evolution)

Dynamics of phenotypic change

- Low mutation regime -

- **Adaptive walk**: Sequential fixation of mutations approaching optimum (SSWM, origin-fixation)
- **Initial phenotypic steps may be large**[1] (unlike Fisher's micro-mutationism)

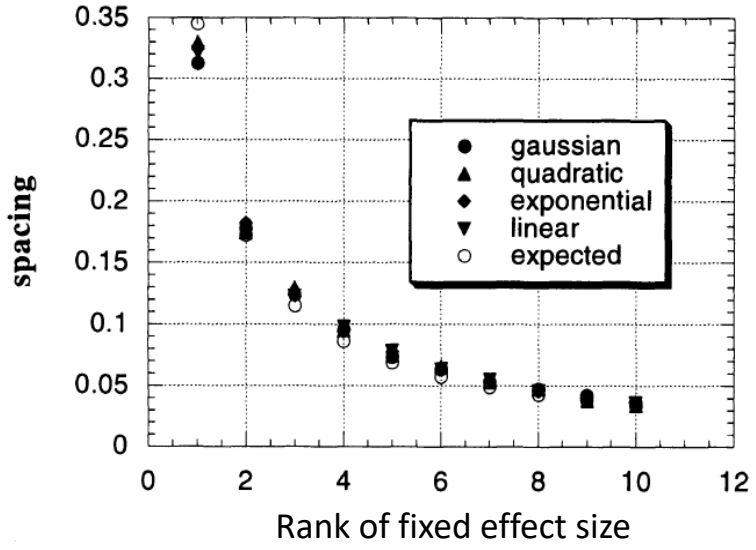


FIG. 8. Spacings between largest and next-to-largest, etc. factors fixed during adaptation.

- Phenotypic effects fixed over entire trajectory are **exponentially distributed**[1]

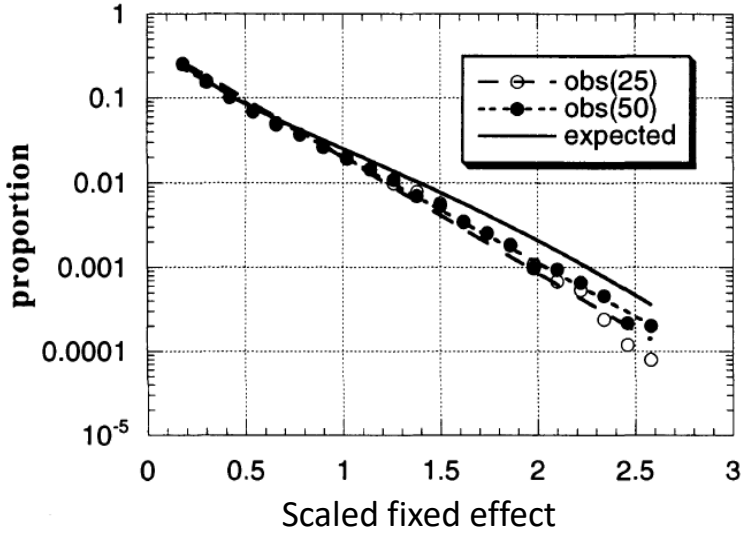


FIG. 6. The factors fixed during adaptation are approximately exponentially distributed (semilog plot).

1: Orr (1998 Evolution)

Dynamics of phenotypic change

- Low mutation regime -

- **Adaptive walk**: Sequential fixation of mutations approaching optimum (SSWM, origin-fixation)
- **Cost of complexity** (number of traits *n*) on rate of adaptation[1]

$$\frac{d\bar{w}}{dt} = -\frac{4N\mu r^2}{n} M\bar{w} \ln \bar{w},$$

$$M = (1/\sqrt{2\pi}) \int_x^\infty (y - x)^2 e^{-y^2/2} dy.$$

$$x = r\sqrt{n}/(2\sqrt{-2 \ln \bar{w}})$$

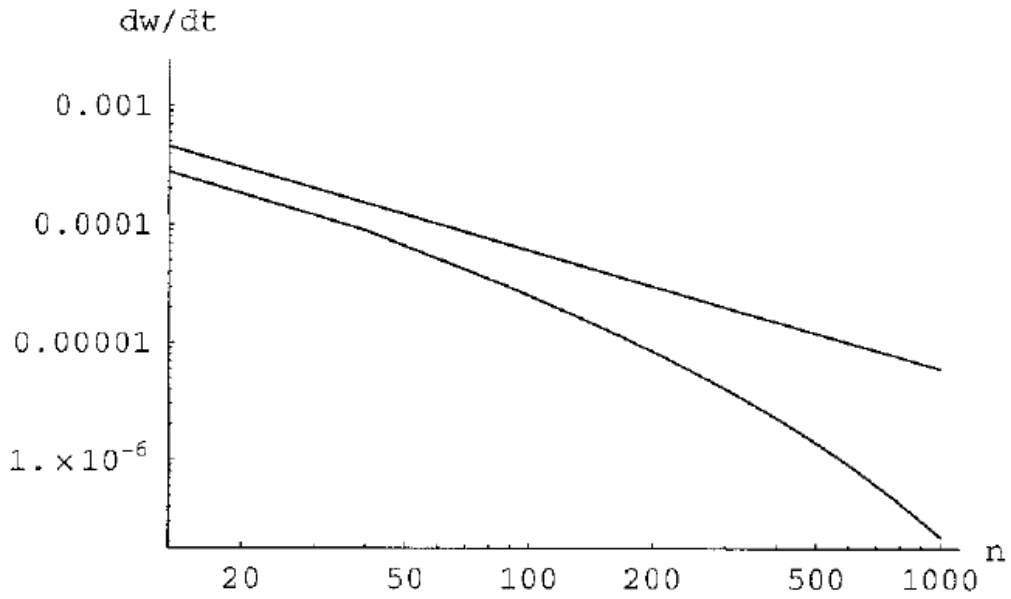


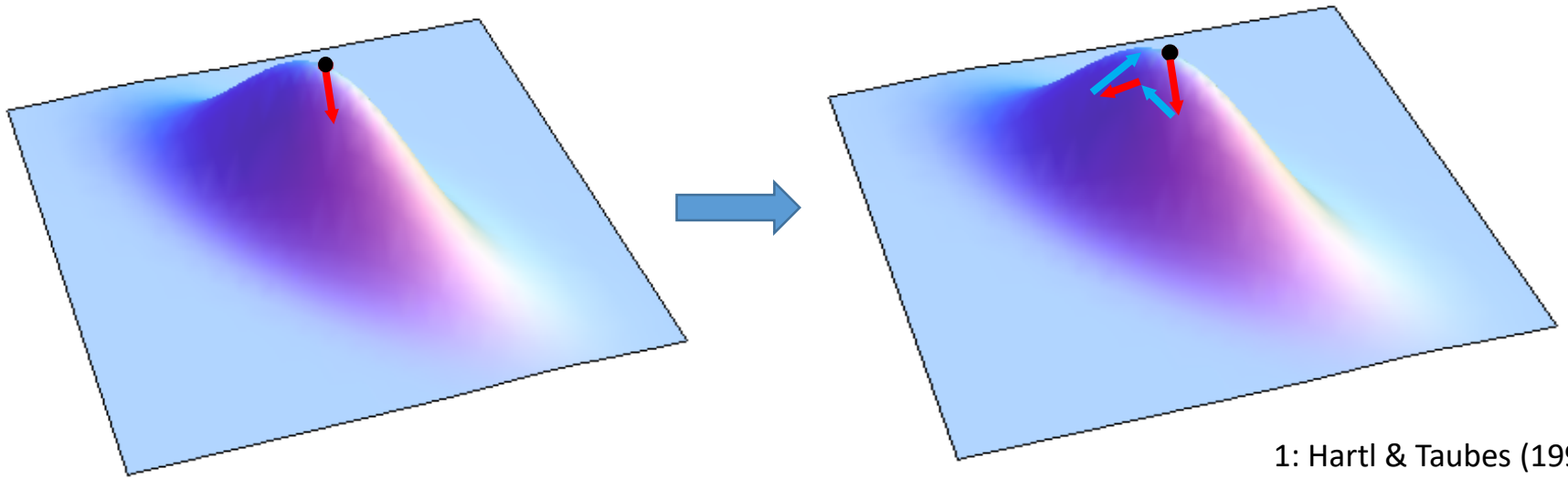
FIG. 2. Rate of increase in fitness as a function of the number of characters, n (log-log plot). The straight line shows the approximate equation (8), in which $d\bar{w}/dt$ declines as n^{-1}. The curved line shows the more exact equation (7b). Note that $d\bar{w}/dt$ declines faster than n^{-1}. For both curves, $z = 1$ and $r = 0.10$.

1: Fisher (1930); Orr (2000 Evolution)

Dynamics of phenotypic change

- Low mutation regime -

- In small populations, **slightly deleterious mutations can fix** by random drift, causing **maladaptation even in constant environment** (fixed optimum)
- This then leads to **compensatory adaptive evolution**
- In long run, the expected **fixed drift load** depends on effective population size and organismal complexity[1]



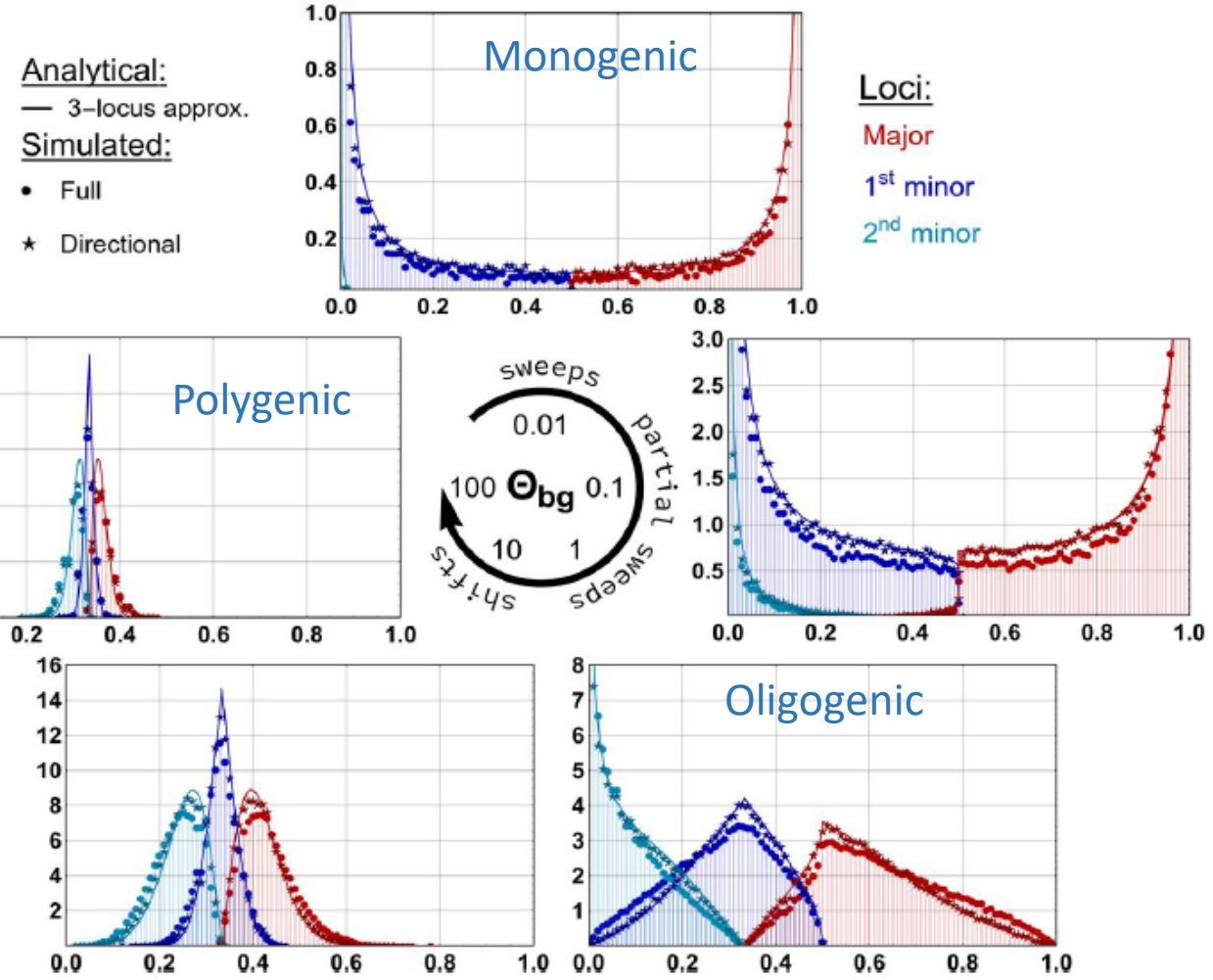
1: Hartl & Taubes (1996); Poon & Otto (2000); Silander et al (2007); Gros & Tenaillon (2009)

Dynamics of phenotypic change

- Intermediate mutation regime (oligogenic) -

- Joint influences of mutation, selection and drift on establishment of alleles contributing to selection response[1,2].
- Assuming same phenotypic effect at all loci, the type of selection response is fully determined by a single parameter [2] : the **background mutation rate Θ_{bg}**
- Response is polygenic if large:
  - mutation rate
  - effective population size (little drift)
  - genetic redundancy (many equivalent loci)

Snapshot at 1/3 of initial distance to optimum



1: Hayward & Sella (2022 Elife)
2: Höllinger et al (2023 Genetics)

Dynamics of phenotypic change

- High mutation regime (polygenic) -

- When many loci with small effects contribute to the trait, genetic values for the phenotype tend to a normal distribution, as in infinitesimal model[1]
- Even with substantial deviations from normality[2], the phenotypic response to selection is well predicted by Lande's equation[3]

$$\Delta\bar{z} = V_a \frac{\partial \ln \bar{W}}{\partial \bar{z}}$$

V_a: additive genetic variance of the trait

$\beta = \frac{\partial \ln \bar{W}}{\partial \bar{z}}$: directional selection gradient, slope of mean fitness landscape[4]

1: Fisher 1918; Barton et al (2017)
2: Turelli & Barton (1994), Hayward & Sella (2022)
3: Lande (1976); 4: Wright (1937)

Dynamics of phenotypic change

- High mutation regime (polygenic) -

- With a Gaussian fitness peak, selection gradient $\beta = \partial \ln \bar{W} / \partial \bar{z} = -S(\bar{z} - \theta)$
  → **linear restoring force** towards optimum θ, deviation $(\bar{z} - \theta)$ declines exponentially[1]

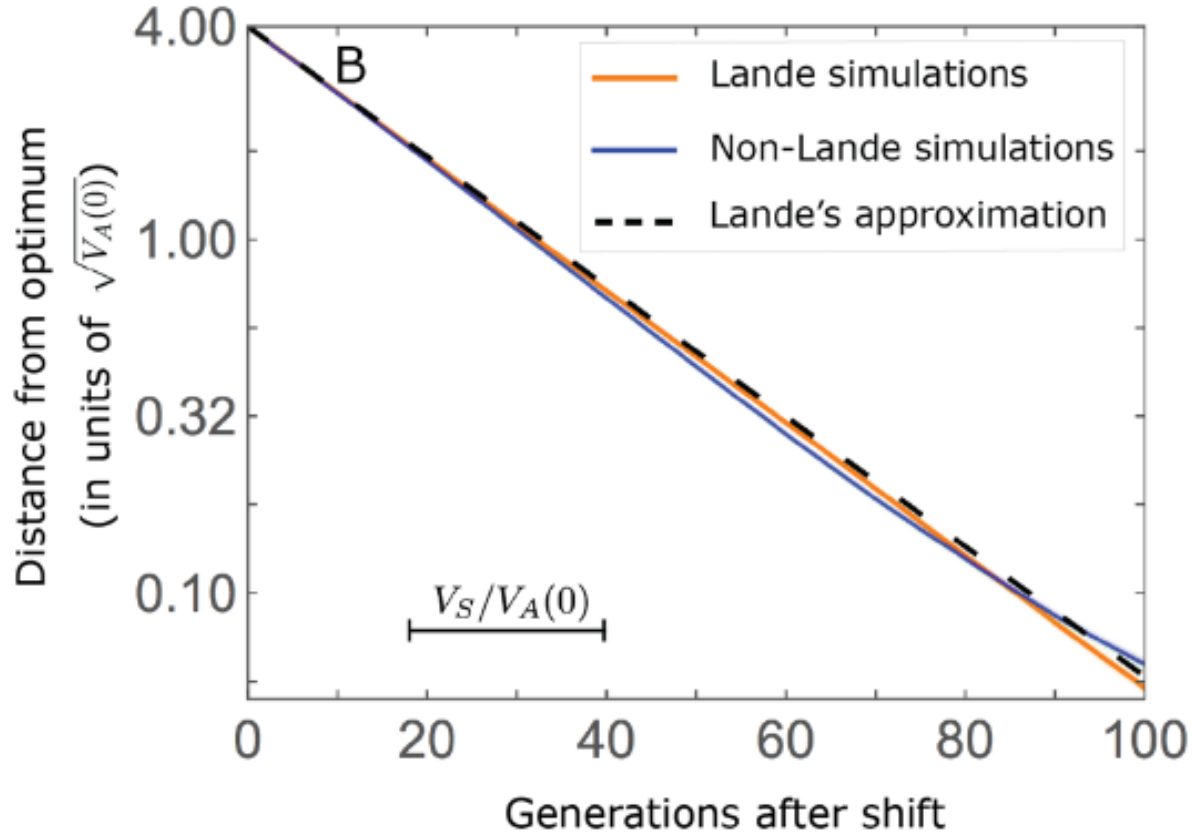


Figure from Hayward & Sella (2022 Elife)

1: Lande (1976)

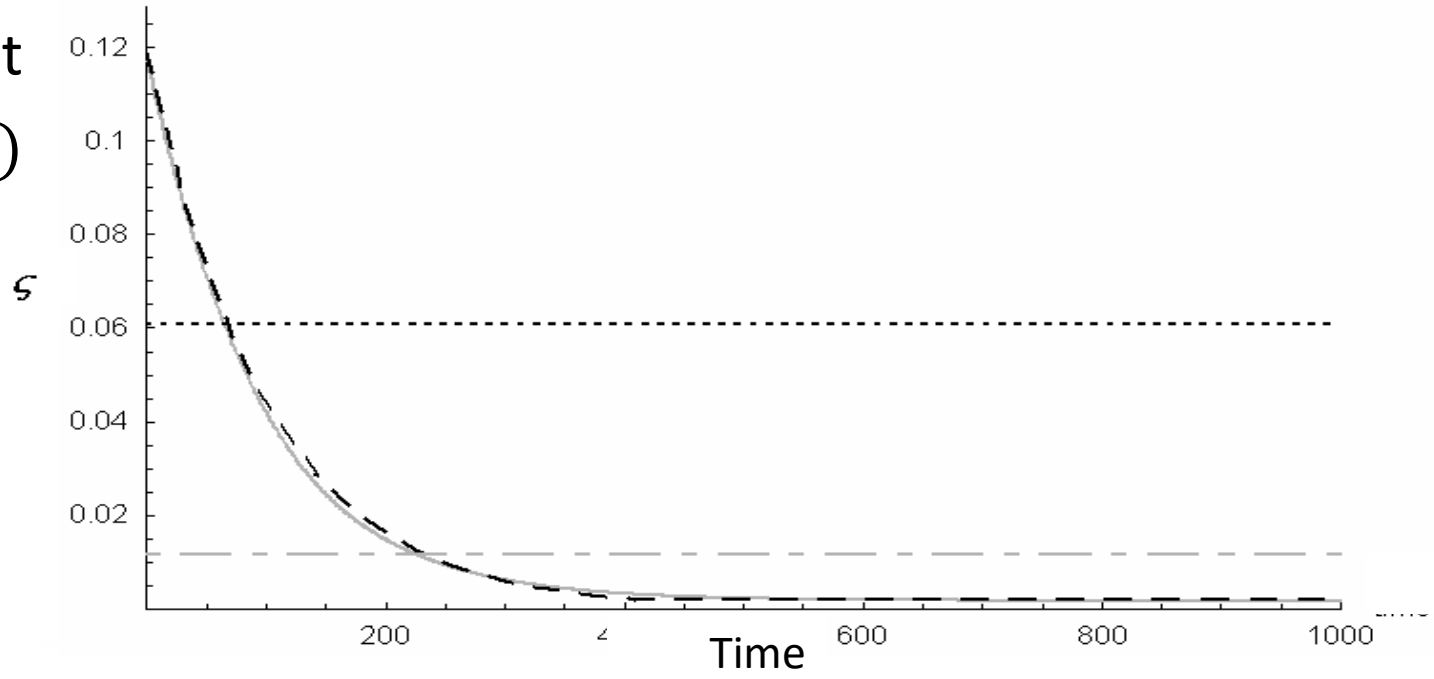
Dynamics of phenotypic change

- High mutation regime (polygenic) -

- Frequency change at loci underlying adaptation are small in short run, proportional to their contribution to genetic variance[1].
- Even for **locus of major effect *a*** on the trait, its mean selection coefficient changes over time, as mean phenotype in genetic background evolves because of other loci[2]

Selection coefficient

$$s = \frac{\Delta p}{pq} \approx -Sa(\bar{z} - \theta)$$



1: Hayward & Sella (2022); 2: Lande (1983); Chevin & Hospital (2008); Jain & Stephan (2015, 2017)

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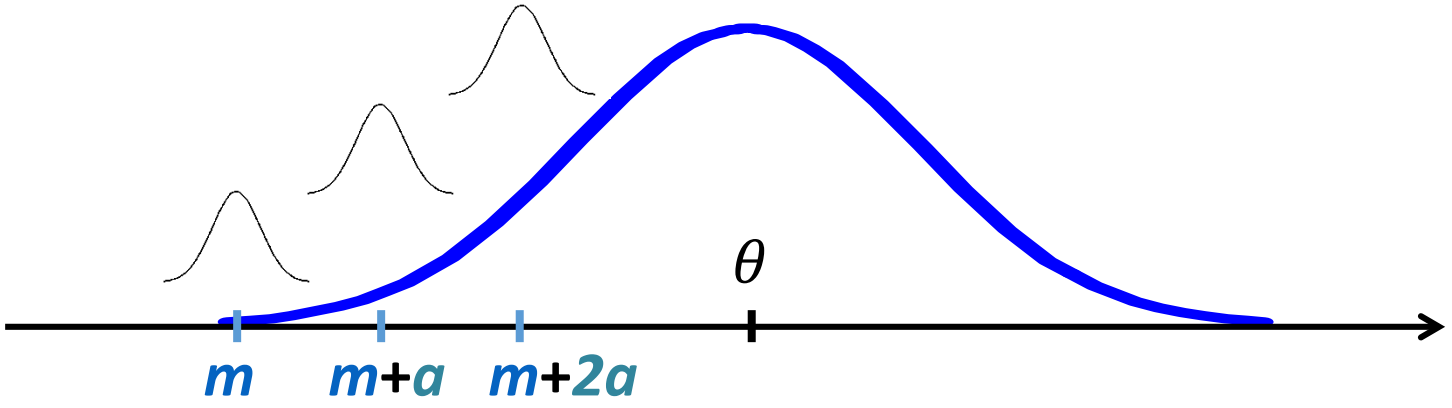

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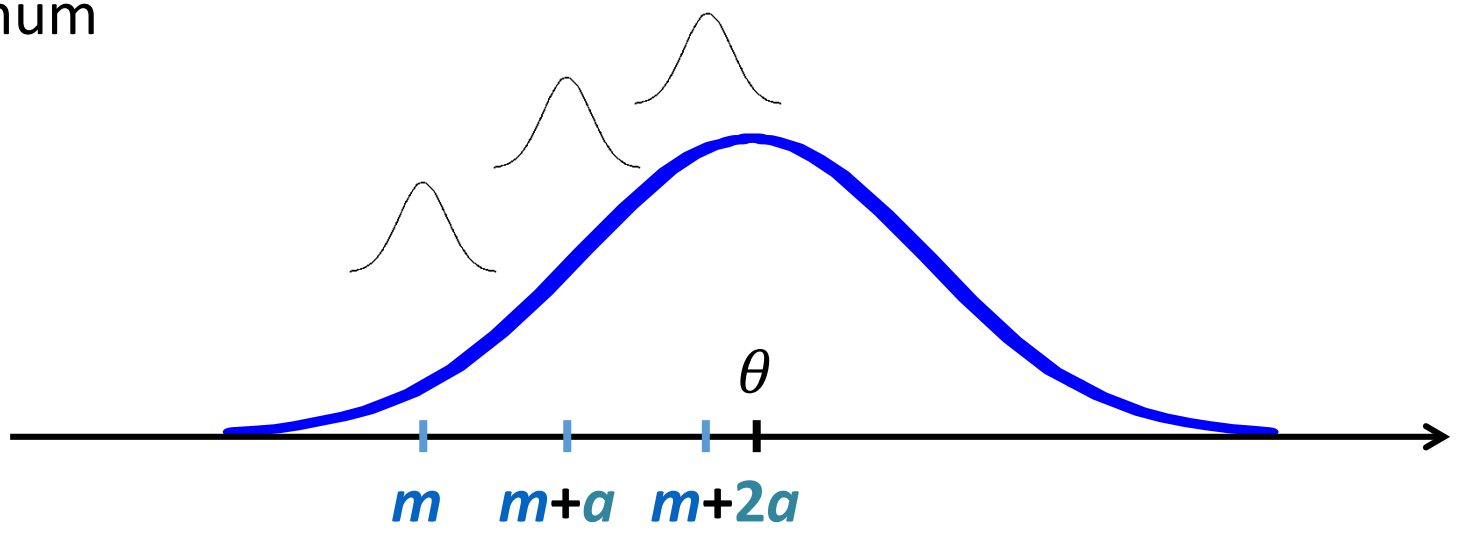

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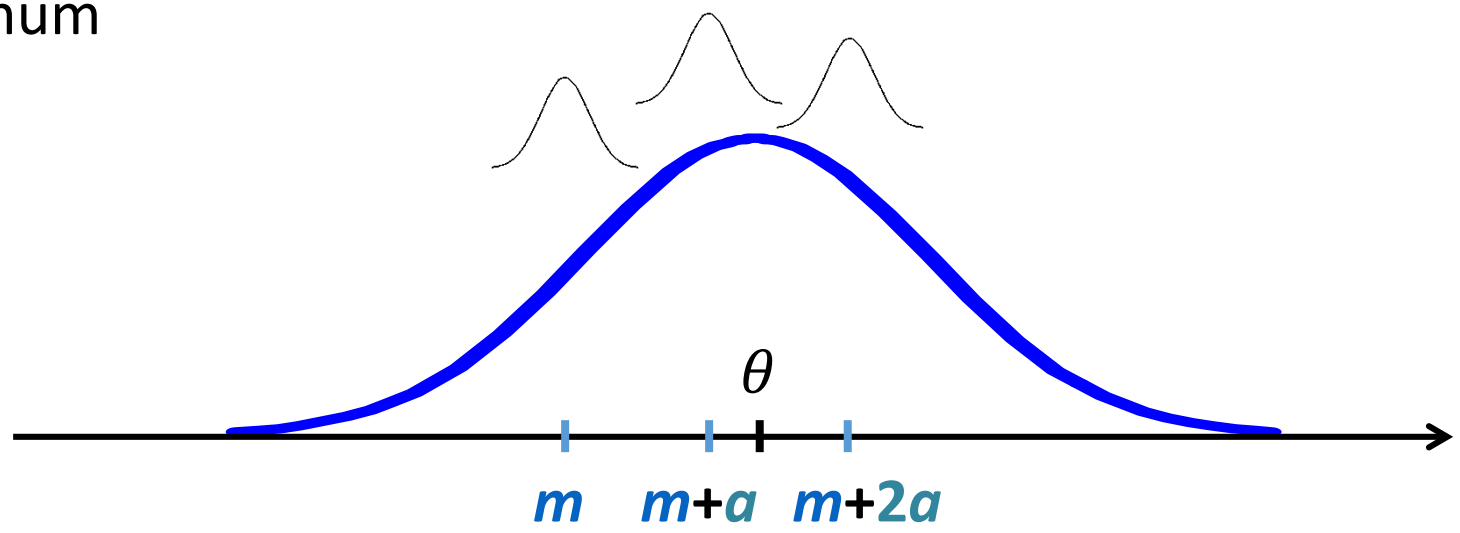

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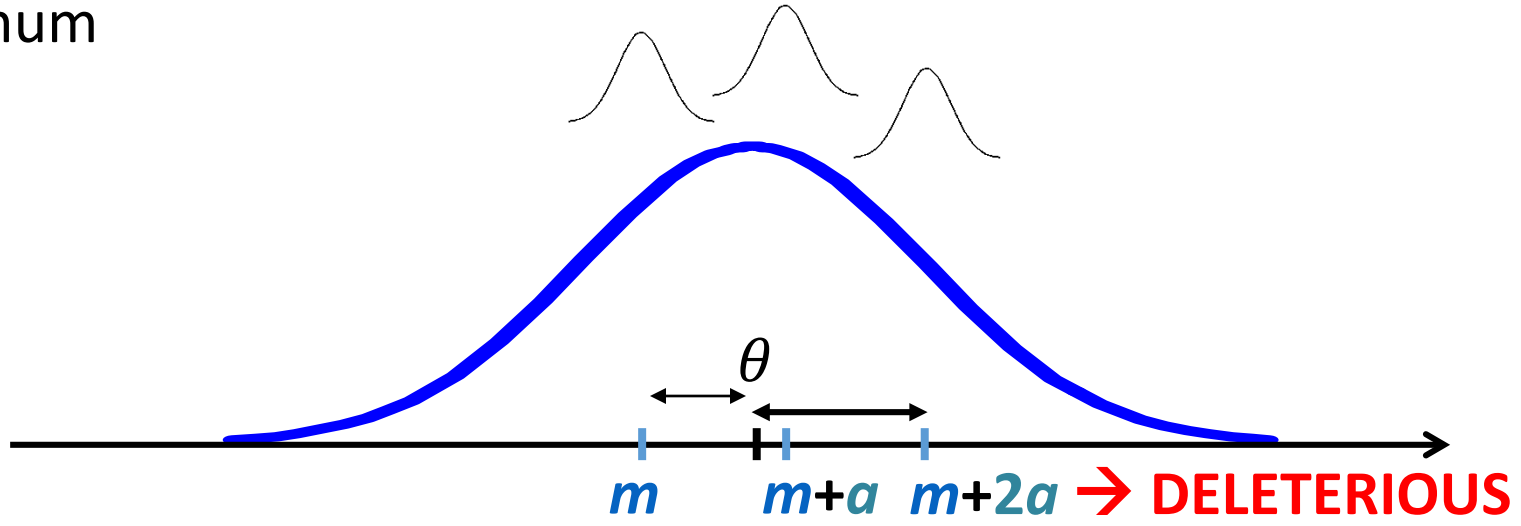
- Even for **locus of major effect *a*** on the trait, its mean selection coefficient changes over time, as mean phenotype in genetic background evolves because of other loci[2]
- Some initially beneficial mutation may even become deleterious as mean background reaches optimum



1: Hayward & Sella (2022);
2: Lande (1983); Chevin & Hospital (2008);
Jain & Stephan (2015, 2017)

Dynamics of phenotypic change

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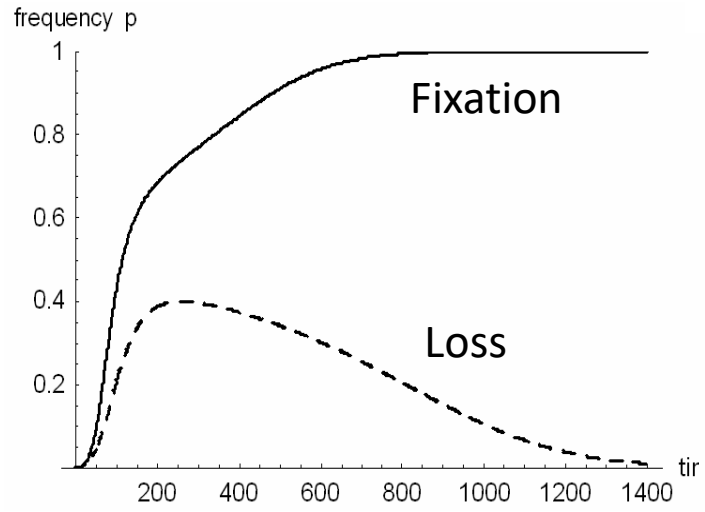

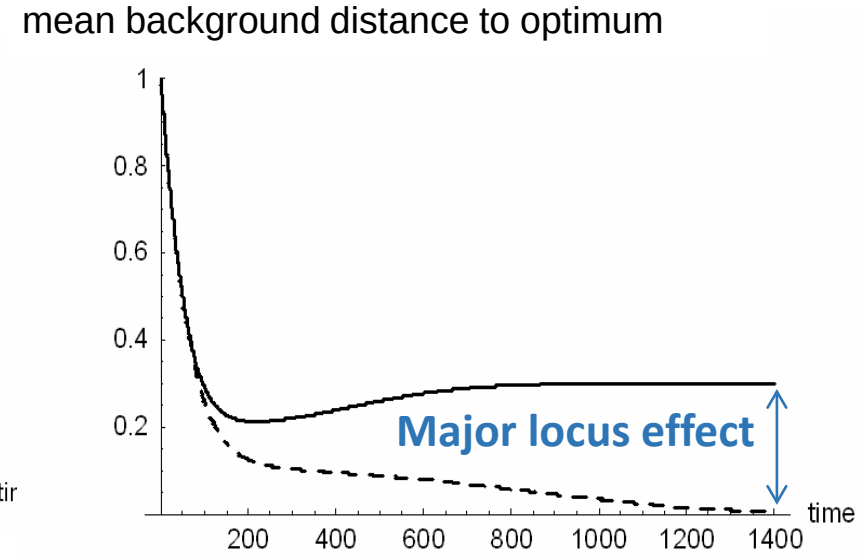

1: Hayward & Sella (2022);
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Dynamics of phenotypic change

- High mutation regime (polygenic) -

- In highly polygenic regime, each individual locus has little predictive power, and may have complex dynamics.
- Genomic selection[1] could be used to predict adaptation based on DNA data, but GWAS are often population-specific: saturation requires huge sample size[2]
- Quantitative genetics instead tracks moments of phenotype distributions, without attention to genetic detail
- When genetic (co)variances can be approximated as constant[3], much analytical progress can be made in **explicit scenarios of adaptation**, where a changing environment causes movements of an optimum phenotype.

To be continued…

1: Meuwissen et al (2001 Genetics)
2: Yengo et al (2022 Nature)
3: Lande (1976); Hayward & Sella (2022)

Thanks!
Questions?

Adaptation to an optimum - history

- **Quantitative genetics**: Wright (1935)

THE ANALYSIS OF VARIANCE AND THE CORRELATIONS BETWEEN RELATIVES WITH RESPECT TO DEVIATIONS FROM AN OPTIMUM.

By SEWALL WRIGHT.

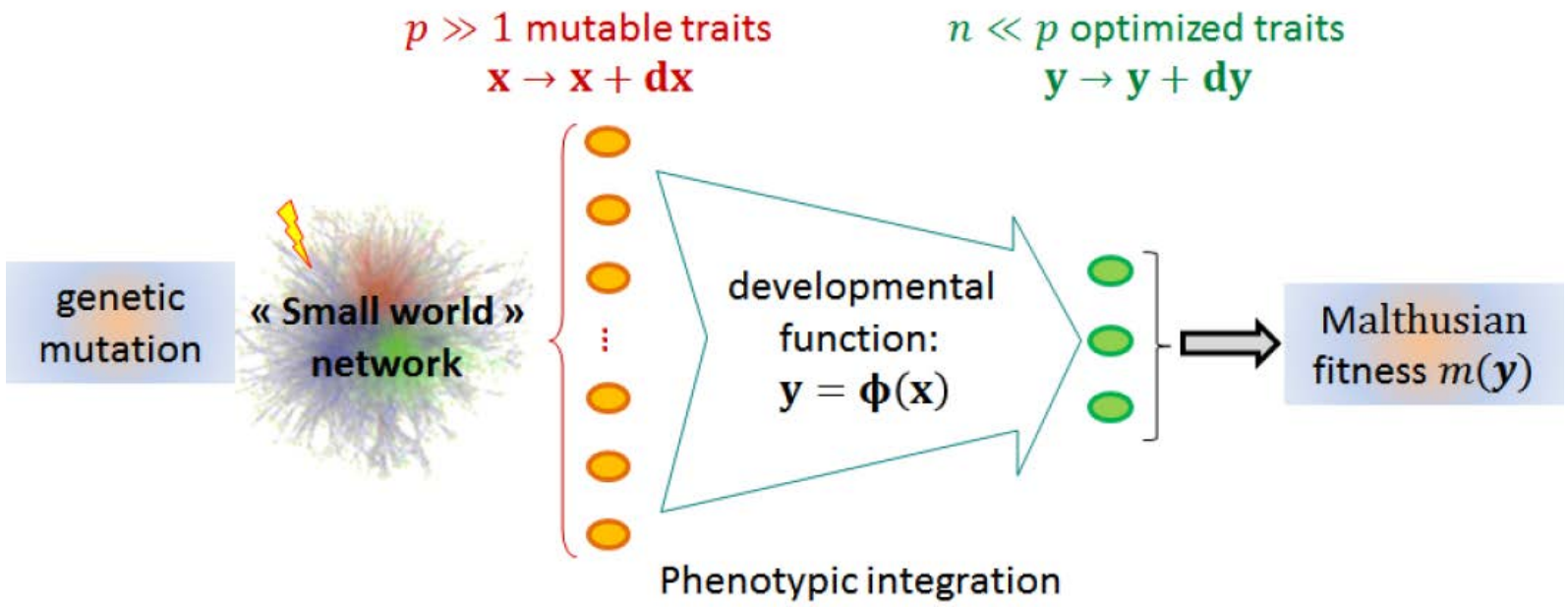
In the present paper it is assumed that the grade of a "primary" character is determined by a number of independent pairs of genes whose effects combine additively (no epistasis).

A "secondary" character is assumed to depend on the deviation of the primary from a certain optimum grade. It is convenient to use the squared deviations in order to bring deviations above and below the optimum to a common sign. It is also more natural in that it avoids an abrupt change at the optimum.

Patterns of genetic variation depend on how close a trait is to fitness of performance

Distribution of mutation phenotypic effects

- (*) Assumptions of this model **can emerge from first principles**.
  Gaussian distribution of mutation effects on traits under stabilizing selection can arise from a network of regulatory and developmental interactions on a larger number of underlying traits



1: Martin (2014 Genetics)