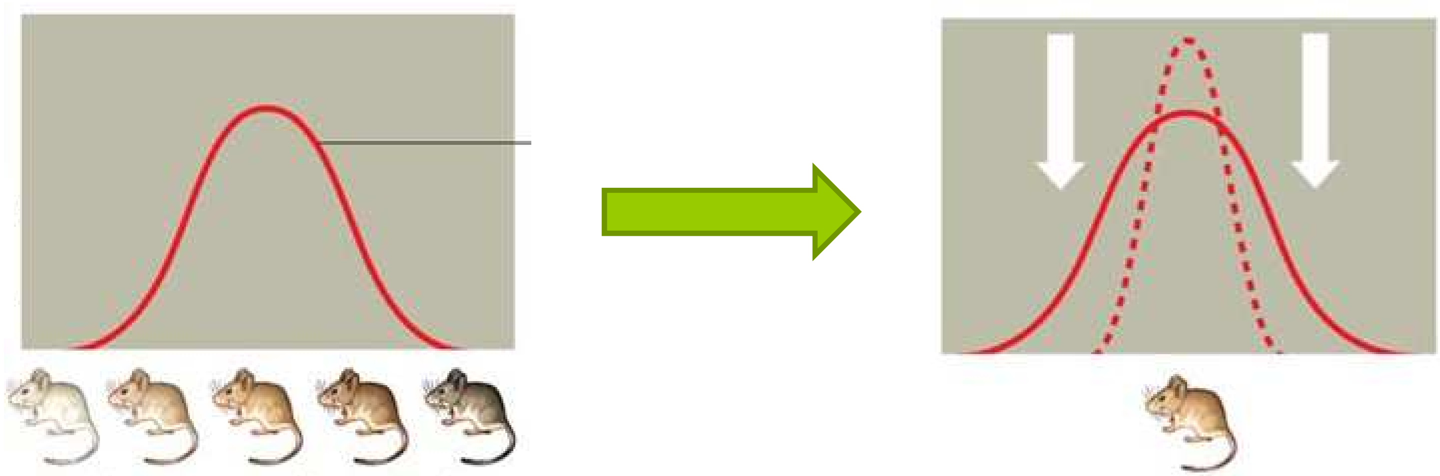
Inbreeding depression due to stabilizing selection on a quantitative character

Emmanuelle Porcher & Russell Lande



Inbreeding depression

- Reduction in fitness of inbred vs. outbred individuals

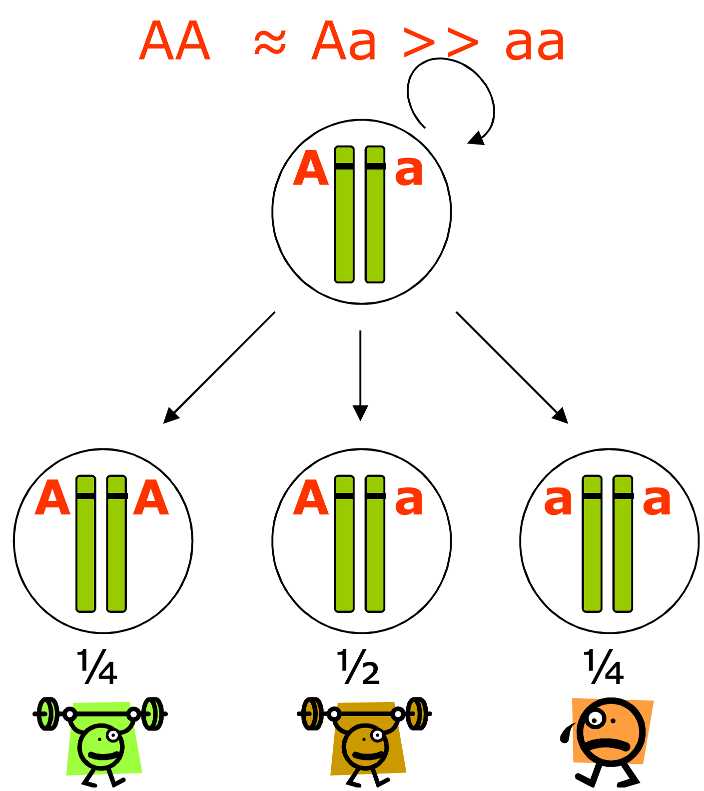
Outcrossed (Connolly 2001) Selfed

- Major force in the evolution of mating systems

Genetics of inbreeding depression

- Main mechanism causing inbreeding depression:
  - Recessive deleterious mutations
  - (Overdominance)

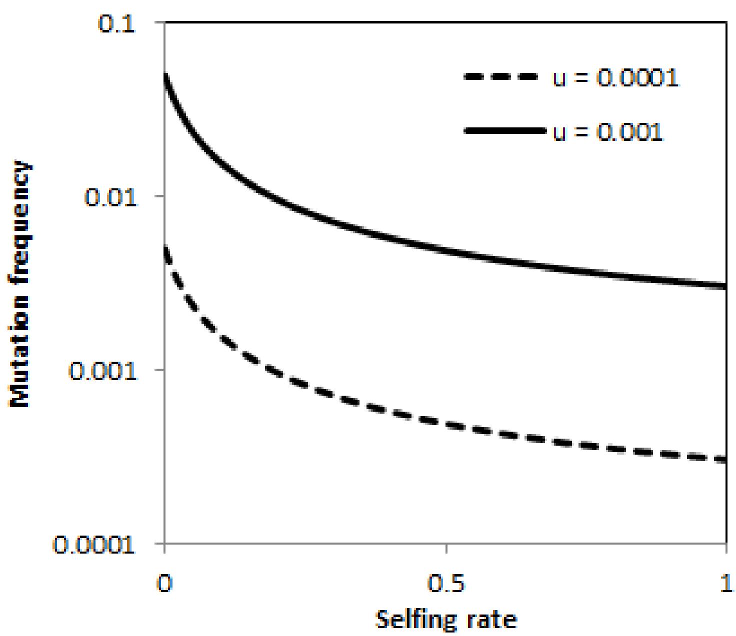
- Frequent assumption: deleterious effects are unconditional



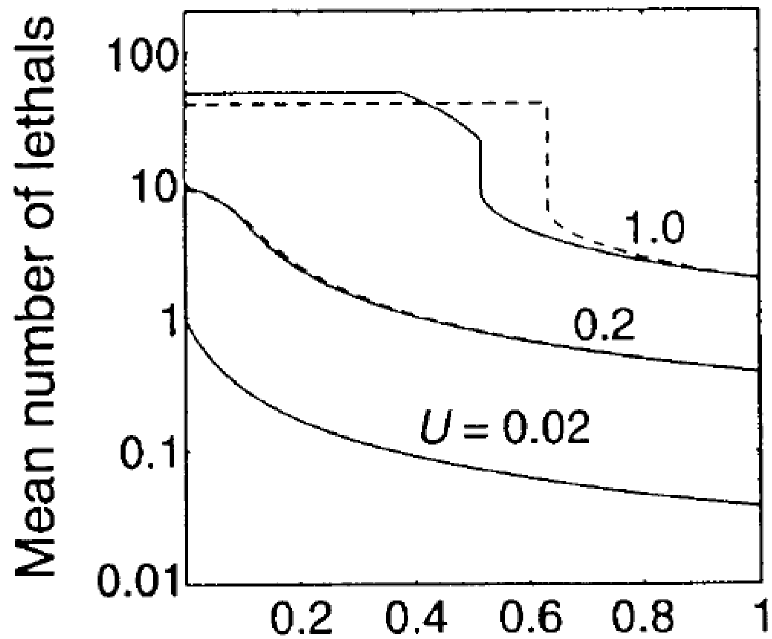
Examples of models of inbreeding depression assuming unconditional deleterious effects

AA	Aa	aa
1	1 - *hs*	1 - *s*

A $\xrightarrow{u}$ a



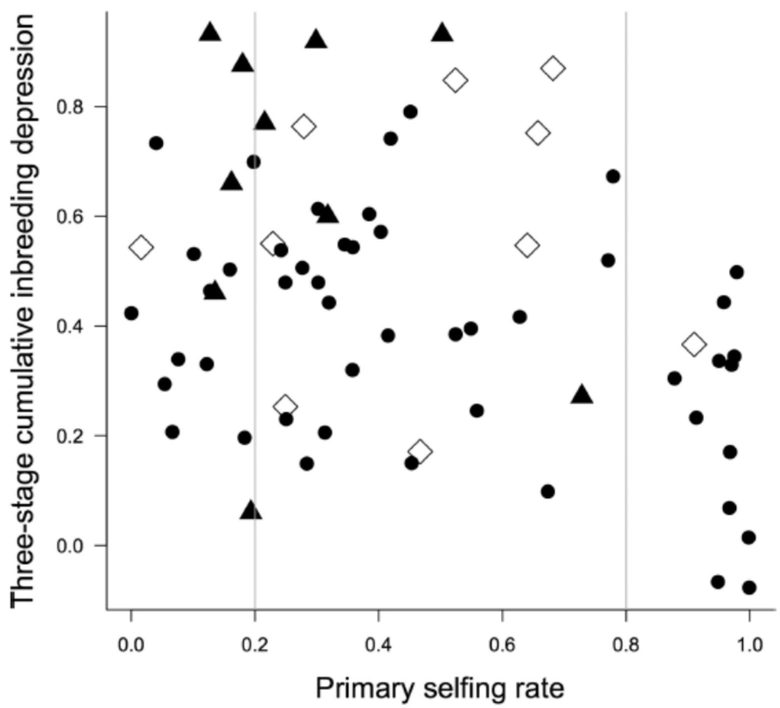
One locus, Ohta & Cockerham 1974



Multilocus, Lande et al. 1994

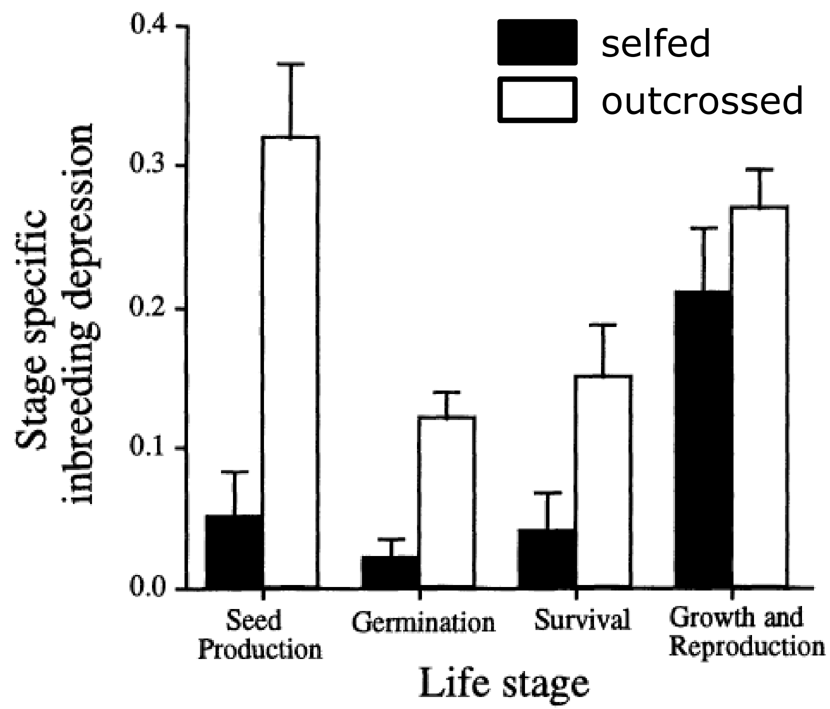
Limitations of models based on unconditionally deleterious alleles

- Not all inbreeding depression is purged at high selfing rates



Winn et al. 2011

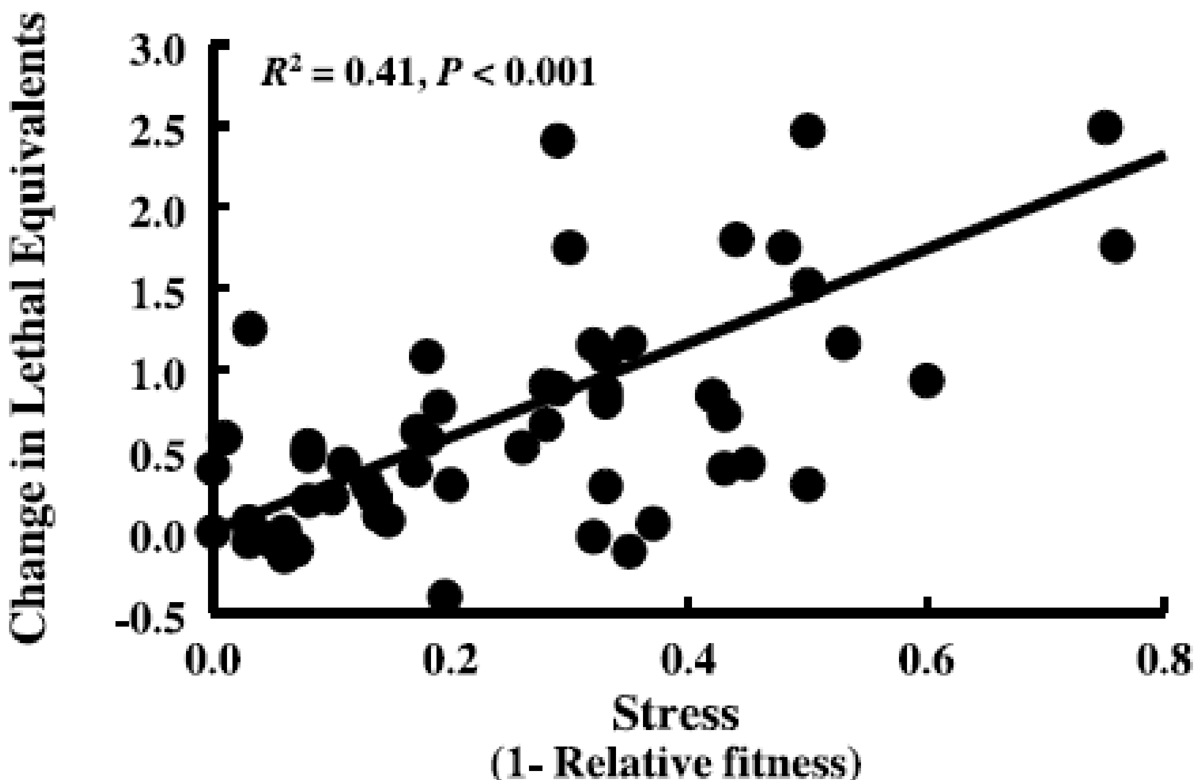
- Late-acting inbreeding depression is not purged



Husband & Schemske 1996

Inbreeding depression changes with the environment

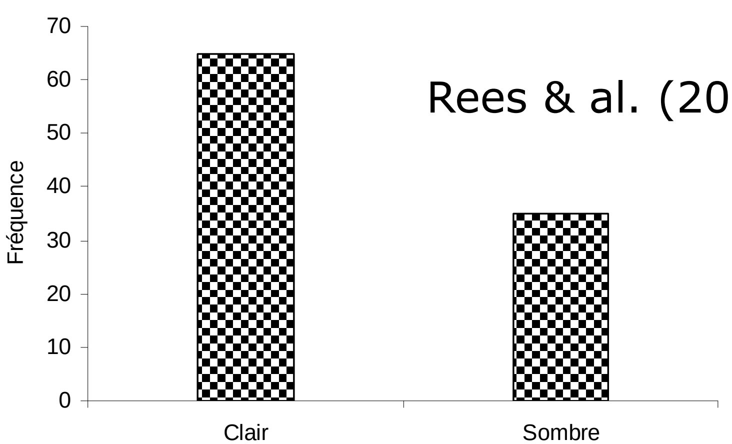
- E.g. stronger inbreeding depression in more stressful environments



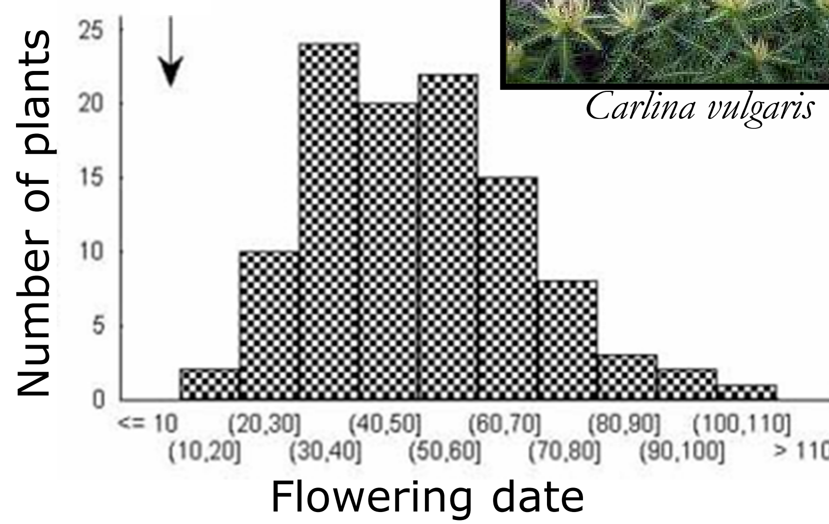
Fox and Reed 2011

Different types of characters under selection

- Qualitative traits
  - Discrete distribution
  - Few (1-2) genes involved
  - No effects of the environment
- Quantitative traits
  - Continuous distribution
  - Numerous genes involved
  - Effects of the environment

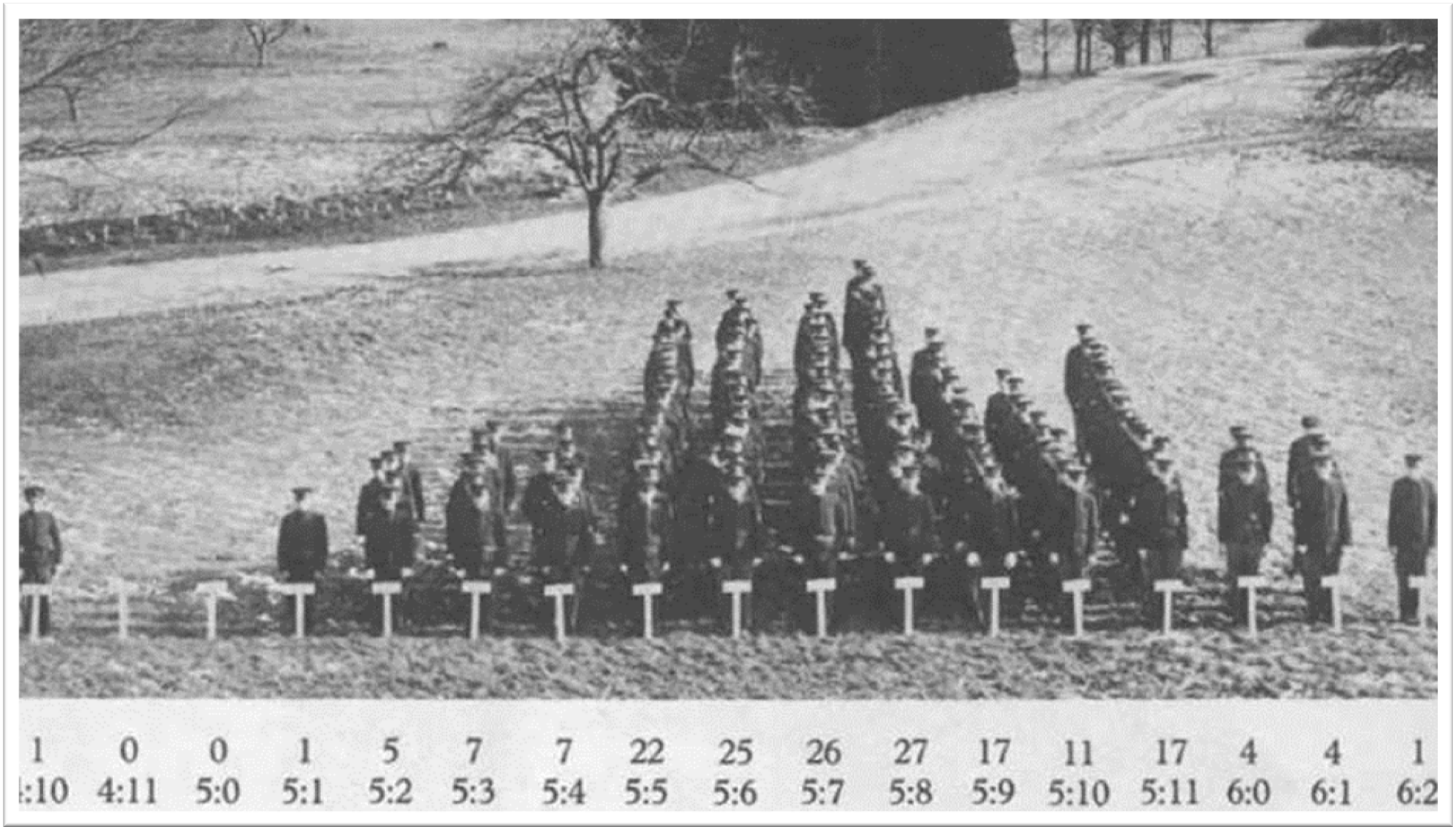


Rees & al. (2004)



Carlina vulgaris

Size, an example of quantitative trait



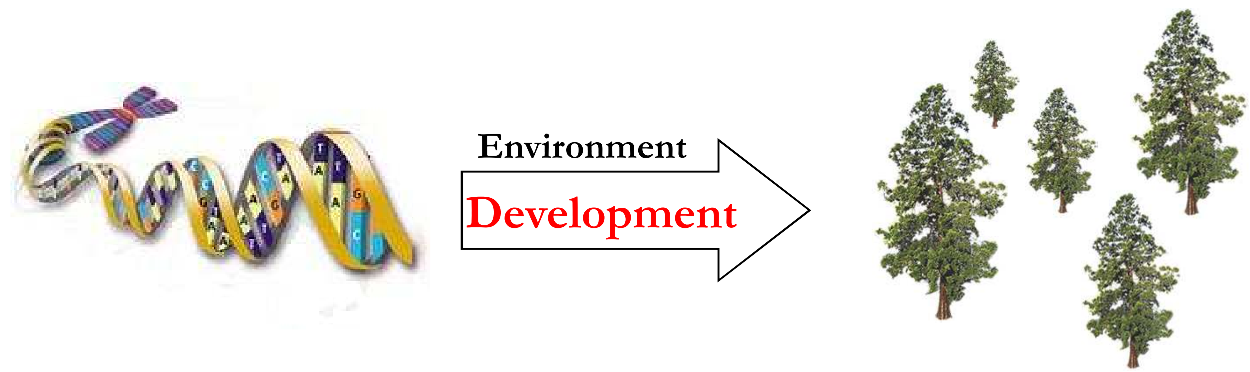
http://staff.stir.ac.uk/steve.paterson/Home_page.htm

Genetic determinism of quantitative traits

Phenotype = Genotype + Environment

Genotype

Phenotype



Gene diversity

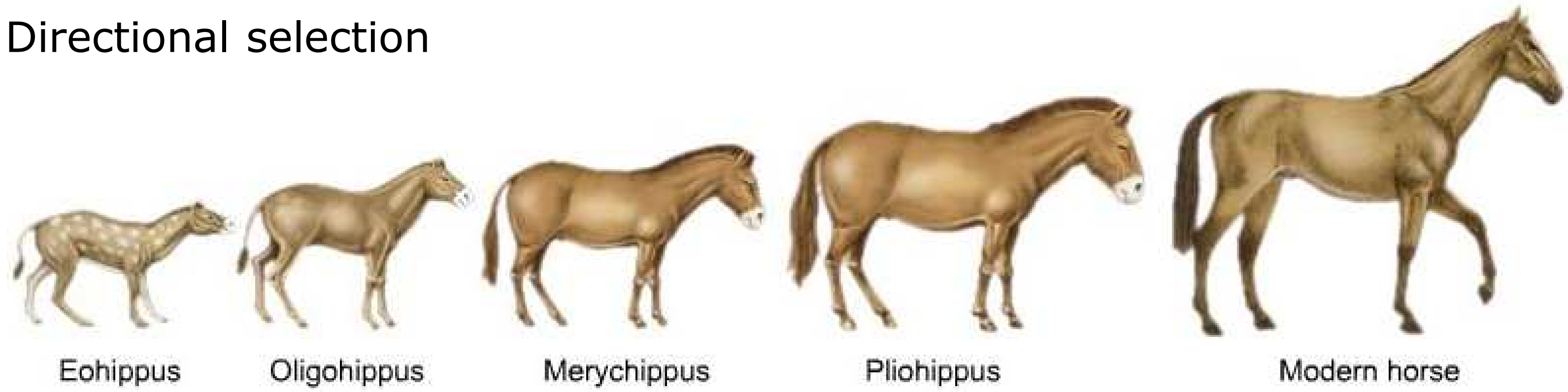
Trait diversity

$$V_P = V_G + V_E$$

$$(P = G + E)$$

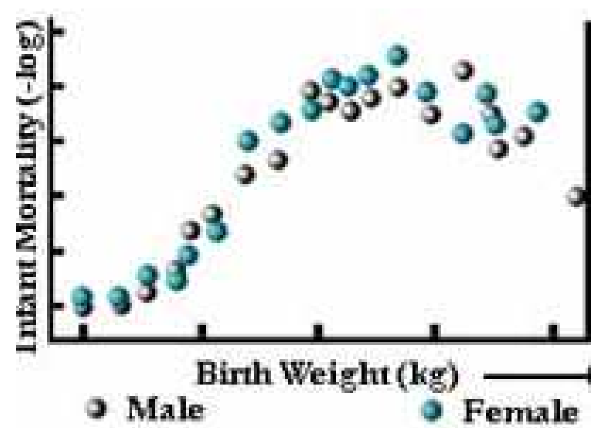
Types of natural selection

- Directional selection



- Disruptive selection

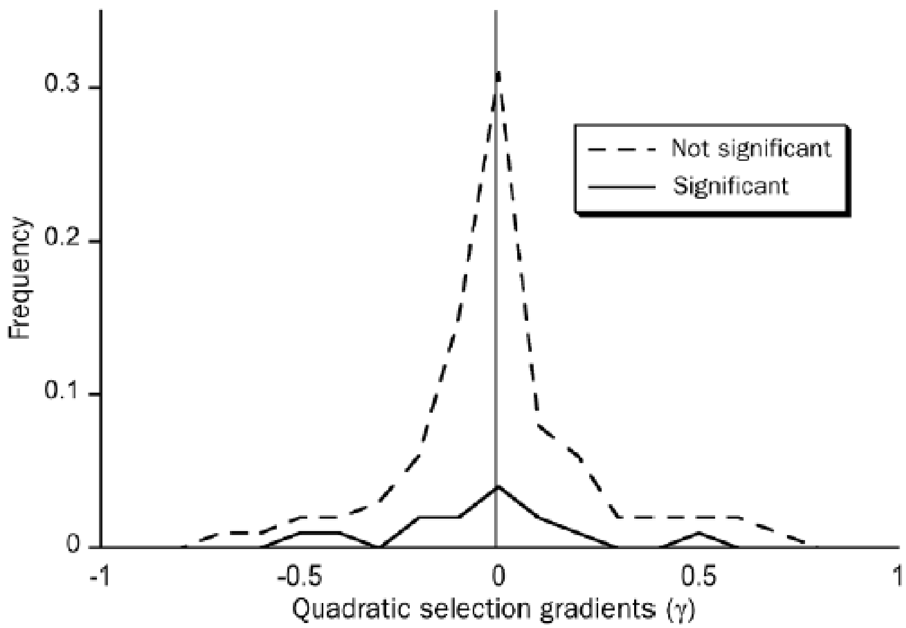
- Stabilizing selection



Stabilizing selection causing inbreeding depression?

- Widespread in natural populations?

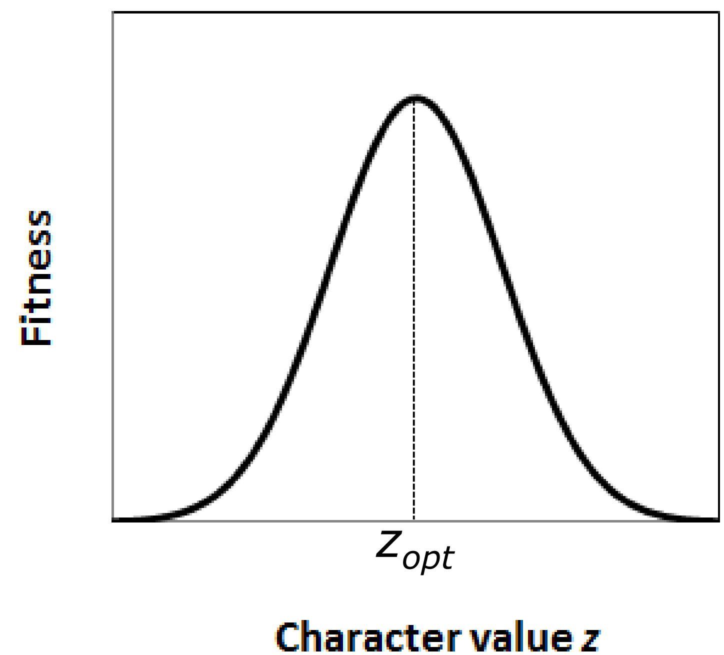
$$w(z) = \alpha + \gamma(z - z_{opt})^2$$



(Kingsolver & Pfennig 2007)

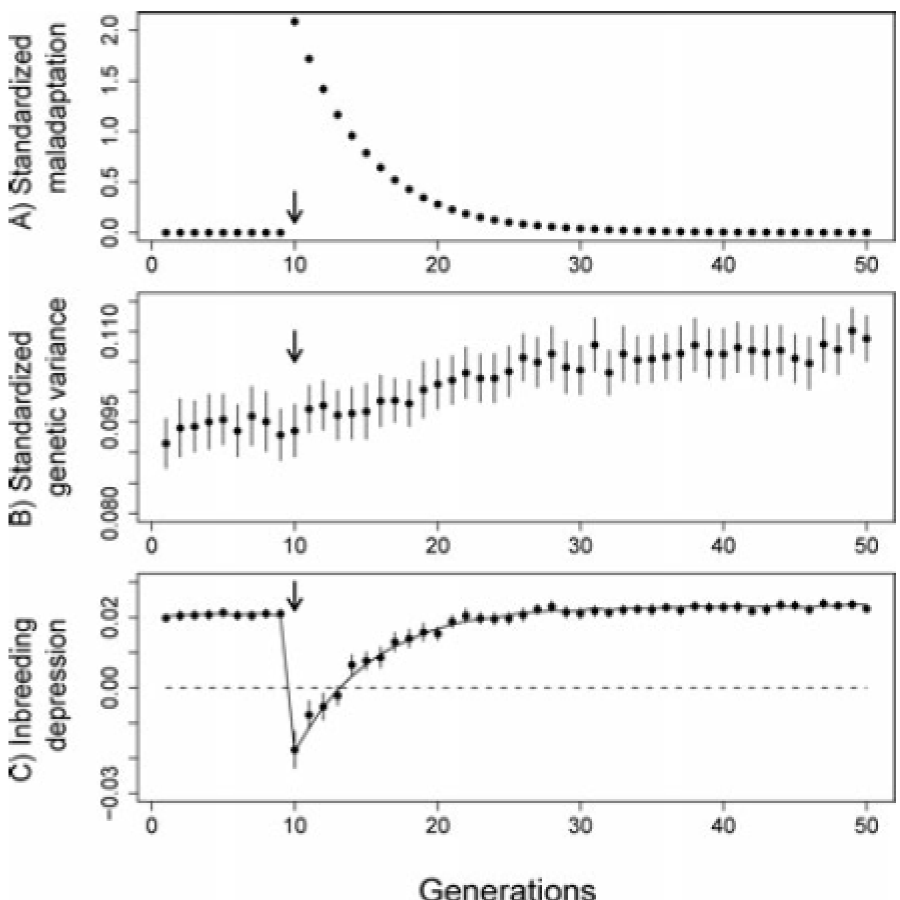
- Fitness of an individual with phenotype *z*:

$$w(z) = \exp\left(-\frac{(z - z_{opt})^2}{2\omega^2}\right)$$



Stabilizing selection causing inbreeding depression?

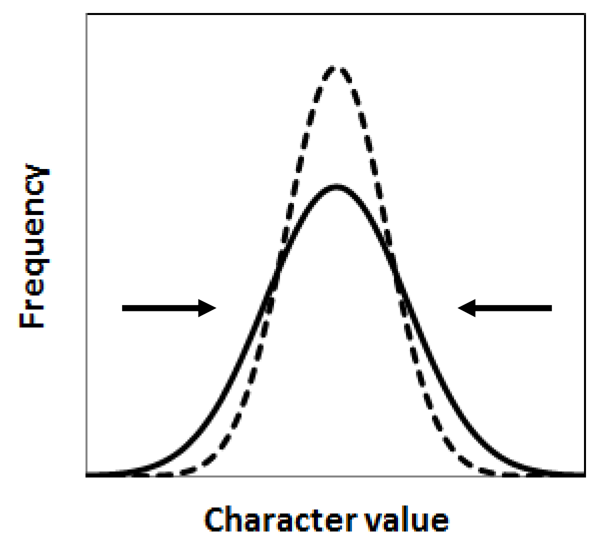
- Deviation from the optimum



Ronce et al. 2009

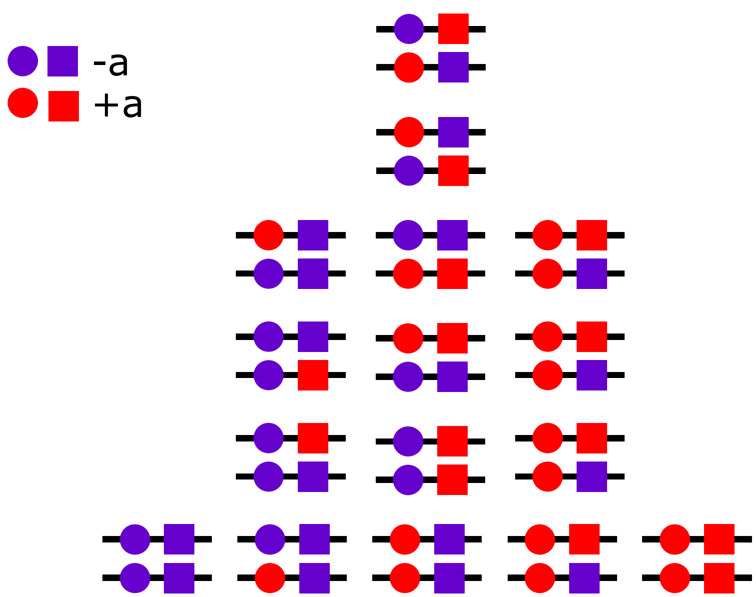
- Change in genetic variance
  - In a constant environment
  - Mean phenotype = z_{opt}
  - Mean fitness of a population

$$\bar{w} = \sqrt{\frac{\omega^2}{\omega^2 + V_P}}$$



A quantitative genetics model

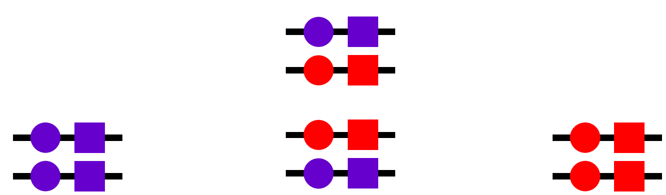
- Assume a character controlled by *n* loci, with infinitely many alleles of purely additive effects
- Phenotypic value of an individual $$z = \sum_{i=1}^{n}(x_i + x_i') + e$$
- Total phenotypic variance *P* = *G* + *E*



No linkage among loci (*C*=0)

Genetic variance in a randomly mating population

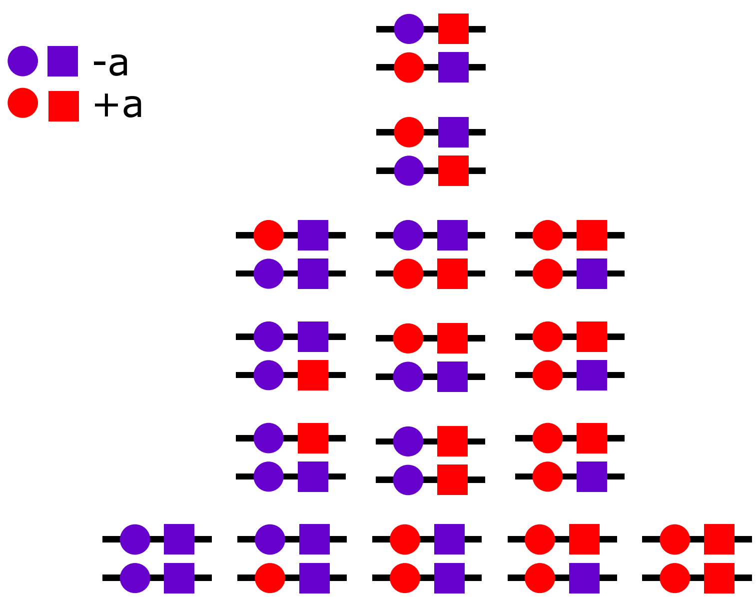
G = *V* + *C*



Positive linkage (*C*>0)

A quantitative genetics model

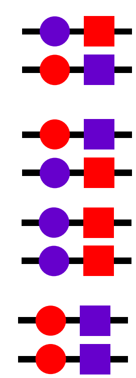
- Assume a character controlled by *n* loci, with infinitely many alleles of purely additive effects
- Phenotypic value of an individual $$z = \sum_{i=1}^{n}(x_i + x_i') + e$$
- Total phenotypic variance *P* = *G* + *E*



No linkage among loci (*C*=0)

Genetic variance in a randomly mating population

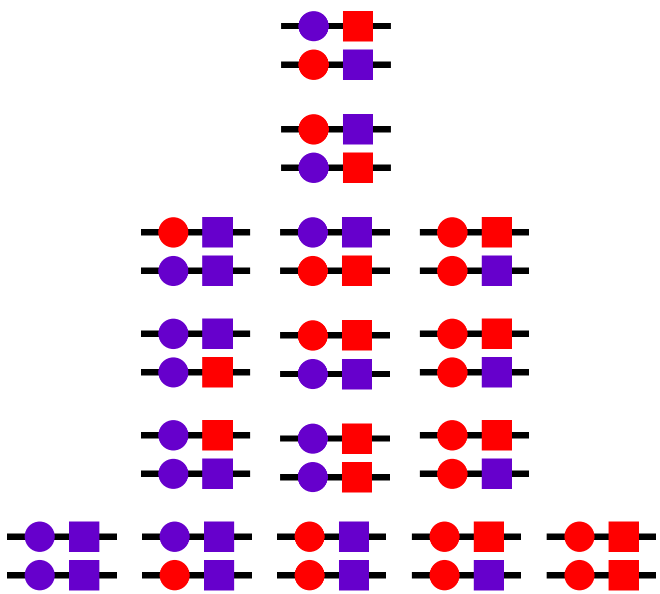
G = *V* + *C*



Negative linkage (*C*<0)

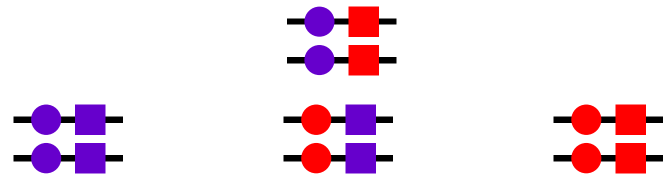
Effect of inbreeding on the genetic variance of a quantitative character

- Randomly mating population
  - $F = 0$



- Completely selfing population
  - $F = 1$

$$G = (1 + F)(V + C)$$



For a given C and V, selfed individuals have higher genetic (phenotypic) variance than outcrossed individuals
⇨ Inbreeding depression due to stabilizing selection

Question

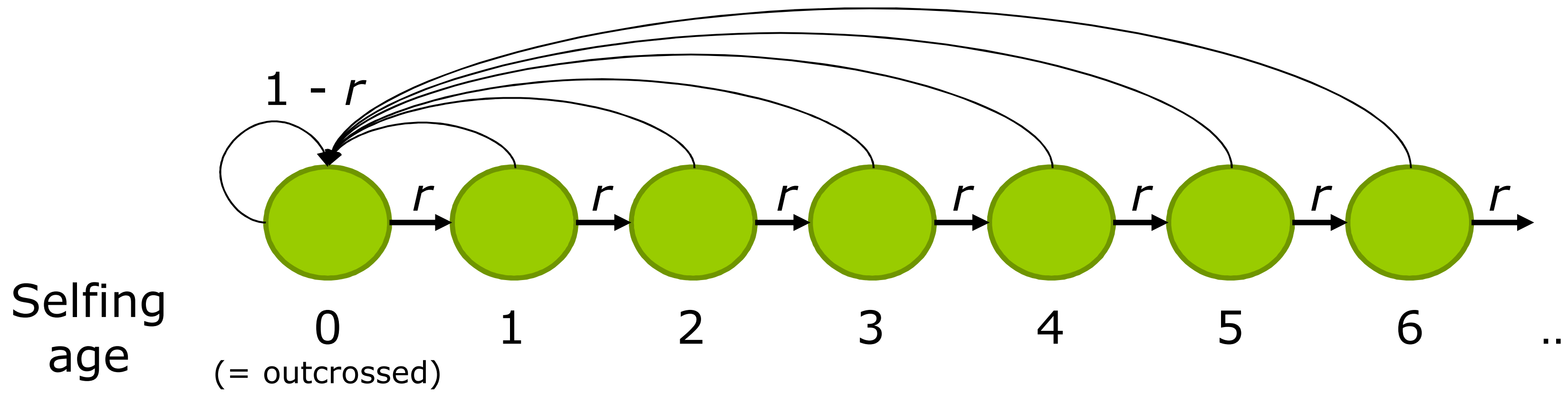
- How do the effects of the mating system and stabilizing selection combine to drive the evolution of genetic variance and inbreeding depression?

- Lande (1977): total genetic variance is independent of the mating system

- Model
  - Infinite population size
  - One character, controlled by *n* loci with additive effects
  - Normal distribution of allelic effects at each locus
  - The character is under stabilizing selection (strength $1/\omega^2$), always at optimum (constant environment)
  - Mutational variance V_m
  - Accounts for the history of different selfing lineages
    - (≠ Lande 1977)

Why consider the different selfing age classes?

- In a mixed mating population (selfing rate *r*):



- Different lineages coexist, with contrasting inbreeding coefficients
  - Creates zygotic disequilibrium (non-random association of homozygosity across loci)
  - Consequences for the evolution of genetic variance

A few equations

- Three main variables across selfing age classes τ:
  - Genic variance $V\tau$
  - Gametic linkage disequilibrium (covariance among loci $C\tau$)
  - Inbreeding coefficient F_τ = correlation of additive effects

- Recursions:

$$V'_{\tau+1} = V_\tau - \frac{G_\tau^2}{2n(P_\tau + \omega^2)} + V_m \qquad V'_0 = \sum_{\tau=0}^{\infty} \frac{p_\tau \overline{w_\tau}}{\overline{\overline{w}}} V'_{\tau+1}$$

$$C'_{\tau+1} = \frac{1+F_\tau}{2} C_\tau - (1 - \frac{1}{n}) \frac{G_\tau{}^2}{2(P_\tau + \omega^2)} \qquad C'_0 = \sum_{\tau=0}^{\infty} \frac{p_\tau \overline{w_\tau}}{\overline{\overline{w}}} C'_{\tau+1}$$

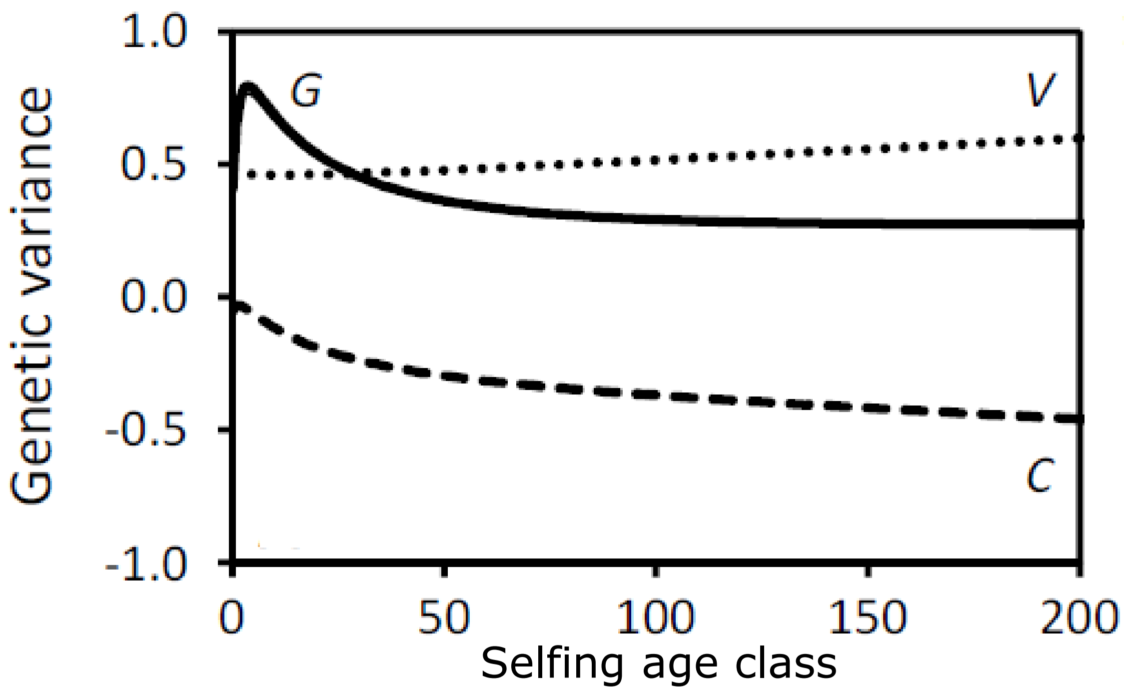
$$F'_{\tau+1} = f(F_\tau, V_\tau, G_\tau, P_\tau, V_m, n, \omega^2) \qquad F'_0 = 0$$

- These are used to derive:
  - $G_\tau = (1+F_\tau)(C_\tau+V_\tau)$ and $P_\tau = G_\tau + V_E$
  - The mean fitnesses (=$f(G_\tau)$), hence the frequencies of each class

Results

- Analytical approximation : change in total genetic variance due to selfing

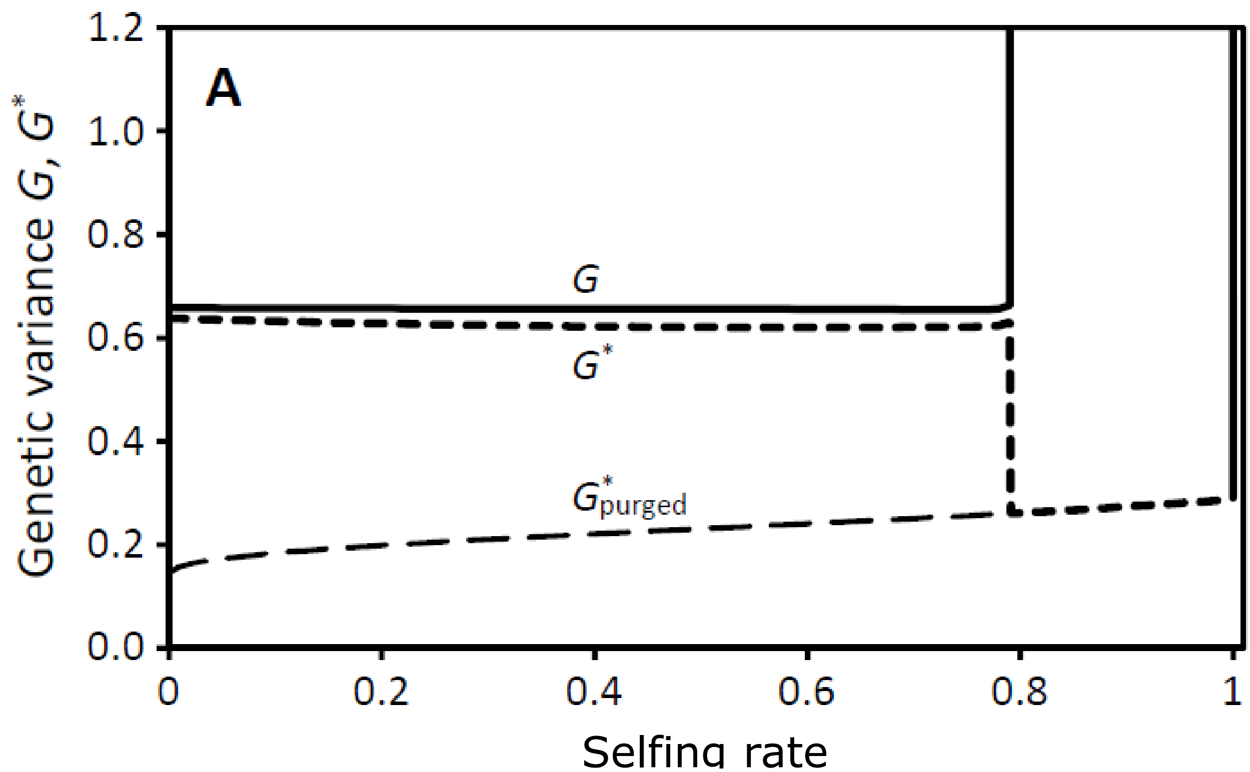
$$G_{(0)} \approx \sqrt{2nV_m\omega^2} \quad > G_{(\infty)} = 2\sqrt{V_m\omega^2}$$



25 traits under selection, n = 10 loci, mutational variance V_m = 0.001, environmental variance V_E = 1, stabilizing selection ω^2 = 20, selfing rate s = 0.78

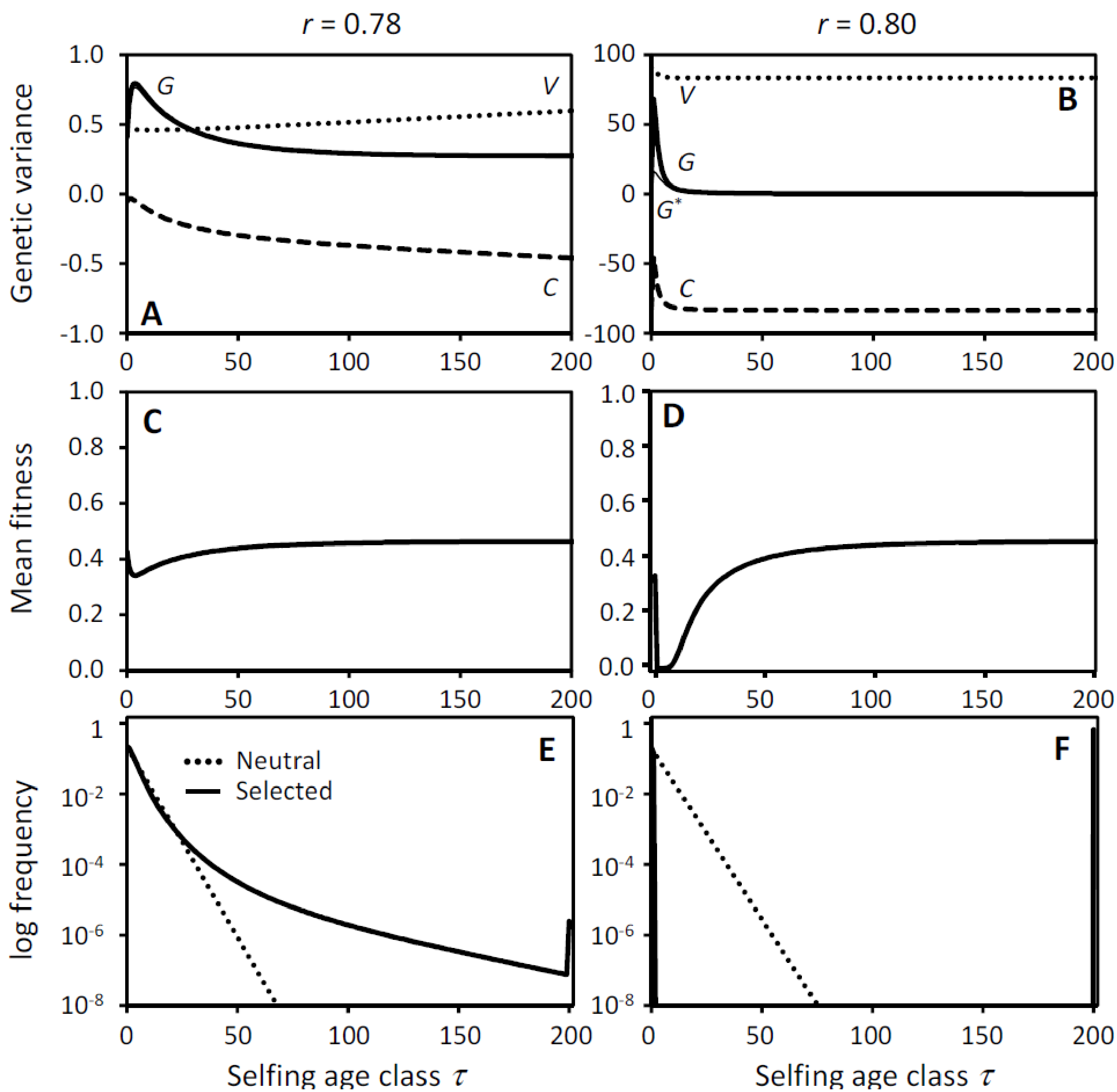
Genetic variance across selfing rates

- Sharp purging of genetic variance measured after selection
  - Associated with a blowup of genetic variance before selection



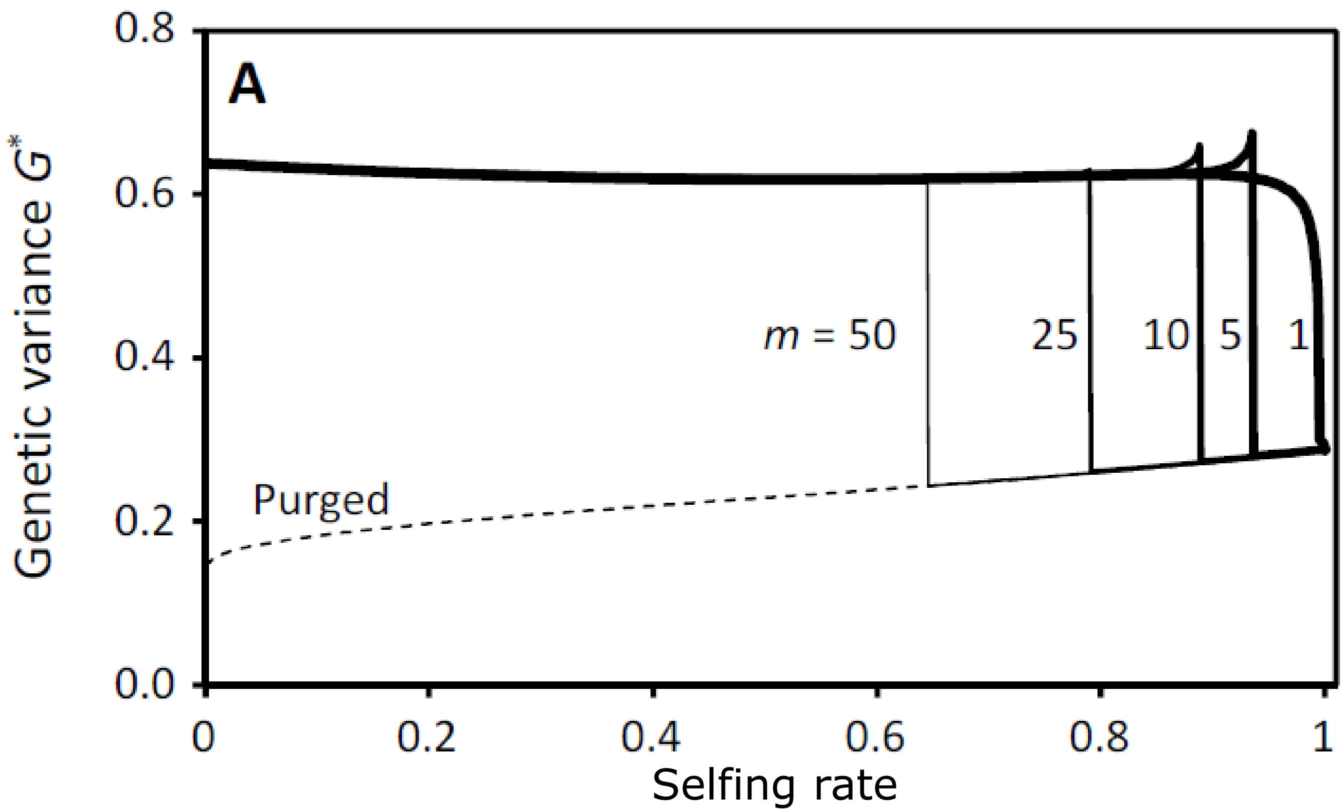
Mechanisms for purging the genetic variance

M ... c
va ...



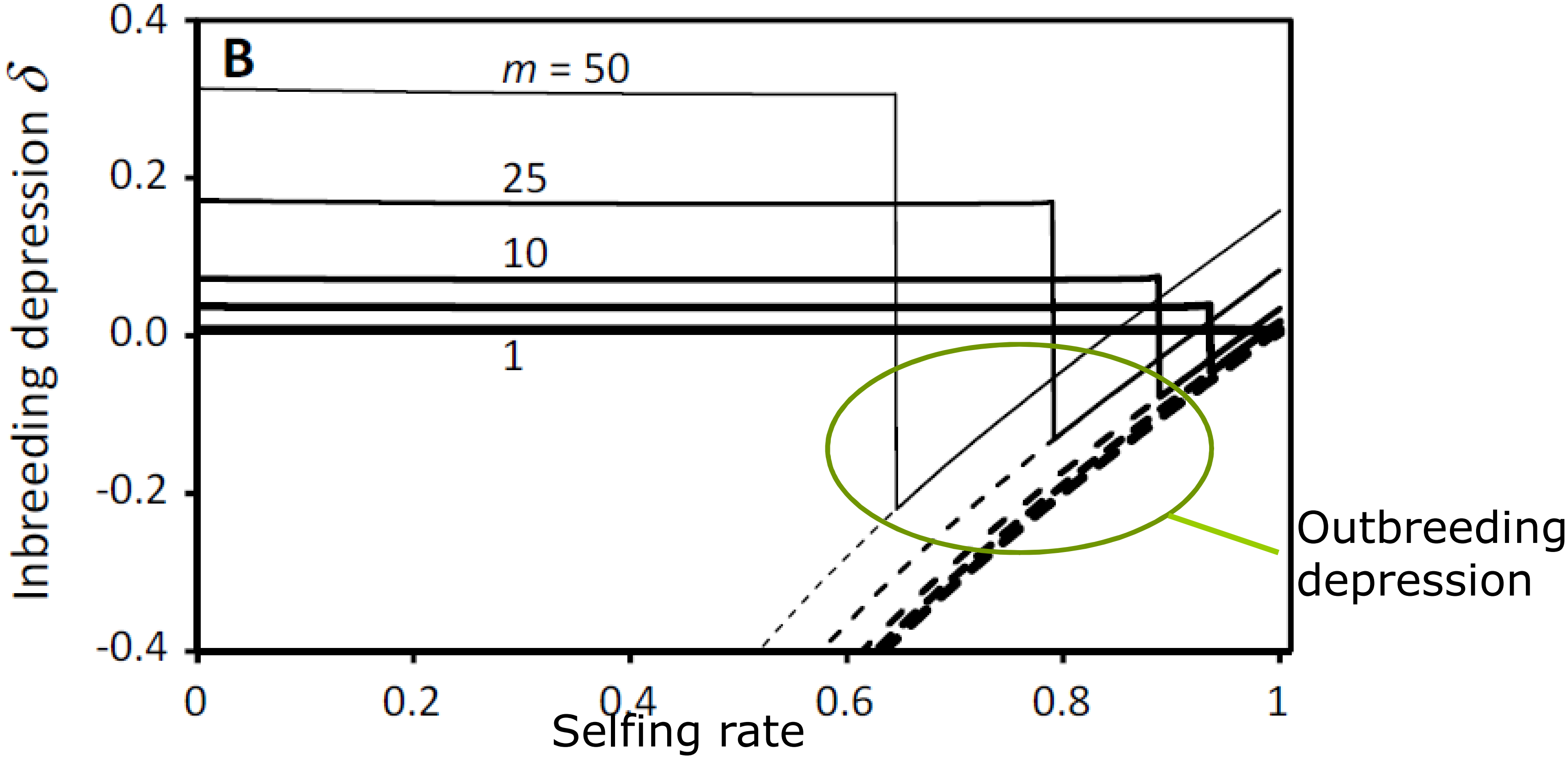
r = 0.78
r = 0.80
Genetic variance
Mean fitness
log frequency
G
V
C
G*
A
B
C
D
E
F
Neutral
Selected
Selfing age class τ
Selfing age class τ

Stabilizing selection on multiple characters facilitates purging



n = 10 loci, mutational variance V_m = 0.001, environmental variance V_E = 1, selection ω^2 = 20

Inbreeding depression caused by selection on multiple characters



n = 10 loci, mutational variance V_m = 0.001, environmental variance V_E = 1, selection ω^2 = 20

High selfing rates as “evolutionary traps”?

- With stabilizing selection on multiple characters
  - Purging and outbreeding depression favor evolution to higher selfing rates
  - Highly selfing lineages accumulate negative linkage disequilibrium
  - Their outcrossed offspring have large genetic variance and are strongly counterselected

Perspectives

- Combination of the two models of inbreeding depression
  - Highly deleterious mutations with unconditional effects
  - Stabilizing selection on multiple characters
  - ⇨ Evolution of selfing rates?
- Finite populations?
- Experimental test of outbreeding depression in highly selfing species?