

# Pseudo-overdominance: a plausible mechanism for maintaining inbreeding depression?

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# Inbreeding depression

## A definition

The fitness of the descendants of selfed individuals ( $W_s$ ) relative to that of the descendants of outcrossed individuals ( $W_o$ ).

$$\delta = 1 - \frac{W_s}{W_o}$$

# Inbreeding depression

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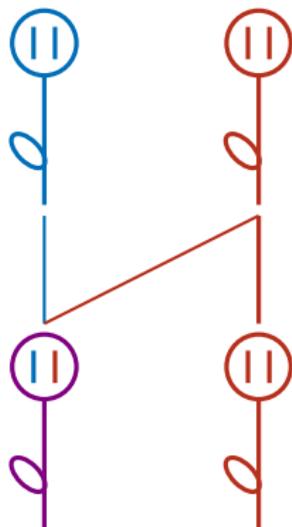
$$\delta = 1 - \frac{W_s}{W_o}$$

→ A dynamic characteristic of populations

# Inbreeding depression

## Theoretical expectations

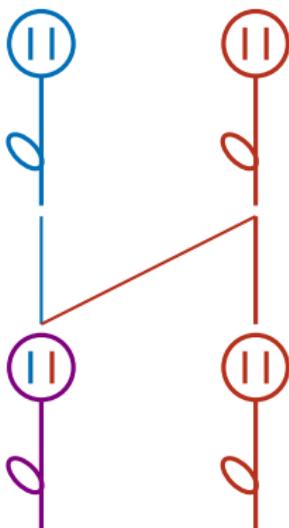
Inbreeding increases homozygosity:



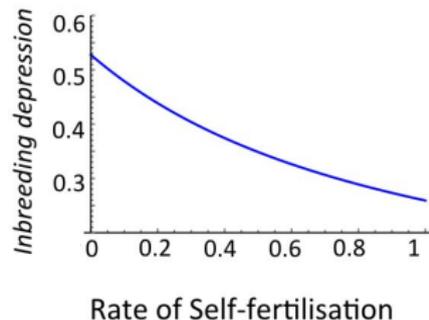
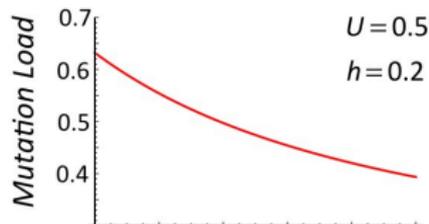
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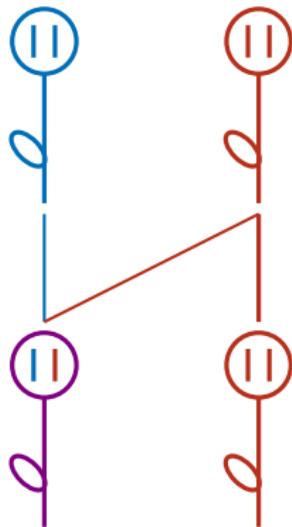
More efficient purge of deleterious mutations



# Inbreeding depression

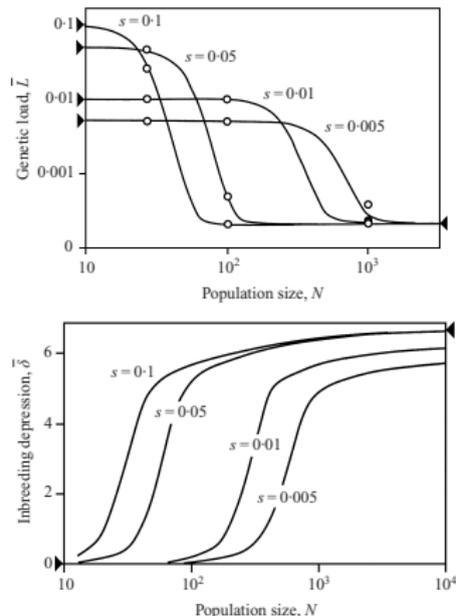
## Theoretical expectations

Inbreeding increases homozygosity:



Bataillon and Kirkpatrick 2000

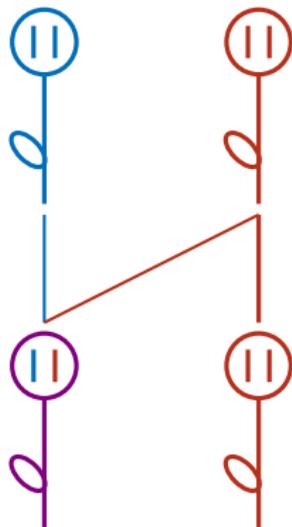
But also fixation



# Inbreeding depression

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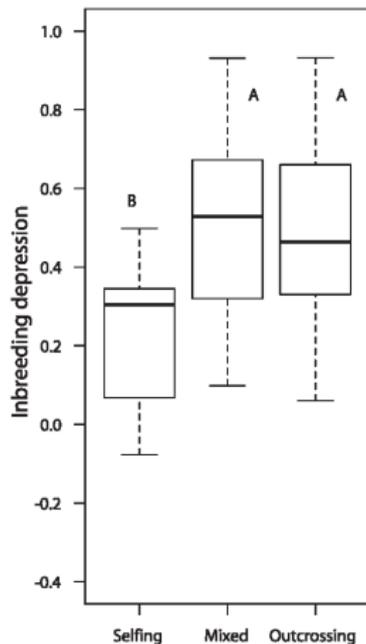
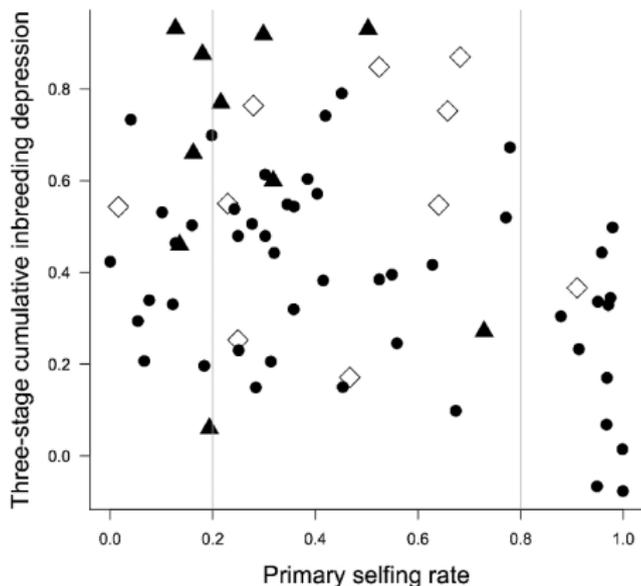


Inbreeding depression reflects heterozygosity within a population.

# Inbreeding depression in selfing populations

“Controversial” findings..

Self-fertilization should reduce  $\delta < 0.5$   
(theoretical condition for the evolution of selfing)



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Selfing should reduce genetic diversity very quickly

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- Selective interference (requires that most mutations be very recessive)

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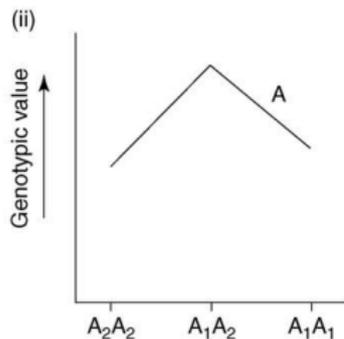
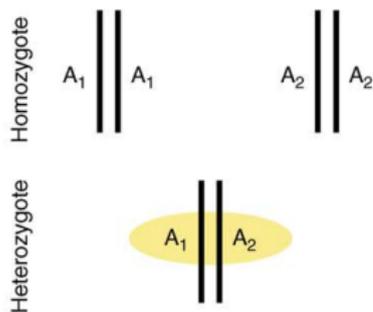
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# Maintaining heterozygosity over time?

Inbreeding depression reflects the heterozygosity maintained in a population.

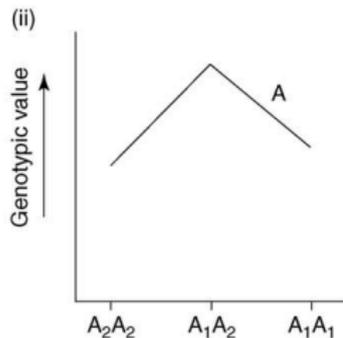
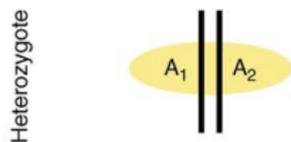
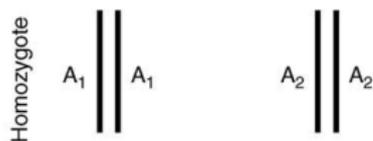
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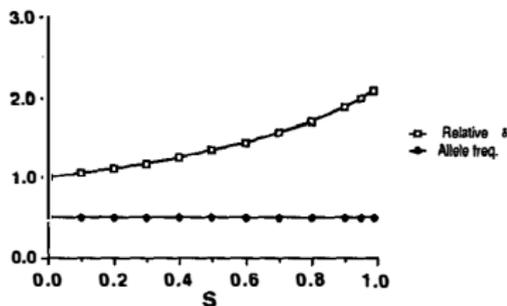
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(ii) Overdominance



Kimura and Ohta (1970):

- More diversity maintained
- Higher inbreeding depression

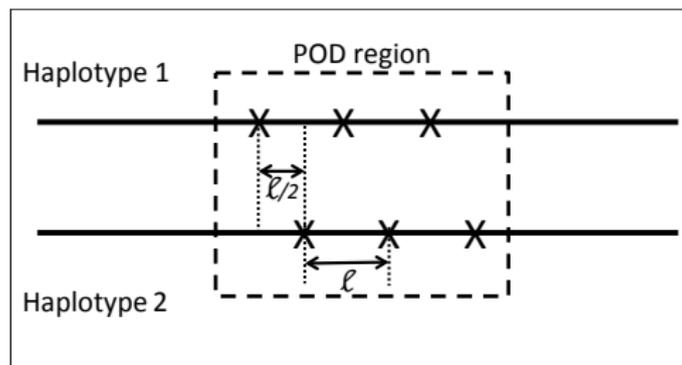


Charlesworth and Charlesworth 1987

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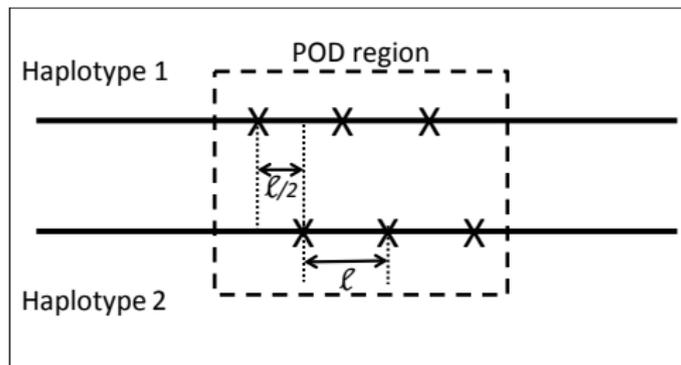
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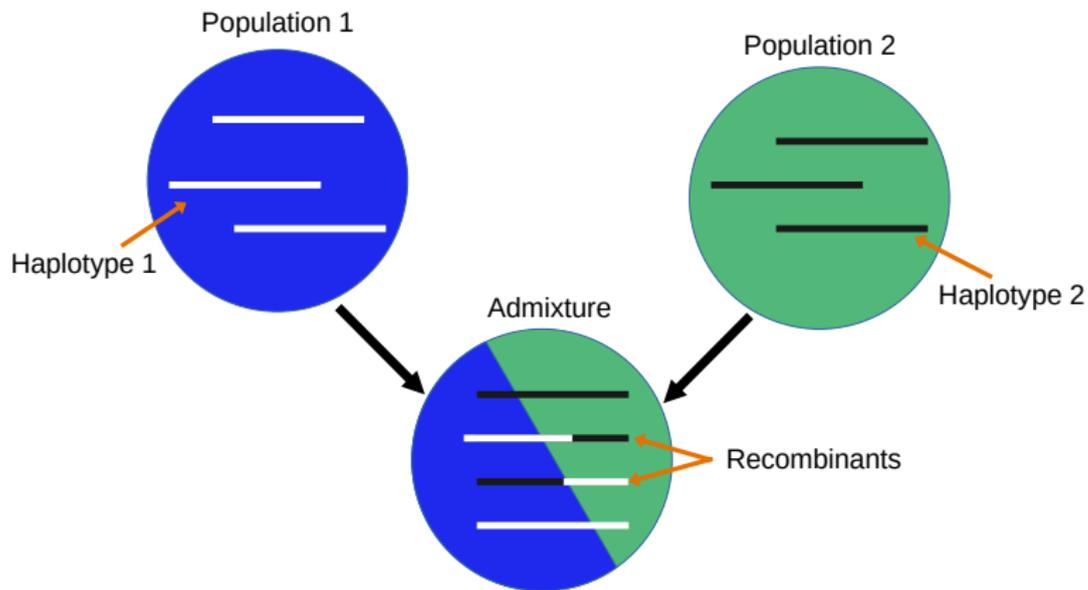
→ Selection against clustered recessive deleterious alleles could resemble overdominant selection

Could pseudo-overdominant selection contribute to maintaining inbreeding depression in selfing populations?

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- What conditions need to be met?
- How long can heterozygosity persist?

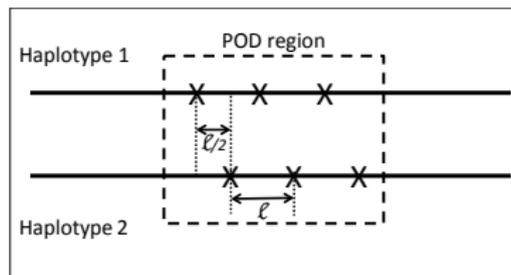
# General model



# Pseudo-overdominance and inbreeding

## Definitions

We consider two haplotypes, each carrying  $n$  mutations:

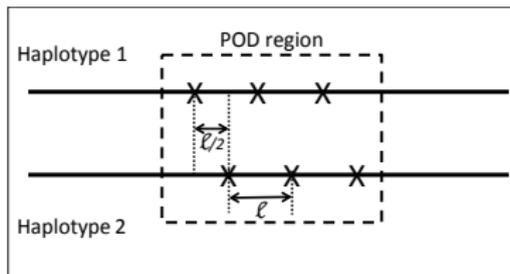


(Ideal case)

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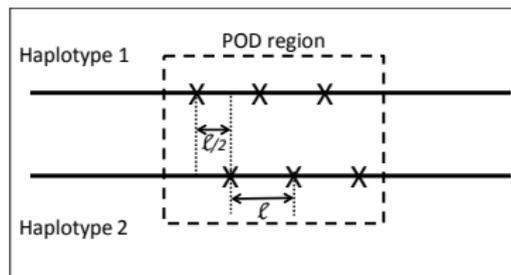
Fitness is multiplicative:

$$W = (1 - hs)^{he}(1 - s)^{ho}$$

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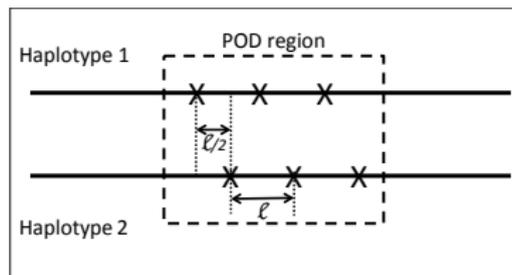
$$W_{ho} = (1 - s)^n$$

$$W_{he} = (1 - hs)^{2n}$$

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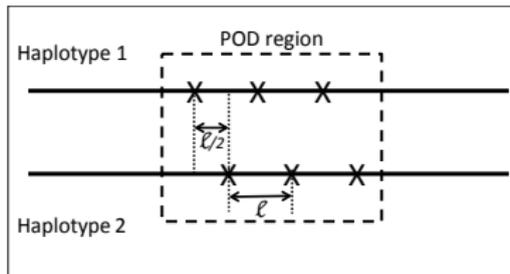
Selection against homozygotes:

$$s_H = 1 - \frac{W_{ho}}{W_{he}}$$

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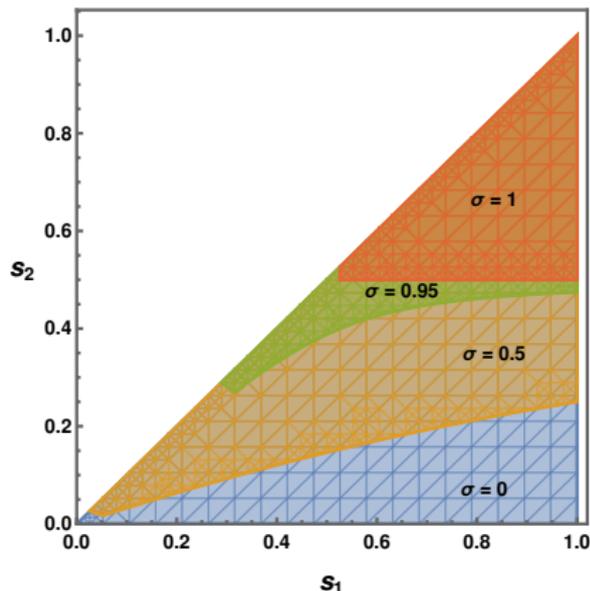
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# Pseudo-overdominance and inbreeding

## Conditions for stability

Expectations from the classical case of overdominant selection  
(Kimura and Ohta 1970)

- Strong selection against homozygotes ( $s_1$  and  $s_2 > 0.5$ )
- Similar selection against either homozygote:  $s_1 = s_2$



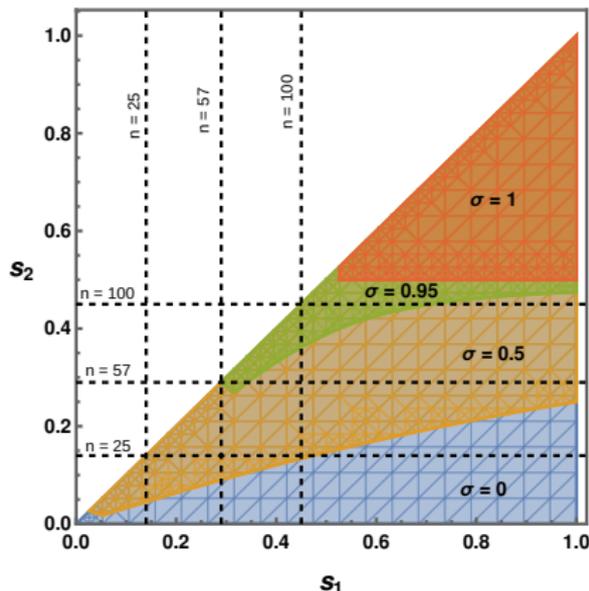
Adapted from Kimura and Ohta 1970

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# Pseudo-overdominance and inbreeding

## Recombination

How will recombinants contribute to the selection dynamics?

We develop a system of ODEs to follow the change in haplotype frequencies ( $\Delta p_x$ , with  $x$  denoting a given haplotype).

# Pseudo-overdominance and inbreeding

## Recombination

How will recombinants contribute to the selection dynamics?

$$\Delta P_1 = \frac{1}{\bar{W}} \left( P_1 \left( (1 - \hat{F})(1 - s_{c,1})P_c + (1 - s_H)((1 - \hat{F})P_1 + \hat{F}) \right. \right. \\ \left. \left. + (1 - \hat{F})P_2 \right) - P_1 \bar{W} \right)$$

the terms  $s_i$  are the coefficients of selection against each combination of haplotypes -  $H_1 H_2$  having an  $s_{1,2} = 0$ .

Here we make the simplifying assumption that  $s_{1,1} = s_{2,2} = s_H$

# Pseudo-overdominance and inbreeding

## Recombination

How will recombinants contribute to the selection dynamics?

$$\Delta_{P_1} = \frac{1}{\bar{W}} \left( P_1((1 - \hat{F})(1 - s_{c,1})P_c + (1 - s_H)((1 - \hat{F})P_1 + \hat{F}) + (1 - \hat{F})P_2) - P_1\bar{W} \right)$$

$$\Delta_{P_2} = \frac{1}{\bar{W}} \left( P_2((1 - \hat{F})(1 - s_{c,2})P_c + (1 - s_H)((1 - \hat{F})P_2 + \hat{F}) + (1 - \hat{F})P_1) - P_2\bar{W} \right)$$

$$\Delta_{P_c} = \frac{1}{\bar{W}} \left( P_c((1 - \hat{F})(1 - s_{c,1})P_1 + (1 - s_c)((1 - \hat{F})P_c + \hat{F}) + (1 - \hat{F})(1 - s_{c,2})P_2) - P_c\bar{W} \right).$$

# Pseudo-overdominance and inbreeding

## Recombination

How will recombinants contribute to the selection dynamics?

Solving this system of ODEs we find:

- Only a one or two haplotype equilibrium is expected
- A recombinant will invade if it is very similar to the initial haplotypes or has one less mutation

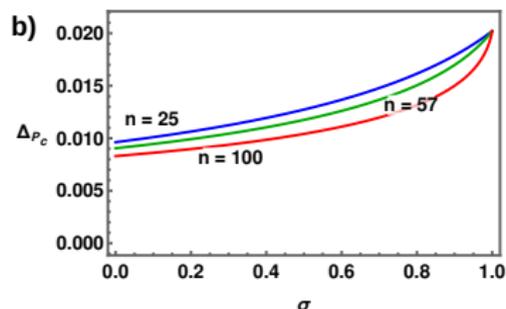
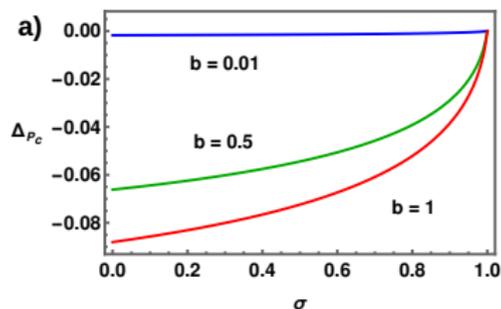
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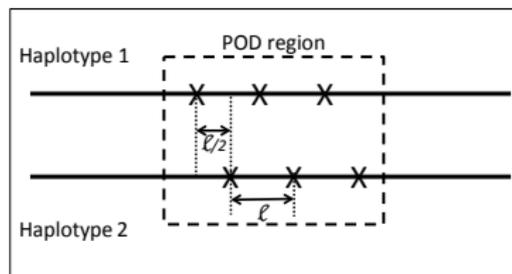
**We predict that, for stable POD selection, mutations will mostly be lost on the edges of the POD zone**

### General parameters:

- Finite population of size  $N$  ( $N = 100, 1000, 5000$ )
- Selfing at rate  $\sigma$  ( $0 \leq \sigma \leq 0.95$ )
- Admixture: 50/50
- Fixed mutation and recombination rates ( $U = 0, 0.1$  and  $0.5$  and  $R = 10cM$ )
- Infinite number of loci
- $s_d = 0.01$  and  $h_d = 0.2$  and  $0.5$
- Simulations run for 4000 generations after admixture

# Simulations run

## Parameter sets



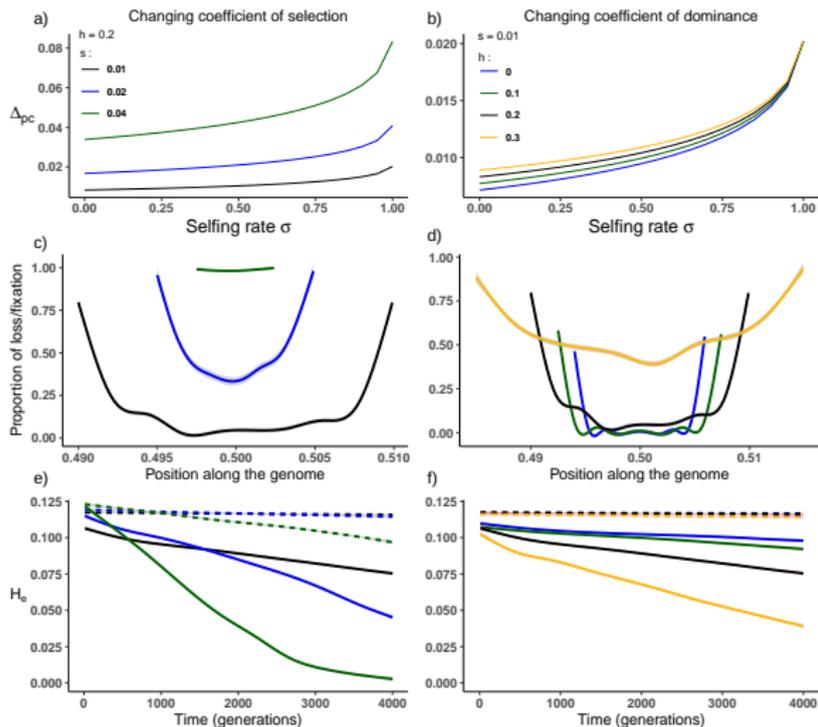
## Within POD's

- Recombination rate between trans mutations  
 $10^{-6}cM \leq \ell \leq 10^{-3}cM$
- Number of mutations  $n = 25, 57, 100$
- selection coefficient  $s$  and dominance  $h$
- Control simulations run with  $s = 0$
- Simulations run with **randomly placed** mutations

- Effects of the types of mutations in the POD zone (ideal case)
- Different haplotype sizes
- Effect of mutations outside the POD zone
- Consequences on inbreeding depression

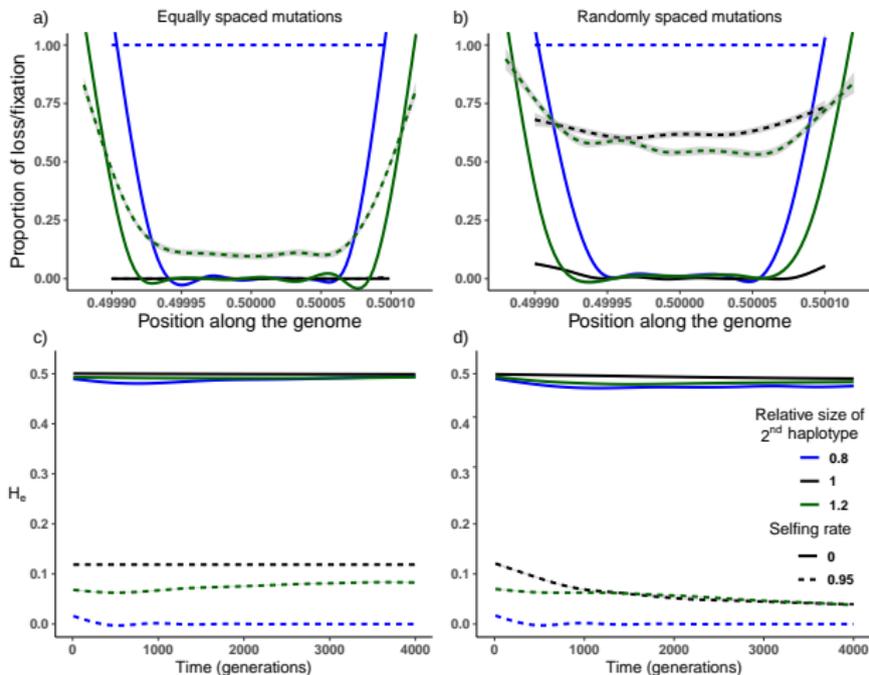
# Results

Effects of  $s$  and  $h$  (ideal case - equally spaced mutations)



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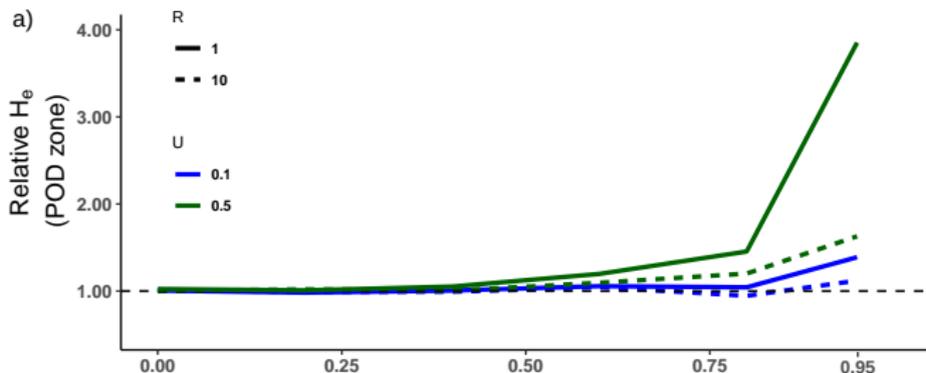
## Variation in haplotype size



# Results

## Background mutations: Diversity within the POD zone

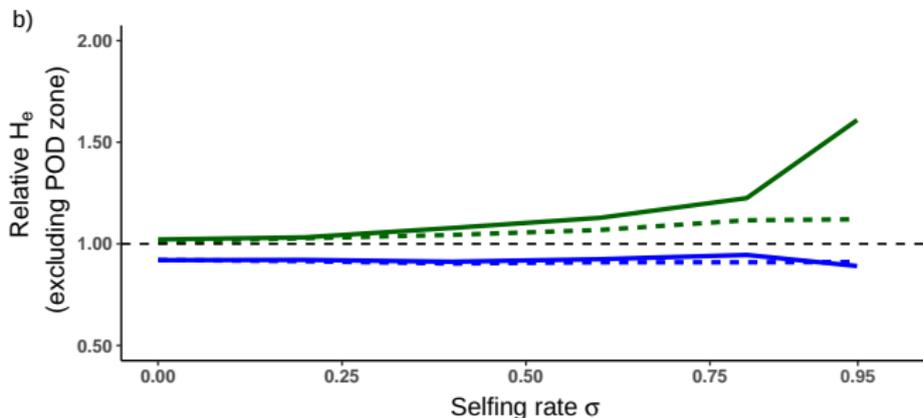
Background mutations can lead to more stable POD selection in highly selfing populations:



# Results

Background mutations: Diversity in the rest of the genome

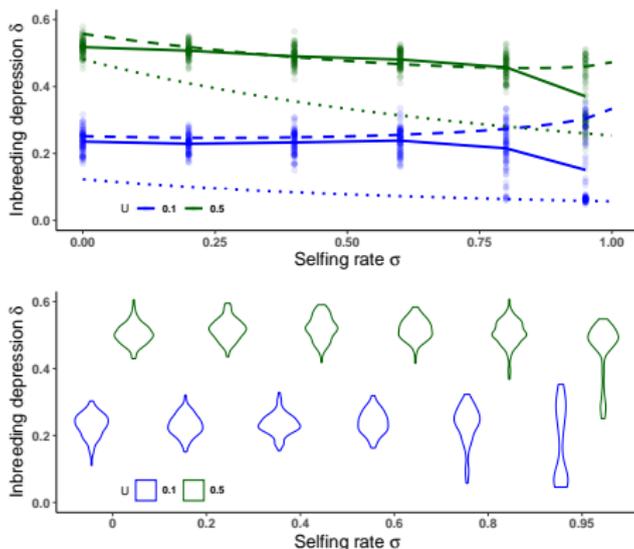
And .. POD selection can lead to more diversity throughout the genome in highly selfing populations:



# Results

## Inbreeding depression

For stable POD selection,  $\delta$  remains close that predicted for overdominant selection:



Even in an ideal setting:

- Strong selection (large  $n$ )
- Tight linkage (small  $\ell$ )
- Alternating and evenly spaced mutations (balanced haplotypes)

pseudo-overdominance can be maintained over many generations,  
but will inevitably be lost.

# Are POD'S a plausible mechanism to explain inbreeding depression?

For POD formation to be favored:

- Nonuniform distribution of deleterious mutations (recombination cold spots)
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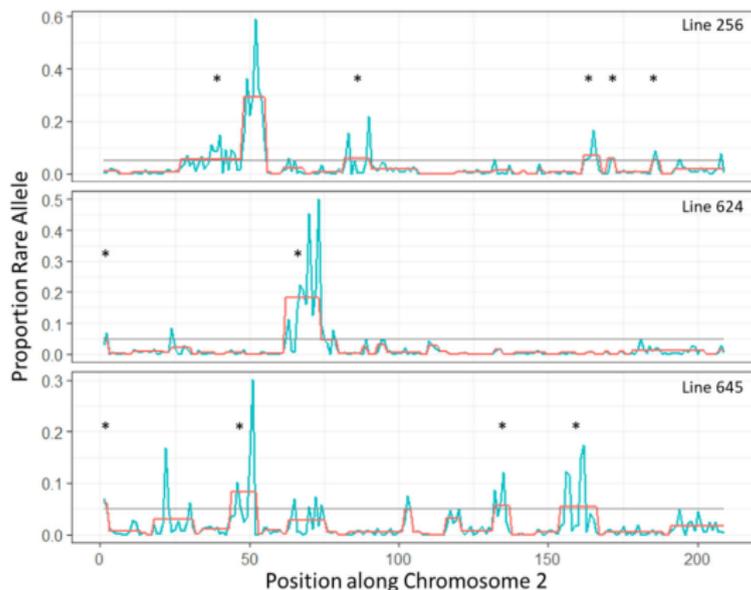
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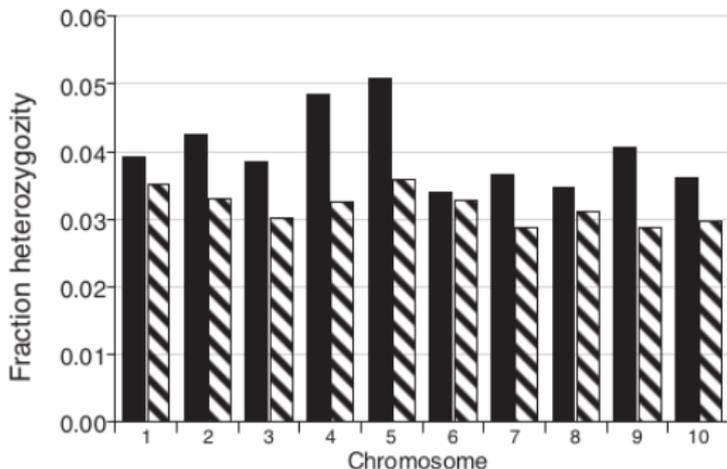
Rare Allele Clusters (RAC) observed in *Mimulus guttatus* lineages



# Are POD'S a plausible mechanism to explain inbreeding depression?

## Residual heterozygosity in Maize:

**Fig. 4.** The proportion of marker genotypes that are heterozygous are shown as calculated for the area within 10 cM on each side of the centromere compared with the remaining chromosome arms. Black bars are within 10 cM on each side of the centromere position; hatched bars represent the rest of the chromosome.

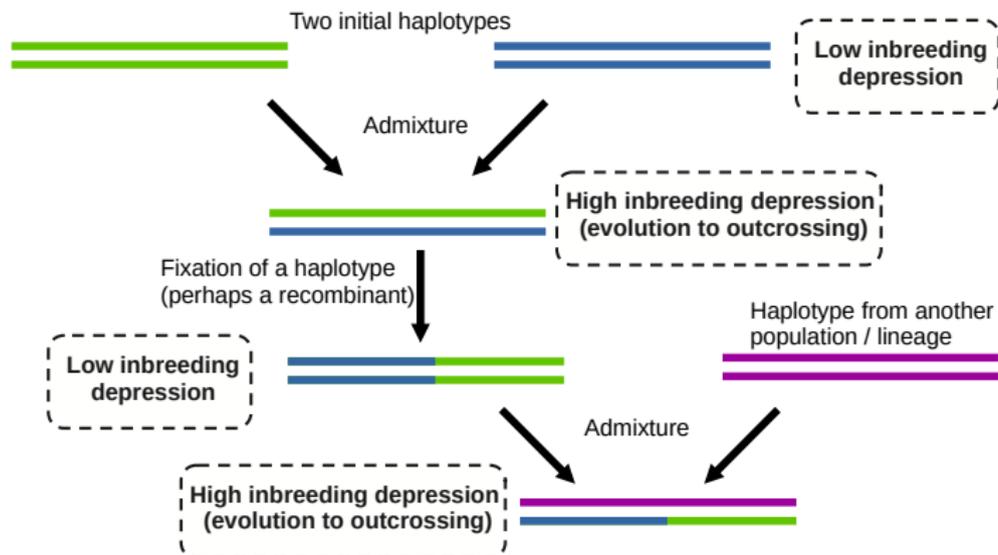


McMullen et al. 2009

→ Higher heterozygosity in centromeric regions (tight linkage) may be cause of heterosis between Maize lines

# Consequences on mating system evolution

## Potential for “cyclical” dynamics



Thank you!

Any questions?