The impact of genetic interactions on response to selection

Örjan Carlborg

Other contributors: Arnaud Le Rouzic and Paul Siegel

Swedish University of Agricultural Sciences
Department of Animal Breeding and Genetics

Epistasis

Epistasis

- Non-additive genetic variation has an impact on the evolutionary properties of a population

Epistasis

- Non-additive genetic variation has an impact on the evolutionary properties of a population
- Hybridization / pairwise QTL detection experiments reveal epistasis for most quantitative traits (*)

Epistasis

- Non-additive genetic variation has an impact on the evolutionary properties of a population
- Hybridization / pairwise QTL detection experiments reveal epistasis for most quantitative traits (*)

(*) Roff and Emerson 2006. Epistasis detected for:
- 79% of life history traits
- 67% of morphological traits

Describing Epistasis

Describing Epistasis

- Usual way to describe epistasis: interaction variance

Describing Epistasis

- Usual way to describe epistasis: interaction variance
- Link with biological description of genetic interactions

Describing Epistasis

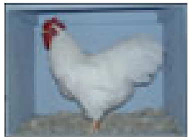
- Usual way to describe epistasis: interaction variance
- Link with biological description of genetic interactions
- A case study: a 4-locus network of interacting loci involved in determining chicken body weight

Genetic architecture of selection response

Dunnington & Siegel, 1996; Jacobsson et al. 2005

Genetic architecture of selection response

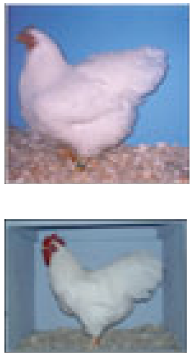
Dunnington & Siegel, 1996; Jacobsson et al. 2005

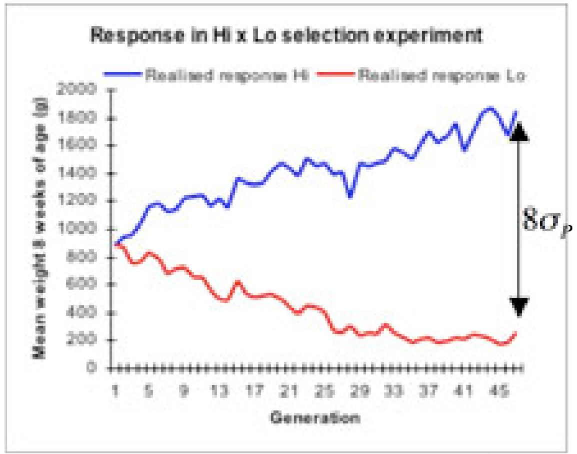


7 partially inbred lines of White Plymouth Rocks were crossed and subjected to…

Genetic architecture of selection response

Dunnington & Siegel, 1996; Jacobsson et al. 2005



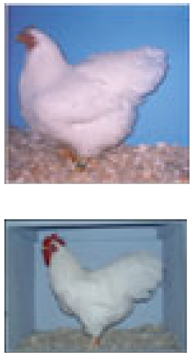


7 partially inbred lines of White Plymouth Rocks were crossed and subjected to…

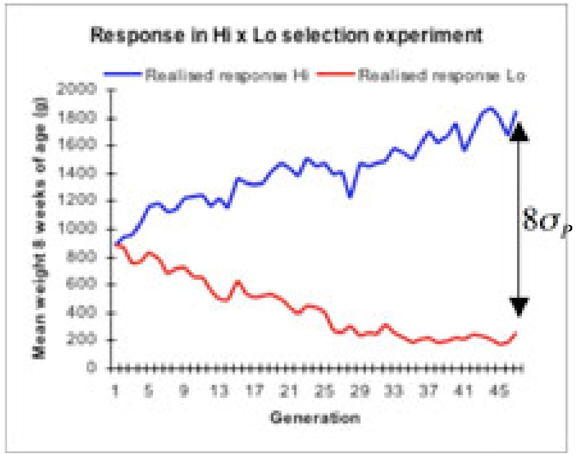
44 generations of bi-directional phenotypic selection for body week at 56 days of age and …

Genetic architecture of selection response

Dunnington & Siegel, 1996; Jacobsson et al. 2005



7 partially inbred lines of White Plymouth Rocks were crossed and subjected to…



44 generations of bi-directional phenotypic selection for body week at 56 days of age and …

the high- and low- selected lines were crossed to generate 800 F_2 individuals

QTL Mapping

New insights to genetic architecture

QTL Mapping

New insights to genetic architecture

QTL Mapping

New insights to genetic architecture

- Genetic mechanisms underlying:

QTL Mapping

New insights to genetic architecture

- Genetic mechanisms underlying:
  - Continued response for many generations

QTL Mapping

New insights to genetic architecture

- Genetic mechanisms underlying:
  - Continued response for many generations
  - New phenotypes outside of original range of phenotypes

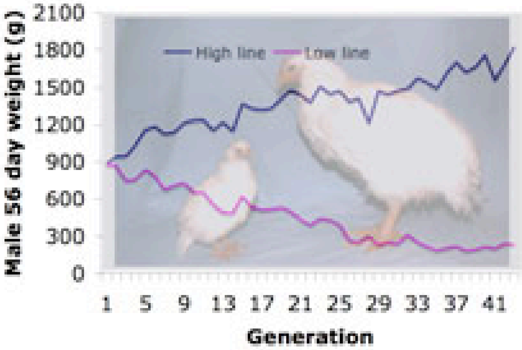
QTL Mapping

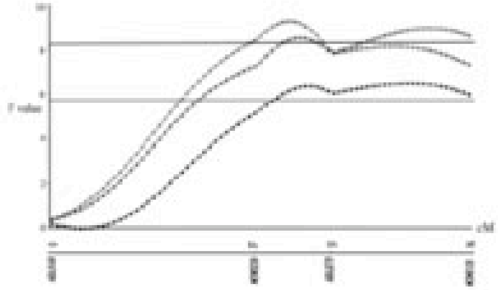
New insights to genetic architecture

- Genetic mechanisms underlying:
  - Continued response for many generations
  - New phenotypes outside of original range of phenotypes
  - Genetic variation not depleted

Standard QTL Mapping

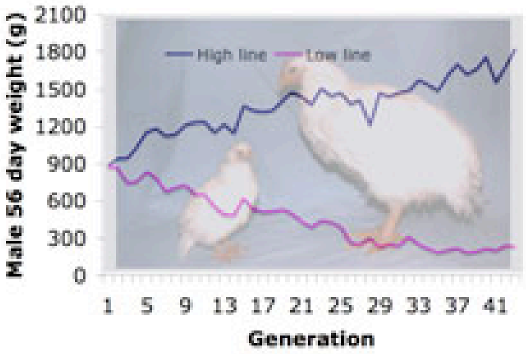
Single QTL

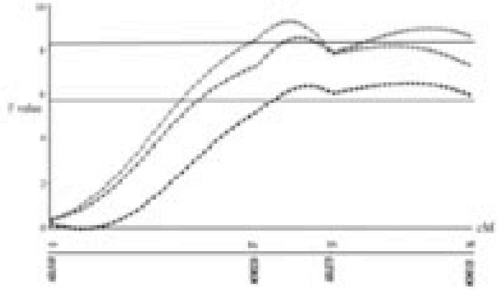




Standard QTL Mapping

Single QTL

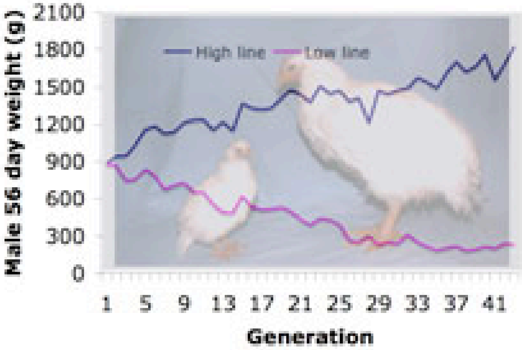


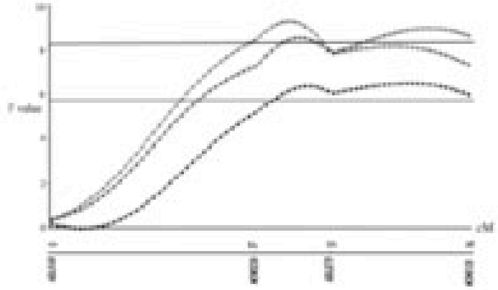


- 1 Genome-wide significant QTL affecting weight at age of selection

Standard QTL Mapping

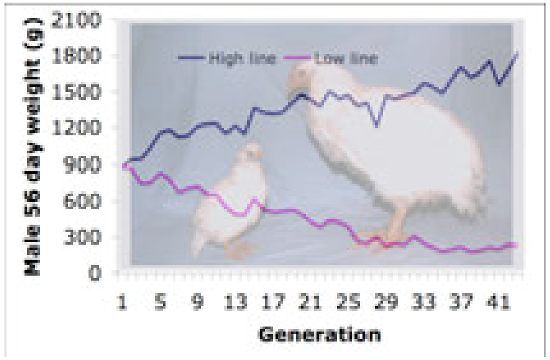
Single QTL

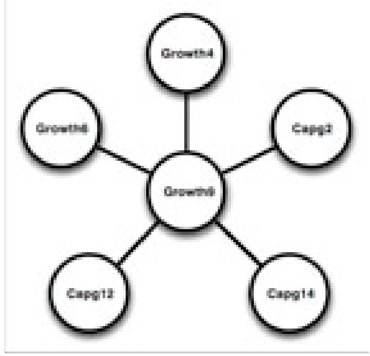




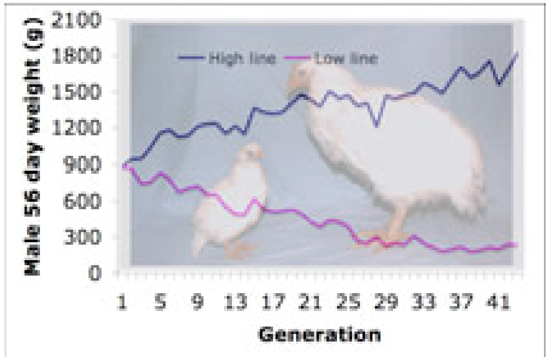
- 1 Genome-wide significant QTL affecting weight at age of selection
- Explains 6% of parental line difference or 3% of residual phenotypic variation in the F_2 population

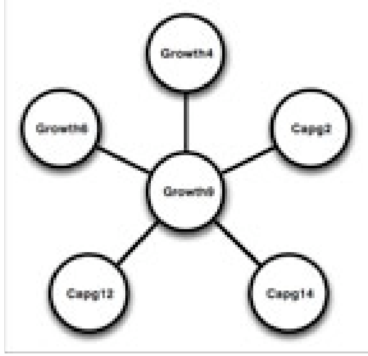
Epistatic QTL Mapping





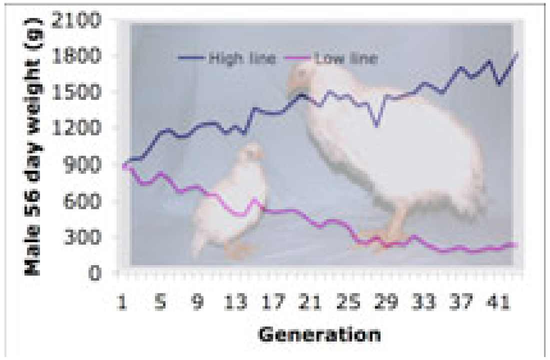
Epistatic QTL Mapping

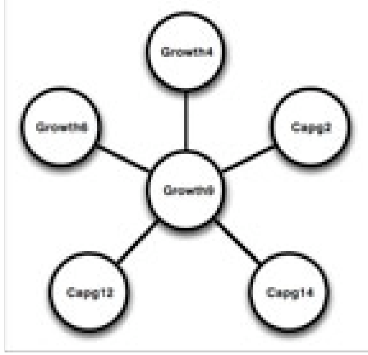




- Radial network of 6 QTL affecting weight at age of selection

Epistatic QTL Mapping

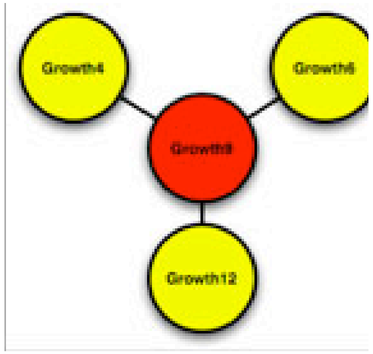


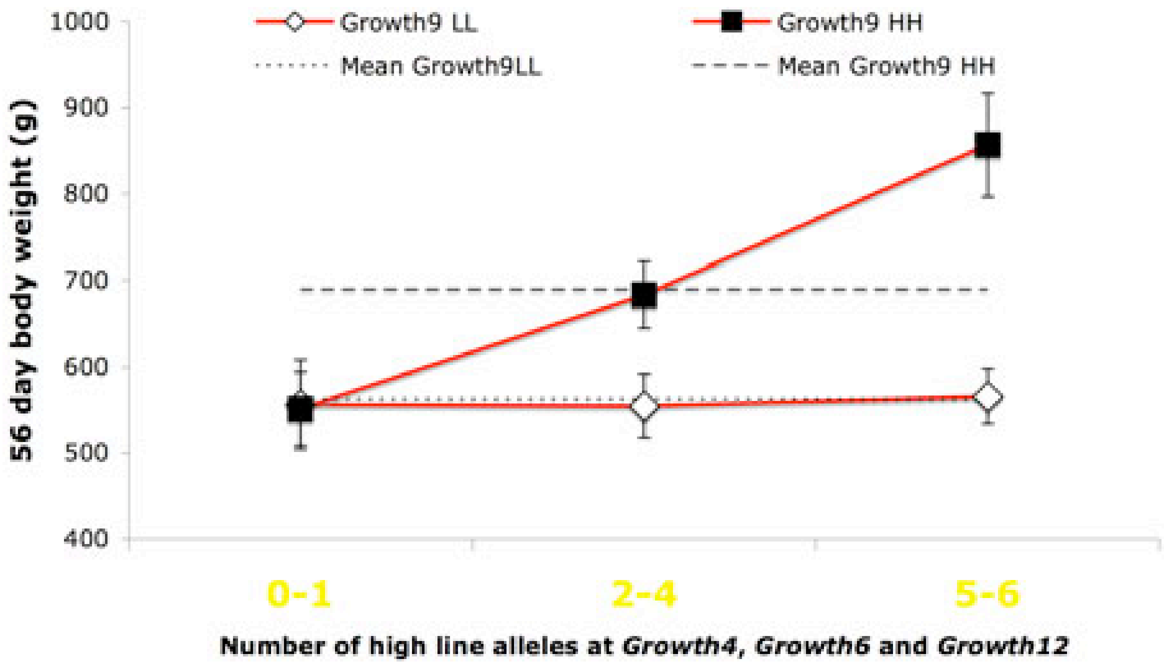


- Radial network of 6 QTL affecting weight at age of selection
- Explains 13% of residual phenotypic variation in the F_2 population

Total network effect

Stratified data

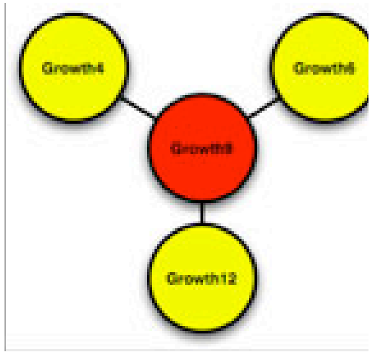


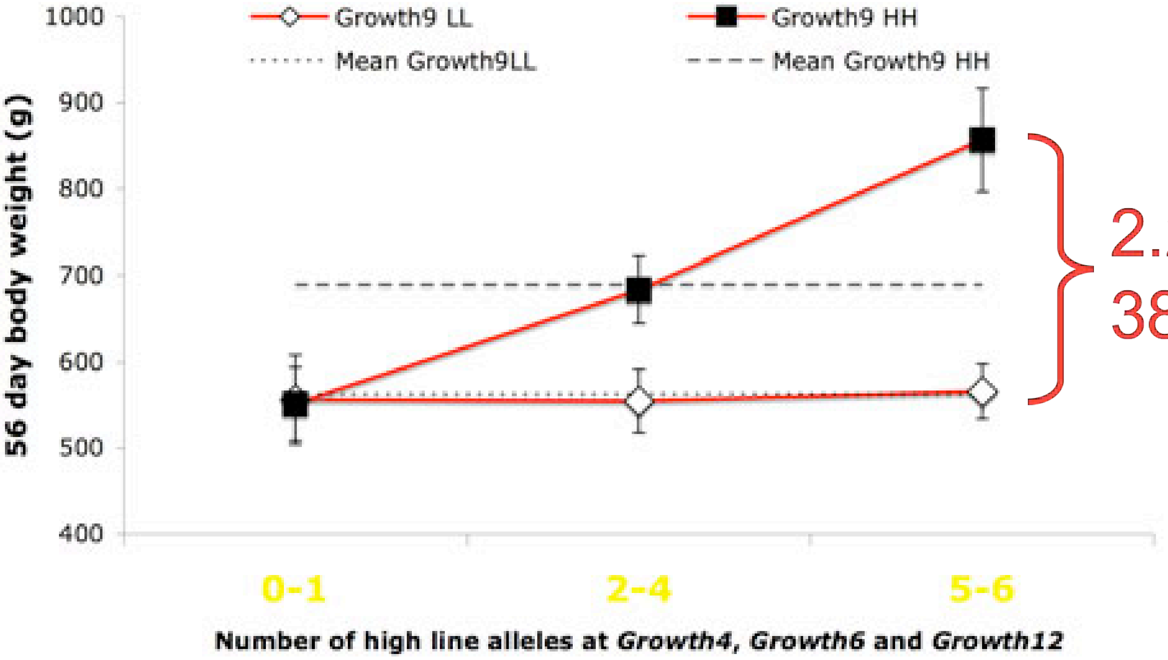


Increasing number of high-line alleles

Total network effect

Stratified data





2.2 σ_P or
38% of F_2 range

Increasing number of high-line alleles

Implications:

Implications:

- Multiple, novel interacting loci

Implications:

- Multiple, novel interacting loci
- An important role of epistasis in response to selection

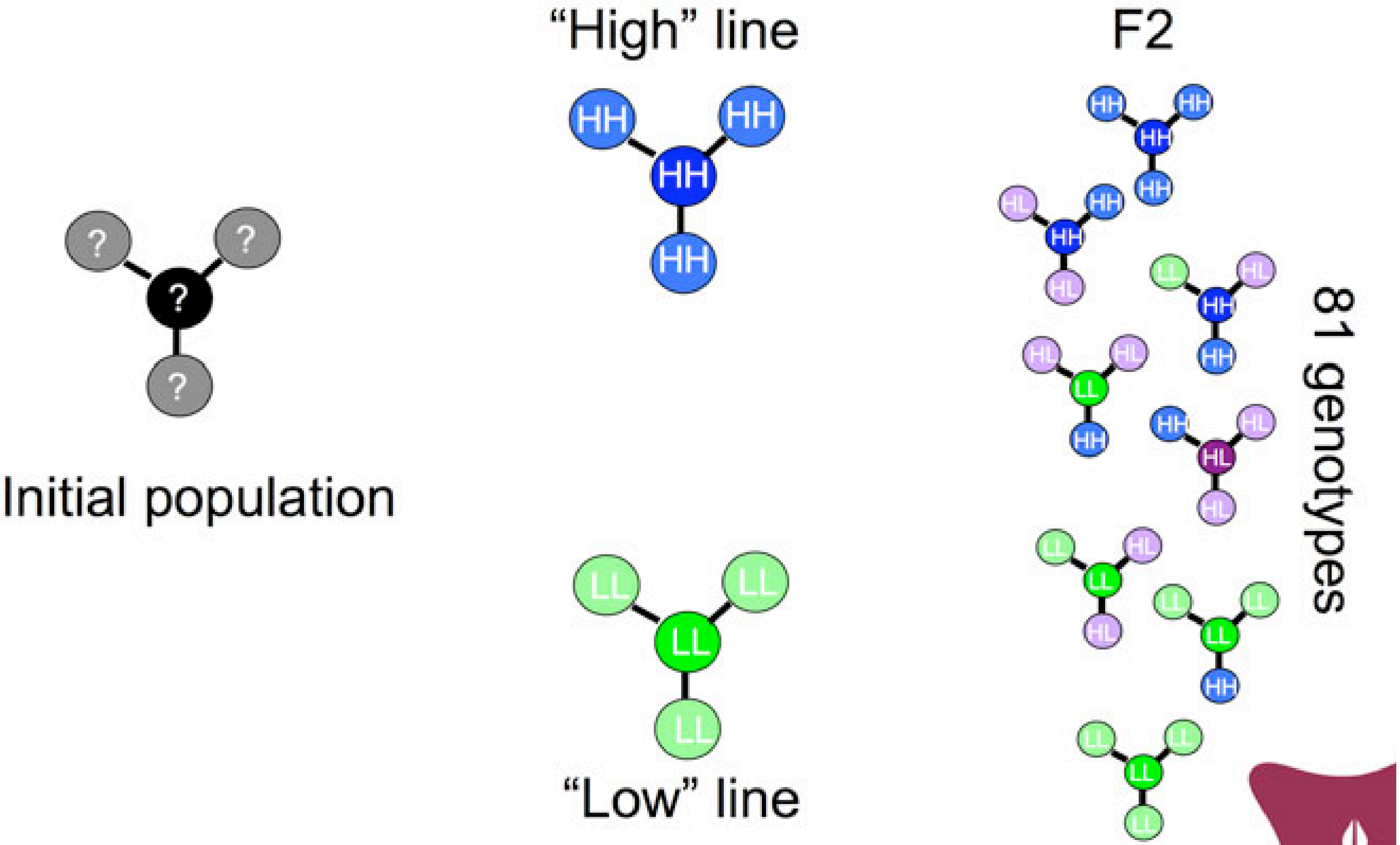
Implications:

- Multiple, novel interacting loci
- An important role of epistasis in response to selection
- A novel genetic mechanism underlying phenotypic change

Do QTL data bring information about the dynamics of the system ?

- Estimate the genotype-phenotype map
- Simulate the behavior of this genetic architecture

Genotype - phenotype map



Initial population

“High” line

“Low” line

F2

81 genotypes

Genotype - phenotype map

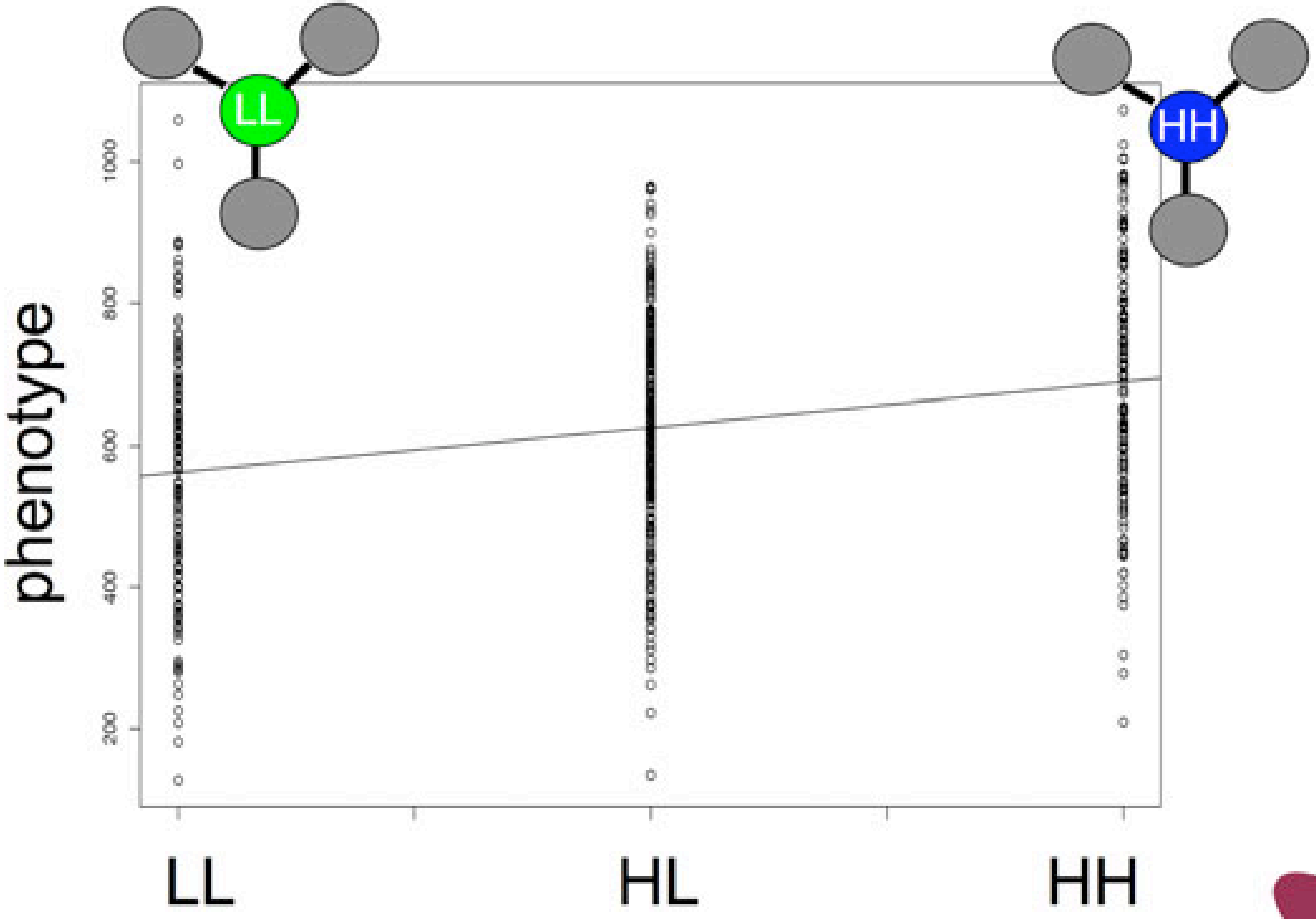
- 528 individuals with high-information on genotypes and phenotypes in the F2 population.

Gr4	Gr6	Gr9	Gr12	Phenotype
HH	HL	HL	HH	608
HL	HL	HH	HH	465
LL	HL	HL	LL	658
…				

- => Phenotypic estimates for each genotype

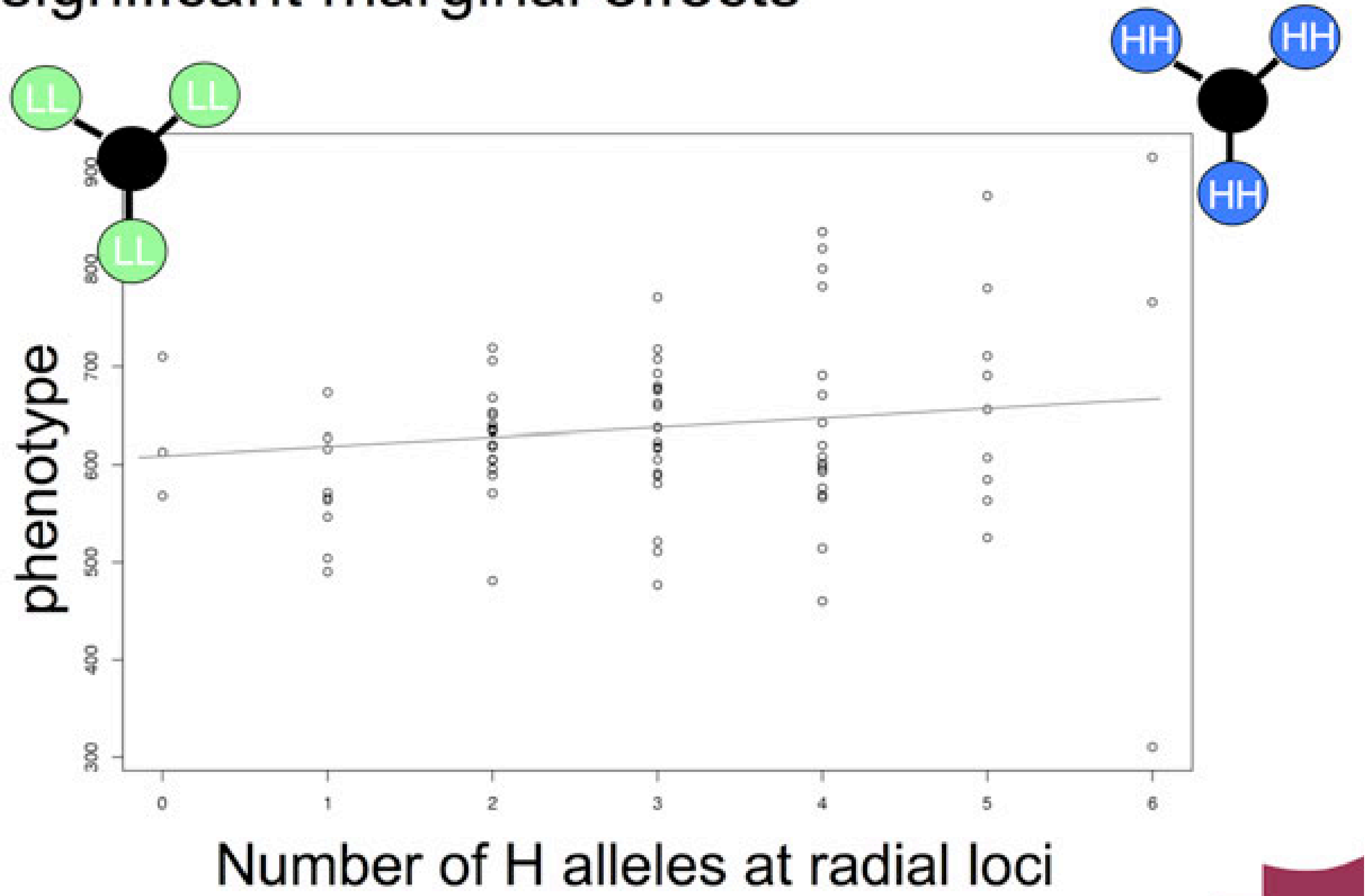
Central locus (Growth9):

Significant maginal effect



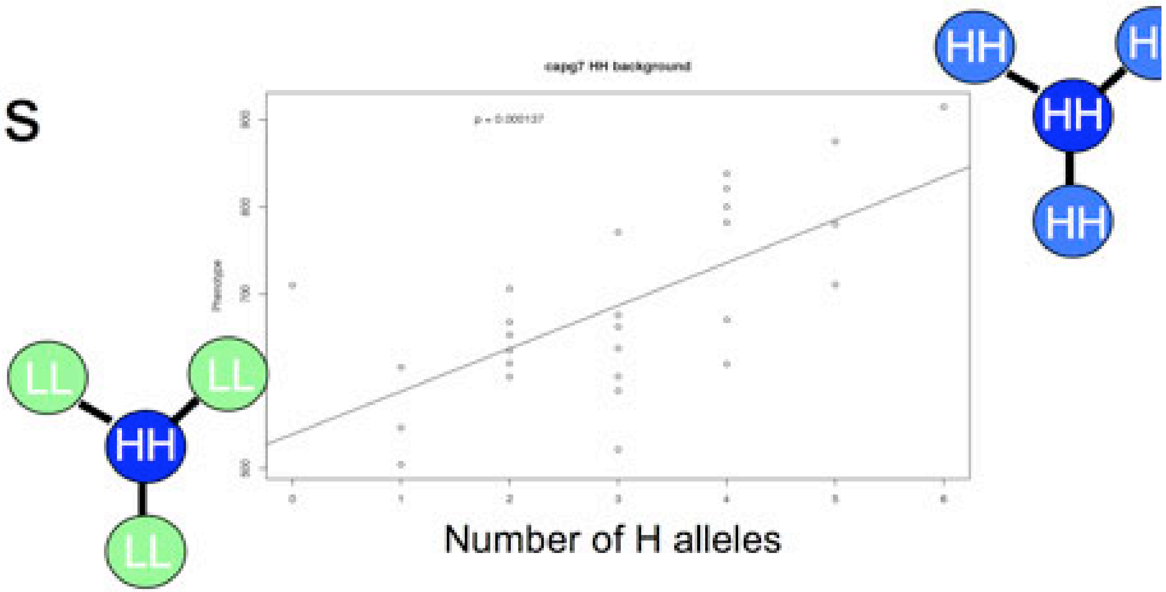
Radial loci (Growth4, 6 and 12)

No significant marginal effects

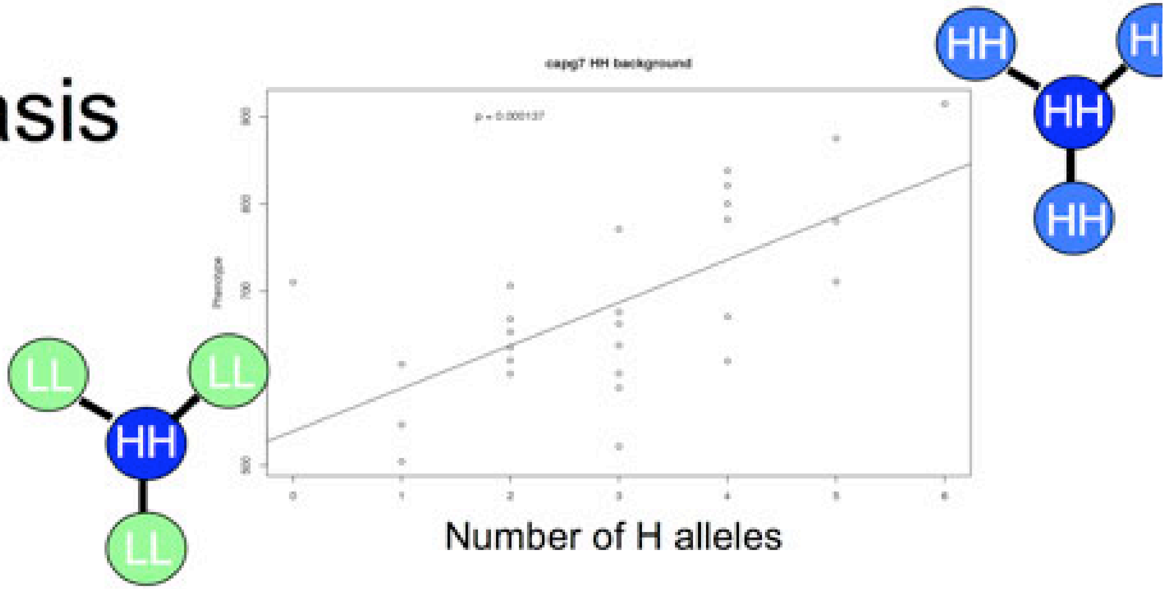


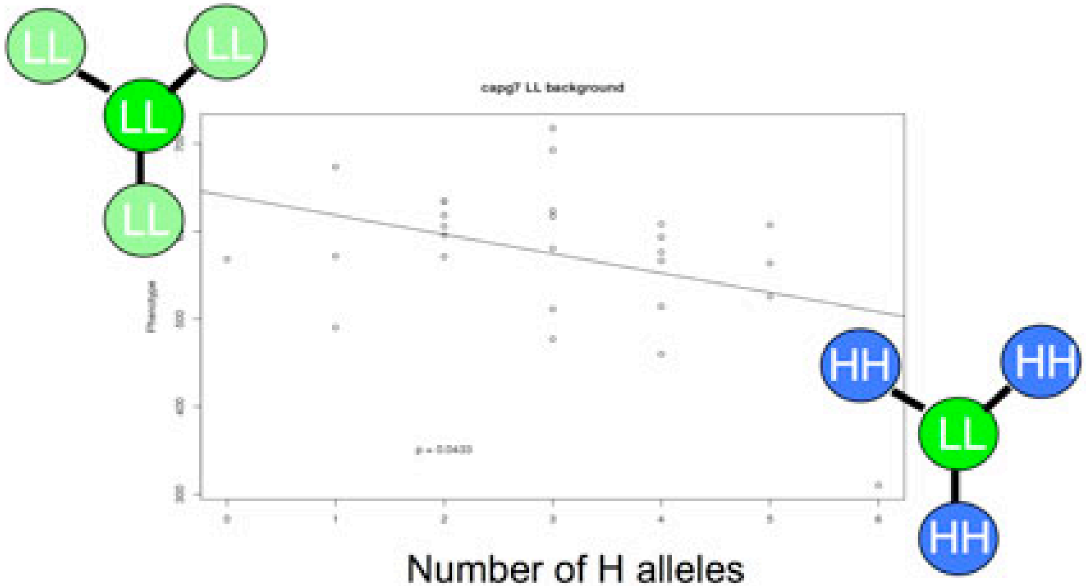
Radial loci:

Strong epistasis



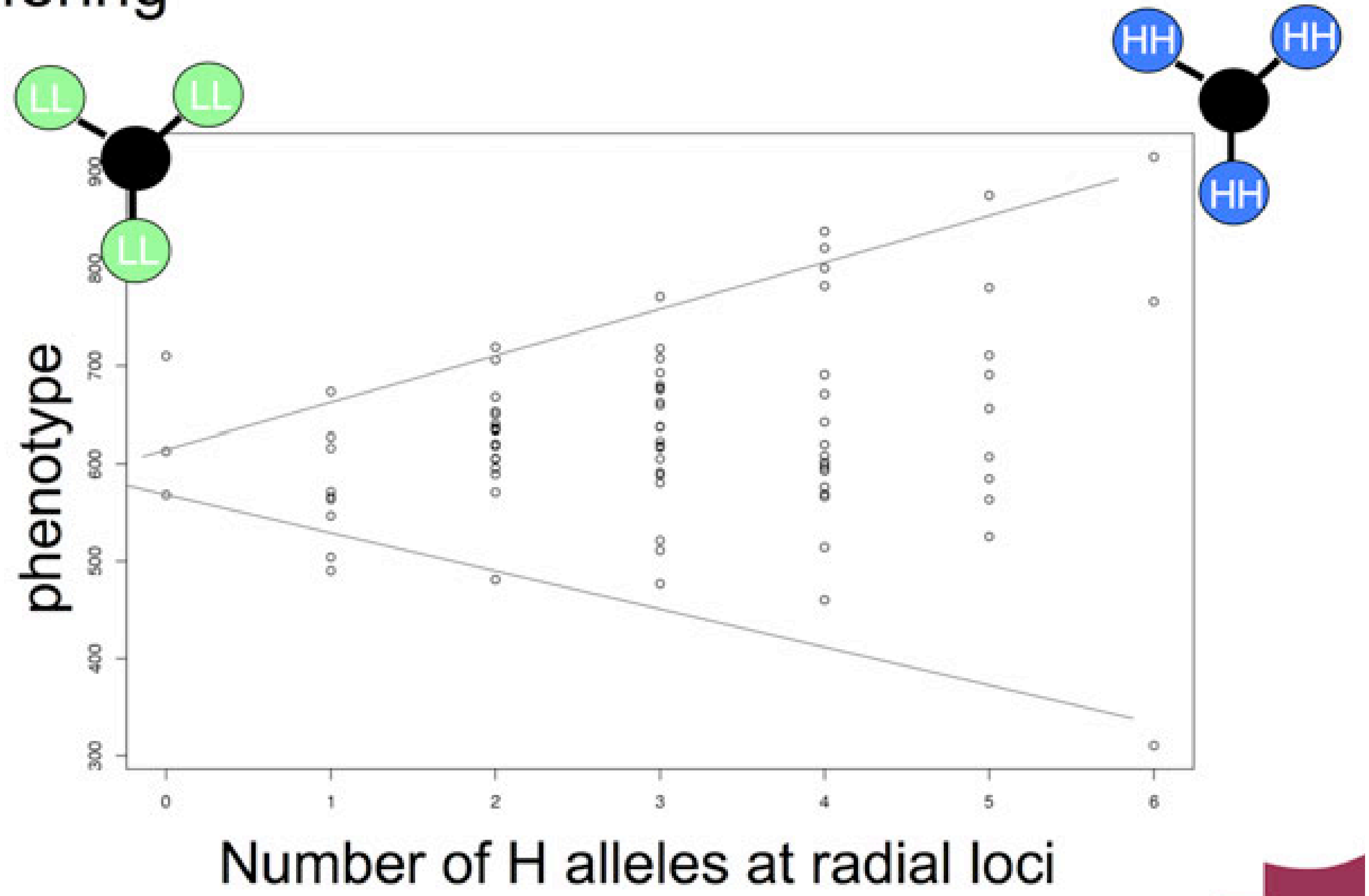
Radial loci:
Strong epistasis





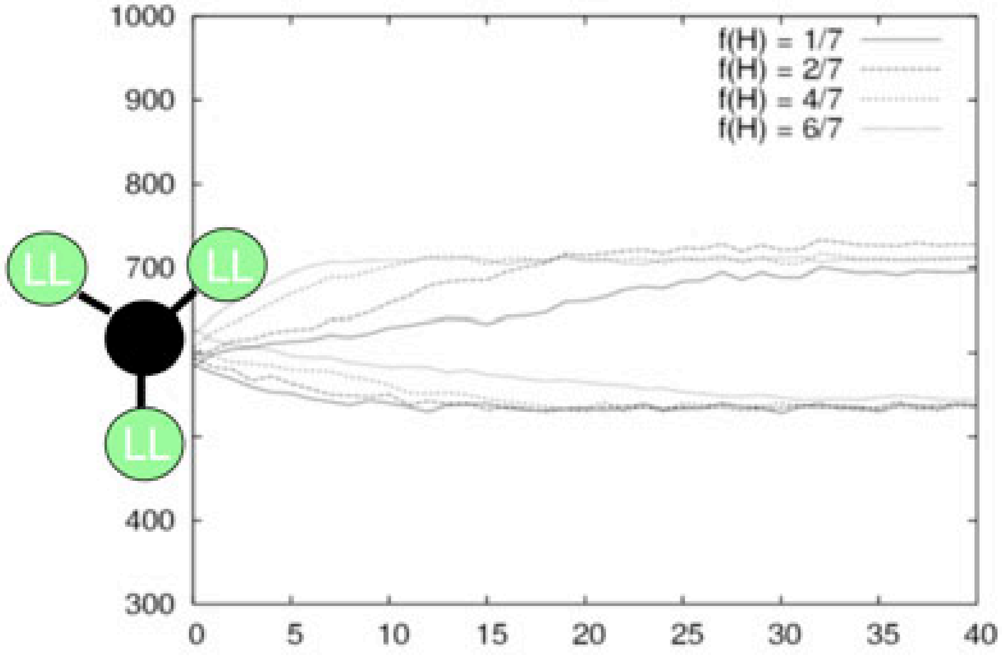
Epistatic effect of radial loci:

Buffering



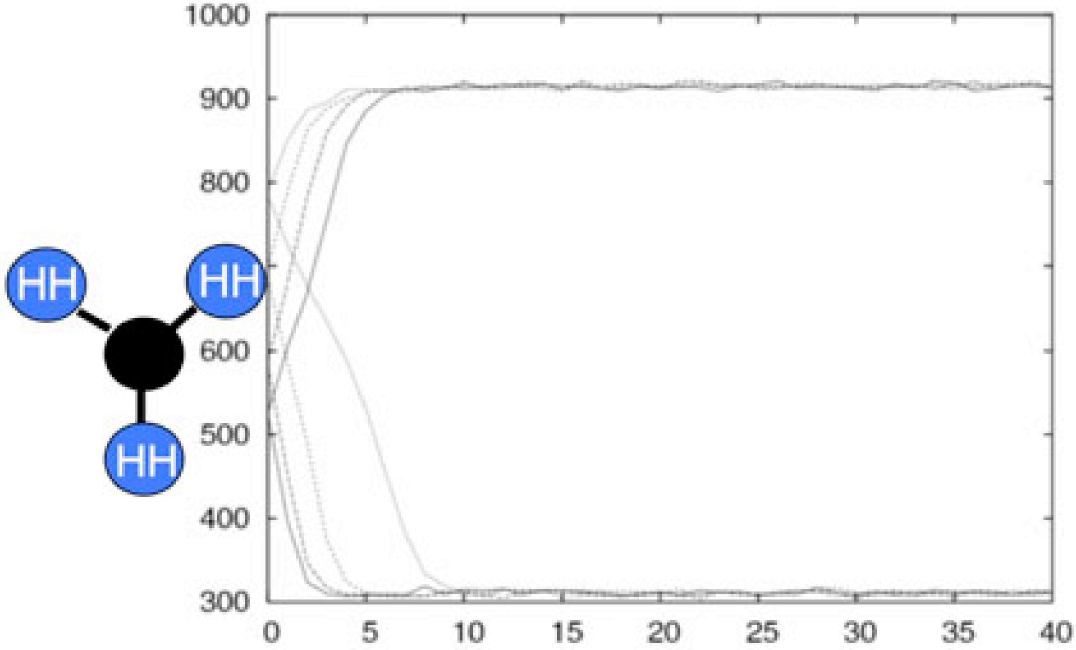
Effects on response to selection

I. Buffered system



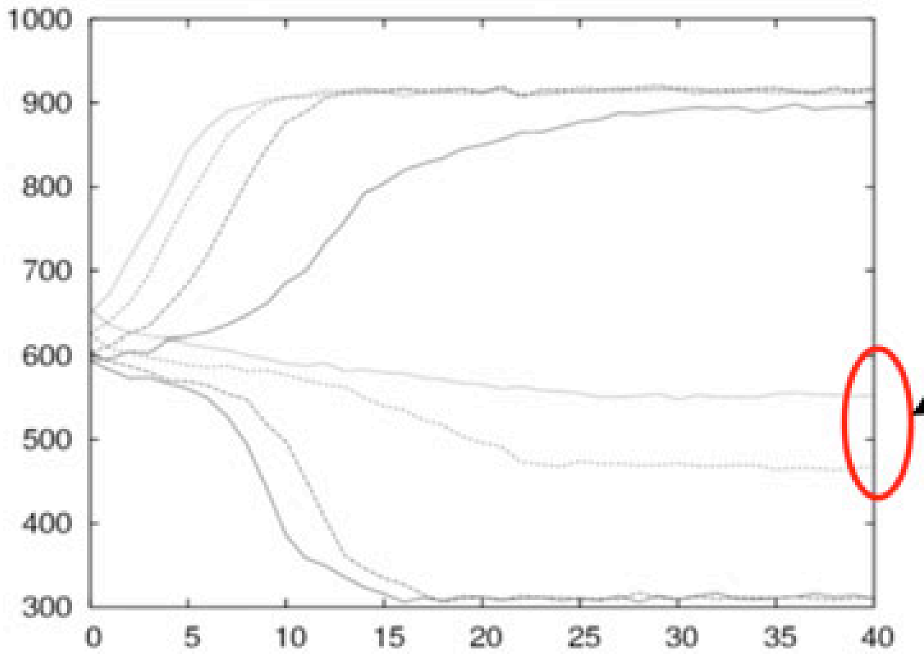
Response to selection

II. Decanalized system



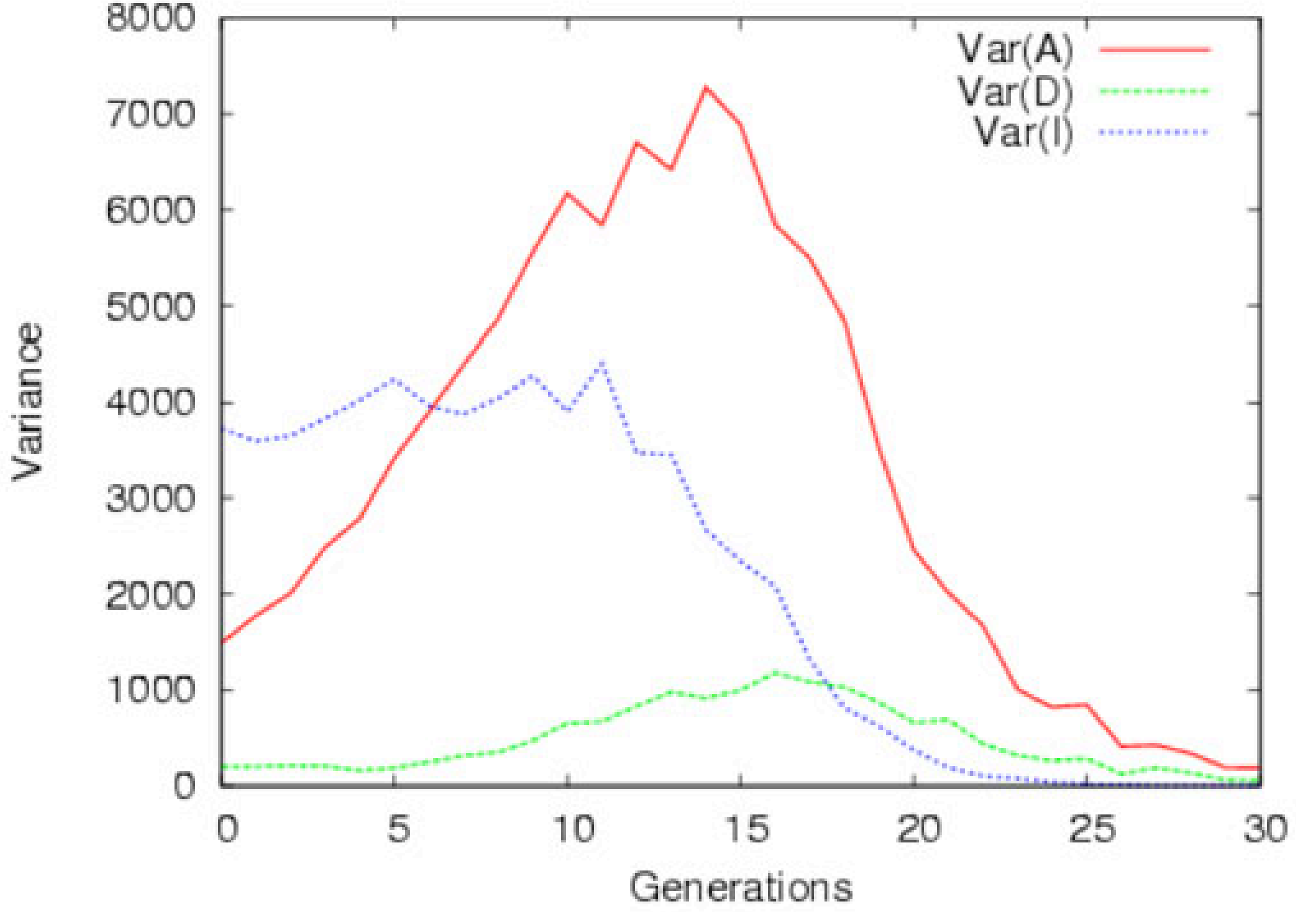
Response to selection

III. Intermediate initial frequencies

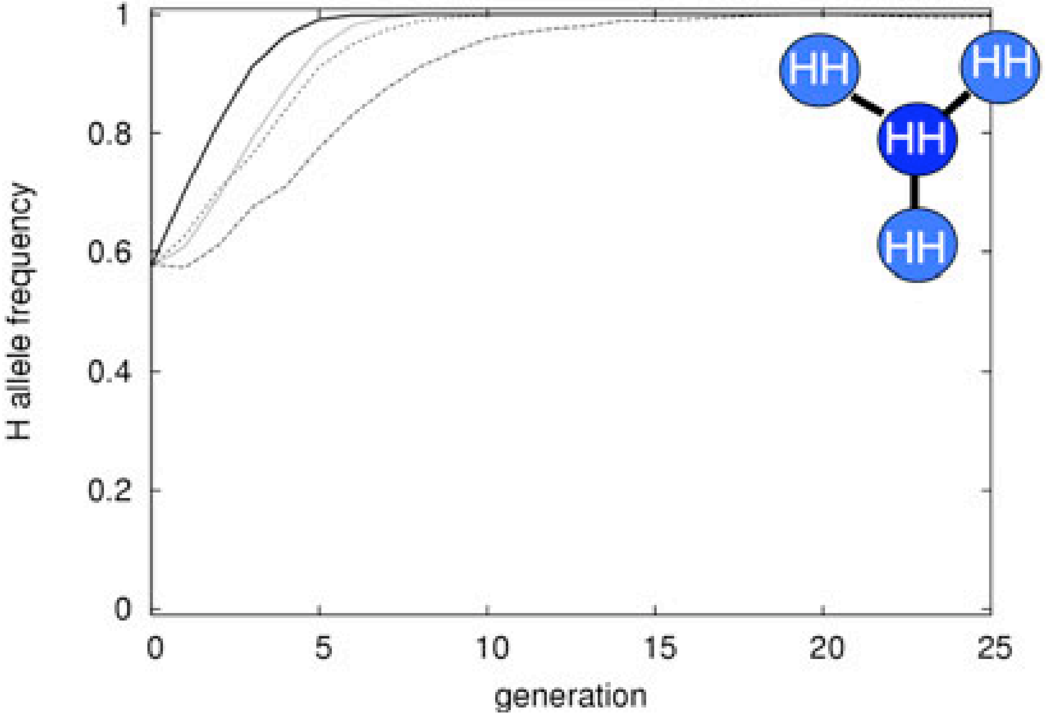


Local optima

Change in genetic variances over time



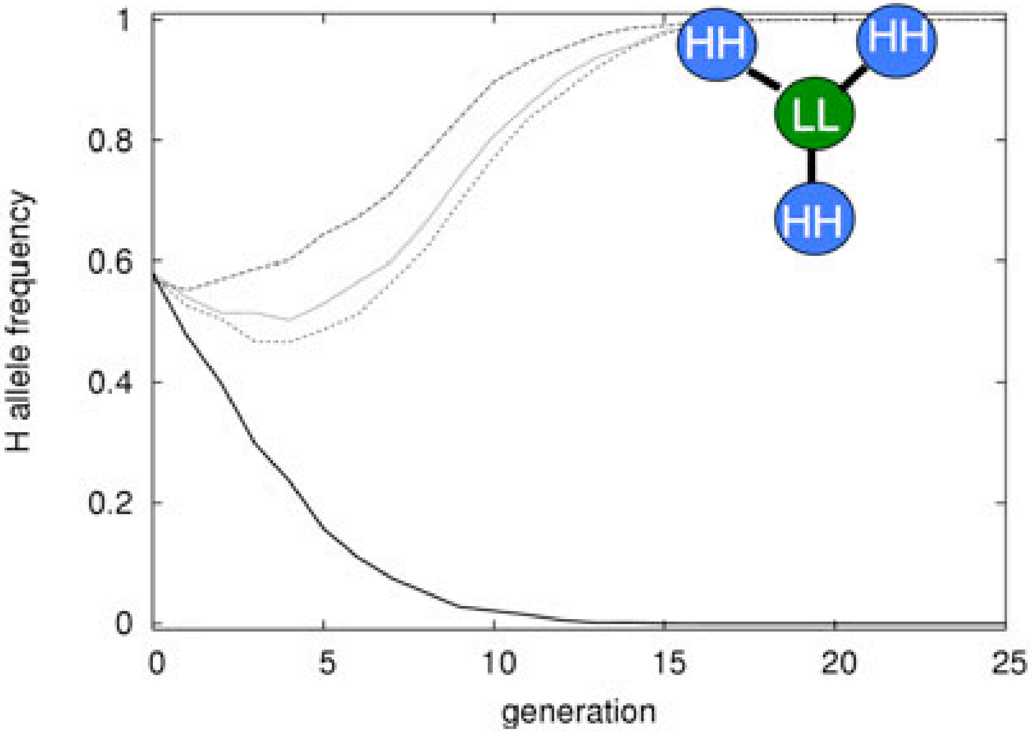
Change in allelic frequencies
I. Selection for increased body weight



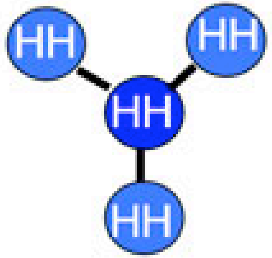
High line

Change in allelic frequencies

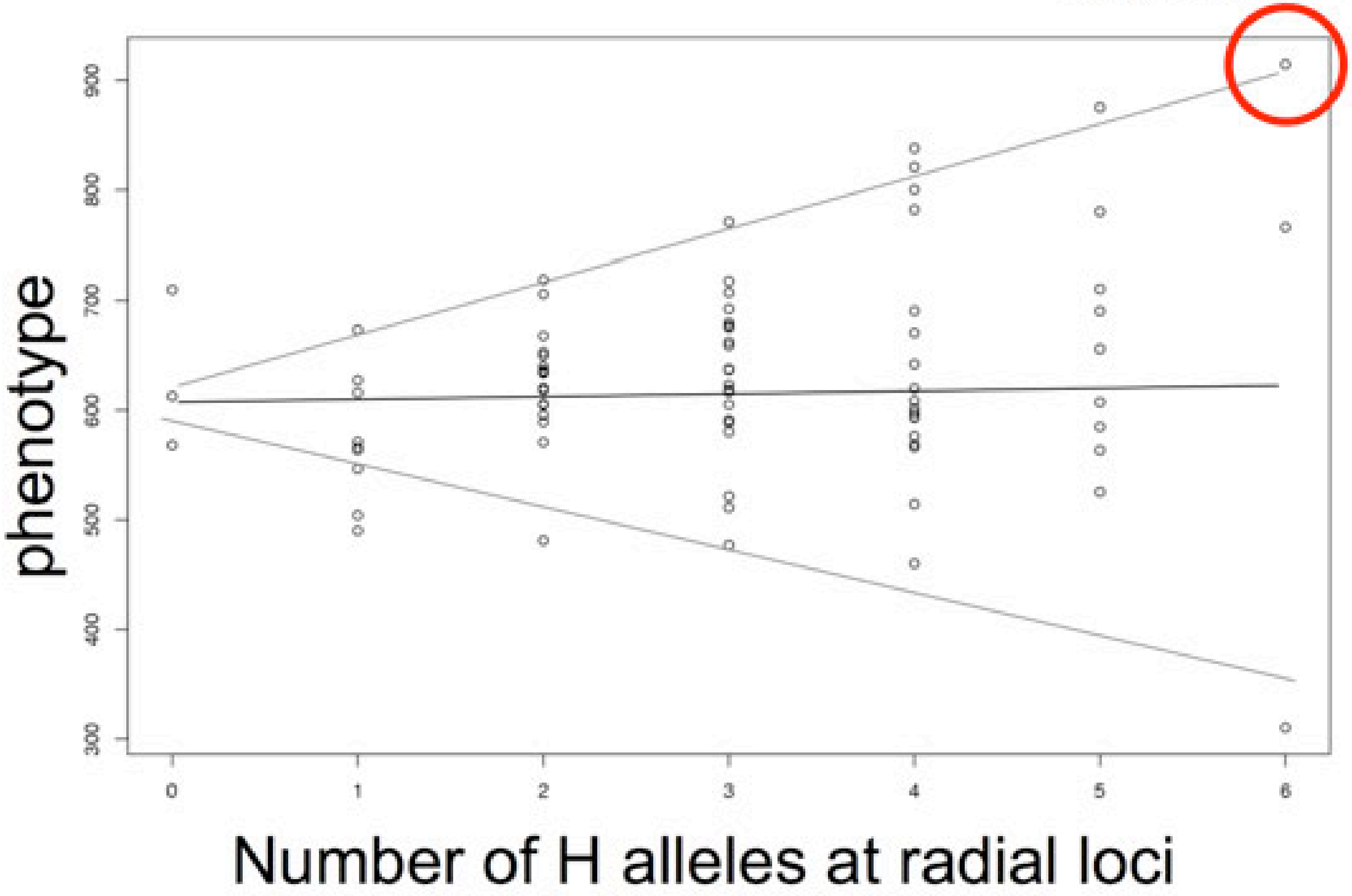
I. Selection for decreased body weight

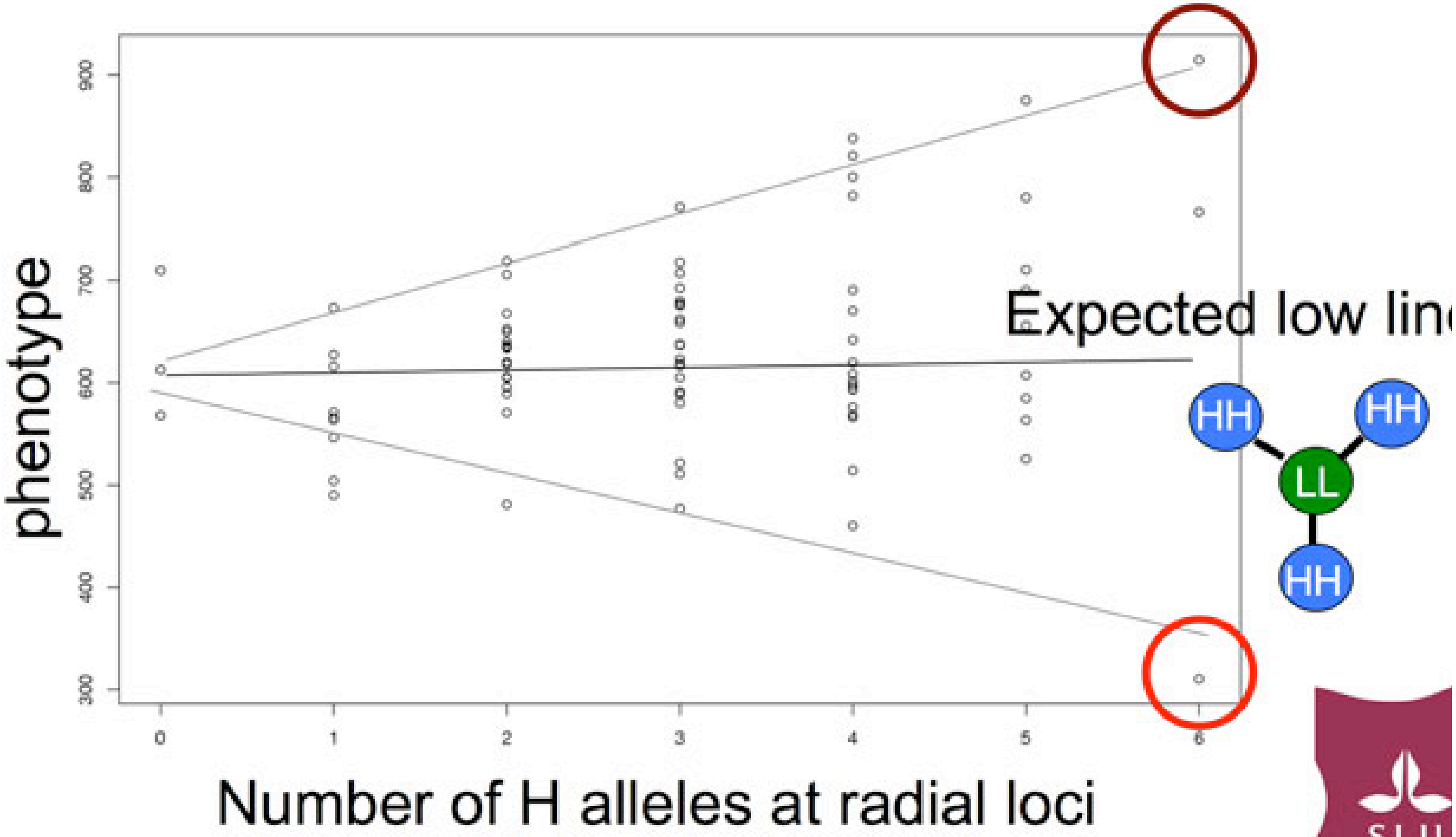


Low line



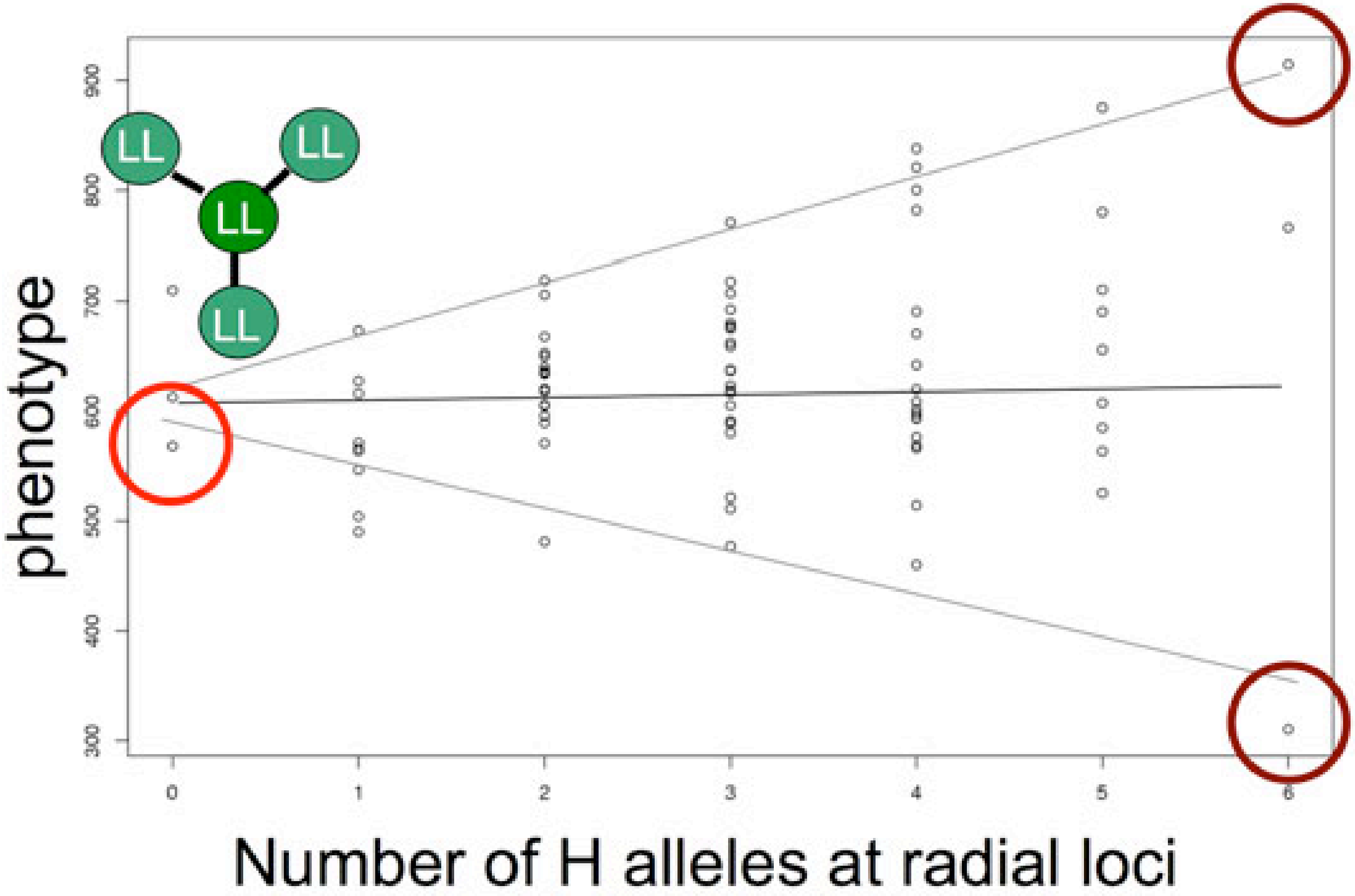
Expected and
observed high lin





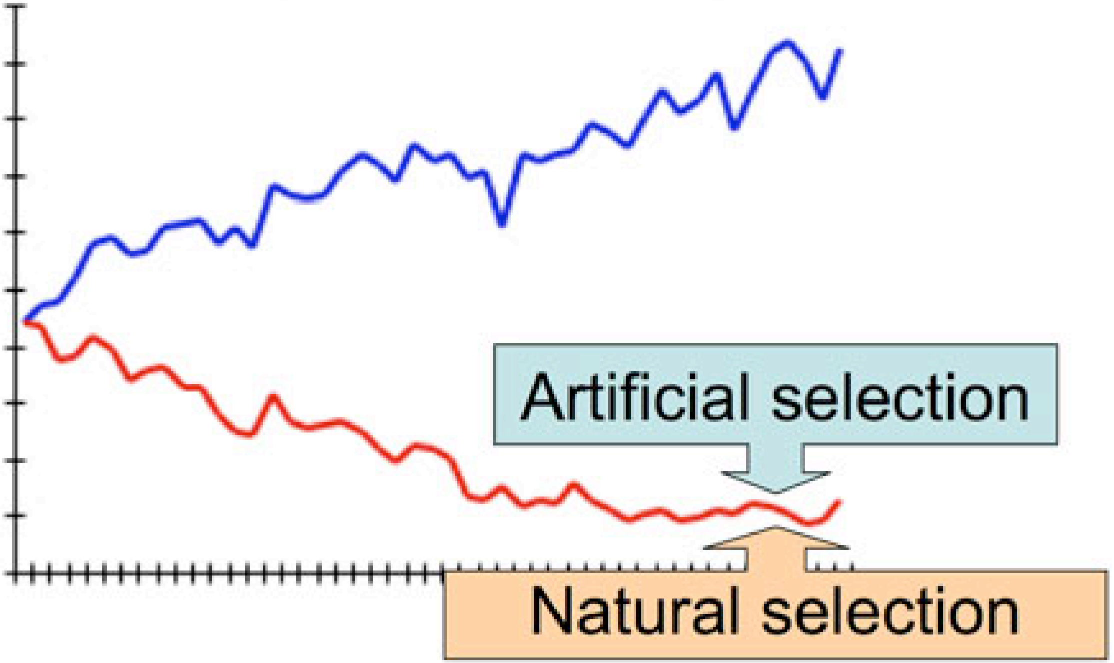
Expected low lin

Observed low line



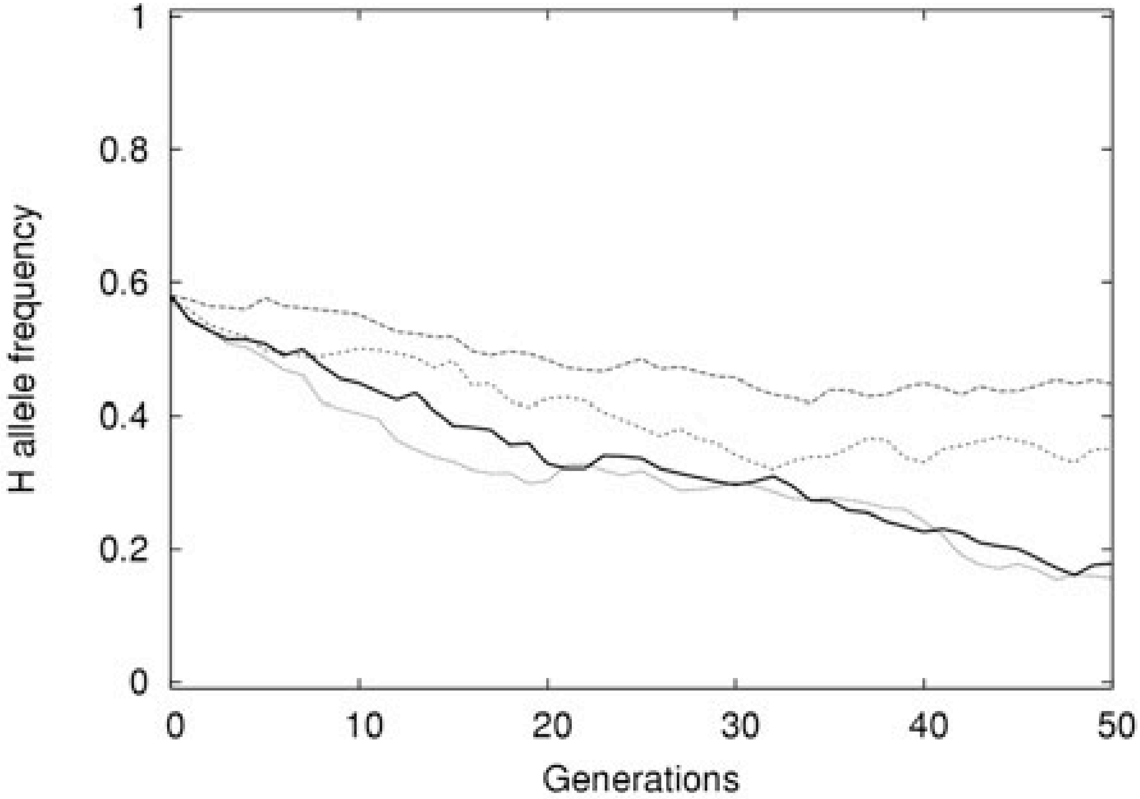
What did happen in the low line?

- Stabilizing selection?


Artificial selection

Natural selection

Simulation of stabilizing selection



Conclusions

- Foundation in experimental data -> realistic features of epistatic genetic architecture
- Local maxima observed - outcome of selection depends on initial allelic frequencies
- Release of “new” selectable genetic variation from interacting network architectures
- Epistasis can partly explain observed selection response
- Epistasis can mislead QTL detection by leading to the fixation of identical genotypes in oppositely selected lines