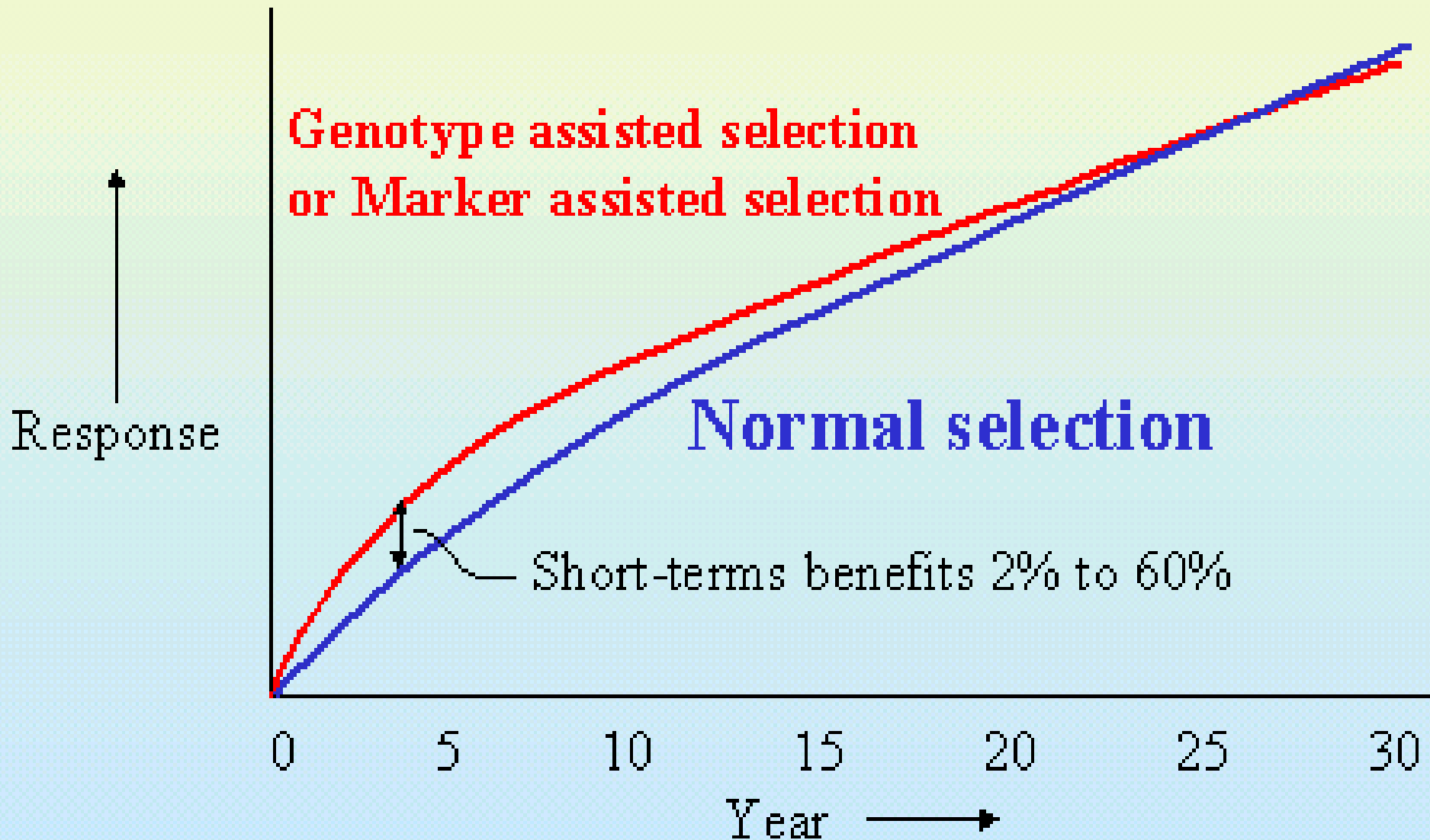


# QTL mapping for practitioners from linkage to gene

Exploitation of genes with major effect

- Detect genotypes based on phenotype only
  - eye and coat colour, genetic defects
  - double muscling, Booroola, Halothene
- Detect with the aid of genetic markers
  - > Location, also those with smaller effect
- Detect actual gene mutation

# Long term response



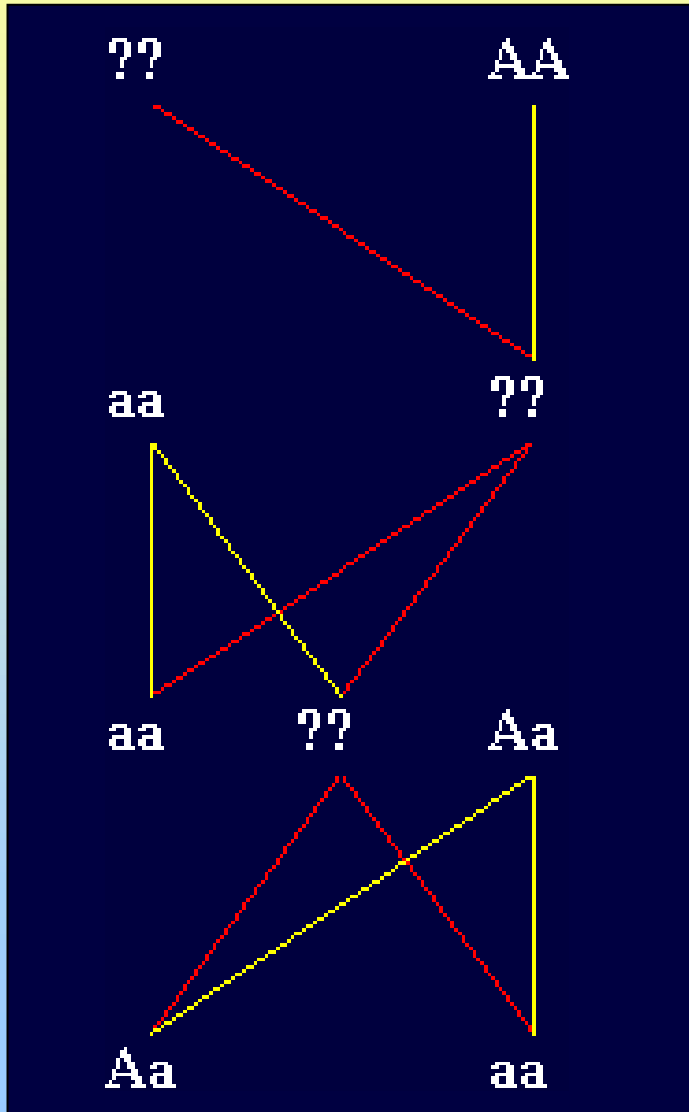
# Segregation Analysis

- For detection of major genes or single gene effects
  - (often without markers)
- Based on phenotypic distributions between/within families
- Use of genotype probabilities
  - e.g. in DNA genotyping strategies
- Can be precursor to marker studies

# Segregation Analysis

- Based on
  - genotype probabilities
  - function (model) to translate phenotypes to genotype probabilities  $g(y|u)$

# Genotype probabilities



- Females have been DNA tested for gene with variants A and a.
- Red lines from males
- Male in second row must be Aa. Why?
- The answer is uncertain for the other two males ...

Male in row	p(aa)	p(Aa)	a(AA)
1	0.6	0.4	0
2	0	1	0
3	2/3	1/3	0

# Segregation analysis

## A systematic approach for complex pedigree

Use information from three sources:

1. Parents

2. Self

$$prob(u) = \frac{prior(u)g(y|u)}{\sum_{v=1}^k prior(v)g(y|v)}$$

3. Mate(s) plus progeny

# $g(y|u)$

probability of expressing a certain phenotype giving the genotype

- 3 distinct genotypes

1 0 0 phenotype 1

0 1 0 phenotype 2

0 0 1 phenotype 3

- complete dominance

1 1 0 phenotype 1

0 0 1 phenotype 2

- incomplete penetrance

1 1 .2 phenotype 1

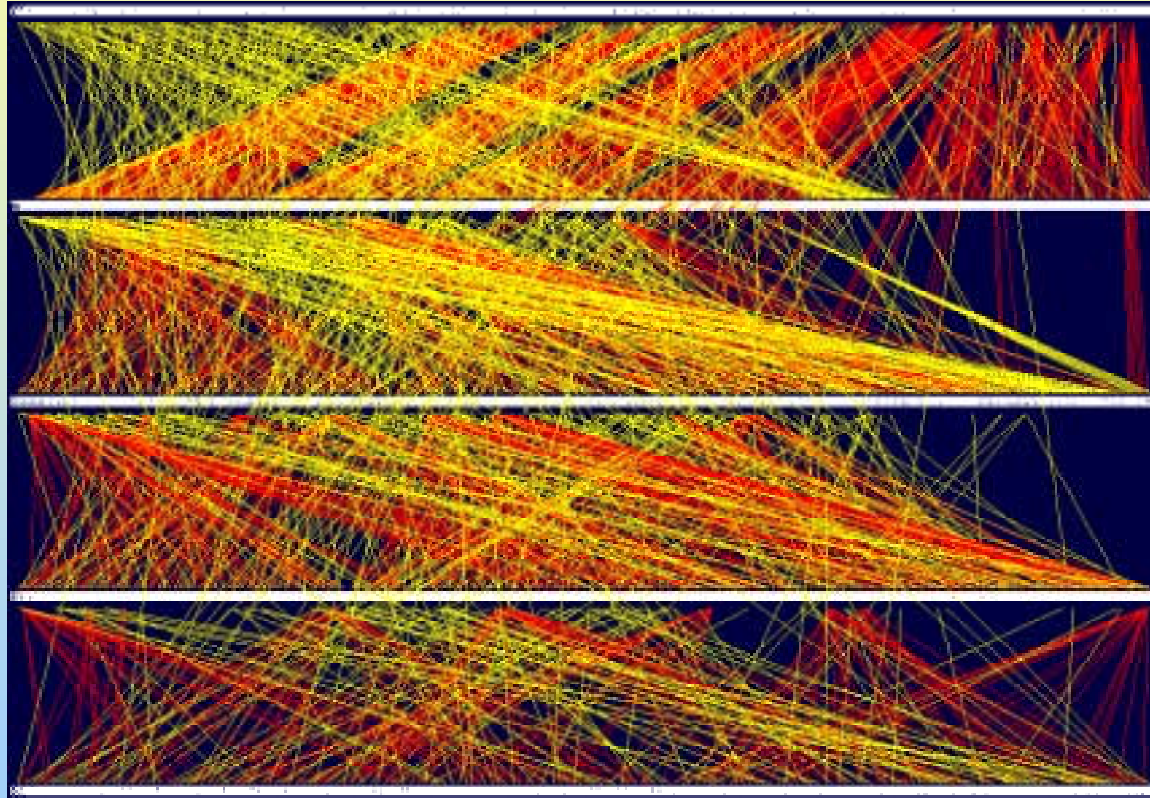
0 0 .8 phenotype 2

# Example in pigs - the halothane gene

- Halothane gene - variants *H* and *h*
- *HH* pigs are normal
- *hh* pigs ...
  - susceptible to halothane gas
  - porcine stress syndrome (**PSS**)
  - pale soft exudative (**PSE**) meat
  - higher lean percent
- *Hh* pigs - mostly like *HH* pigs



# Example in pigs - the halothane gene



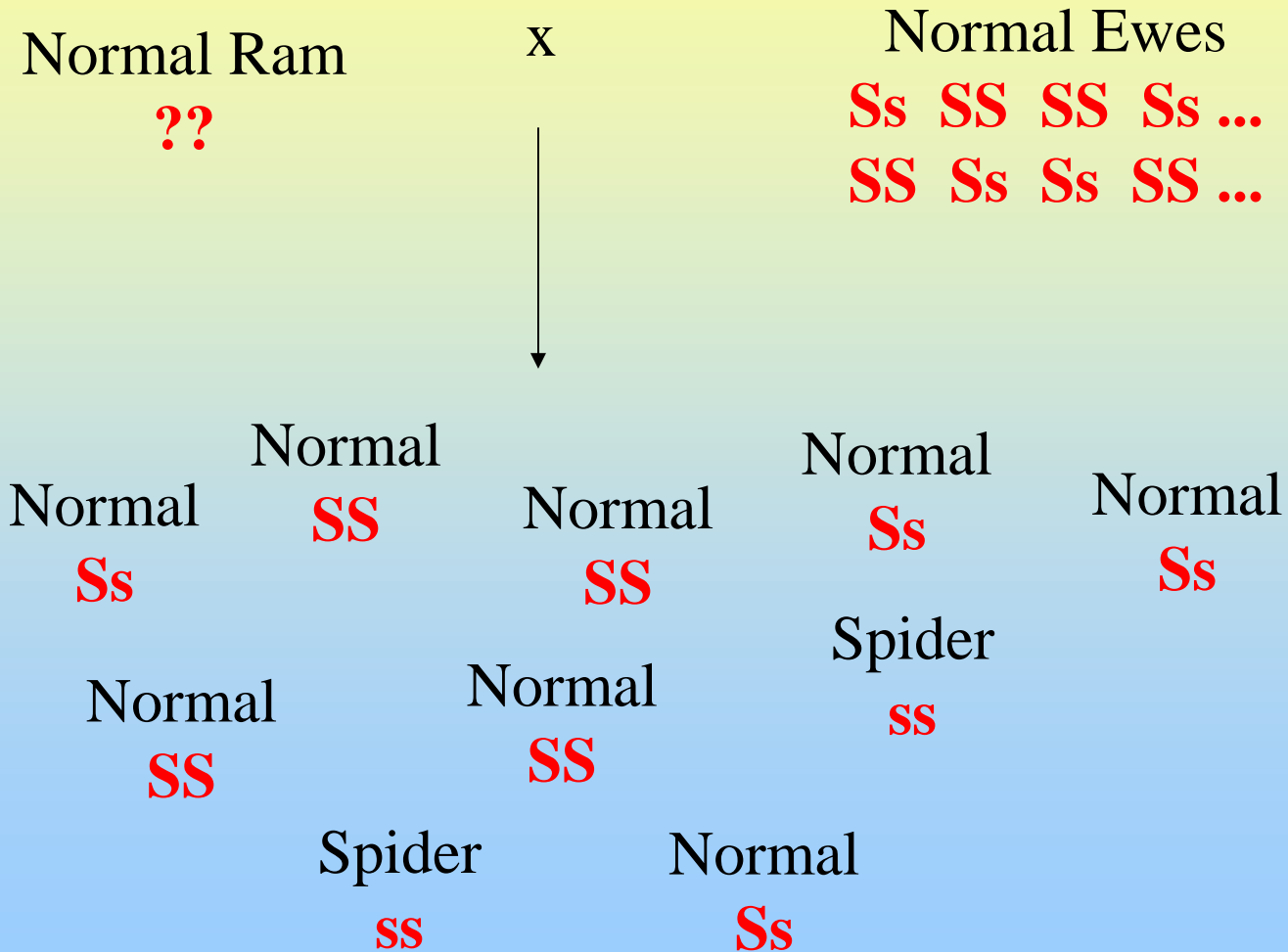
- A slightly bigger problem.
- 60,000 pigs get probabilities (or certainties) from only 113 DNA tests
- Results used in determining effect of halothane variants and in making selection decisions.

# Example in sheep - the spider syndrome

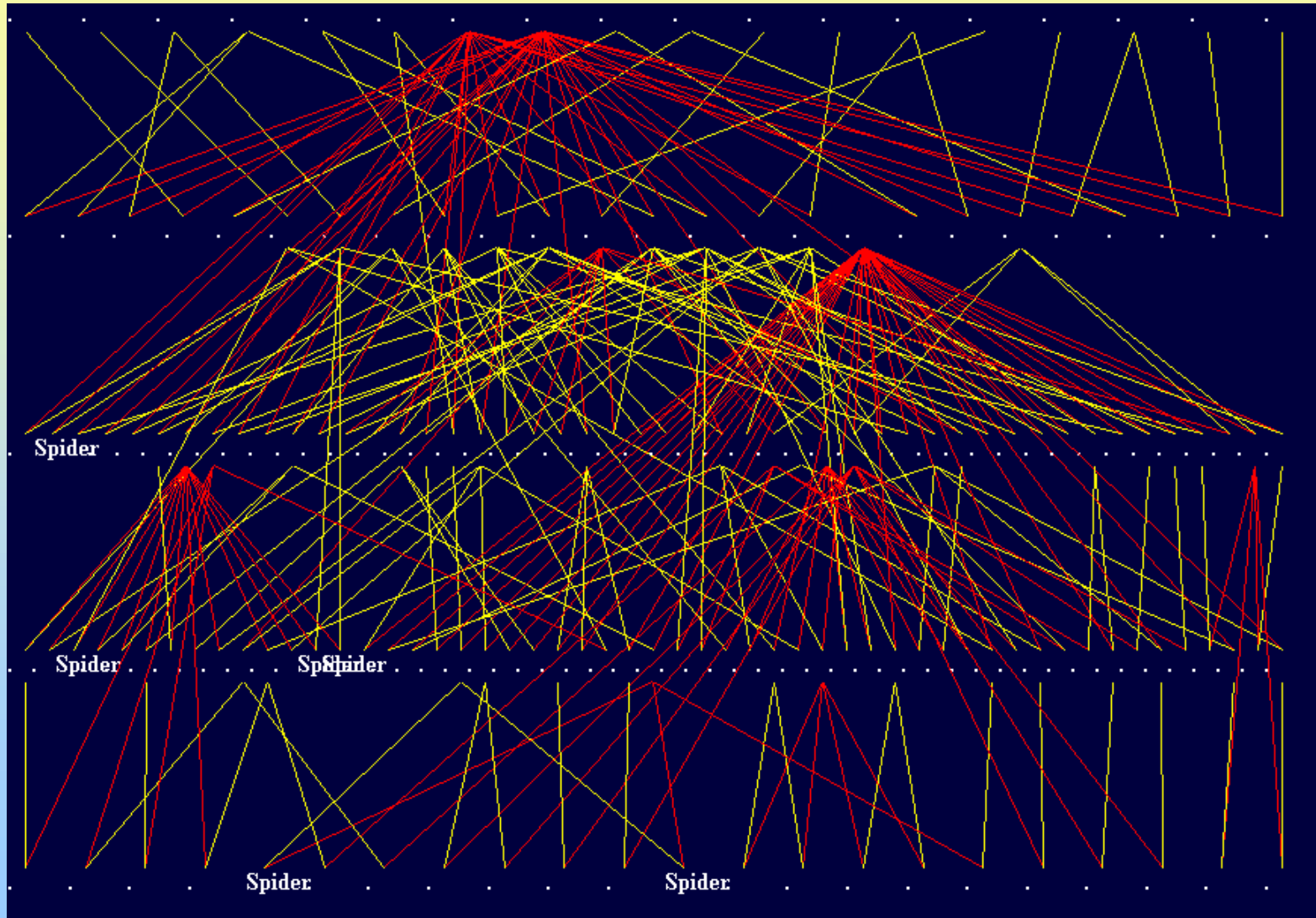


- Spider gene - variants  $S$  and  $s$
- $SS$  and  $Ss$  sheep are normal
- $ss$  sheep are 'spider'
- DNA test is now available

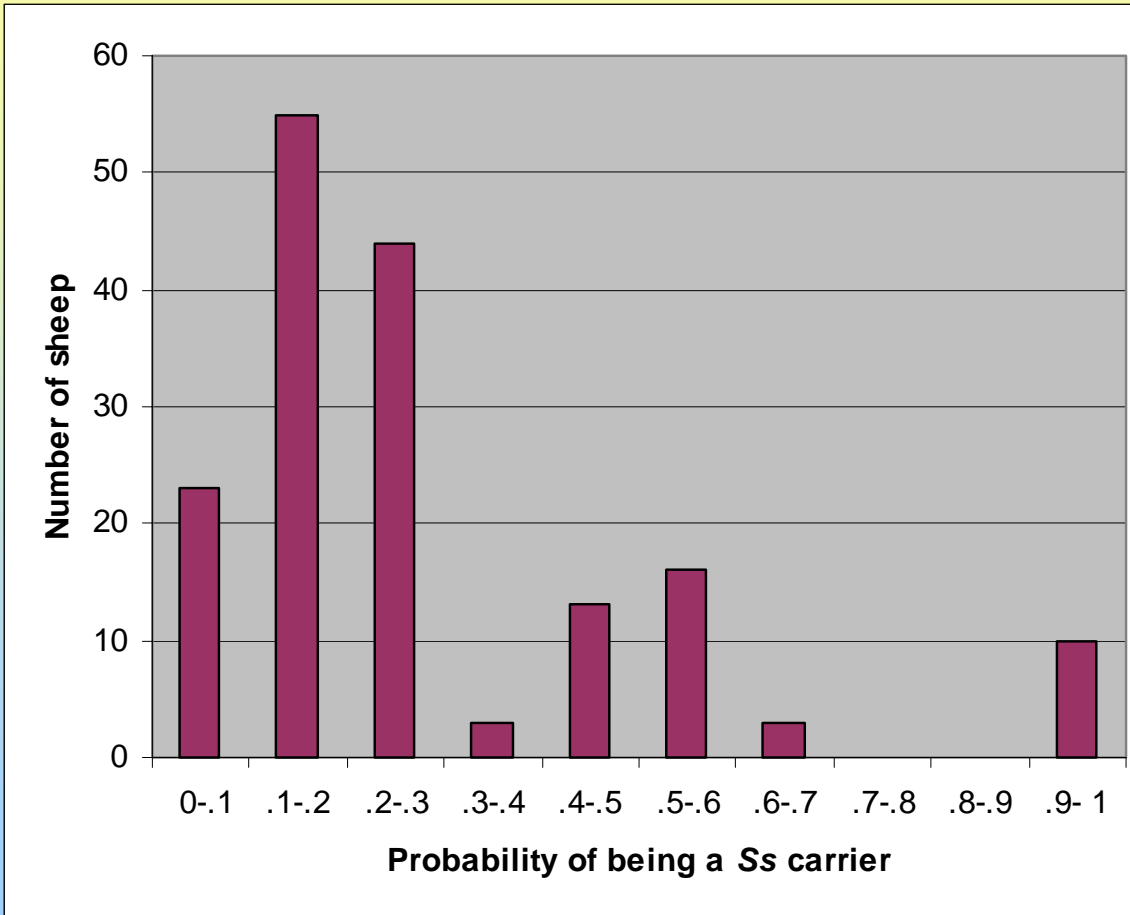
# Progeny test to detect carriers



# Information from all relatives to detect carriers



# Example in sheep - the spider syndrome



- 167 sheep, including 6 spiders - progeny of 3 rams and 3 ewes.
- A small number of spiders lambs gives a lot of information at the population level.
- Can use mixture of DNA test and phenotypic observations.

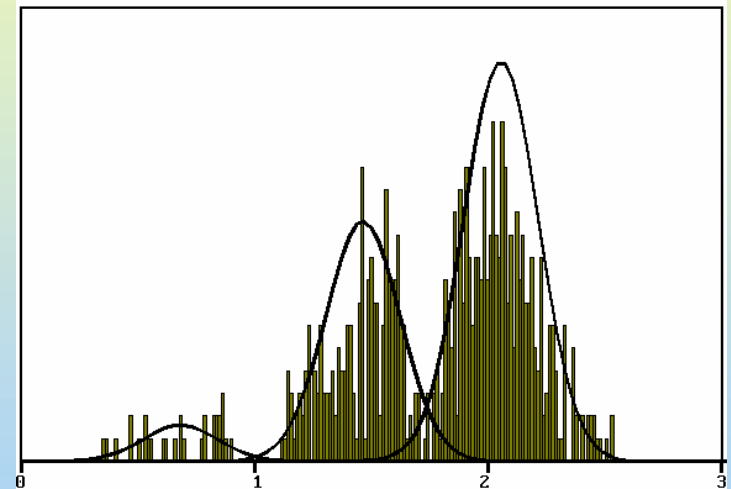
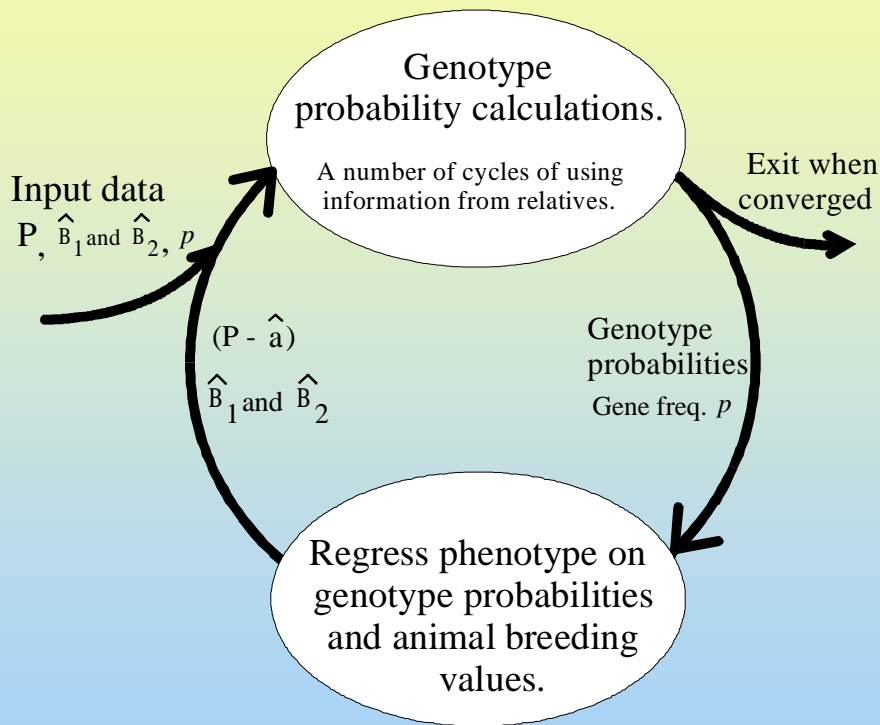
# Conclusions so far

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- Segregation analysis is available to help identify carriers of unwanted genes, and extend value of DNA tests.
- The resulting genotype probabilities can be used in many ways.
  - Evaluate gene variants.
  - Select to exploit or get rid of gene variants.

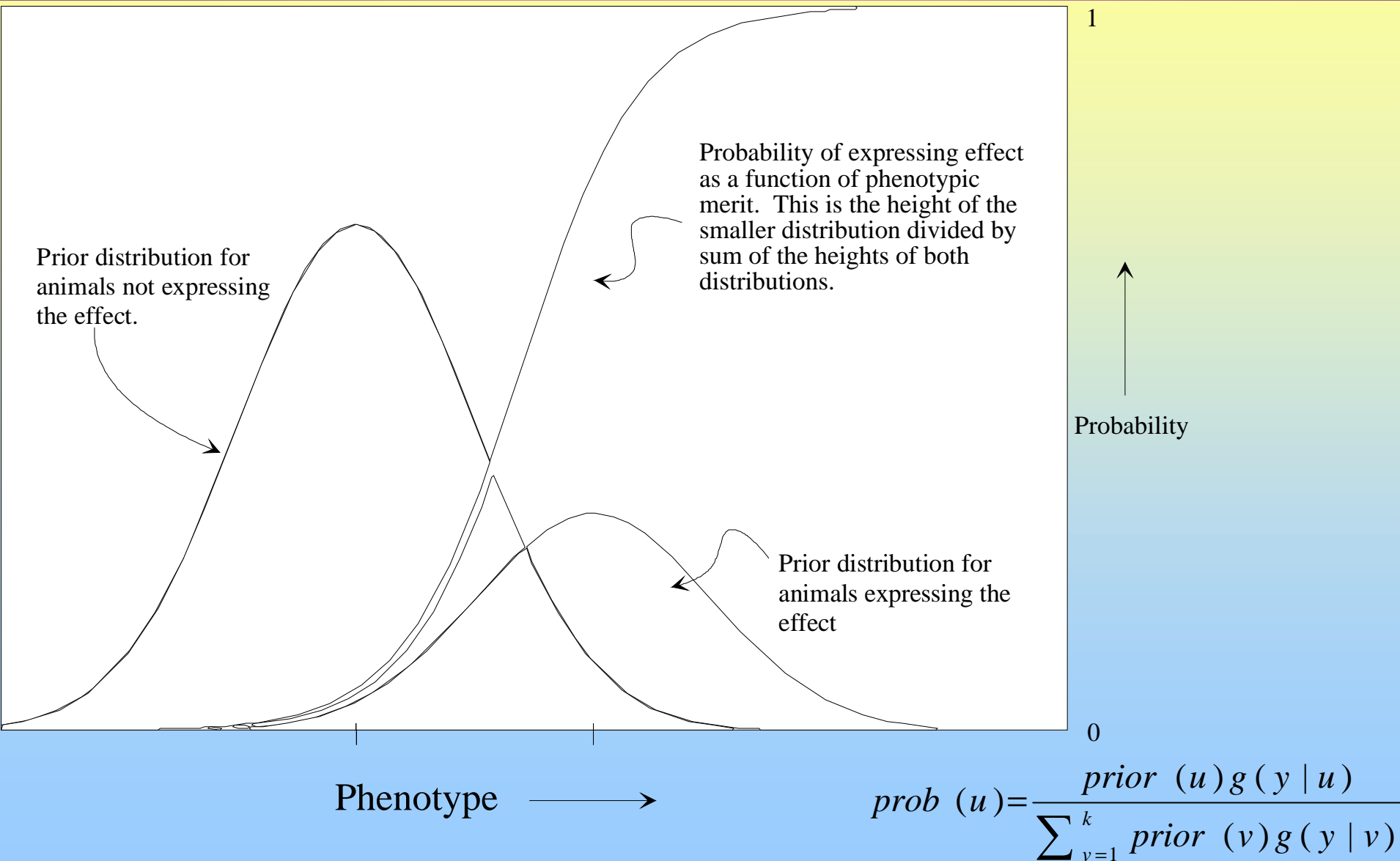
# QTL detection without markers

Kinghorn, B.P.; Kennedy, B.W.; Smith, C. (1993) A method of screening for genes of major effect. *Genetics* 134, 351-360.



Susceptibility to ticks

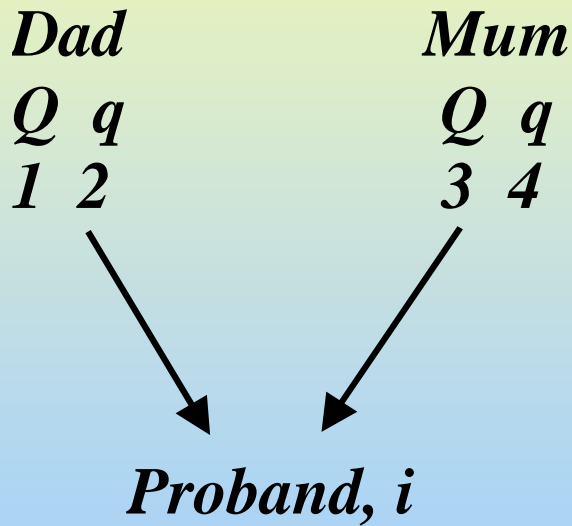
# Regression method: Genotype probabilities ...





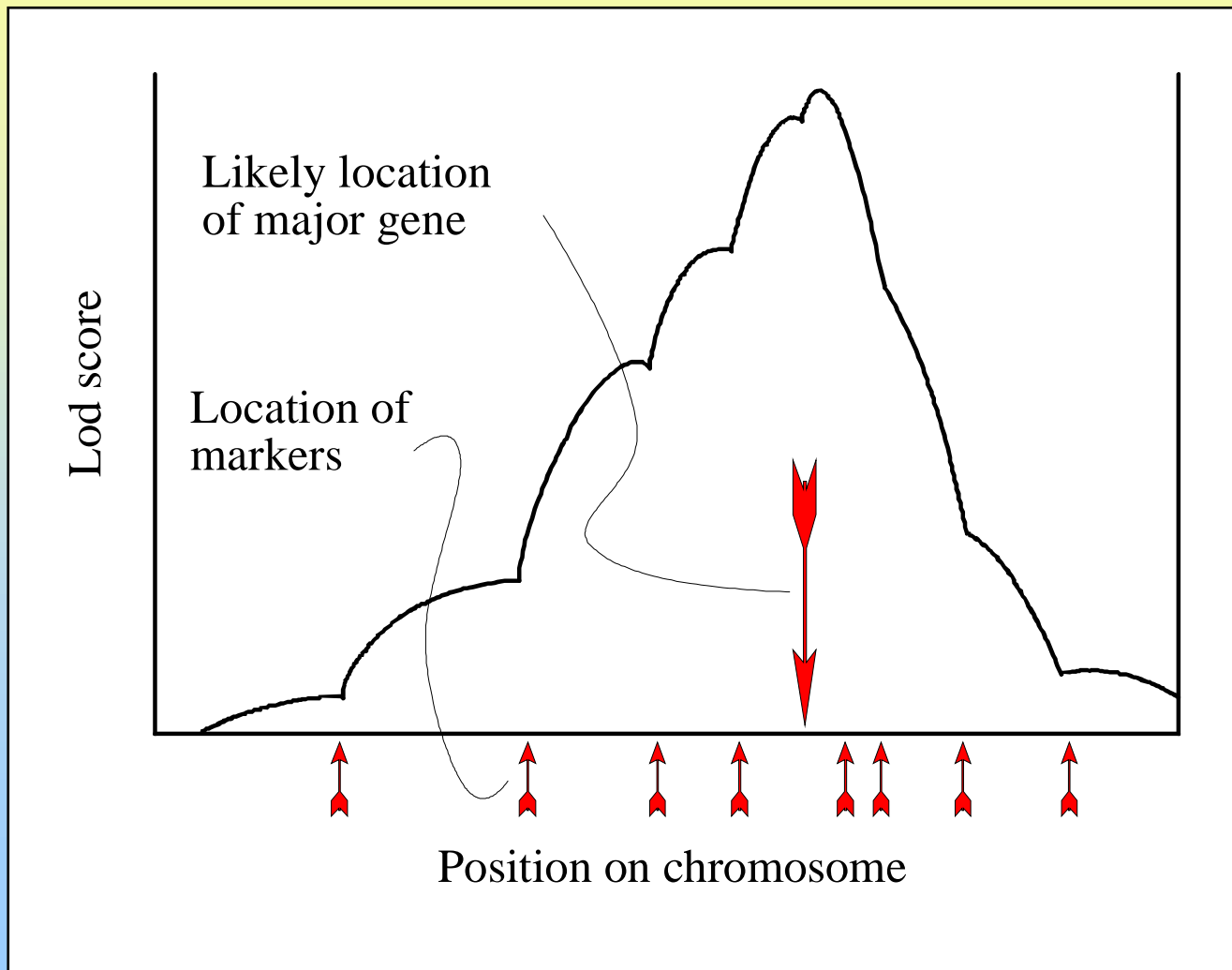
# Regression method:

## Adding marker information:



	Proband QTL genotype conditional probability		
Proband Marker Genotype	QQ	Qq	qq
none	<b>0.25</b>	<b>0.5</b>	<b>0.25</b>
1 3	<b><math>(1-r)^2</math></b>	<b><math>2r(1-r)</math></b>	<b><math>r^2</math></b>
1 4	<b><math>r(1-r)</math></b>	<b><math>r^2+(1-r)^2</math></b>	<b><math>r(1-r)</math></b>

# QTL detection with markers



# Segregation Analysis

- -ve
  - Need to wait for phenotype
  - Could be sensitive to aberrations in variance
- +ve
  - cheap way of obtaining genotype information
  - can be used to suggest segregation and heteroz's
  - can be used in combination with gene markers