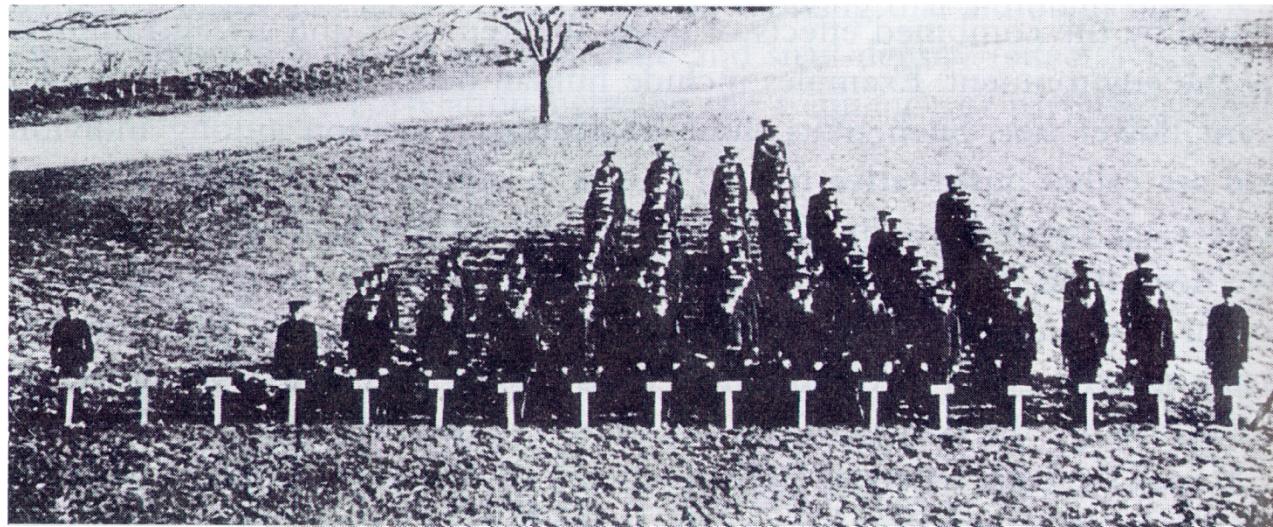


“Genética Quantitativa,
Arquitetura Genética e
Evolução Morfológica”

(a)



(b)

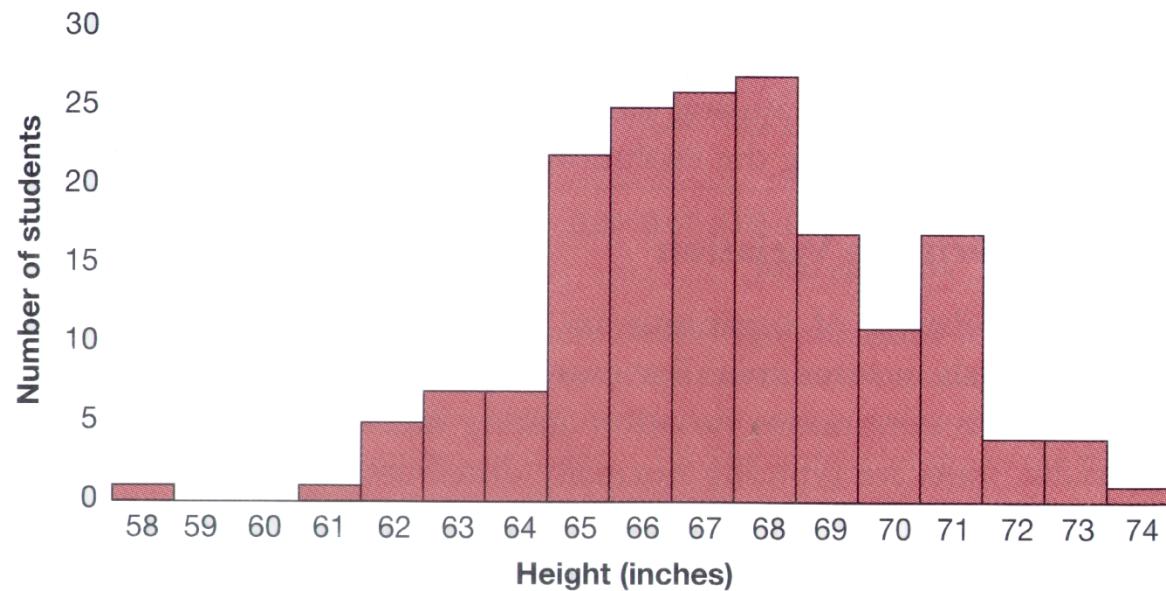
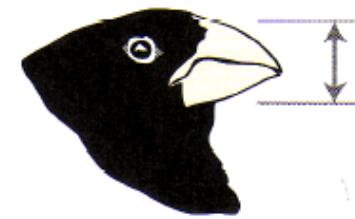
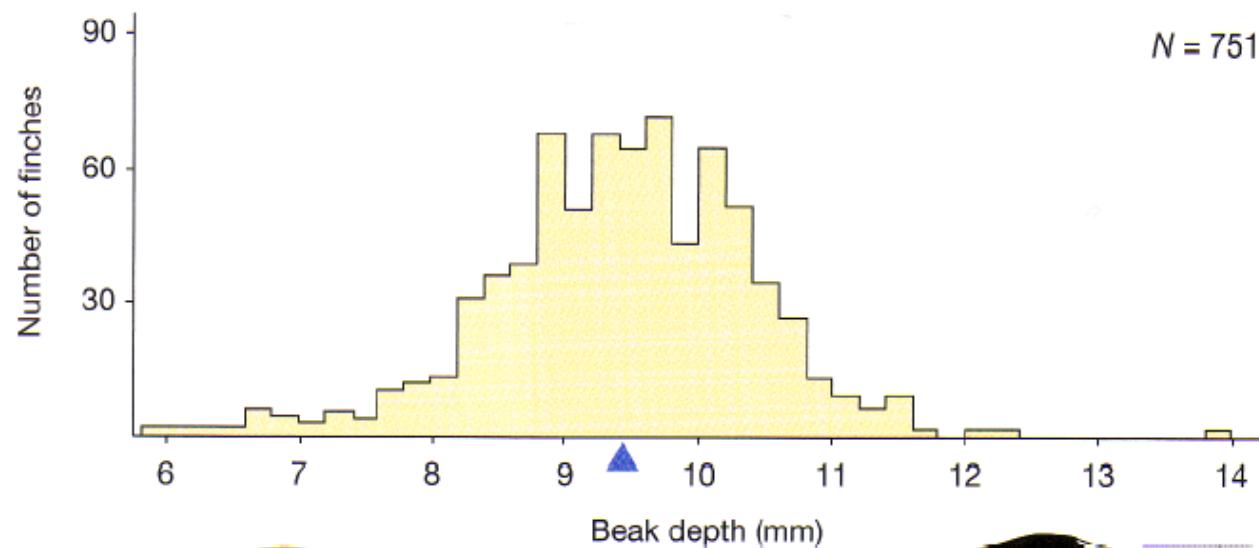


Figure 6.11 Normally distributed variation in a trait

(a) A photograph, published in the *Journal of Heredity* in 1914 by Albert Blakeslee, of a group of students at Connecticut Agricultural College sorted by height. The arrangement of the students forms a living histogram. (b) A graphical histogram representing the distribution of heights among the students shown in (a).

Figure 3.3 Beak depth in medium ground finches This histogram shows the distribution of beak depth in medium ground finches on Daphne Major in 1976, at the start of the Grant study. A few birds have shallow beaks, less than 8 mm deep. Most birds have medium beaks, 8 to 11 mm deep. A few birds have deep beaks, more than 11 mm deep. (*N* stands for sample size; the blue arrow along the *x* axis indicates the mean, or average.)

When variation in the characteristics of organisms is plotted, it is common to observe a bell-shaped curve like the one formed by this histogram. The extent, cause, and nature of variation in traits is a focus of Chapter 4 and Chapter 7.



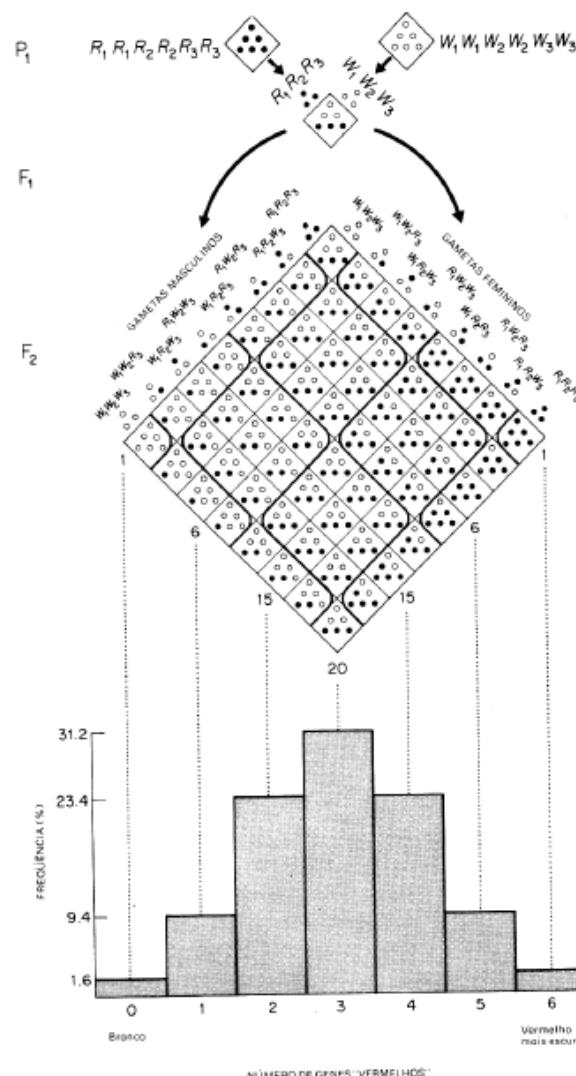
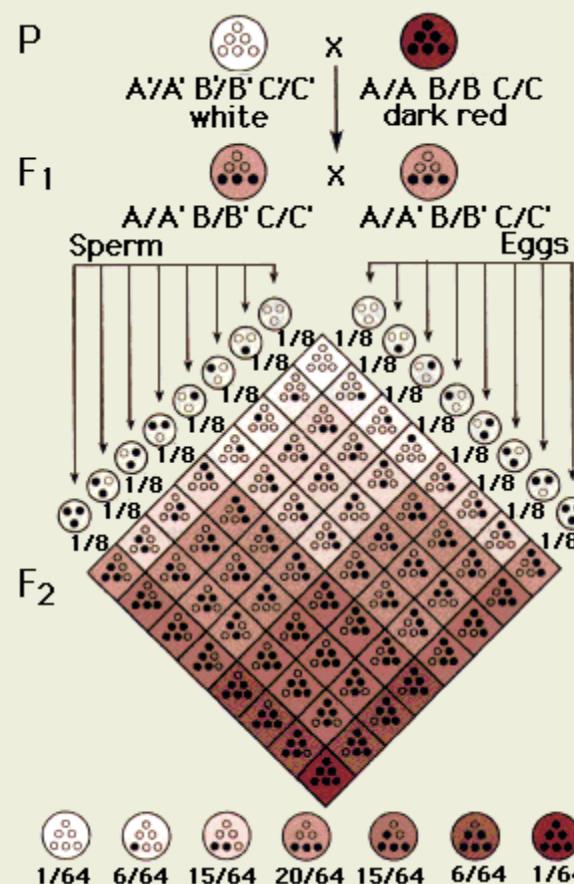
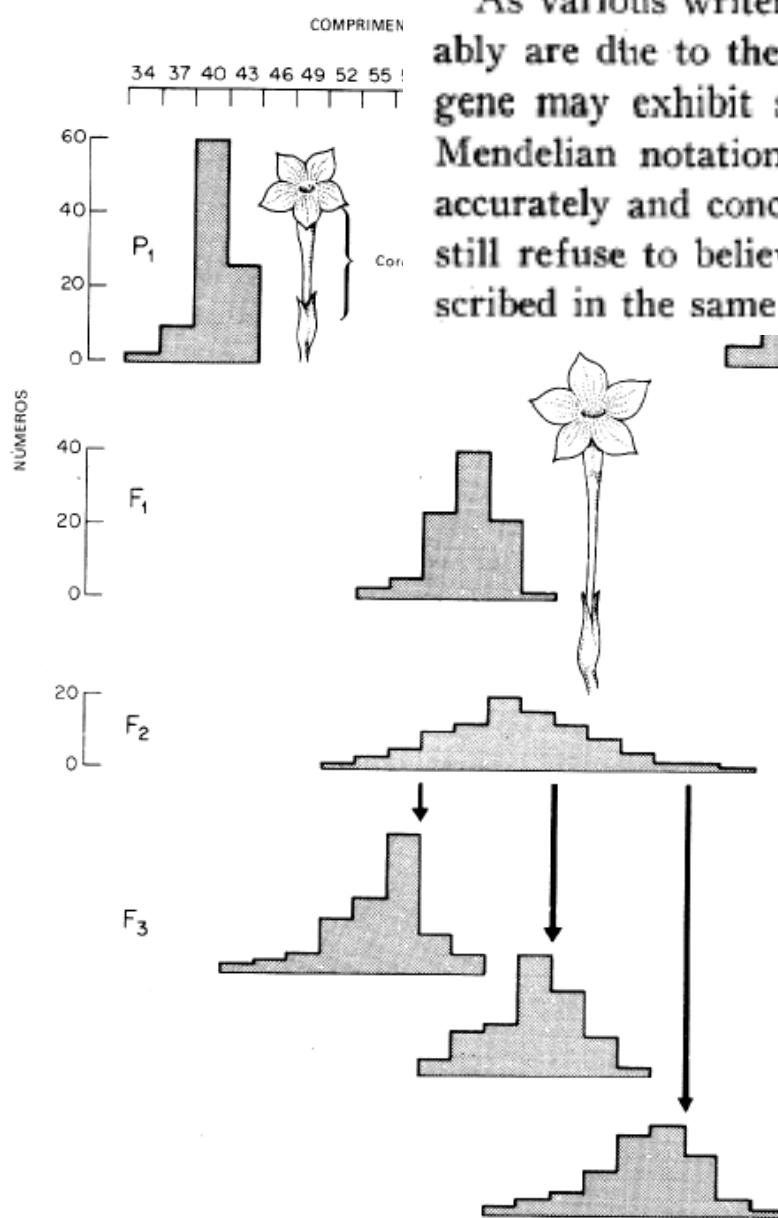


FIGURA 11.1 Herança da cor do grão no trigo. Cada ponto preto representa um gene “vermelho”. (Redesenhado com pequena modificação e com permissão da Macmillan Publishing Co., Inc., de *Genetics*, por Monroe W. Strickberger.)



Nilsson-Ehle (1909)





As various writers have pointed out, all Mendelizing characters probably are due to the interaction of several genes, and presumably every gene may exhibit several somatic effects, yet no one doubts that the Mendelian notation describes the inheritance of such things as color accurately and concisely. It is strange, therefore, that some geneticists still refuse to believe that the inheritance of size characters can be described in the same way, without further assumptions.

STUDIES ON SIZE INHERITANCE IN NICOTIANA

E. M. EAST

Harvard University, Bussey Institution, Forest Hills, Massachusetts

[Received January 6, 1916]

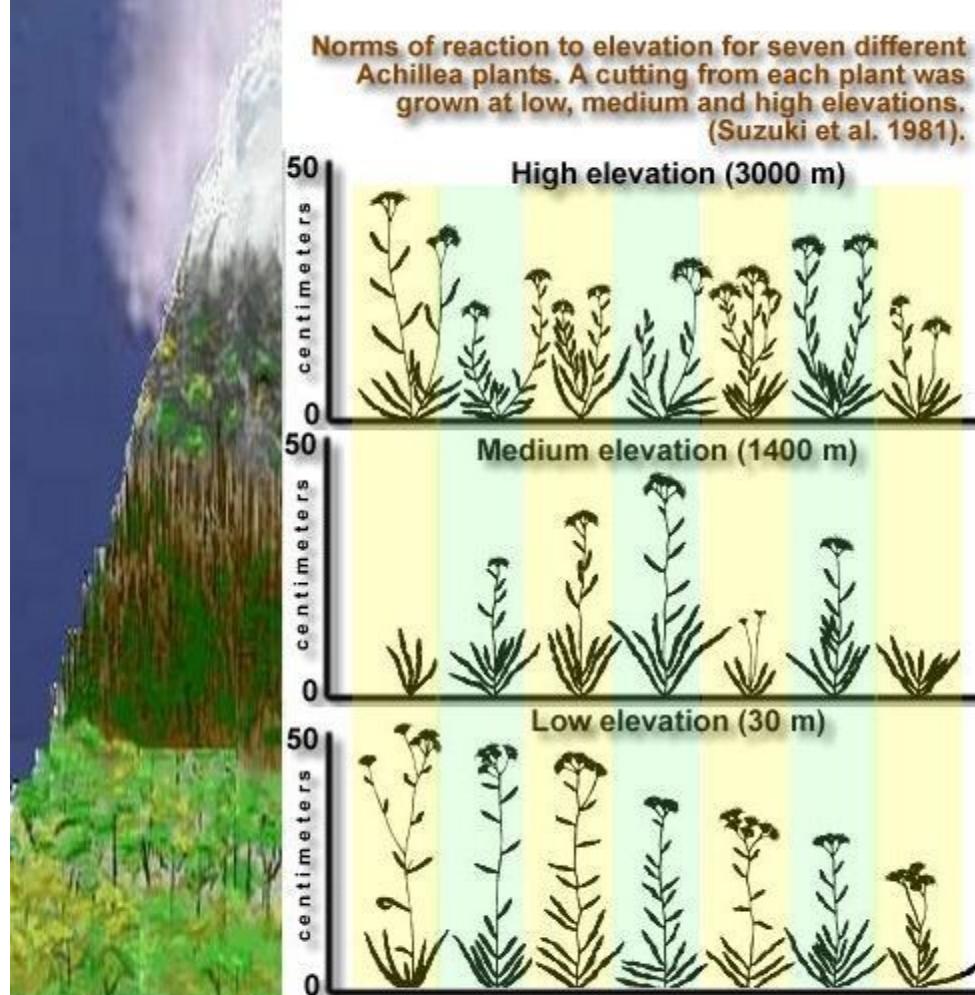
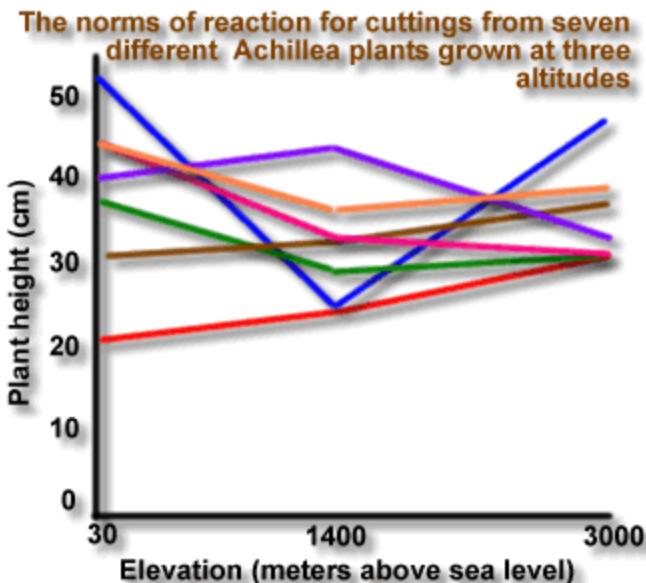
GENETICS 1: Mh 1916

FIGURA 11.2 Experimentos de cruzamento referentes ao tamanho da flor em *Nicotiana longiflora*. (Dados de East, 1915. Redesenhado e ligeiramente modificado com permissão da Macmillan Publishing Co., Inc., de *Genetics*, por Monroe W. Strickberger.)

E. M. East (1916)

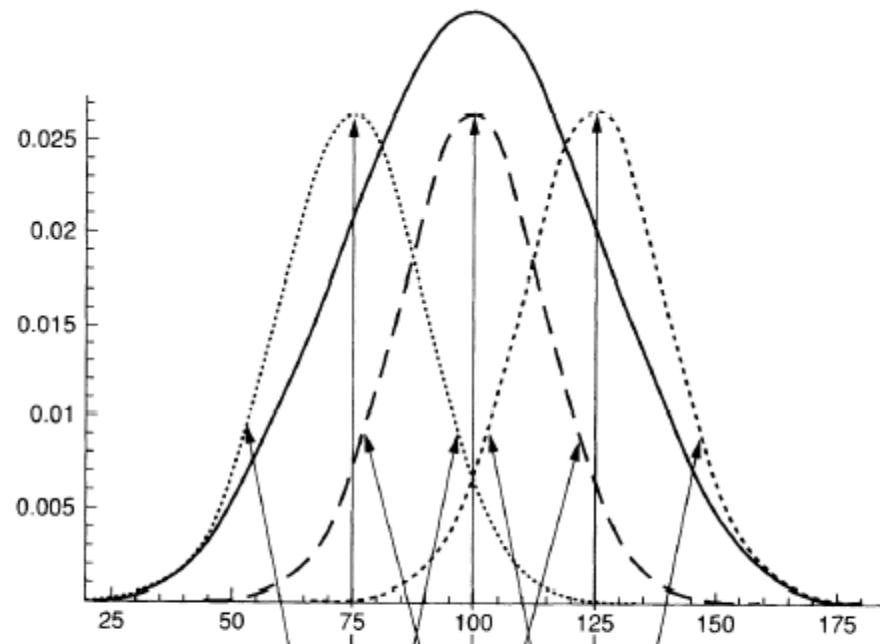
Efeitos genéticos e não genéticos em caracteres quantitativos

Expressos em termos de variância genética e não genética





Sir Ronald Aylmer Fisher
(1890-1962)



Reproduced by permission of the Royal Society of Edinburgh from Transactions of the Society,
vol. 52: 399-433 (1918)

9

XV.—The Correlation between Relatives on the Supposition of Mendelian Inheritance. By R. A. Fisher, B.A. *Communicated by* Professor J. ARTHUR THOMSON. (With Four Figures in Text.)

(MS. received June 15, 1918. Read July 8, 1918. Issued separately October 1, 1918.)

ronmental variation, a thin dashed line the phenotypic distribution associated with Aa , and a thin dotted line with aa . The thick solid line indicates the overall phenotypic distribution in the population that represents a mixture of the three genotypic specific distributions as weighted by the genotype frequencies.

Sem variação ambiental

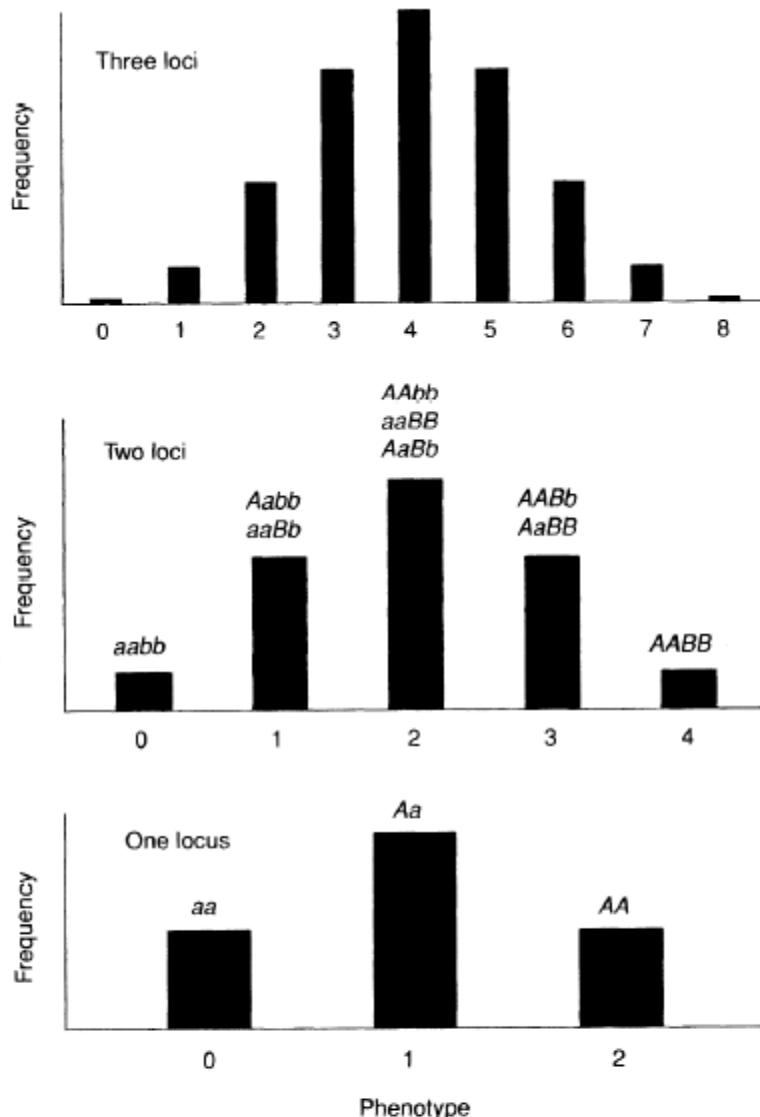
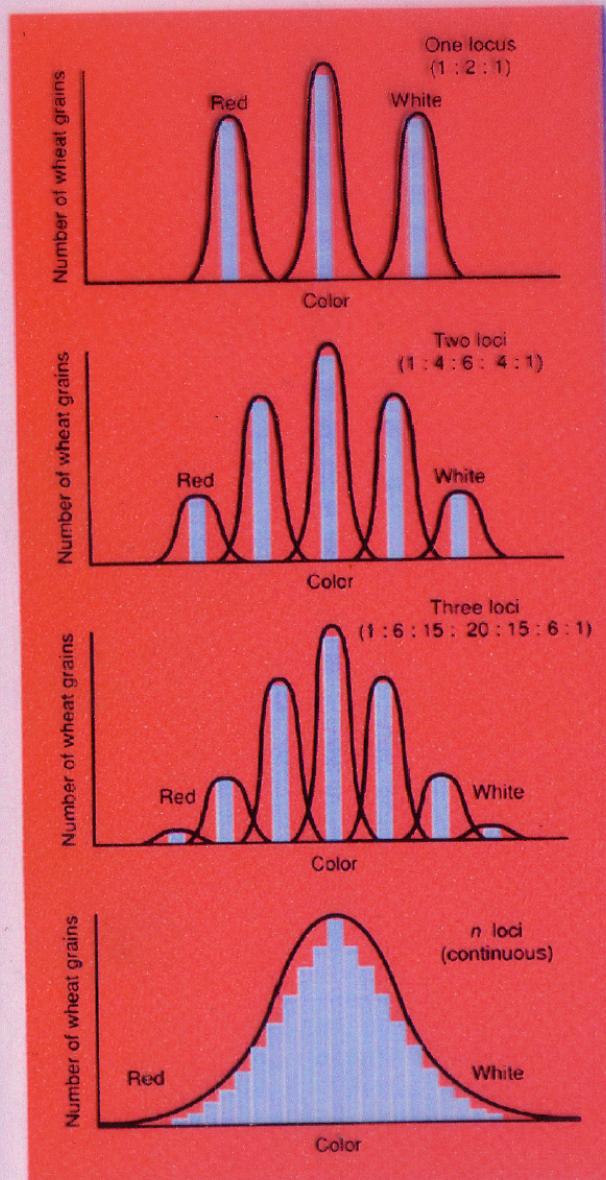


Figure 8.5. Approximate continuous phenotypic distribution produced by increasing number of loci affecting phenotypic variation. A simple genotype-to-phenotype model is assumed in which each allele indicated by a lowercase letter contributes 0 to the phenotype, and each allele indicated by a capital letter contributes +1, with the overall phenotype simply being the sum over all alleles and all loci. At the bottom of the figure, the phcnotypic distribution associated with a one-locus, two-allele model with equal allele frequencies is shown, the middle panel shows the phenotypic distribution associated with a two-locus, two-allele model with equal allele frequencies, and the top panel shows the phenotypic distribution associated with a three-locus, two-allele model with equal allele frequencies (the genotypes associated with the phenotypic categories are not indicated in that case). As the number of loci increases, the

COM variação ambiental

Figure 18.5 The change in shape of the distribution as increasing numbers of loci control grain color in wheat. If each locus is segregating two alleles with each affecting the same trait, eventually a continuous distribution will be generated in the F_2 generation.

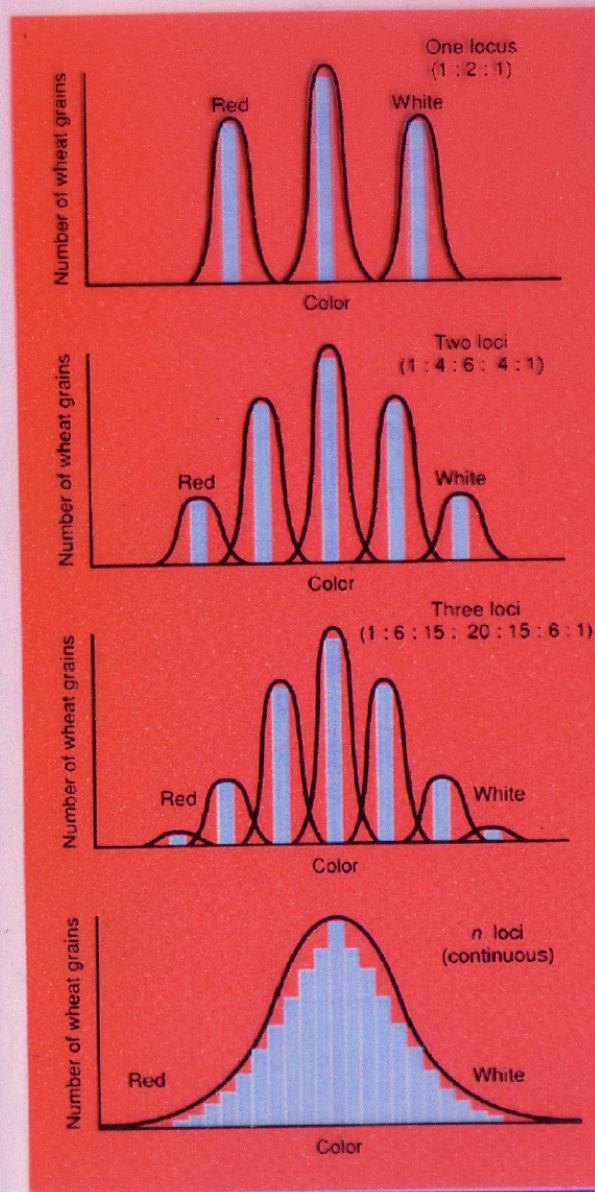


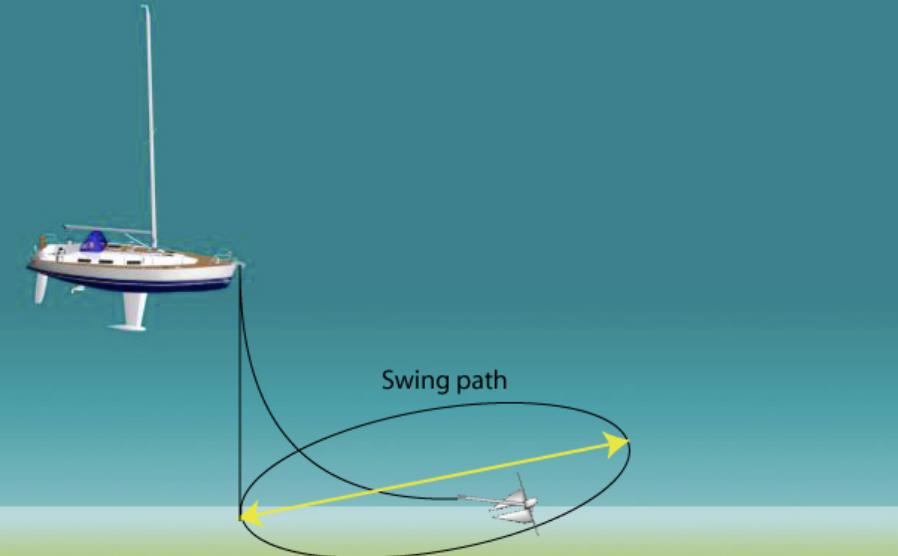
O que acontece quando a variação ambiental é ainda maior que nestes gráficos?

Mensagem: Em geral não conseguimos seguir os efeitos individuais dos genes.

Você consegue ver isto na figura abaixo com 3 loci?

Figure 18.5 The change in shape of the distribution as increasing numbers of loci control grain color in wheat. If each locus is segregating two alleles with each affecting the same trait, eventually a continuous distribution will be generated in the F_2 generation.





Analogia Náutica

- Profundidade rasa
- Ancôra no fundo
- Posição relativa fixa (ou com pouca variação em relação a terra)

Genética Mendeliana

- 1 ou poucos loci
- Genética mendeliana
- Identifica os efeitos de loci específicos e de alelos em uma escala conveniente

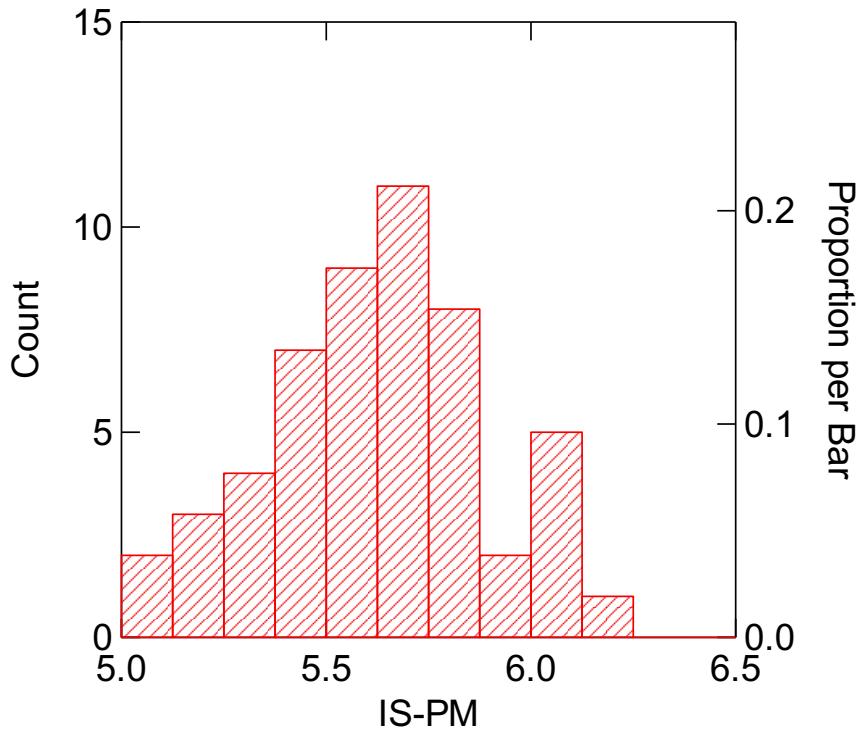
Analogia Náutica

- Profundidade oceânica (alto mar)
- Ancôra flutuante (sea anchor)
- Posição relativa as ondas e ao vento

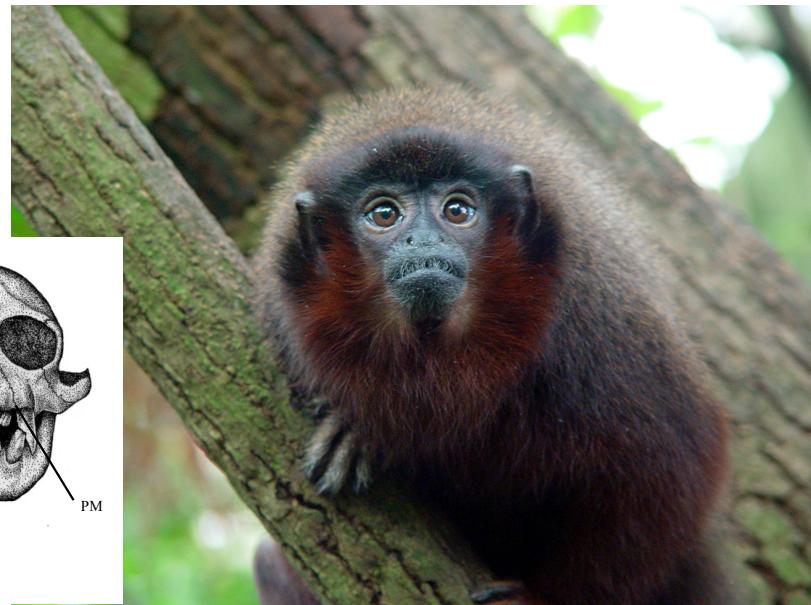
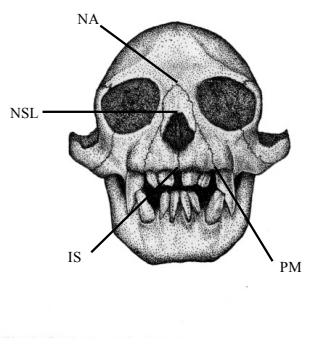
Genética Quantitativa

- Muitos loci
- Genética Quantitativa
- Identifica os efeitos de múltiplos loci em uma escala relativa a média

Média fenotípica e variância de um caráter fenotípico



	IS-PM
N of cases	52
Mean	5.626
Variance	0.072



$$\bar{x} = \frac{1}{n} \sum_{i=1}^n x_i$$

$$s^2 = \frac{1}{n-1} \sum_{i=1}^n (x_i - \bar{x})^2,$$

Média e variância de uma distribuição

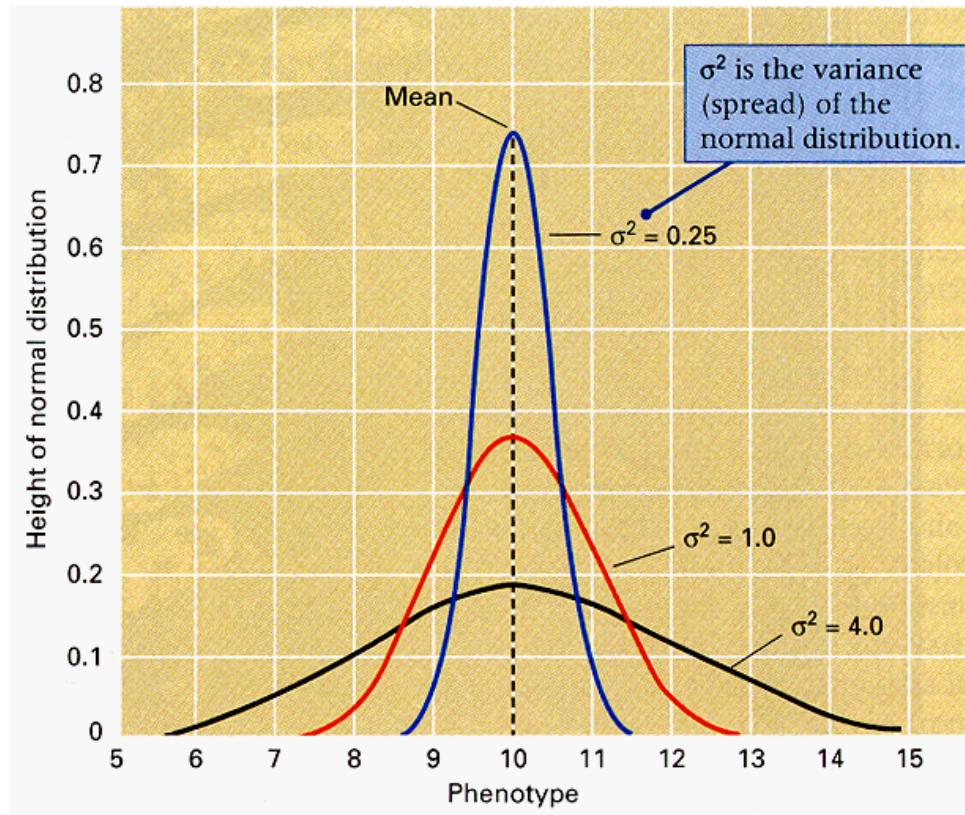


Figure 14.4 Graphs showing that the variance of a distribution measures the spread of the distribution around the mean. The area under each curve covering any range of phenotypes equals the proportion of individuals having phenotypes within the range.

Valor fenotípico = valor genotípico + desvio ambiental

$$P = G + E$$

Valores genotípicos

São as médias dos valores fenotípicos de cada classe genotípica:

Por exemplo, se uma amostra populacional foi separada em três classes genotípicas, AA, Aa e aa, As médias dos valores fenotípicos de cada genótipo são os seu valores genotípicos (mm em vermelho):

AA

33,7

Aa

21,5

aa

17,4

Desvio Ambiental

É a variação em torno das médias dos valores fenotípicos de cada classe genotípica:

Por exemplo, se uma amostra populacional foi separada em três classes genotípicas, AA, Aa e aa, As médias dos valores fenotípicos de cada genótipo são os seu valores genotípicos (mm em vermelho) mas existe variação em torno desta média (em verde):

AA

Aa

aa

28,3 - 33,7 – 39,02

18,06 - 21,5 - 24,94

14,61 - 21,5 - 20,18

Valor fenotípico = valor genotípico + desvio ambiental

$$P = G + E$$

Teoria completa e suficiente sobre a herança baseada apenas nestes valores?

Organismos de reprodução sexuada passam adiante seus genes e não seus genótipos!

Valor fenotípico = valor genotípico + desvio ambiental

$$P = G + E$$

Organismos de reprodução sexuada passam adiante seus genes e não seus genótipos!

Vamos juntar a informação sobre os valores dos fenótipos + herança mendeliana + grau de parentesco (genealógico)

Logo, para deduzir as propriedades de uma população em conjunto com a sua estrutura familiar nós temos que lidar com a transmissão do “valor” dos pais para os filhos e isto não pode ser feito por meio dos valores genotípicos apenas, porque os pais passam adiante apenas seus genes e não seus genótipos intactos para a próxima geração, genótipos sendo criados novamente em cada geração pela fusão de gametas.

Precisamos de uma medida de “valor” que se refere aos genes e não aos genótipos

Efeito médio de um alelo em particular é o desvio médio em relação a média da população daqueles indivíduos que recebem este alelo de um dos pais com o outro alelo vindo ao acaso da população.

Colocando isto de outra forma:

Pegue um número de gametas todos carregando o alelo A_1 , una estes gametas com outros gametas vindo **ao acaso** da população; a média dos genótipos assim produzidos **desvia da média populacional** por uma quantidade que é o *efeito médio* do gene A_1 .

Qual a importância disto?

É um conceito que permite fazer a ligação entre a genética Mendeliana Clássica (na qual a segregação de genes individuais pode ser seguida através das gerações) com a genética quantitativa (aonde isto não é possível), permitindo atribuir ao indivíduo uma medida de valor que pode ser mensurada... Este “valor” é chamado de **valor de acasalamento**

NOTE-SE: Efeito médio de uma alelo é um conceito dual: individual e populacional (“tomado ao acaso”)

É o efeito médio dos genes dos pais que irá determinar o valor genotípico (fenotípico) médio da sua prole.

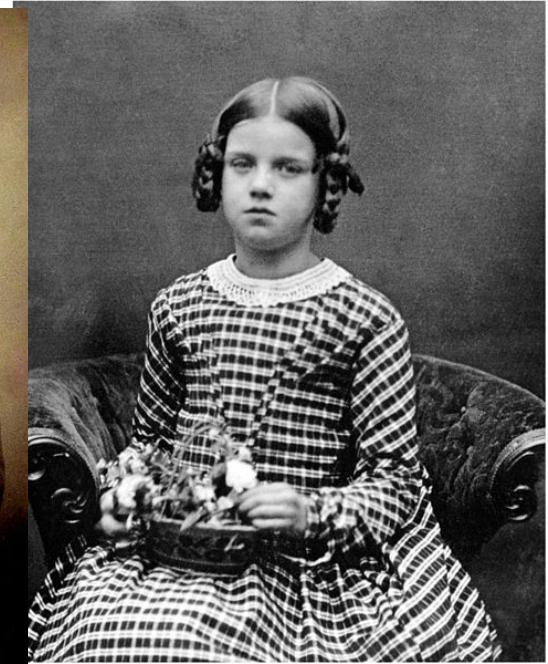
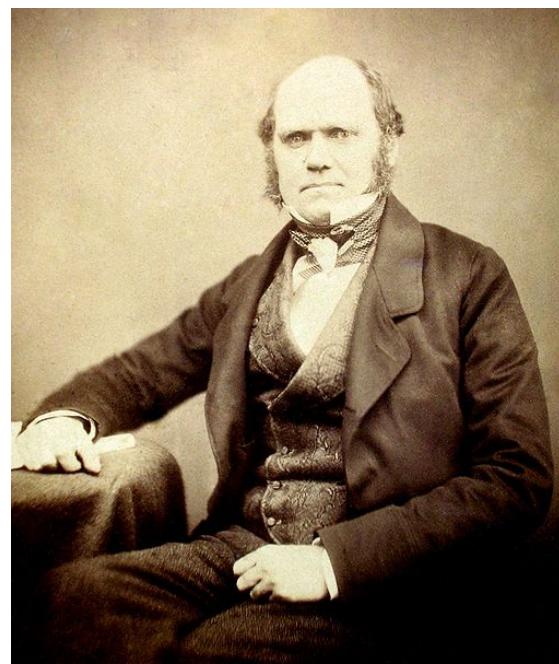
O valor de um indivíduo, avaliado pelo valor médio da sua prole é chamado **Valor de Acasalamento**. Portanto ao contrário do efeito médio de uma alelo (que em geral não é medido), o **Valor de Acasalamento** pode ser medido:

Valor de Acasalamento

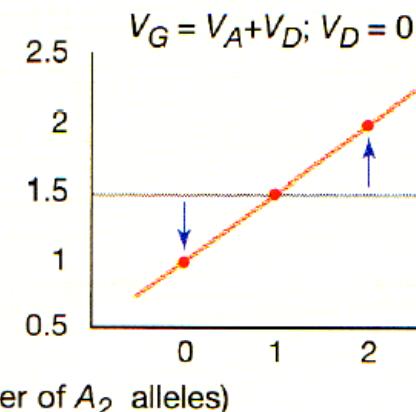
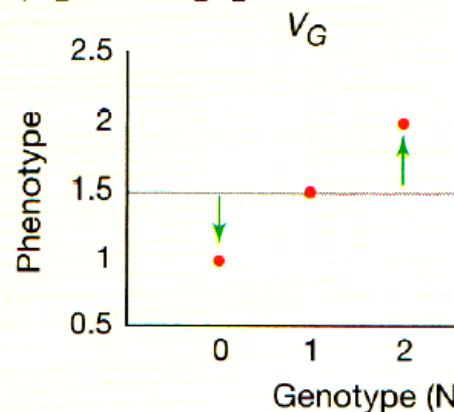
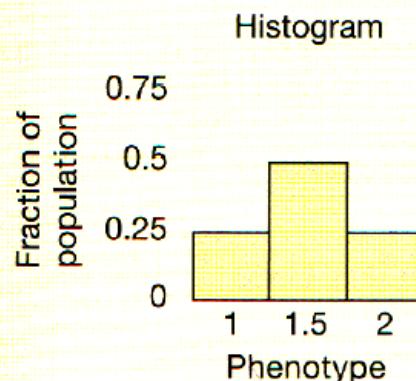
“Se um indivíduo é acasalado com um número de outros indivíduos tomados ao acaso da população, então seu valor de acasalamento é duas vezes o desvio médio da prole em relação á média da população”

O valor é multiplicado por 2 por que cada indivíduo parental contribui com metade dos genes da prole (outra metade vindo da população ao acaso)

Valor de Acasalamento - Base da semelhança por parentesco



(a) No dominance. Phenotypes: $A_1A_1 = 1$; $A_1A_2 = 1.5$; $A_2A_2 = 2$



(b) Complete dominance. Phenotypes: $A_1A_1 = 1$; $A_1A_2 = 2$; $A_2A_2 = 2$

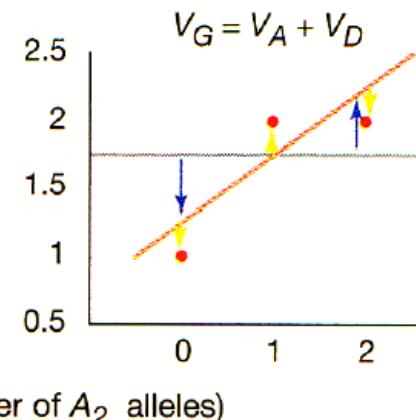
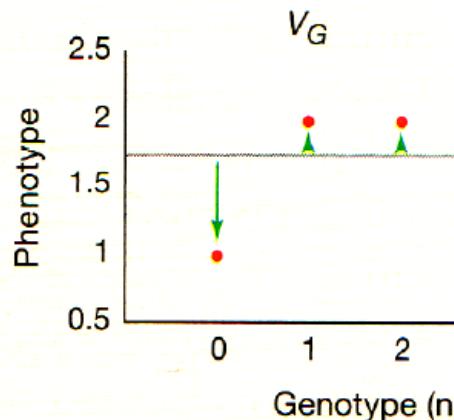
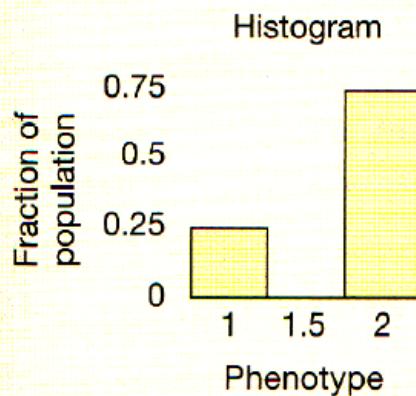


Figure 7.21 Additive genetic variation versus dominance genetic variation in a trait controlled by two alleles at a single locus

Box 7.5 Additive genetic variation versus dominance genetic variation

Here we use a numerical example to distinguish between additive genetic variation and dominance genetic variation. To simplify the discussion, we will analyze genetic variation at a single locus with two alleles as though were analyzing a quantitative trait. We will assume that there is no environmental variation in the trait in question: An individual's phenotype is determined solely and exactly by its genotype. The alleles at the locus are A_1 and A_2 ; each has a frequency of 0.5, and the population is in Hardy–Weinberg equilibrium. We will consider two situations: (1) the alleles are codominant; (2) allele A_2 is dominant over allele A_1 .

Situation (1): Alleles A_1 and A_2 are codominant.

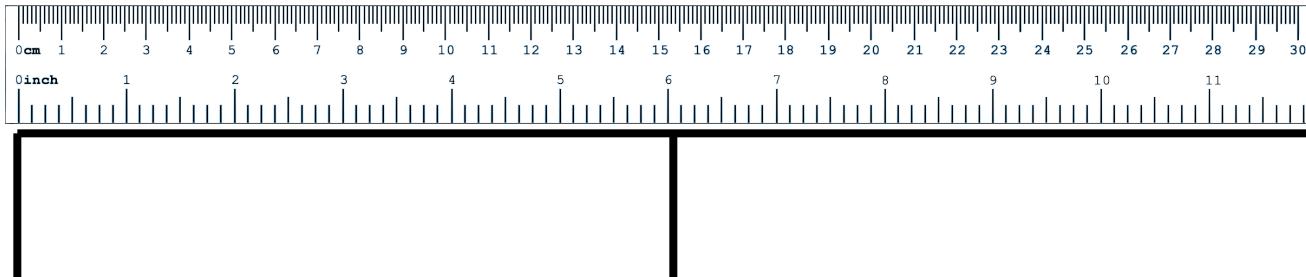
A_1A_1 individuals have a phenotype of 1. In A_1A_2 and A_2A_2 individuals, each copy of allele A_2 adds 0.5 to the phenotype. At the left in Figure 7.21a is a histogram showing the distribution of phenotypes in the population. At the center and right are scatterplots that allow us to analyze the genetic variation in the population. The x -axis represents the genotype, calculated as the number of copies of allele A_2 . The y -axis represents the phenotype. The horizontal gray line shows the mean phenotype for the population ($= 1.5$). The plot at center shows that the total genetic variation V_G is a function of the deviations of the datapoints from the population mean (green arrows). We can quantify V_G by calculating the sum of the squared deviations. The plot

at right shows the best-fit line through the datapoints (red). The additive genetic variation V_A is defined as that fraction of the total genetic variation that is explained by the best-fit line (blue arrows). In this case, the best-fit line explains all of the genetic variation, so $V_G = V_A$. There is no dominance genetic variation.

Situation (2) Allele A_2 is dominant over allele A_1 .

This time, A_1A_1 individuals again have a phenotype of 1. The effects of substituting copies of A_2 for copies of A_1 are not strictly additive, however: The first copy of A_2 (which makes the genotype A_1A_2) changes the phenotype from 1 to 2. The second copy of A_2 (which makes the genotype A_2A_2) does not alter the phenotype any further. At left in Figure 7.21b is a histogram showing the distribution of phenotypes in the population. At center and right are scatterplots that allow us to analyze the genetic variation in the population. The plot at center shows that the total genetic variation V_G is a function of the deviations of the datapoints (green arrows) from the population mean (gray line; $= 1.75$). The plot at right shows the best-fit line through the datapoints (red). The additive genetic variation V_A is that fraction of the total genetic variation that is explained by the best-fit line (blue arrows). The dominance genetic variation V_D is that fraction of the total genetic variation left unexplained by the best-fit line (yellow arrows). In this case, the best-fit line explains only part of the genetic variation, so $V_G = V_A + V_D$.

Efeito aditivo

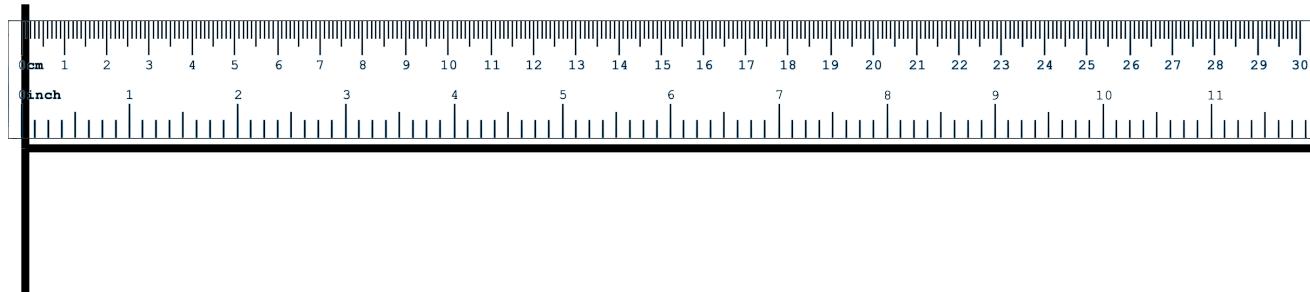


AA Aa aa

O valor genotípico do heterozigoto é a média dos valores genotípicos dos homozigotos. Cada alelo “a” adiciona um valor constante, daí o nome.

Efeito de dominância

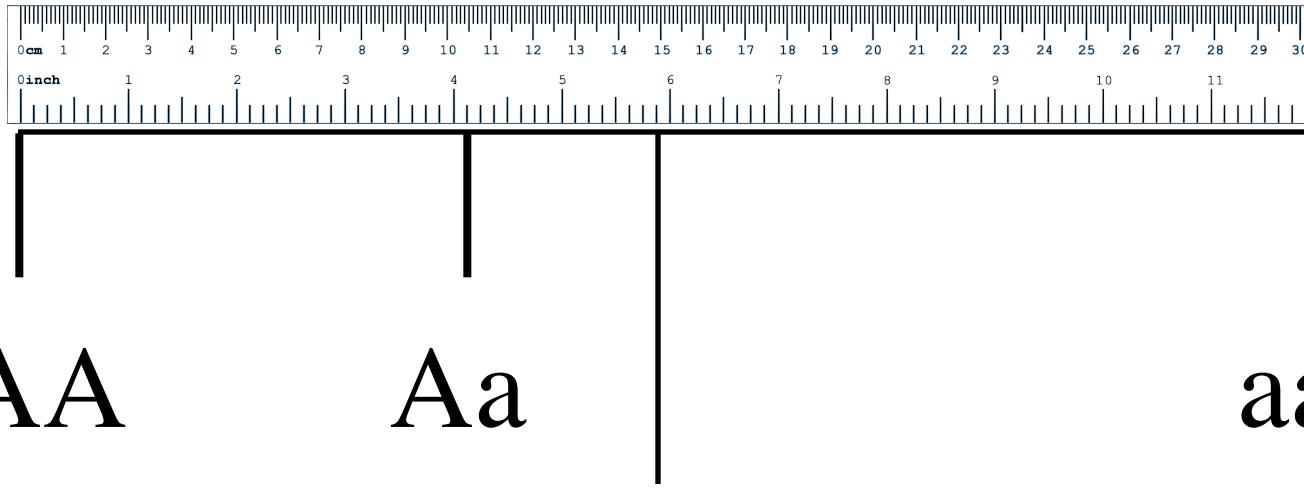
Aa



AA aa

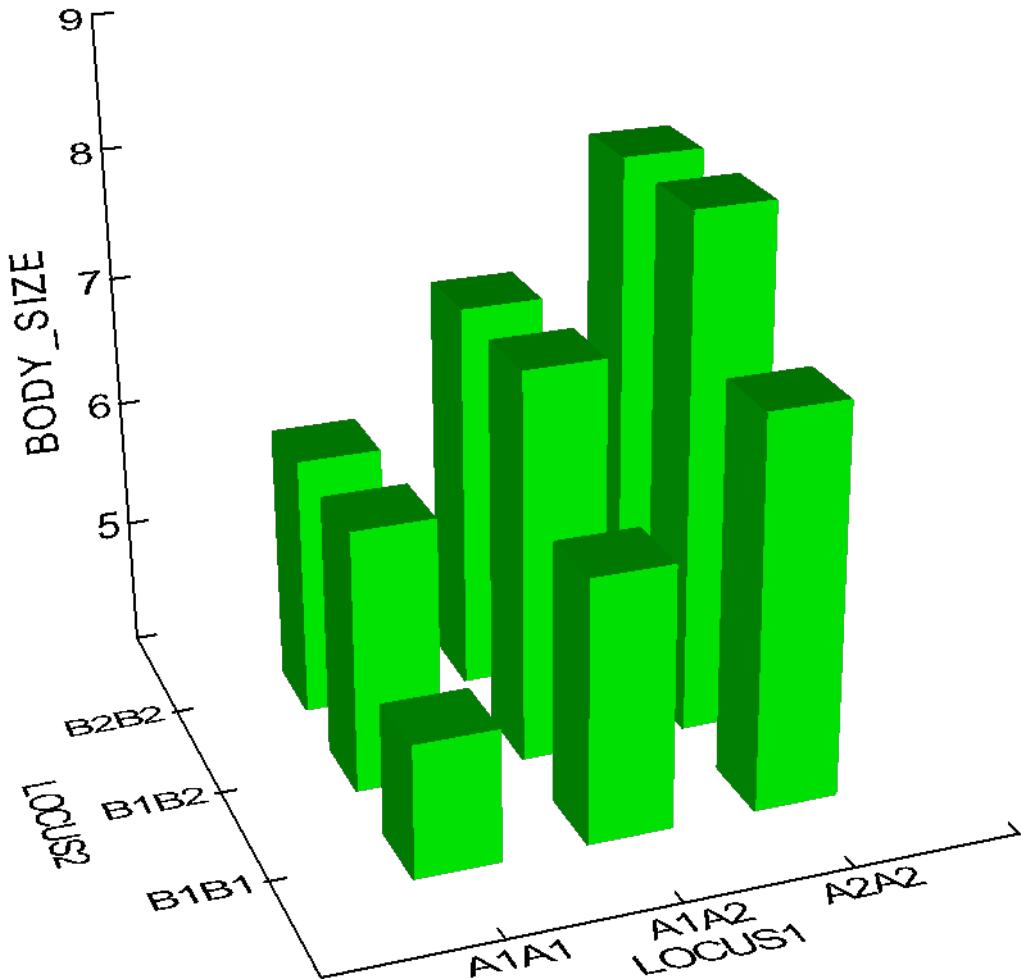
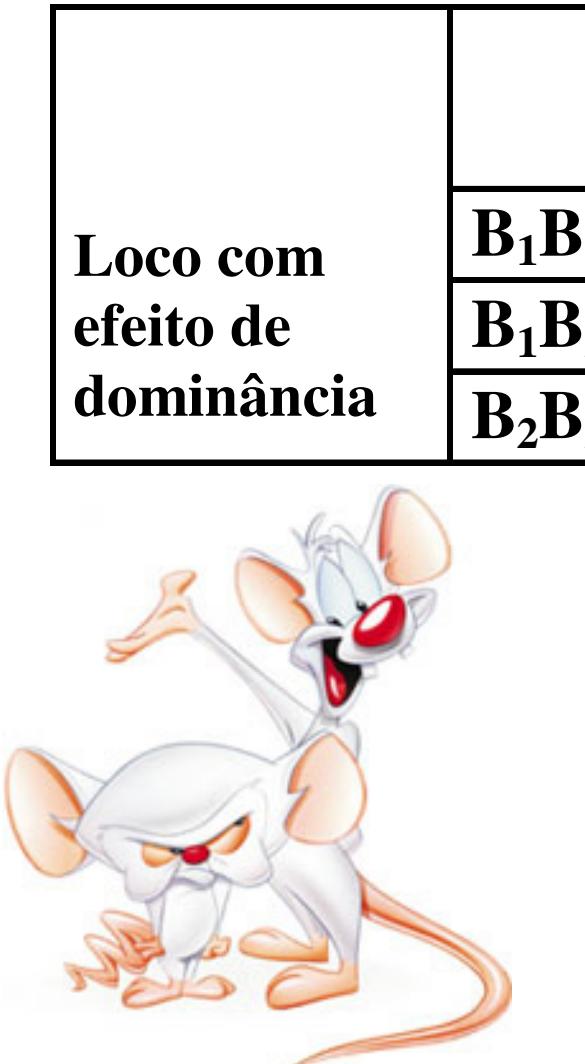
O valor genotípico do heterozigoto é igual ao valor genotípico de um dos homozigotos. O alelo “A” domina sobre o alelo “a”, bastando haver um único “A” para a manifestação do fenótipo.

Efeito parcialmente dominante



O valor genotípico do heterozigoto está entre a média dos valores genotípicos dos homozigotos e o valor de um deles.

Efeitos dominantes e aditivos (ignorando-se efeitos ambientais)



Efeito aditivo

Genótipo	<i>aabb</i>	<i>Aabb</i>	<i>AAbb</i>	<i>AABb</i>	<i>AABB</i>
Escala quantitativa	0	1	2	3	4

Efeito de dominância

Genótipo	<i>aabb</i>	<i>Aabb</i>	<i>AAAb</i>	<i>AABb</i>	<i>AABB</i>
Escala quantitativa	0	2	2	4	4

Efeito de dominância + efeito de epistasia

Genótipo	<i>aabb</i>	<i>Aabb</i>	<i>AAAb</i>	<i>AABb</i>	<i>AABB</i>
Escala quantitativa	0	0	0	4	4

Aditivo – efeitos dos alelos

Dominância – interação entre alelos

Epistático – interação entre genes

Variância fenotípica = Variância genética + Variância ambiental

$$V_p = V_g + V_e$$

$$V_g = V_a \text{ (aditiva)} + V_d \text{ (dominância)} + V_i \text{ (epistática)}$$

$$V_p = V_a + V_d + V_i + V_e$$

TABELA 11.1 Componentes da variação para quatro caracteres da *Drosophila melanogaster*. Cada componente é expresso como percentagem da variância fenotípica total (segundo Falconer, 1964).

	<i>Caráter</i>			
	1 cerdas	2 tórax	3 ovários	4 ovos
Variância fenotípica	100	100	100	100
Variância genética aditiva	52	43	30	18
Variância genética não aditiva	9	6	40	44
Variância ambiental	39	51	30	38

Caracteres:

1. número de cerdas nos 4.^º e 5.^º segmentos abdominais (Clayton, Morris e Robertson, 1957; Reeve e Robertson, 1954);
2. comprimento do tórax (Robertson, 1957);
3. tamanho dos ovários, isto é, número de ovariólos em ambos os ovários (Robertson, 1957);
4. número de ovos postos em 4 dias (4.^º ao 8.^º após a emergência) (Robertson, 1957).

Tipos de variância

Variância fenotípica: é a variância total da população. Inclui efeitos genéticos e não genéticos.

Variância genética: é a variância que é devida as diferenças genéticas existente entre os indivíduos da população. Exclui a variação causada por fatores ambientais.

Variância Aditiva = parte da variância genética que é devida aos efeitos individuais dos alelos – Variância dos valores de acasalamento

Variância de Dominância - surge da interação entre alelos de um locus (interação entre alelos de um mesmo locus)

Variância Epistática - surge da interação entre loci (interação entre alelos de diferentes loci)

Quadro 23.2 Proporção de variância aditiva (s_a^2) e variância de dominância (s_d^2) na covariância genética entre vários indivíduos relacionados

Parentes	Proporção estimada de	
	s_a^2	s_d^2
Cov (gêmeos idênticos)	1	1
Cov (pais-prole)	$\frac{1}{2}$	0
Cov (meio-irmãos)	$\frac{1}{4}$	0
Cov (irmãos)	$\frac{1}{2}$	$\frac{1}{4}$

$$COV(x, y) = \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{n-1}$$

$$s^2 = \hat{\sigma}^2 = \frac{\sum (X_i - \bar{X})^2}{(n-1)}$$

$$r_{(x,y)} = \frac{COV(x,y)}{s_x s_y}$$

$$h^2 = Va/Vp = b = COV_{xy} / S_x^2$$

(VARIÂNCIA DOS PAIS S_x^2)

Onde x são as médias dos pais e y dos filhos

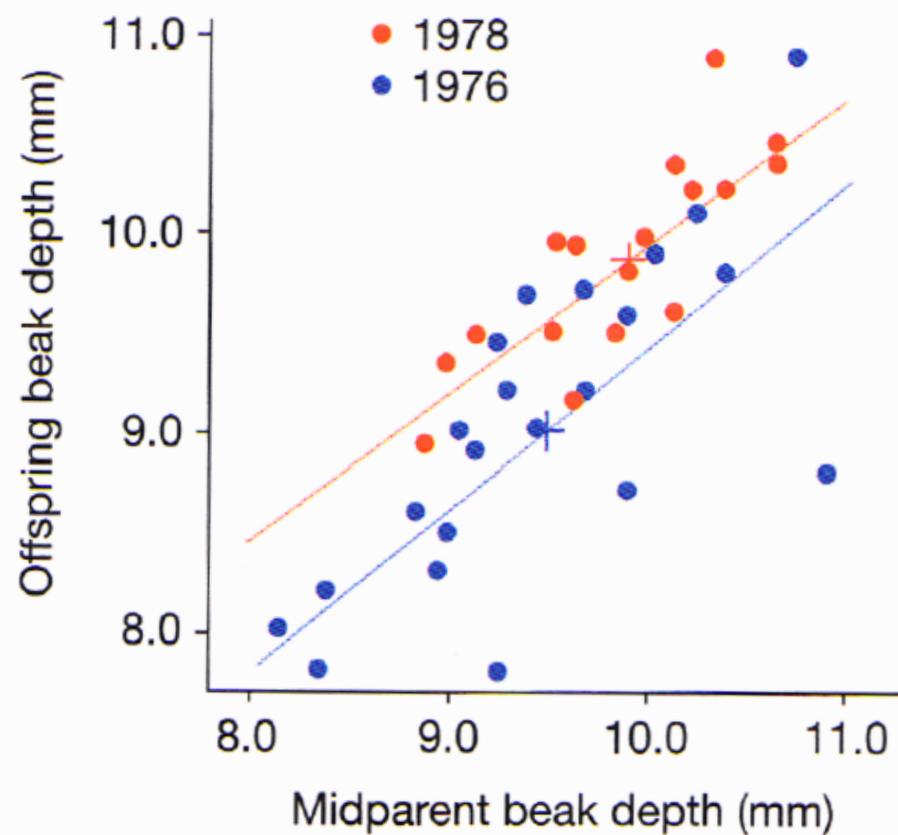
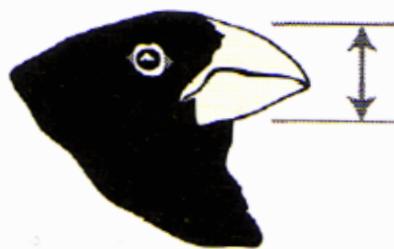


Figure 3.4 Heritability of beak depth in *Geospiza fortis* This graph shows the relationship between the beak depth of parents and their offspring. Midparent value is the average of the maternal and paternal measurements. Using this measurement is important because male *G. fortis* are bigger than females.

Precisamos de uma medida de “valor” que se refere aos genes e não aos genótipos

Efeito médio de um alelo em particular é o desvio médio em relação a média da população daqueles indivíduos que recebem este alelo de um dos pais com o outro alelo vindo ao acaso da população.

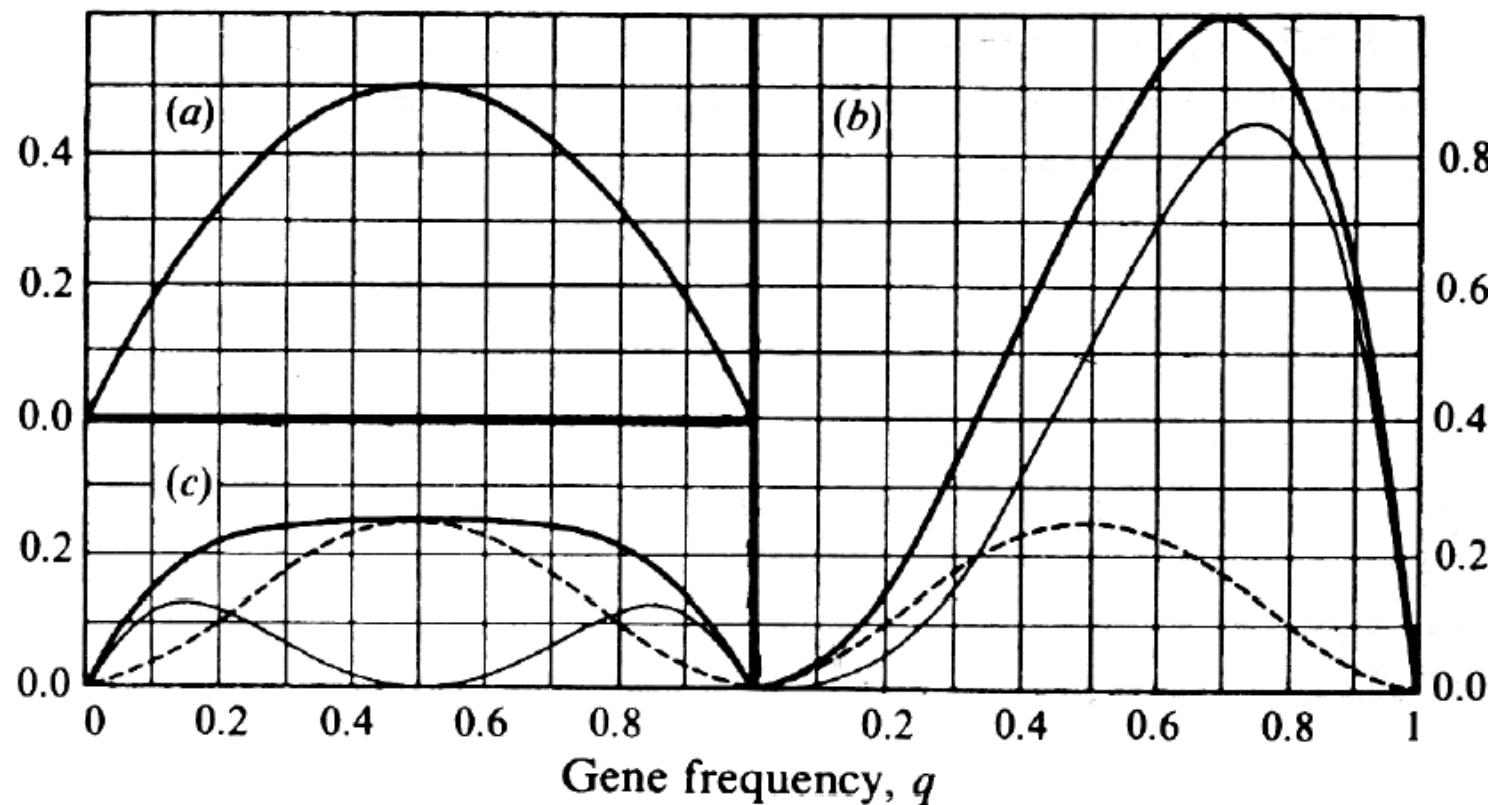
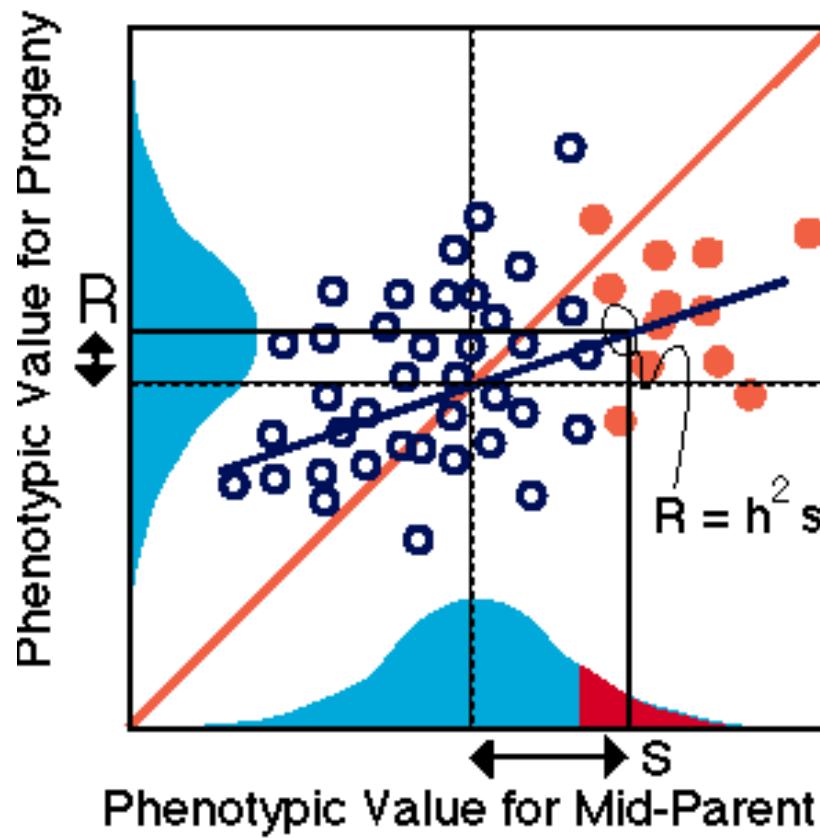


Fig. 8.1. Magnitude of the genetic components of variance arising from a single locus with two alleles, in relation to the gene frequency. Genotypic variance – thick lines; additive variance – thin lines; dominance variance – broken lines. The gene frequency, q , is that of the recessive allele. The degrees of dominance are: in (a) no dominance ($d = 0$); in (b) complete dominance ($d = a$); and in (c) ‘pure’ overdominance ($a = 0$). The figures on the vertical scale, showing the amount of variance, are to be multiplied by a^2 in graphs (a) and (b), and by d^2 in graph (c).

A equação de resposta a Seleção Direcional



$$R = h^2 S$$

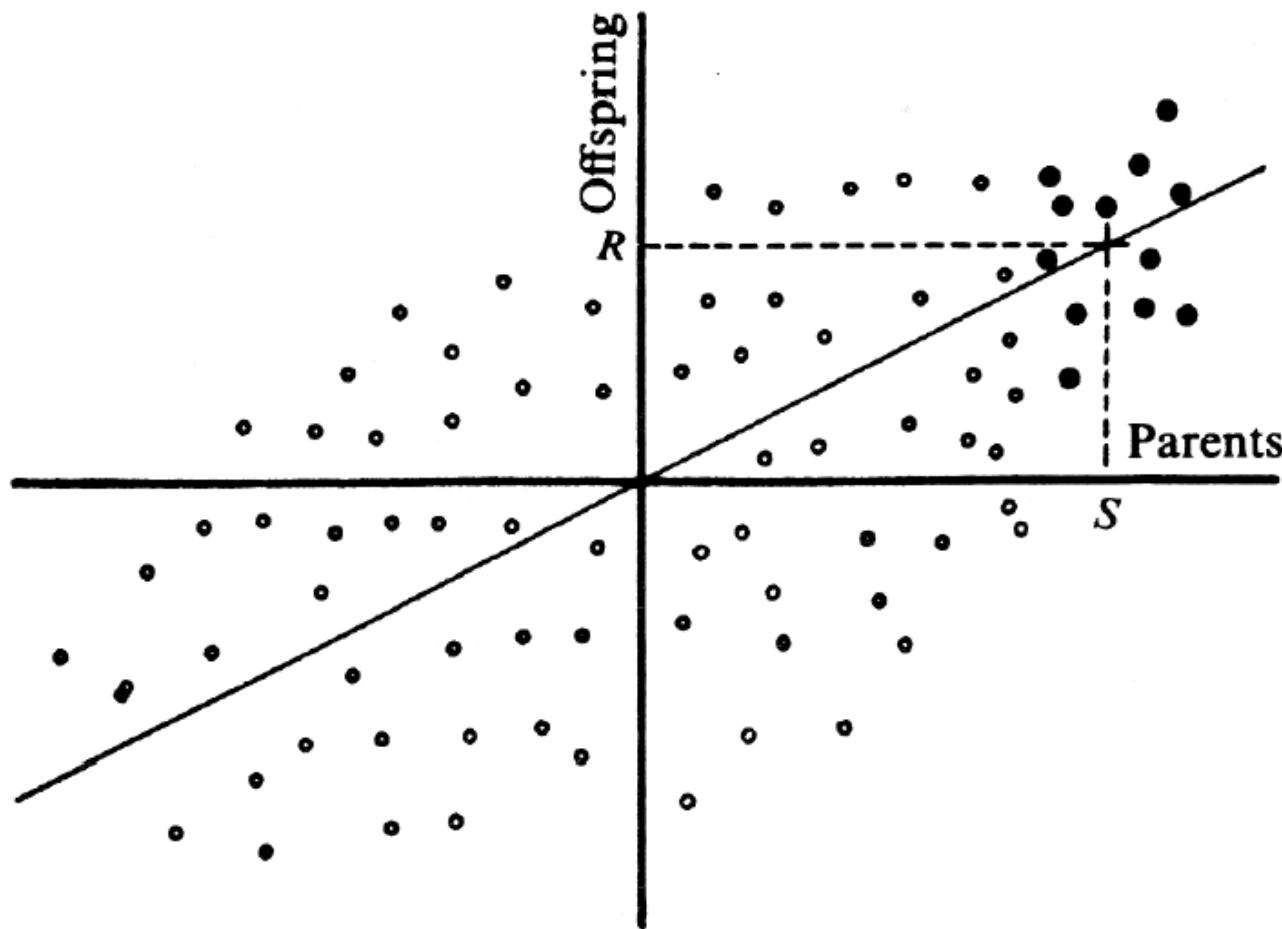
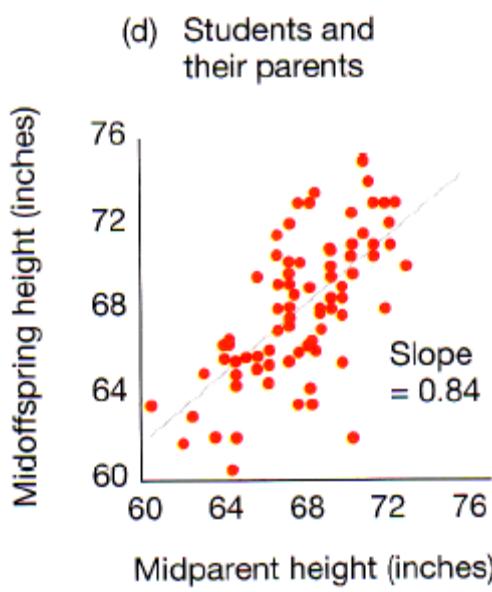
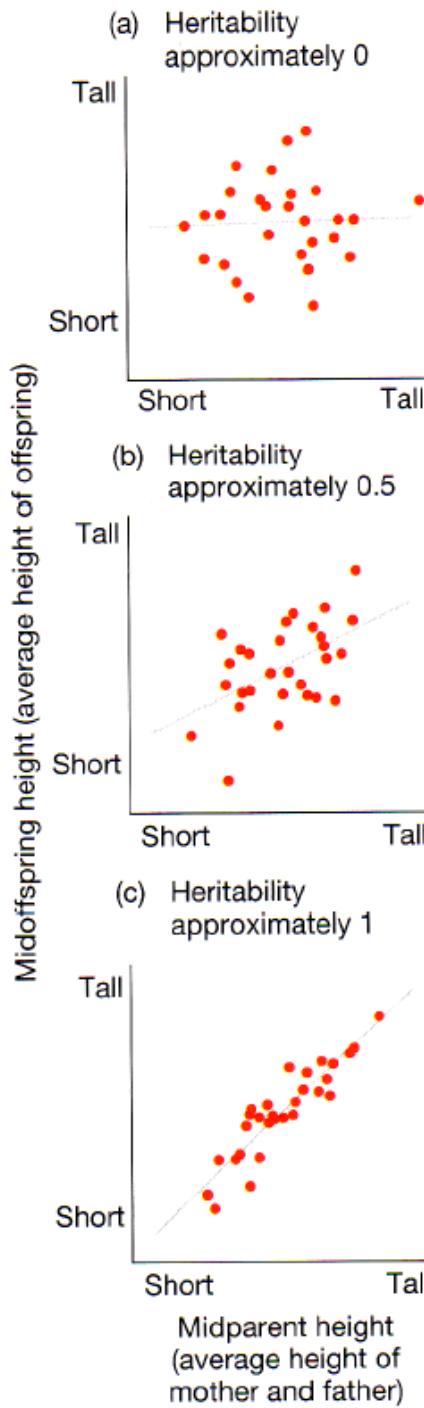
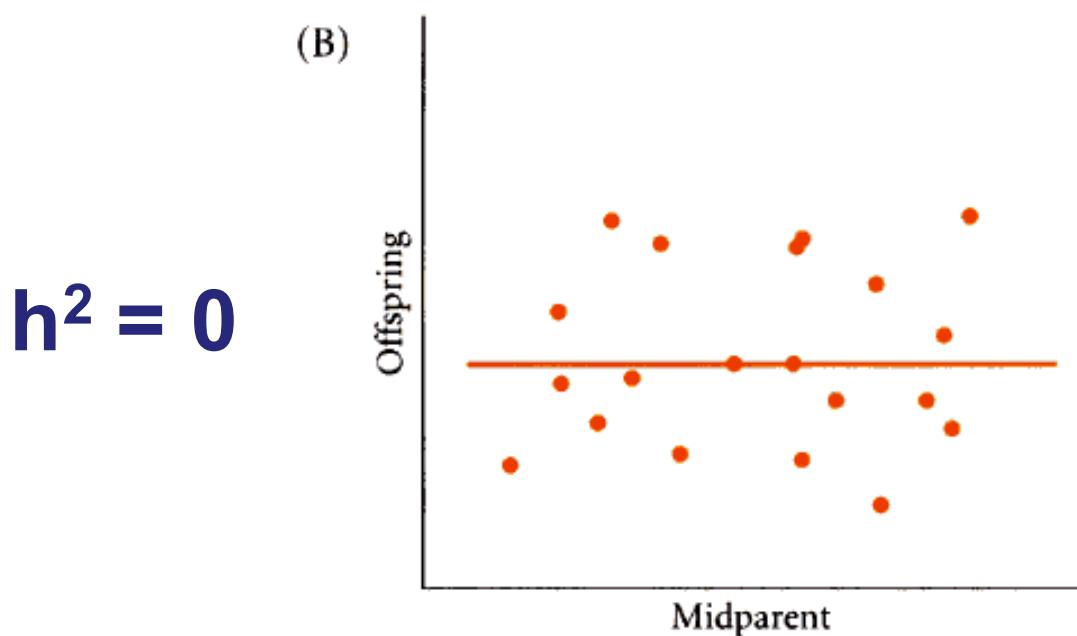
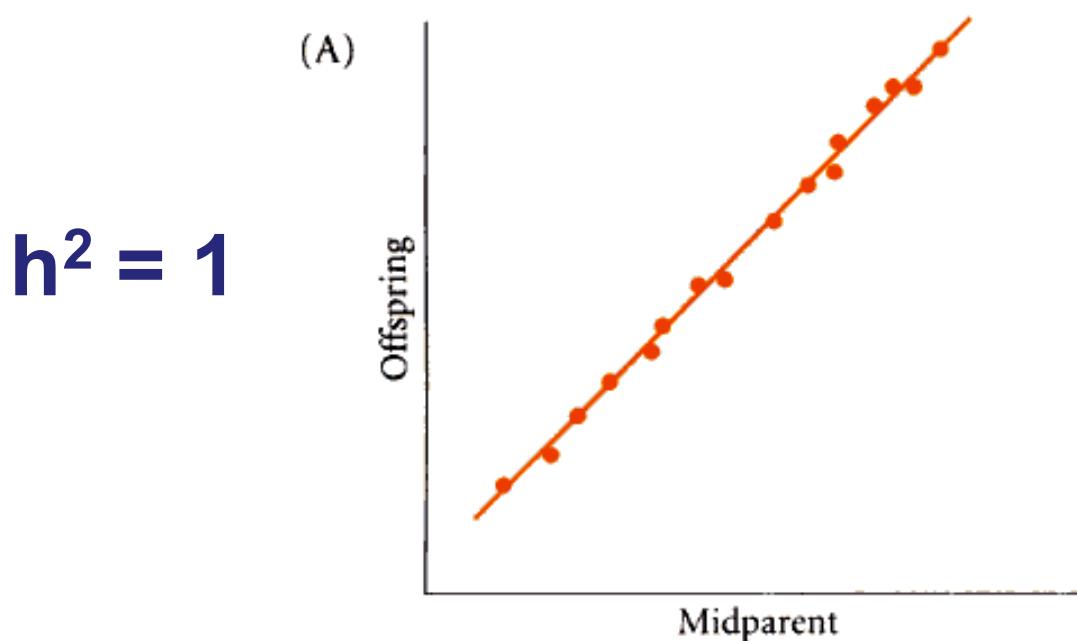


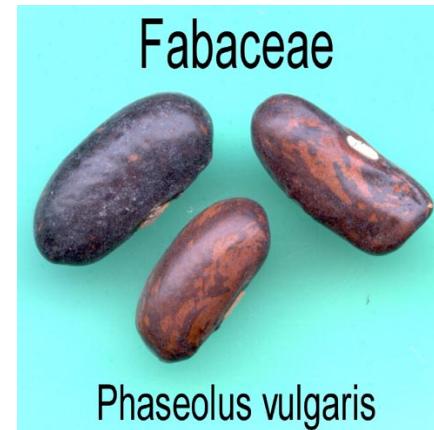
Fig. 11.1. Diagrammatic representation of the mean values of progeny plotted against the mid-parent values, to illustrate the response to selection, as explained in the text.





QTL = “Quantitative Trait Loci”

Une a Genética quantitativa com a biologia molecular na busca da identificação dos genes responsáveis pela variação fenotípica



Karl Sax – 1923 Genetics –

3 “marcadores fenotípicos”, 1 caráter continuo = peso do grão



Example 21.1

The first example of an association between a marker locus and a quantitative trait was reported by Sax (1923), between a pigment locus and seed size in the bean, *Phaseolus vulgaris*. One of the parental lines, Improved Yellow Eye 1317, was homozygous for the dominant pigmentation factor, P , and had seeds that weighed on average 48 centigrams (cg). The other parental line, White 1228, was homozygous for the recessive pigmentation factor, p , and had an average seed weight of 21.0 cg. The genotypes at the pigmentation locus and average seed weights in the F_2 of the cross were:

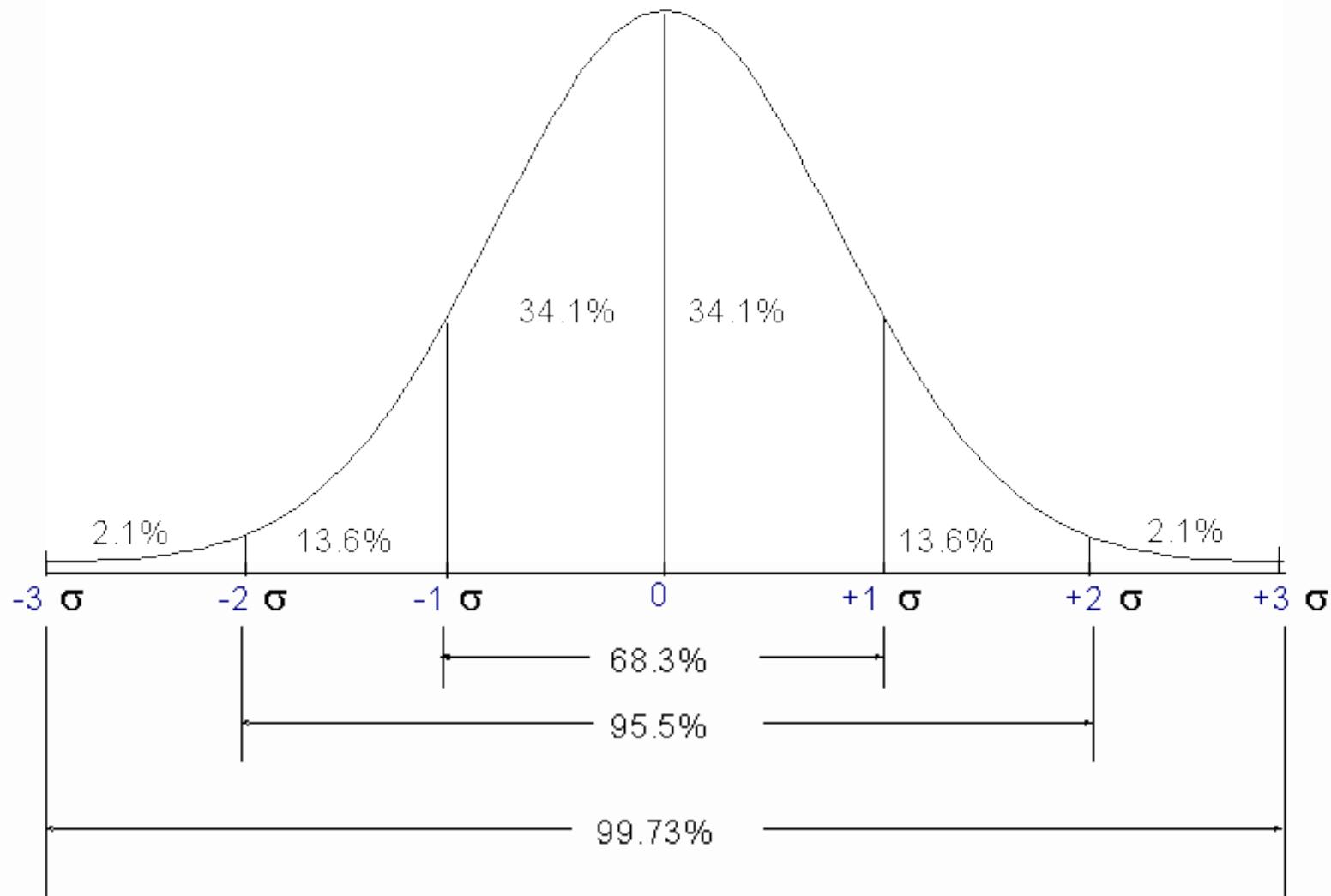
Genotype	PP	Pp	pp
Seed weight (cg)	30.7	28.3	26.4

(The genotypes of the pigmented F_2 were deduced from the presence or absence of unpigmented pp progeny in the F_3 .) Equation [21.1a] gives the estimate of $a(1 - 2c)$ as $(30.7 - 26.4)/2 = 2.15$ cg. The effect is perfectly additive because the marker heterozygote is almost exactly midway between the two homozygotes. Equation [21.1b] gives $d(1 - 2c)^2 = -0.25$ cg. The difference in seed weight between the PP and pp genotypes in the F_2 (4.3 cg) accounts for 16 per cent of the total difference in seed weight between the two parental strains (27 cg). This is a large effect associated with the marker, but the conclusions we can draw about a QTL are limited. First, part, or even all, of the effect may have been due to the P locus itself having a pleiotropic effect on seed weight. Second, if there is a QTL linked to the P locus, its effect ($2a$) is correctly estimated as 4.3 cg only if there is no recombination with the marker ($c = 0$). The effect could equally have been due to a less closely linked QTL with a larger effect. And, third, the QTL identified may have been not one but two or more linked loci.



Métodos para mapear QTL's

- Desenho experimental para estimar efeitos e posição de mapa de QTL's são extensões dos métodos utilizados para mapear "genes maiores" (= 3 x ou mais desvios padrões) ou "mendelianos" -----BASEADOS NO DESEQUILÍBRIO DE LIGAÇÃO
- Desequilíbrio entre alelos em locus ou loci "marcadores" e alelos no "gene(s) quantitativo" ligado a este marcadores.
- Precisamos então:
 - 1) Um mapa de ligação dos loci marcadores polimórficos que cubra o genoma totalmente
 - 2) Variação para o caráter contínuo dentro e entre populações ou linhagens



Escolha dos marcadores:

- 1) Altamente polimórficos (indivíduos diferentes provavelmente carregam alelos diferentes naquele locus)
- 2) Abundantes (assim cobrindo completamente o genoma)
- 3) Neutros (tanto sem efeito em relação ao caráter quantitativo quanto a aptidão)
- 4) co-dominantes (todos os genótipos podem ser identificados)

Até recentemente marcadores fenotípicos (como em Sax 1923) ou proteínas

----Mas não são exatamente “bons” marcadores

A partir da década de 80....

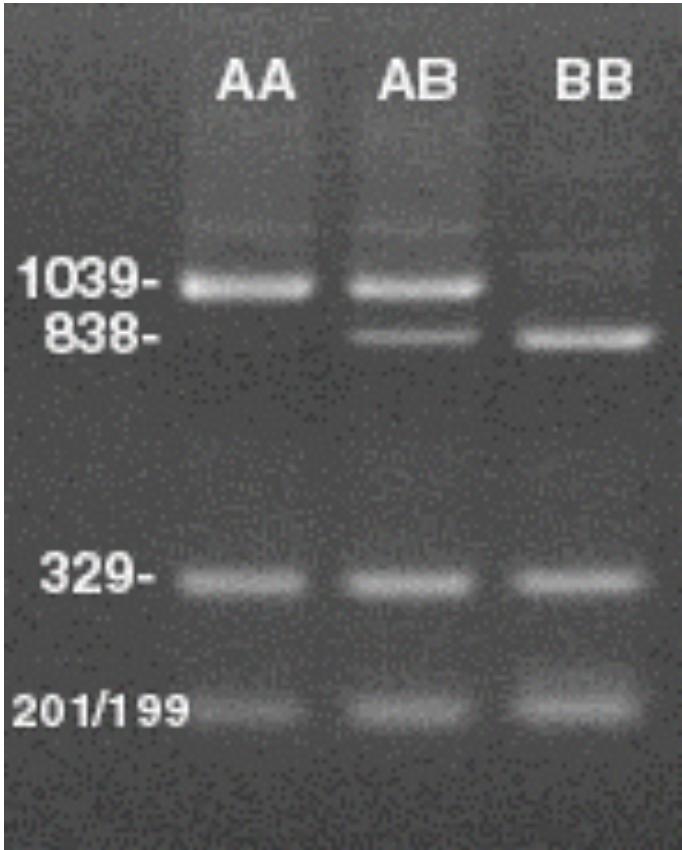
RFLP's, VNTR, Mini-satélites, micro-satélites, RAPD, etc

AA AB BB

1039-
838-

329-

201/199

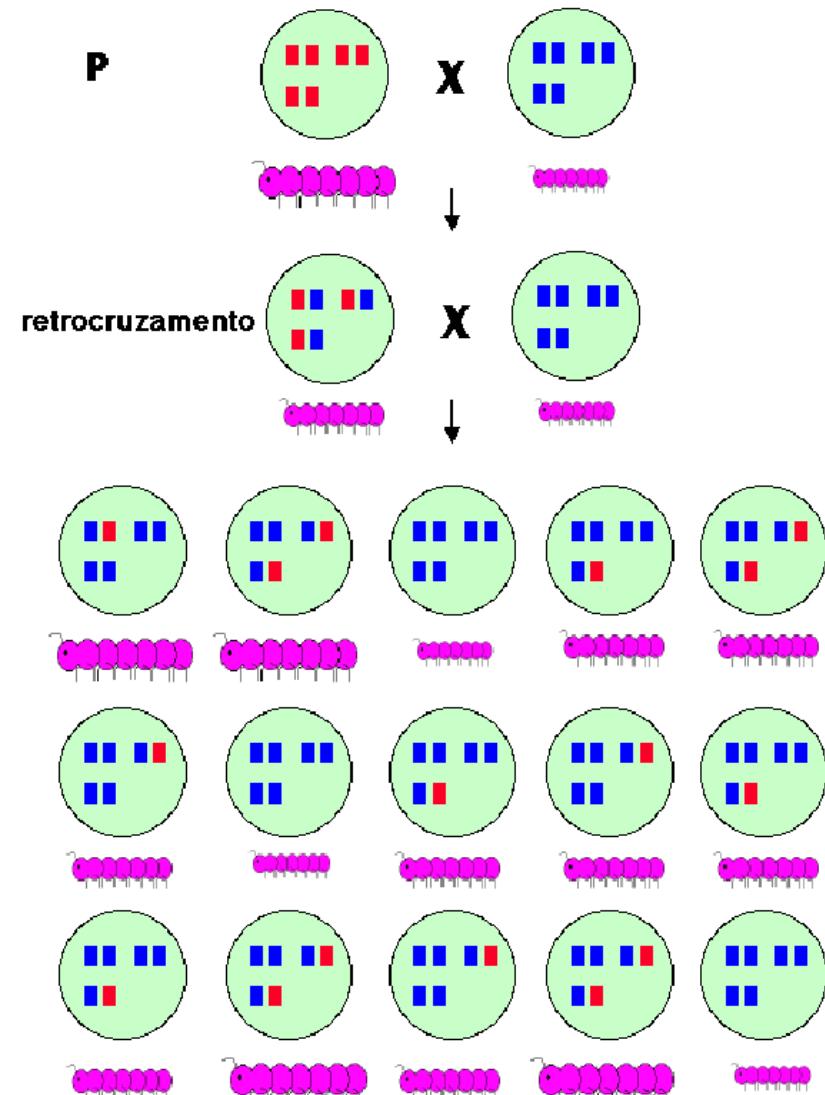
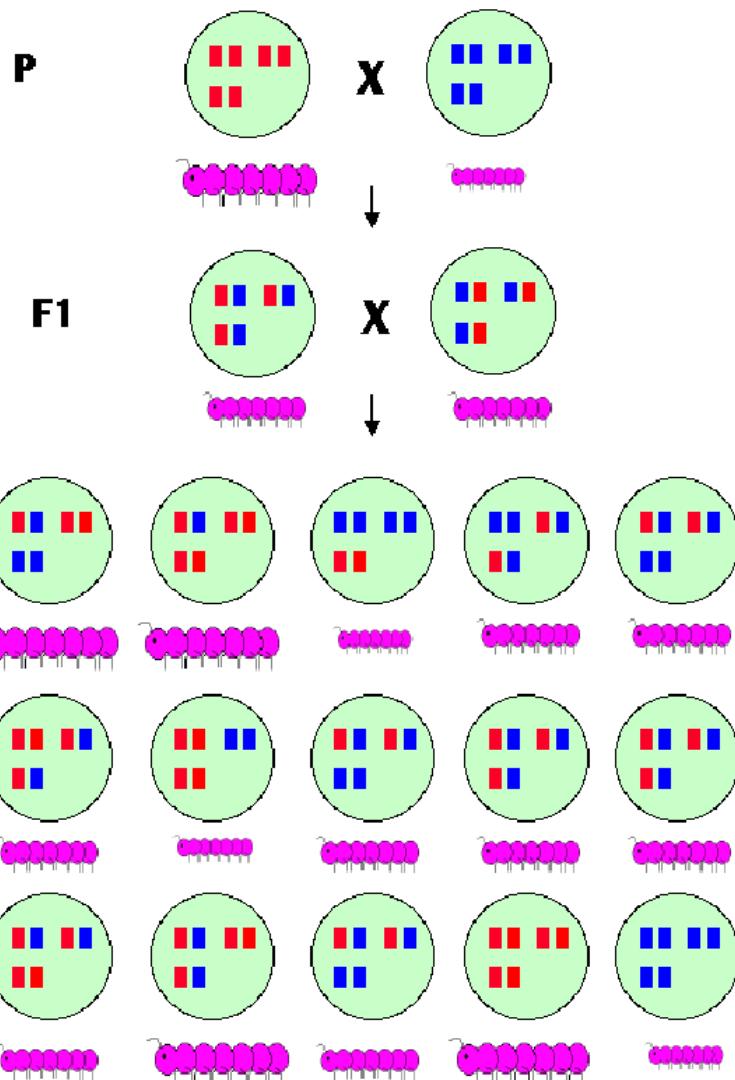


Princípio

Identificamos os QTL's por ligação aos loci marcadores: indivíduos são genotipados para os loci marcadores e medidas são tomadas para o(s) caracteres fenotípicos de interesse

- Se existe diferença no fenótipo médio entre as classes genotípicas dos marcadores, então pode-se inferir a presença de um QTL's ligado ao marcador. Marcadores podem ser considerados individualmente ou em conjunto

Cruzamento entre linhagens (populações) que diferem para o caráter em questão ou populações segregantes



Distância (arbitr.)	Média dos valores fenotípicos	
	para genótipo	para genótipo
0	24,7	24,7
10	24,7	24,7
20	24,0	25,4
30	22,1	27,3
40	19,3	30,1
50	19,3	30,1
60	22,1	27,3
70	24,0	25,4
80	24,7	24,7
90	24,7	24,7

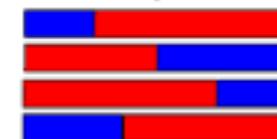
parents



F1



F1 gametes

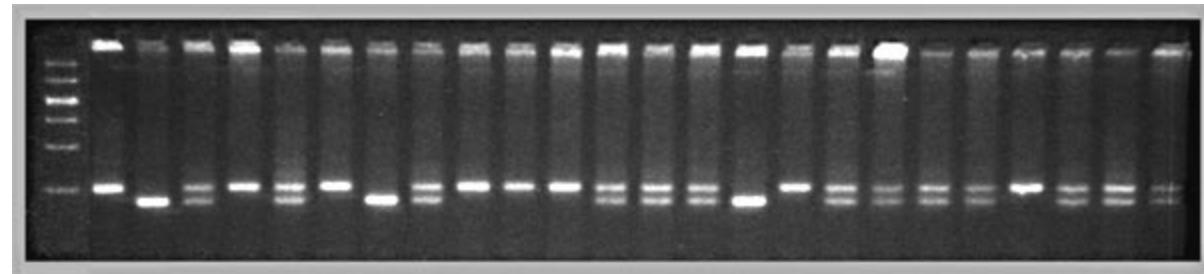
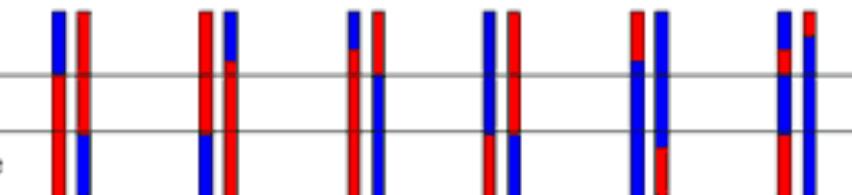


phenotype



QTL

genotype



Distância (arbítr.)	Média dos valores fenotípicos para genótipo	Média dos valores fenotípicos para genótipo
	 	 
0	23,4	24,9
10	27,4	22,4
20	25,6	26,5
30	20,2	28,4
40	21,3	29,0
50	20,2	30,3
60	24,3	25,8
70	22,3	23,9
80	24,5	25,6
90	26,3	24,7

Aqui começa a entrar o poder da Estatística junto com um modelo genético. Se fôssemos fazer uma comparação **independente** para cada marcador teríamos que fazer duas considerações:

1. Em uma série de comparações independentes, é esperado que algumas delas (em 5% dos casos para ser mais exato) sejam significativas **por acaso**. Sabendo disso, corremos o risco de não podermos detectar um QTL que exista realmente pois apenas poderíamos considerar efeitos muito mais fortes que aqueles detectados pelo nível de 5%, padrão em experimentos biológicos, para evitar conclusões espúrias.
2. Os desvios ao acaso que existem em qualquer experimento ocorrem em ambos os sentidos.

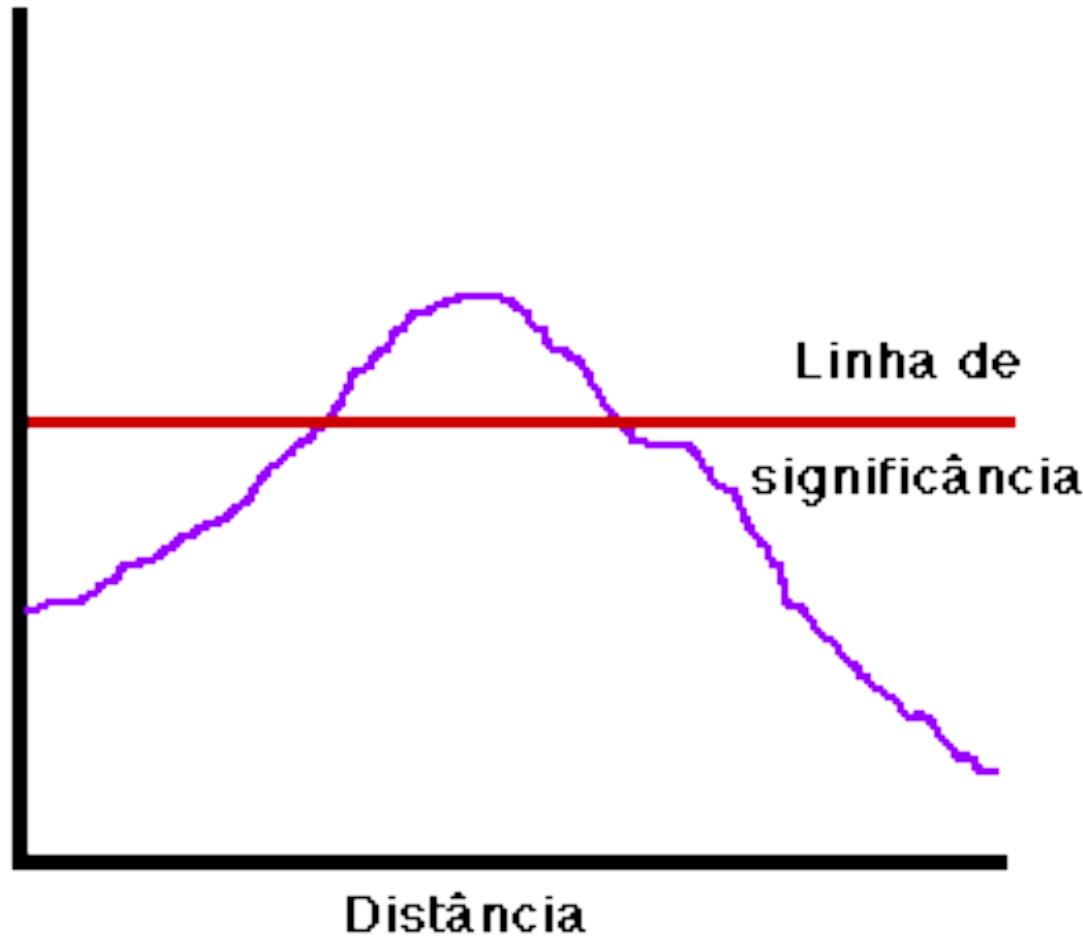
Para evitar esses problemas, é importante que utilizemos informações de todos os marcadores em conjunto.

Felizmente temos um meio para isso que é o método de máxima verossimilhança. É possível entendê-lo intuitivamente.

Imaginemos um número infinito de pontos dispostos sobre uma linha (uma premissa bastante razoável pois os genes estão arranjados linearmente sobre o cromossomo). Cada ponto terá uma determinada distância de cada um dos marcadores. Quanto maior for a distância, menor a probabilidade de que o marcador esteja detectando os efeitos daquele ponto.

Admitimos isso pois a probabilidade de recombinação aumenta com a distância. Calculamos então, para cada um dos pontos imaginários, os efeitos detectados por cada um dos marcadores multiplicados por uma função que é **inversamente proporcional** à distância entre o ponto e o marcador. Colocando isso em um gráfico teremos algo do tipo:

Efeito combinado inversamente proporcional à distância



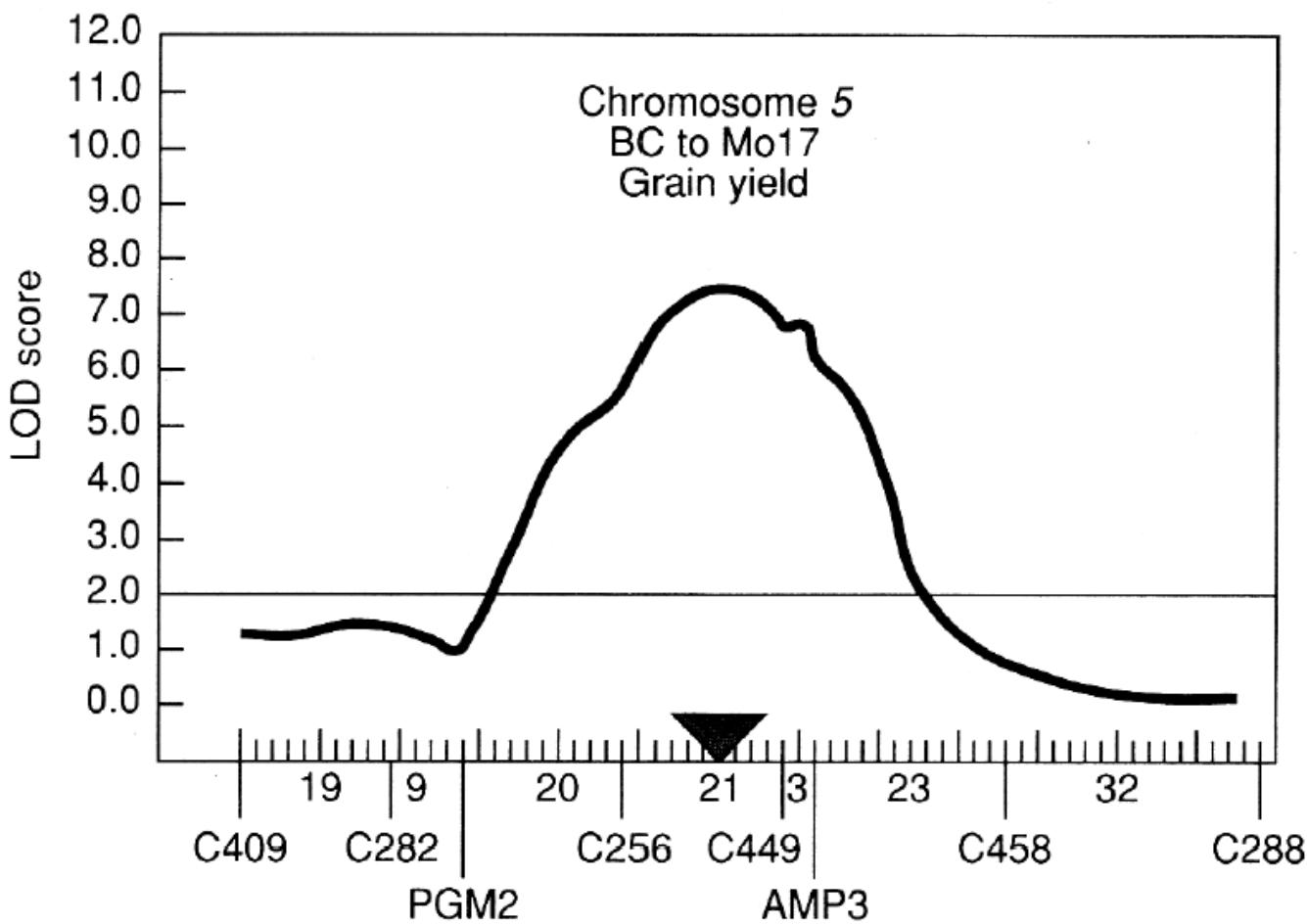


Fig. 21.2. Plot of LOD score against chromosomal position for QTLs affecting grain yield on maize Chromosome 5, for a backcross of the F_1 between two élite maize inbred lines, B73 and Mo17, to the Mo17 parent. The positions of isozyme (PGM2 and AMP3) and RFLP (labelled C---) markers are given on the x -axis, with the distances between markers given in cM. The most likely position of a QTL for yield is indicated by the shaded triangle, corresponding to the peak in LOD score. (*The unpublished figure and data have kindly been provided by C.W. Stuber.*)

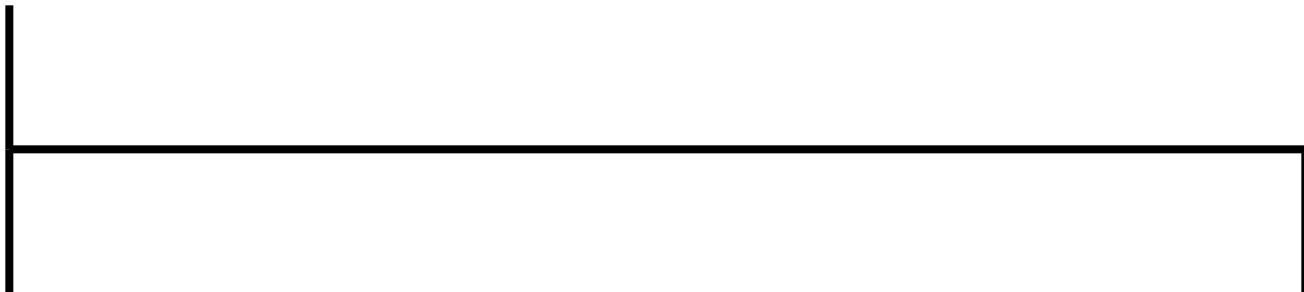
Efeito aditivo



O valor genotípico do heterozigoto é a média dos valores genotípicos dos homozigotos. Cada alelo “a” adiciona um valor constante, daí o nome.

Efeito de dominância

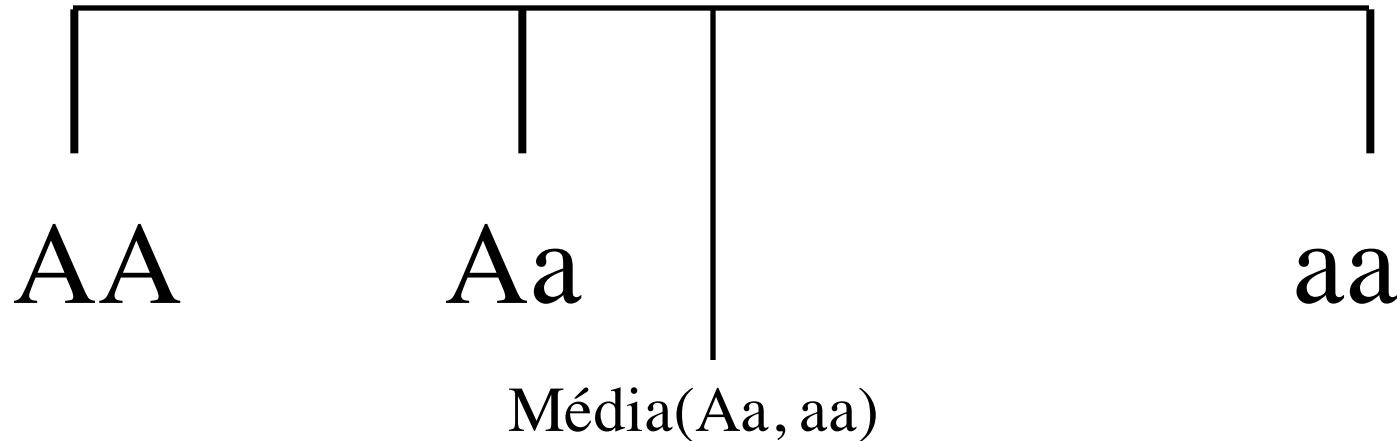
Aa



AA aa

O valor genotípico do heterozigoto é igual ao valor genotípico de um dos homozigotos. O alelo “A” domina sobre o alelo “a”, bastando haver um único “A” para a manifestação do fenótipo.

Efeito parcialmente dominante



O valor genotípico do heterozigoto está entre a média dos valores genotípicos dos homozigotos e o valor de um deles.

Poucos ou muitos genes? Qual a intensidade dos efeitos???

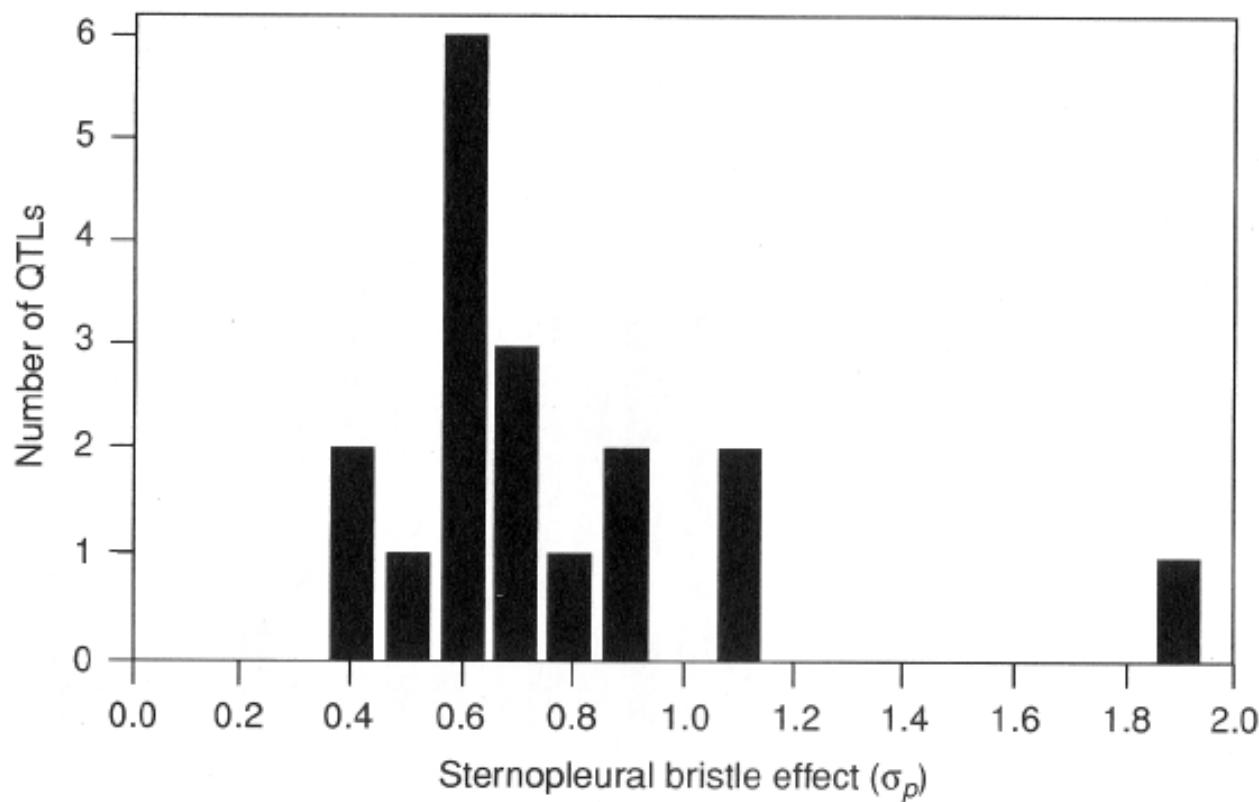


Fig. 21.3. Distribution of effects (a) of QTLs affecting sternopleural bristle number on Chromosome 3 of *Drosophila melanogaster*, in phenotypic standard deviation units. (Adapted from Shrimpton and Robertson, 1988b.)

São todos aditivos? Têm dominância? Completa ou parcial?

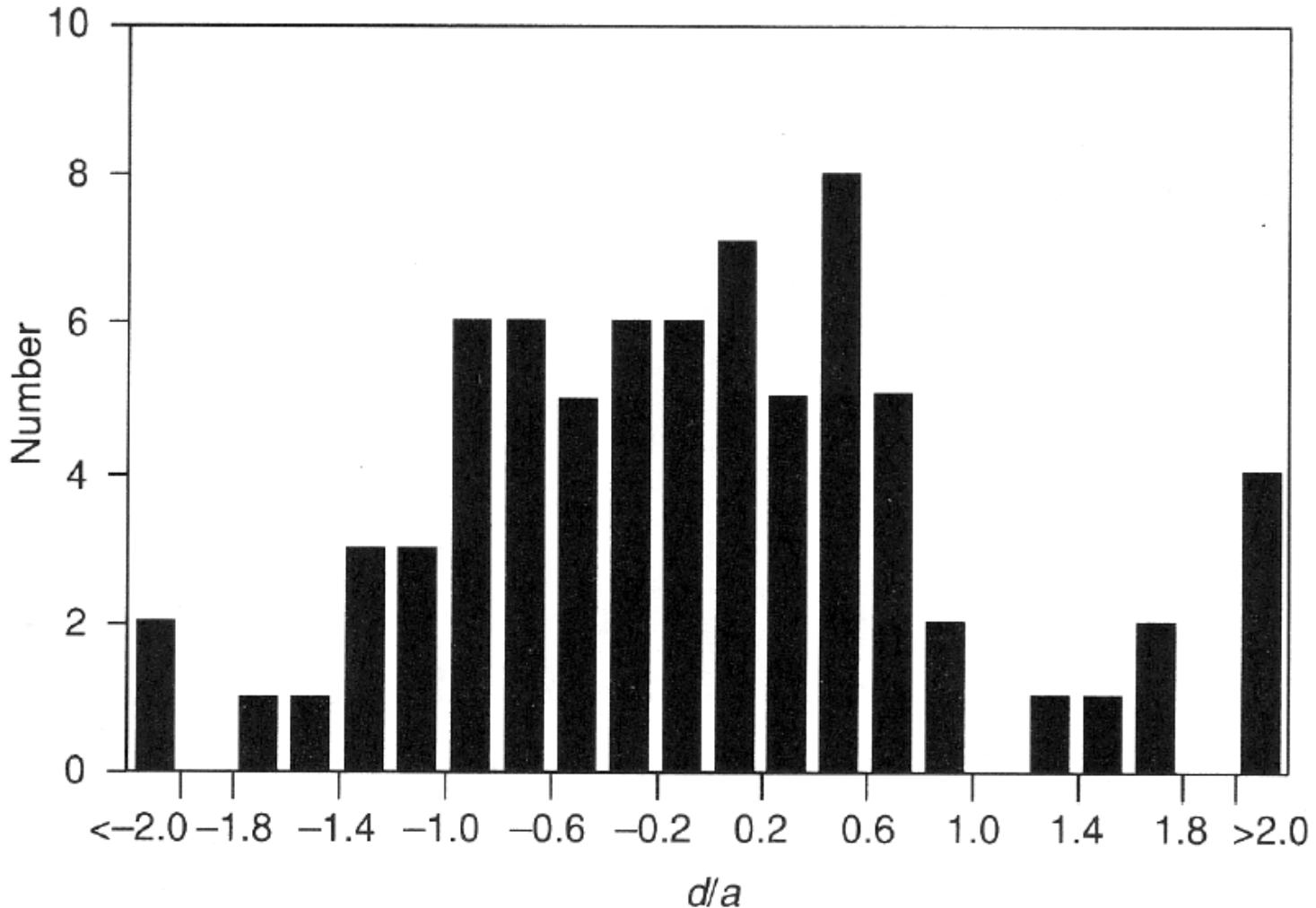
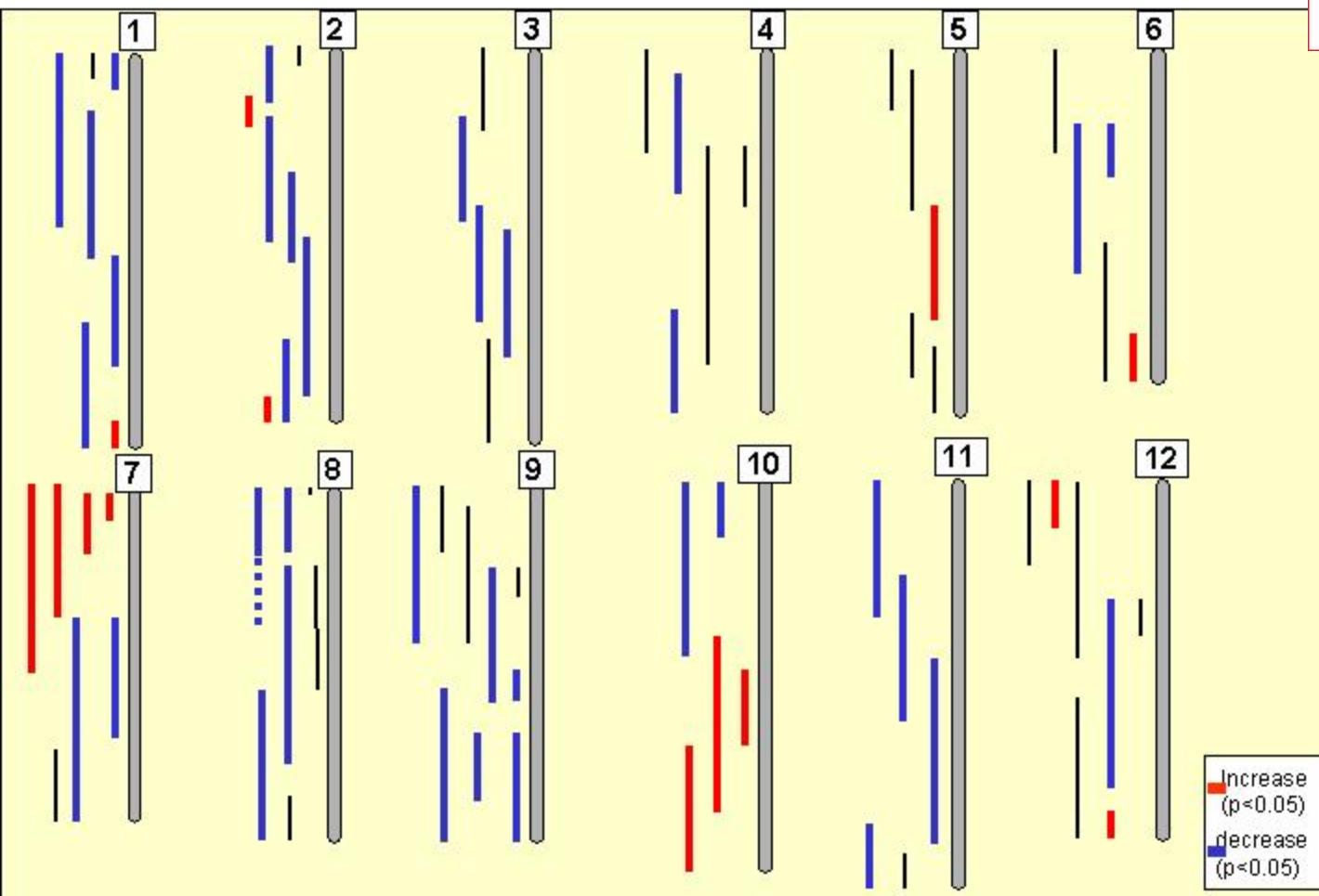
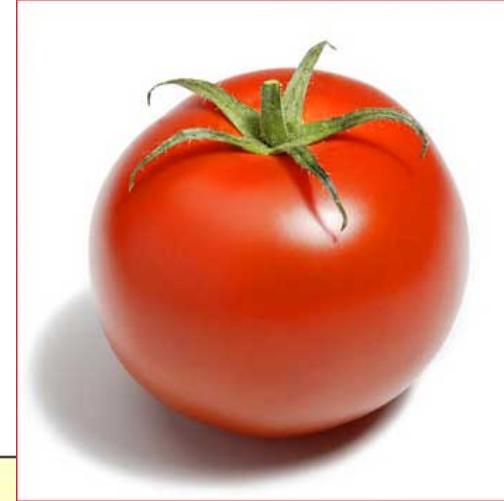


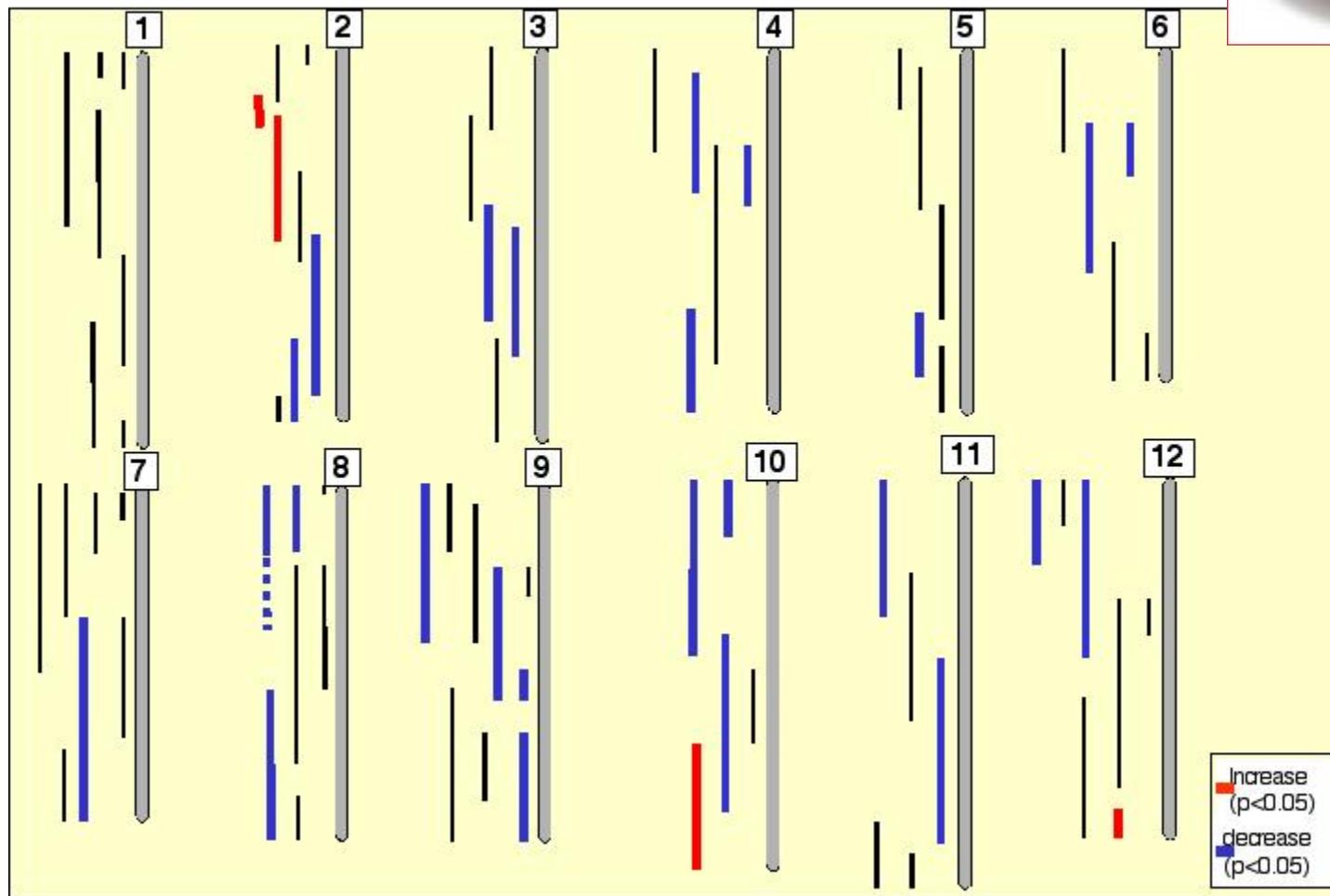
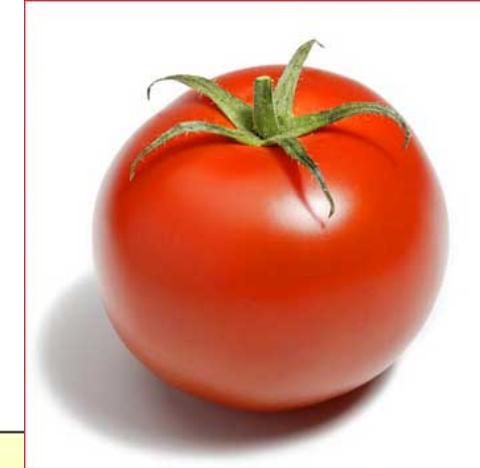
Fig. 21.4. Distribution of degrees of dominance (d/a) among 74 QTLs affecting vegetative traits of tomatoes, detected in the F_2 of a cross between the cultivated tomato and a wild species. (Adapted from deVicente and Tanksley, 1993.)

Fruit Weight QTL map in Combined experiment



Fruit Length QTL map in Akko - 2002 - Wet experiment

<http://zamir.sgn.cornell.edu/>



We report a bovine linkage map constructed with 1236 polymorphic DNA markers and 14 erythrocyte antigens and serum proteins. The 2990-cM map consists of a sex-specific, X chromosome linkage group and 29 sex-averaged, autosomal linkage groups with an average interval size of 2.5 cM.

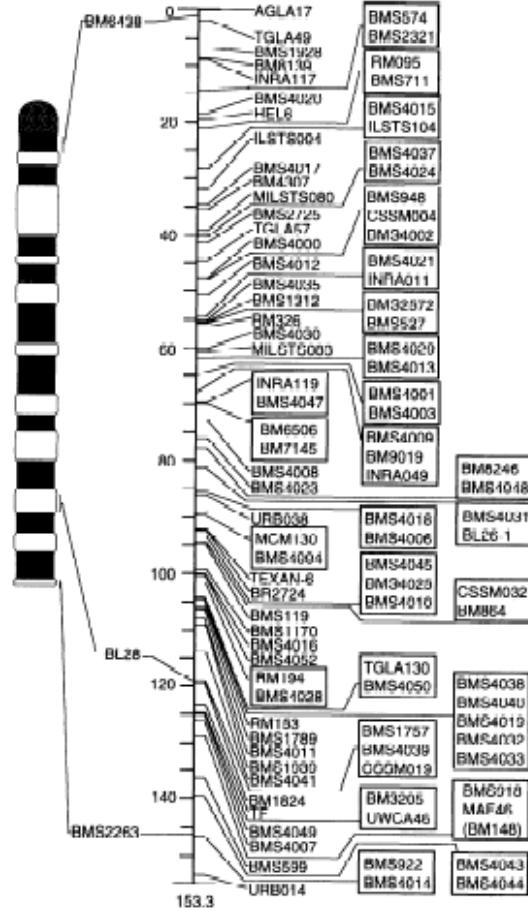


A second-generation linkage map of the bovine genome.

S M Kappes, J W Keele, R T Stone, R A McGraw, T S Sonstegard, T P Smith, N L Lopez-Corrales and C W Beattie

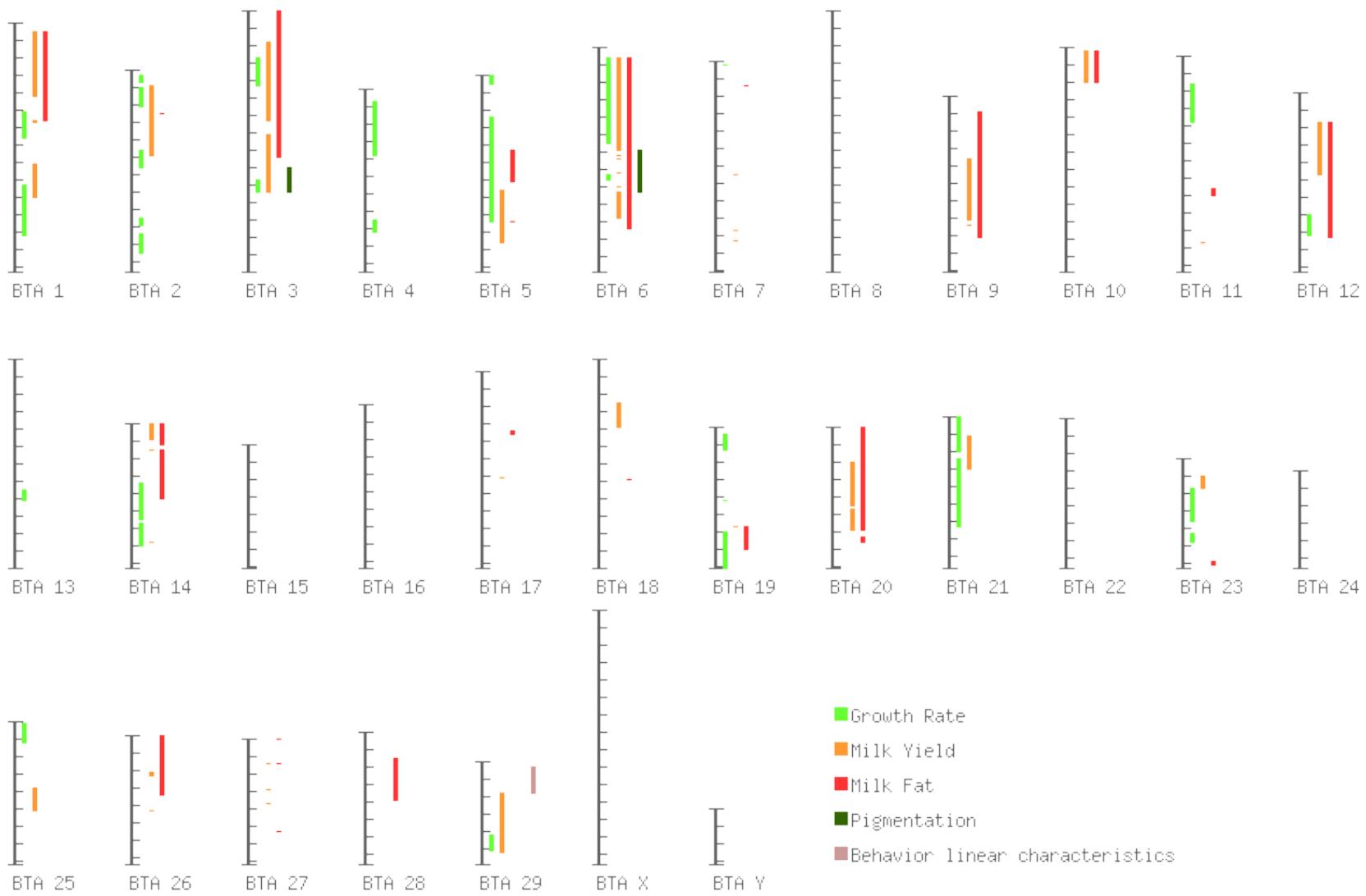
Genome Res. 1997 7: 235-249

Access the most recent version at doi:[10.1101/gr.7.3.235](https://doi.org/10.1101/gr.7.3.235)

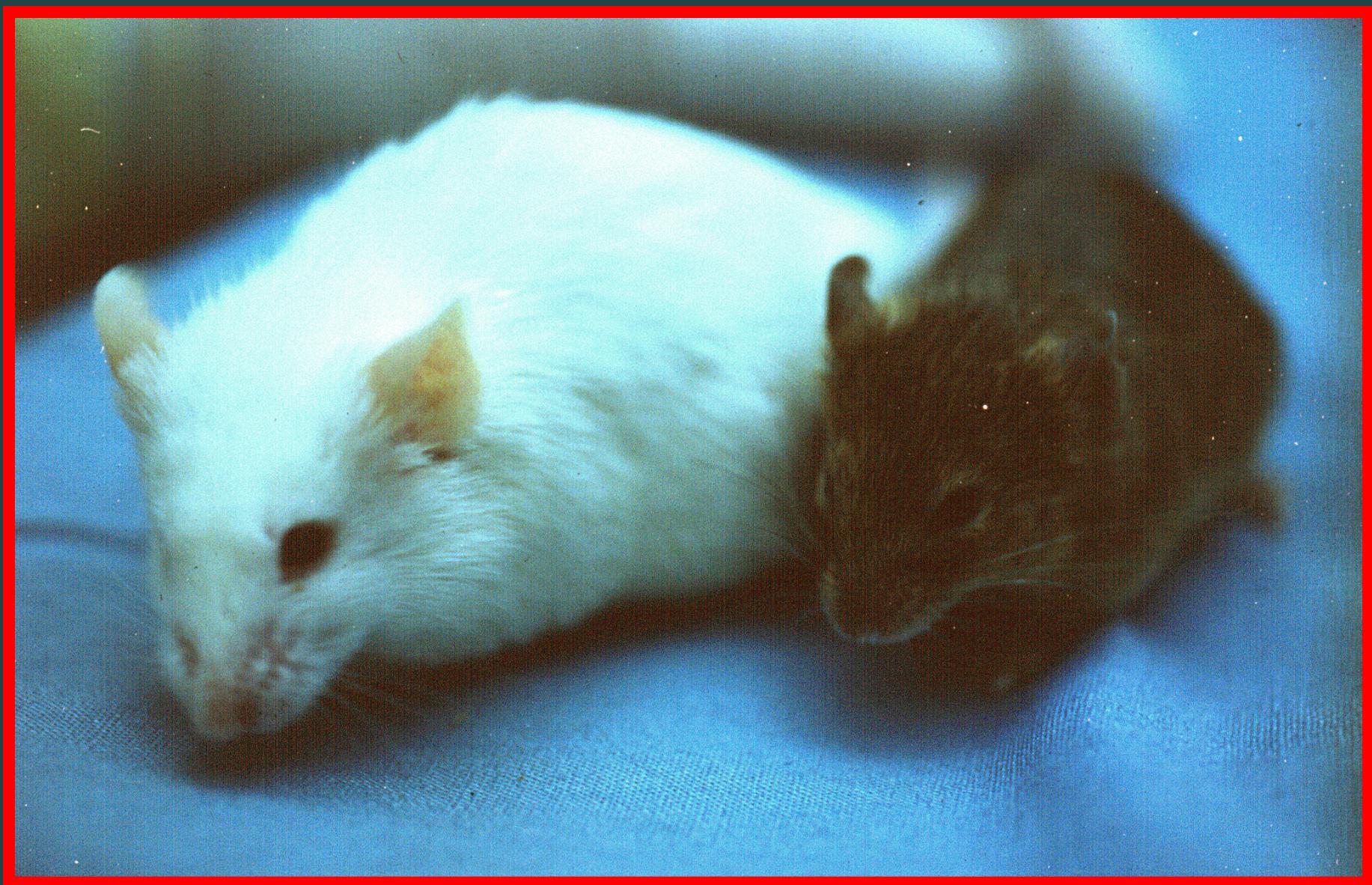


BTA1

Figure 1 Linkage group for bovine chromosome one. The linkage group is oriented next to the R-banded karyotype (ISCNDA 1990) of the chromosome and labeled below for *Bos taurus* (BTA1). Linkage groups for all 29 autosomes and the X and Y chromosomes are presented at the *Genome Research* web site (<http://www.cshl.org/gr/>). BTA1 is shown here. Markers with physical assignments are at left; their assignments (Table 1) are represented on the R-banded chromosome. Markers in parenthesis (see Web site) are a second set of primers for the same microsatellite as the marker above. No recombination events were detected between markers within a box; therefore, the order in which they are presented is arbitrary. In general, marker order in intervals ≤ 5 cM should be considered tentative as their statistical support was often less than a lod score of 3.0.



Large Female and Small Male

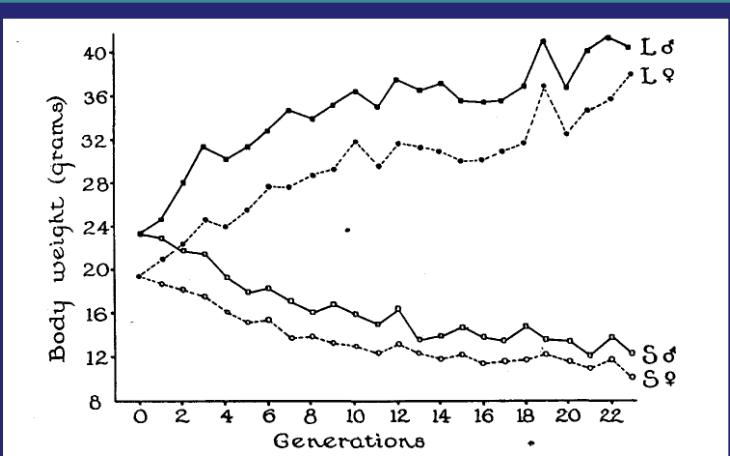


SM/J



MacArthur, 1939

- Selected for Decreased Body Weight at 60 days
- Cross of 7 Inbred Strains
- 8 inbred parents (black & tan used twice)
- Transferred to Jackson Labs in 1940s

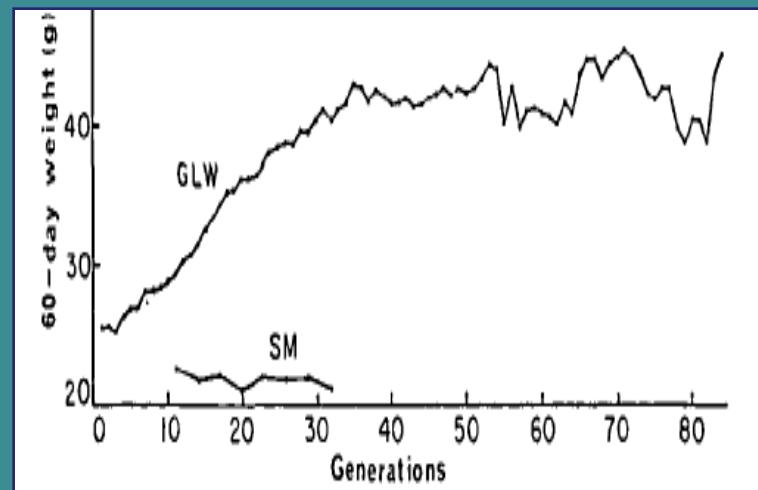


LG/J



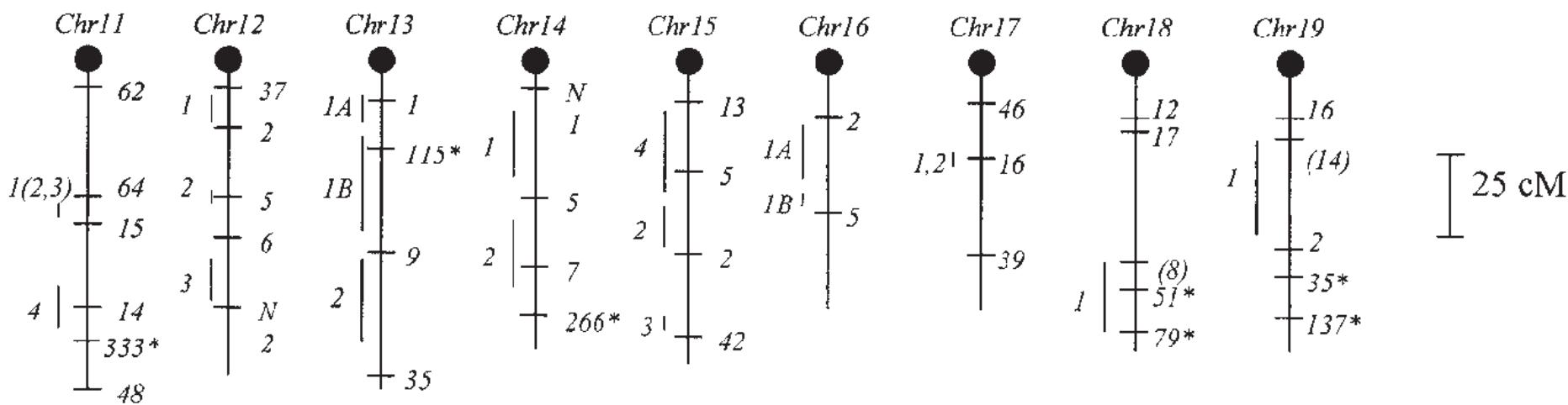
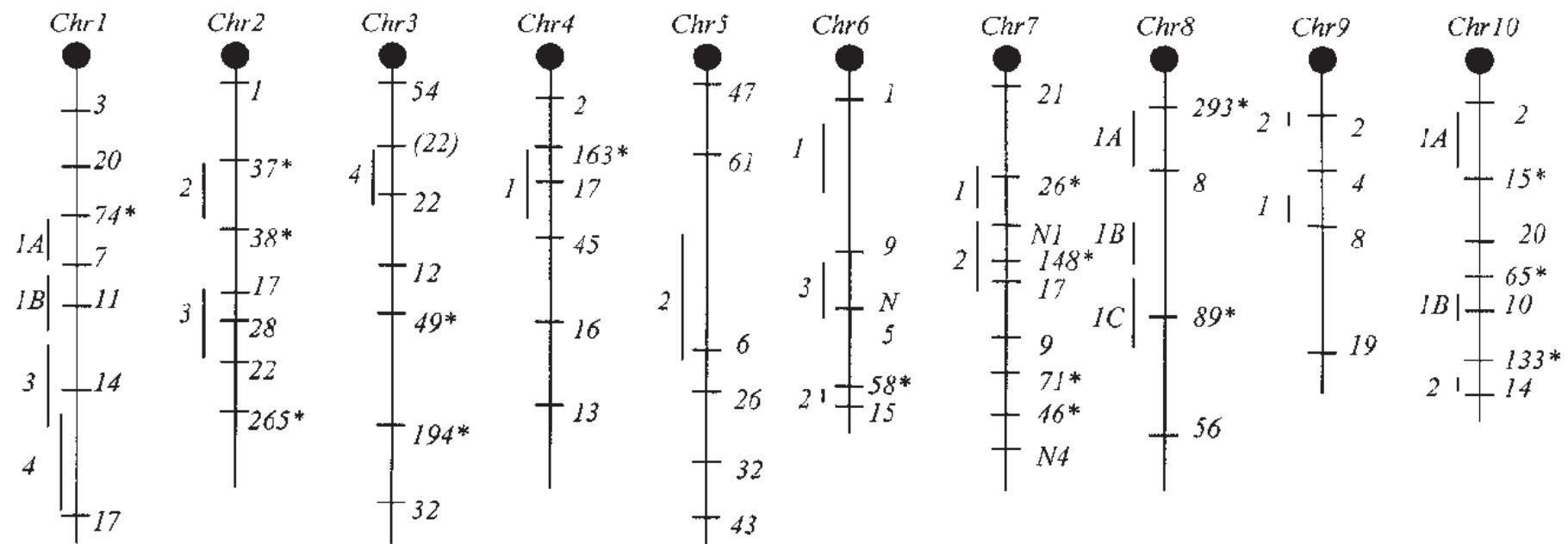
Goodale, 1930

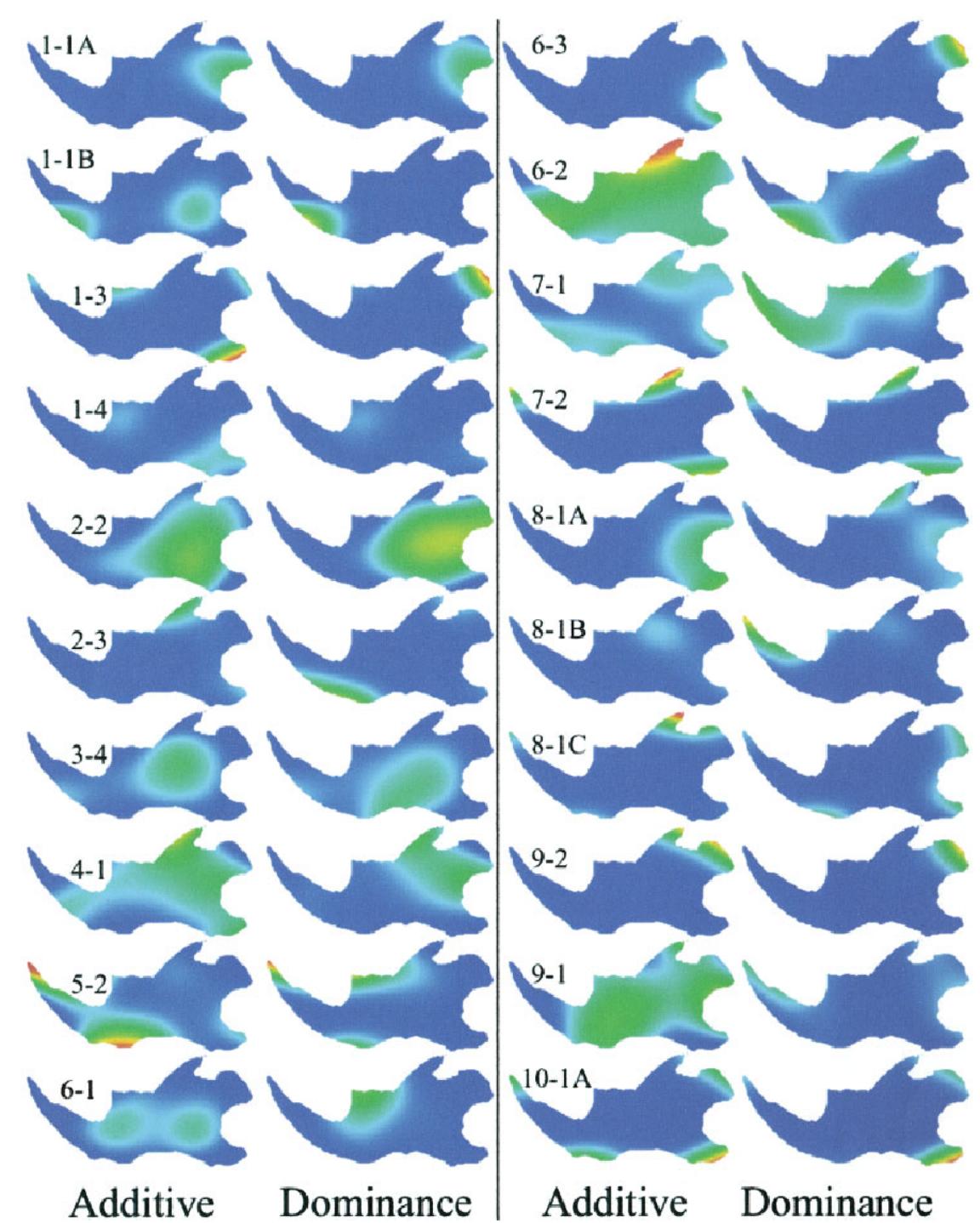
- Selected for Increased Body Weight at 60 days
- Albinos from commercial breeder
- 5 ♂ and 11 ♀ parents
- Transferred to Jackson Labs in 1948



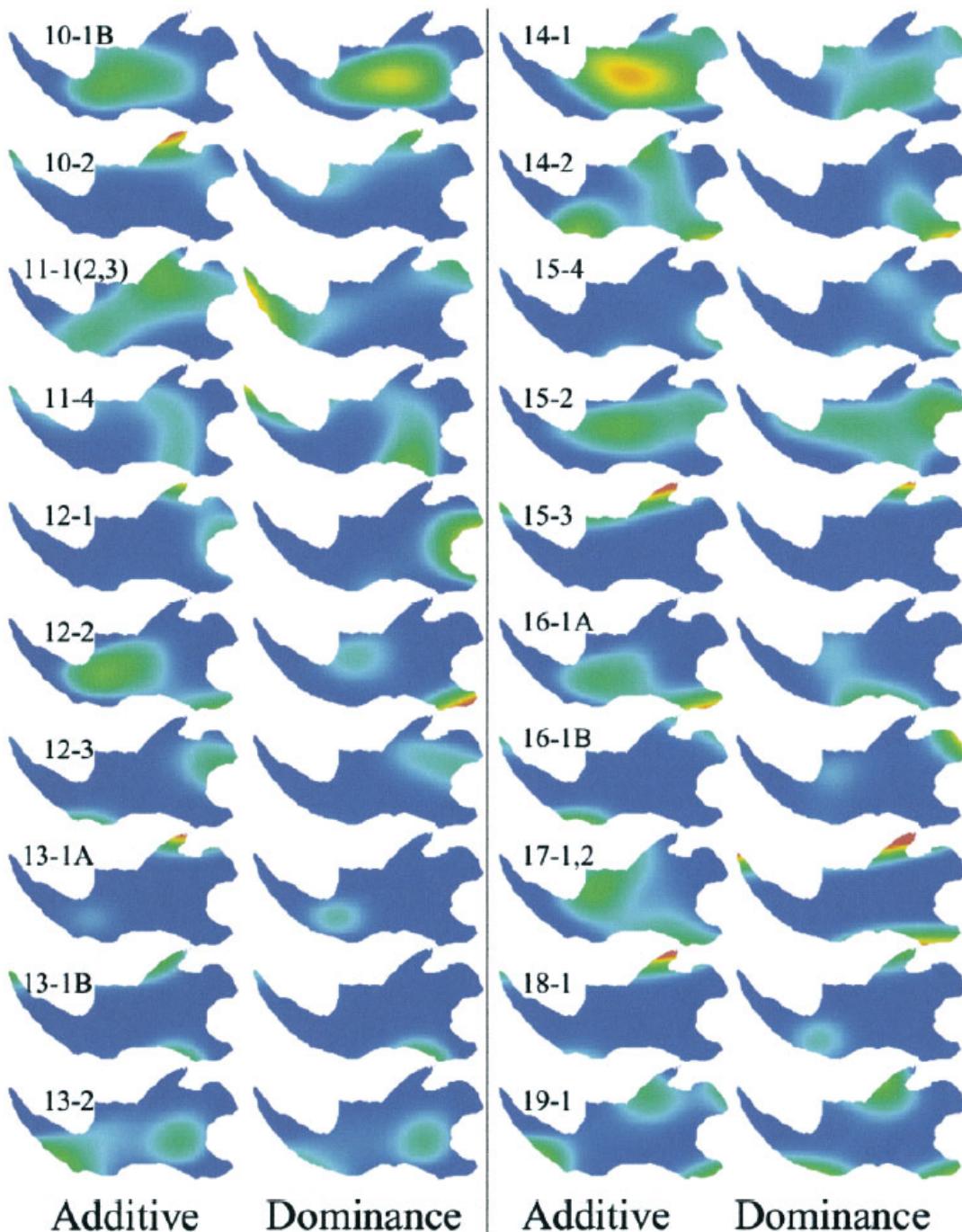
Outro complicador na herança e evolução de caracteres quantitativos

Pleiotropia = efeito de um loco sobre mais de um caráter





Têm pleiotropia?????



Pleiotropic Effects on Mandibular Morphology I. Developmental Morphological Integration and Differential Dominance

THOMAS H. EHRICH, TY T. VAUGHN, SAFINA F. KOREISHI,
ROBIN B. LINSEY, L. SUSAN PLETSCHER, AND JAMES M. CHEVERUD
Department of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, MO 63110

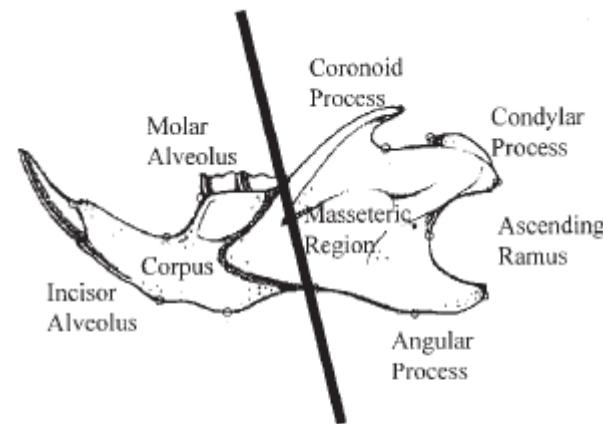


Fig. 1. Developmental regions of the mouse mandible (adapted from Atchley, '93). Each region derives from a different condensation of mesenchymal tissues and is affected by different associated tissues during development. See text for details.

TABLE 2: List of mandibular QTLs¹

Name	Traits	Lower CL	Upper CL	Position	Marker	Marker Dist.	LOD
<i>QTMAN1-1A</i>	2, 4, 11	34	50	38	<i>D1Mit74</i>	8	13.63
<i>QTMAN1-1B</i>	9, 14	46	64	52	<i>D1Mit7</i>	8	4.54
<i>QTMAN1-3</i>	3, 7, 19	70	96	86	<i>D1Mit14</i>	6	6.64
<i>QTMAN1-4</i>	6, 8, 18	92	120	104	<i>D1Mit14</i>	24	3.77
<i>QTMAN2-2</i>	2, 3, 4, 6, 8, 9, 10, 11, 17, 21	48	58	54	<i>D2Mit370</i>	8	14.55
<i>QTMAN2-3</i>	2, 6, 13, 14, 21	94	112	104	<i>D2Mit28</i>	6	6.69
<i>QTMAN3-4</i>	9, 10, 11, 12, 14, 15, 18	30	52	46	<i>D3Mit22</i>	2	4.73
<i>QTMAN4-1</i>	1, 4, 7, 9, 10, 11, 14, 16, 118, 19, 20, 21	28	40	36	<i>D4Mit17</i>	4	9.56
<i>QTMAN5-2</i>	6, 11, 12, 13, 16, 17, 19	56	78	74	<i>D5Mit61</i>	54	4.69
<i>QTMAN6-1</i>	9, 17, 19, 20	16	36	26	<i>D6Mit1</i>	26	7.30
<i>QTMAN6-3</i>	3, 6	60	74	66	<i>D6Mit9</i>	16	5.17
<i>QTMAN6-2</i>	1, 11, 13, 14, 18, 21	92	96	94	<i>D6Mit58</i>	2	10.61
<i>QTMAN7-1</i>	2, 3, 6, 9, 11, 12, 14, 15, 17, 19, 20, 21	24	36	30	<i>D7Mit21</i>	30	15.79
<i>QTMAN7-2</i>	1, 7, 8, 21	36	54	52	<i>D7Nds1</i>	8	4.61
<i>QTMAN8-1A</i>	4, 7, 9, 21	4	22	14	<i>D8Mit293</i>	14	6.94
<i>QTMAN8-1B</i>	6, 11, 16	42	58	50	<i>D8Mit8</i>	26	13.52
<i>QTMAN8-1C</i>	1, 2, 3, 6, 13	66	84	80	<i>D8Mit89</i>	4	12.78
<i>QTMAN9-2</i>	1, 3	0	4	0	<i>D9Mit2</i>	0	4.11
<i>QTMAN9-1</i>	1, 2, 4, 6, 10, 12, 13, 17, 19, 20	20	28	24	<i>D9Mit4</i>	10	12.48
<i>QTMAN10-1A</i>	2, 3, 7, 13	4	22	14	<i>D10Mit2</i>	14	10.82
<i>QTMAN10-1B</i>	9, 10, 17, 19, 20	62	72	70	<i>D10Mit10</i>	2	14.37
<i>QTMAN10-2</i>	1, 4, 11, 16, 18, 21	82	88	84	<i>D10Mit133</i>	8	18.81
<i>QTMAN11-1 (2,3)</i>	1, 2, 3, 4, 10, 11, 13, 14, 15, 17, 18, 20, 21	50	52	52	<i>D11Mit64</i>	6	26.81
<i>QTMAN11-4</i>	8, 9, 11, 16, 18	80	92	84	<i>D11Mit14</i>	2	9.50
<i>QTMAN12-1</i>	1, 4, 6, 12	6	14	10	<i>D12Mit37</i>	10	16.68
<i>QTMAN12-2</i>	7, 8, 10, 17, 18, 20	42	46	44	<i>D12Mit5</i>	2	14.80
<i>QTMAN12-3</i>	2, 4, 11, 13	56	68	62	<i>D12Mit6</i>	10	10.97
<i>QTMAN13-1A</i>	1, 17	0	6	0	<i>D13Mit1</i>	0	3.77
<i>QTMAN13-1B</i>	8, 21	16	42	30	<i>D13Mit115</i>	20	7.09
<i>QTMAN13-2</i>	9, 13, 14, 18	66	84	74	<i>D13Mit9</i>	12	9.49
<i>QTMAN14-1</i>	1, 2, 3, 6, 9, 10, 12, 18, 19, 20	14	32	22	<i>D14Nds1</i>	22	9.23
<i>QTMAN14-2</i>	7, 9, 11, 13, 17, 21	50	74	58	<i>D14Mit5</i>	14	9.50
<i>QTMAN15-4</i>	6, 11, 12	0	26	12	<i>D15Mit13</i>	12	4.52
<i>QTMAN15-2</i>	2, 4, 8, 10, 16, 18, 20	28	40	34	<i>D15Mit5</i>	10	10.90
<i>QTMAN15-3</i>	1, 19, 21	72	76	76	<i>D15Mit2</i>	26	5.29
<i>QTMAN6-1A</i>	7, 8, 10, 12, 17, 20	8	24	16	<i>D16Mit2</i>	16	7.47
<i>QTMAN6-1B</i>	1, 3, 13, 18	24	30	30	<i>D16Mit2</i>	30	6.02
<i>QTMAN17-1,2</i>	1, 7, 8, 9, 11, 12, 17, 18, 20, 21	4	8	8	<i>D17Mit46</i>	8	14.92
<i>QTMAN18-1</i>	1, 13, 17, 21	24	46	36	<i>D18Mit51</i>	10	9.61
<i>QTMAN19-1</i>	3, 7, 10, 11, 13, 14, 18, 21	12	38	26	<i>D19Mit14</i>	20	5.15

¹Assignment of QTL names is described in the text. The traits listed are those that are statistically significantly associated with the QTL. QTL position is given relative to the most proximal marker scored on the chromosome and relative to the nearest proximal marker. Lower and upper

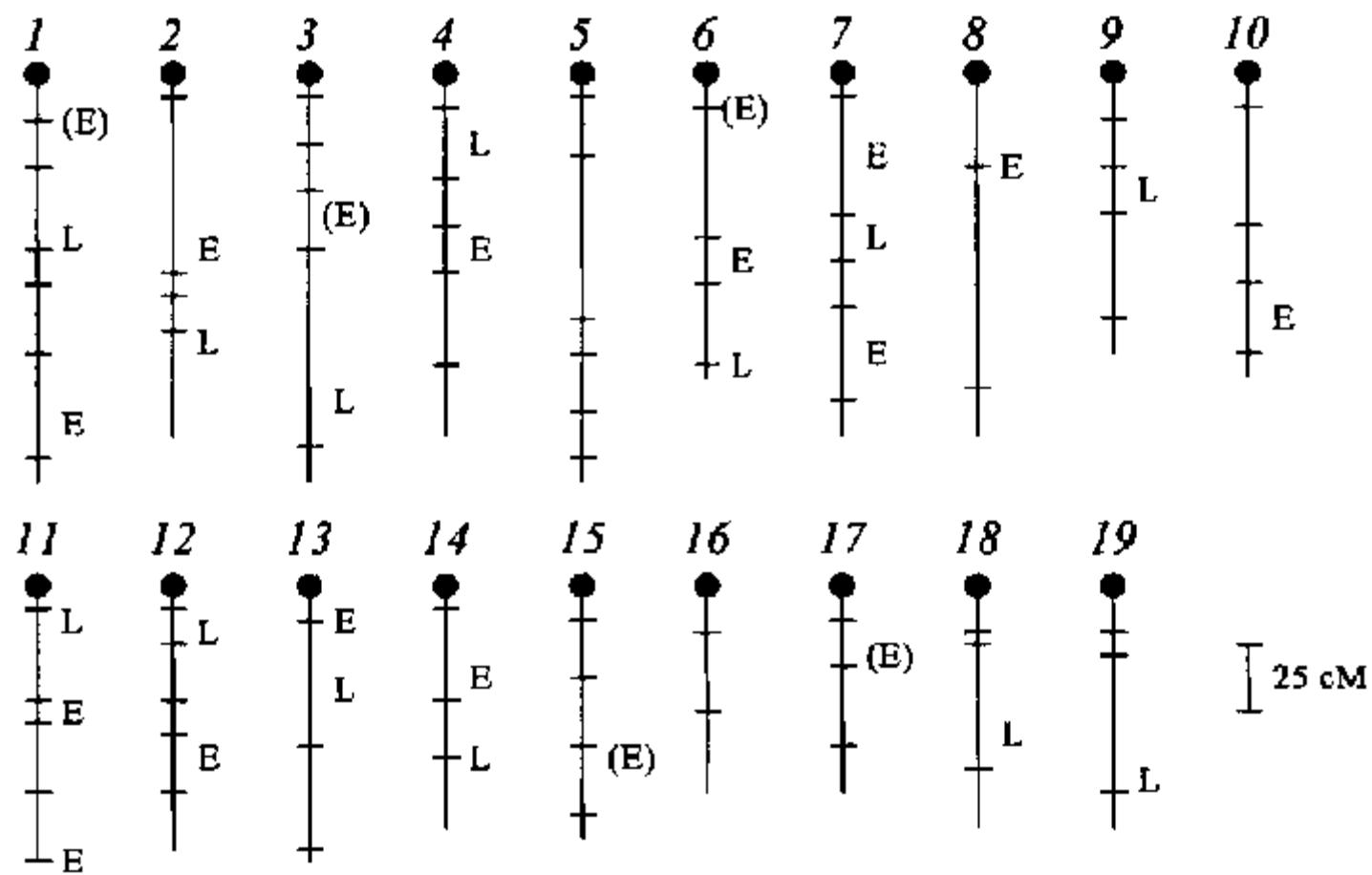


FIGURE 2.—Relative positions of QTLs affecting early (E) and late (L) growth. Parenthetical entries represent locations with exclusive effects on early or late weights but not on growth itself.

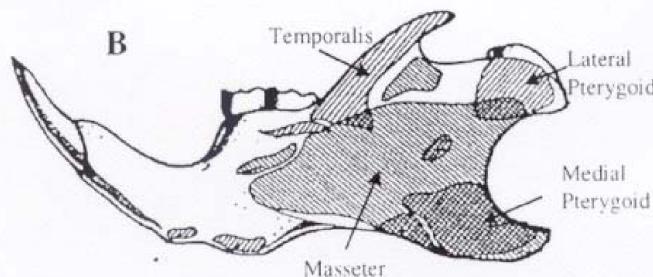
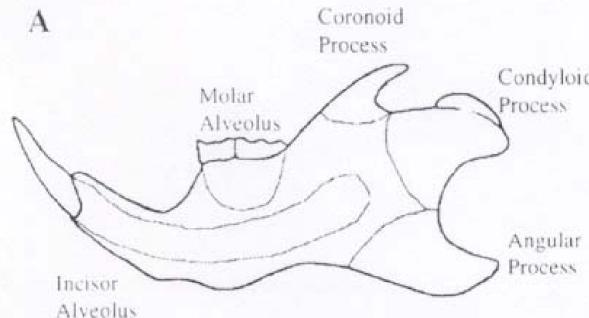


Fig. 7.3.—*A*, Mandibular condensations that coalesce to form the adult mandible. *B*, Mandibular muscle attachment areas. (Modified from Atchley and Hall 1991.)

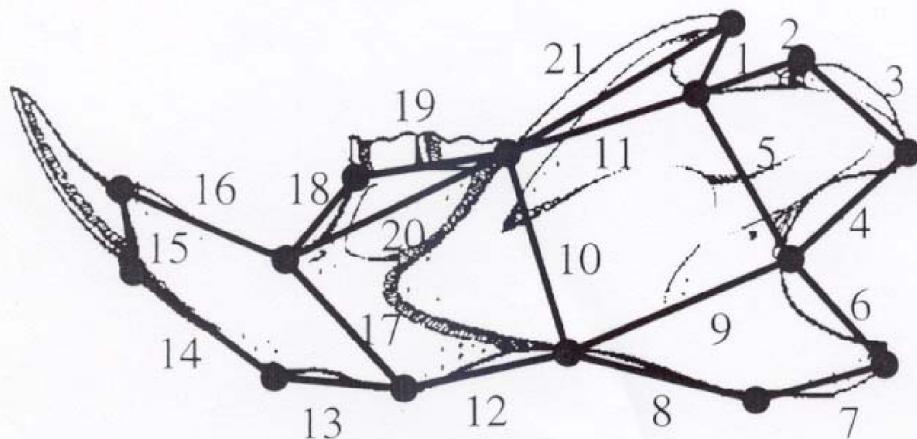


Fig. 7.4.—Linear measurements calculated from two-dimensional coordinates of murine mandibles (Cheverud et al. 1997; Cheverud 2000a). The dots indicate landmark locations.

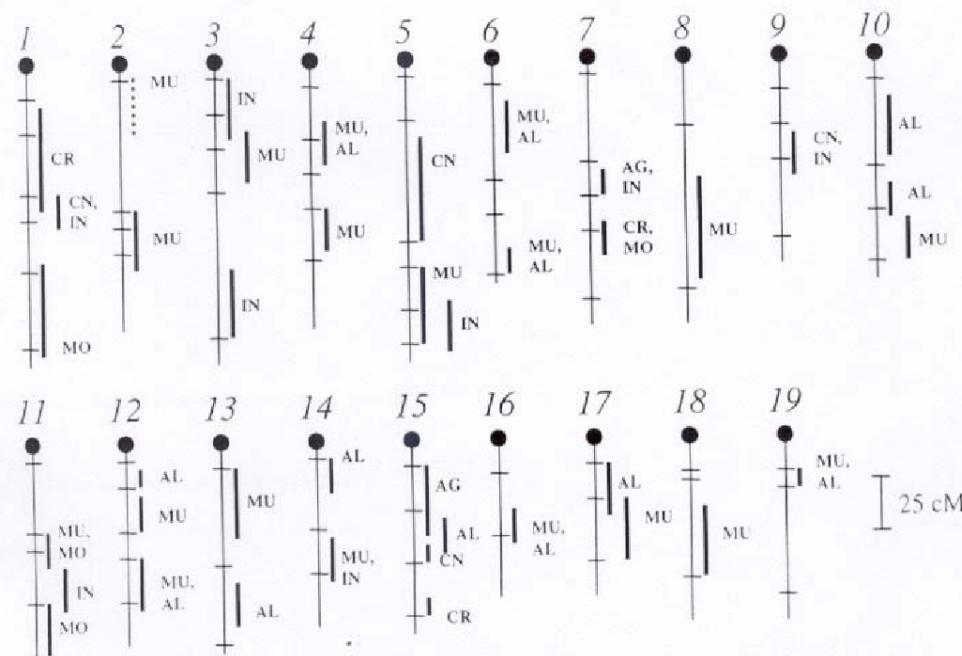


Fig. 7.5.—Genetic map positions of QTLs affecting mandibular morphology shown with 95% confidence regions. CR indicates that the QTL affects the coronoid process; CN, the condylloid process; AG, the angular process; MU, all the muscle attachment regions of the ascending ramus; IN, the incisor alveolus; MO, the molar alveolus; and AL, the total alveolar region. The dashed region on chromosome 2 indicates a region that was not sufficiently mapped in the first F_2 intercross to allow precise QTL placement. (After Cheverud 2000a.)

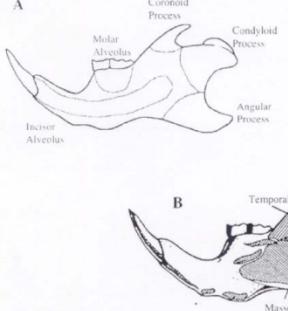


Fig. 7.3.—*A*, Mandibular condensations that coalesce to form the adult molar areas. (Modified from Atchley and Hall 1991.)

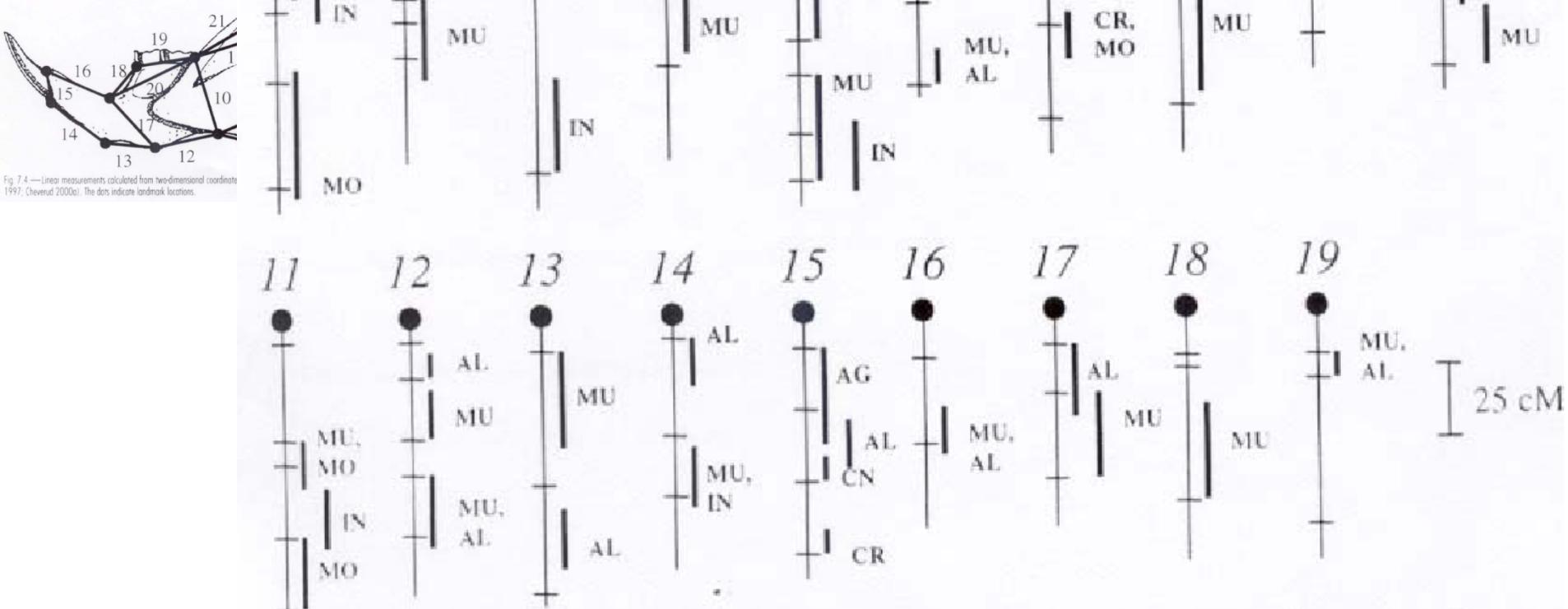


Fig. 7.5.—Genetic map positions of QTLs affecting mandibular morphology shown with 95% confidence regions. CR indicates that the QTL affects the coronoid process; CN, the condyloid process; AG, the angular process; MU, all the muscle attachment regions of the ascending ramus; IN, the incisor alveolus; MO, the molar alveolus; and AL, the total alveolar region. The dashed region on chromosome 2 indicates a region that was not sufficiently mapped in the first F_2 intercross to allow precise QTL placement. (After Cheverud 2000a.)

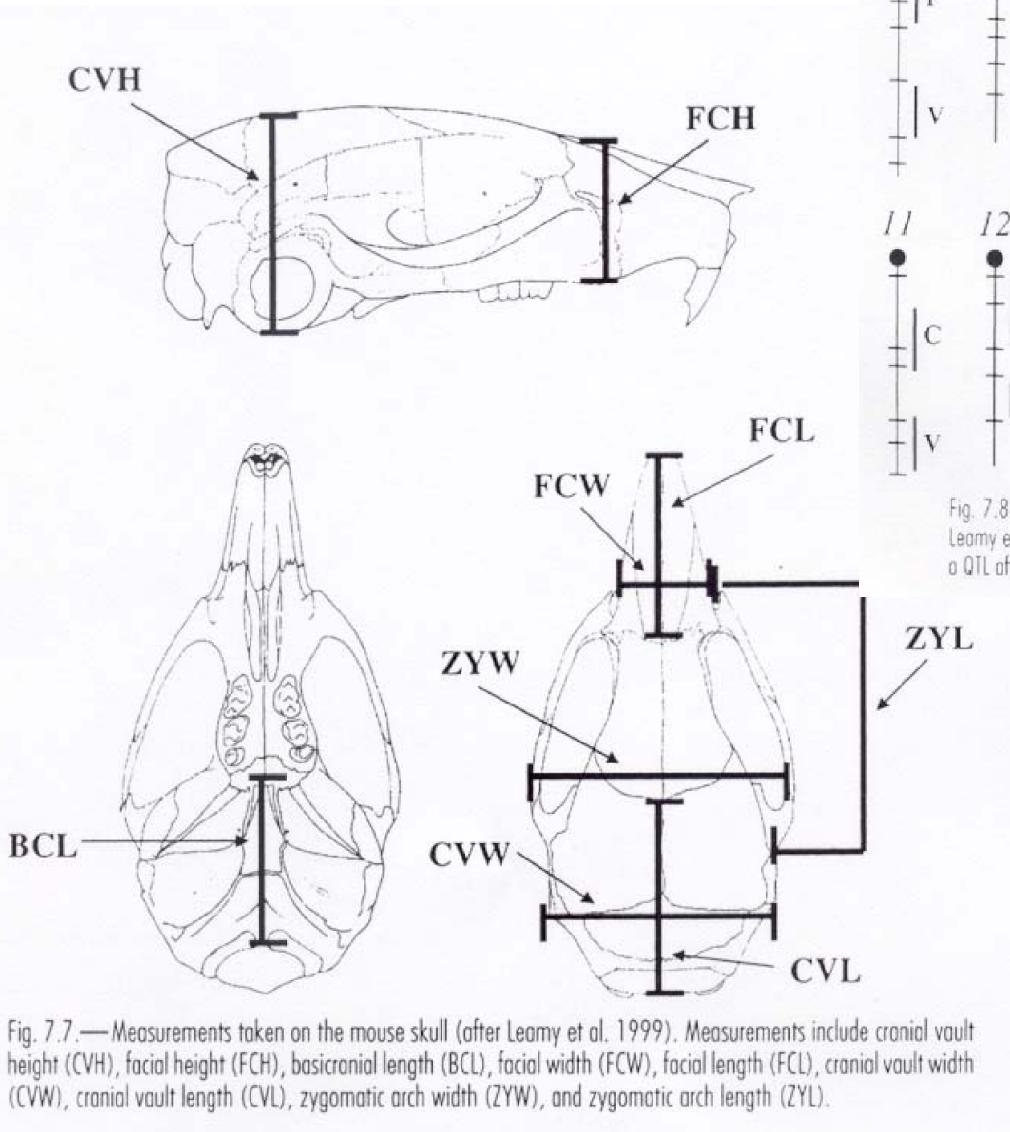


Fig. 7.7.—Measurements taken on the mouse skull (after Leamy et al. 1999). Measurements include cranial vault height (CVH), facial height (FCH), basicranial length (BCL), facial width (FCW), facial length (FCL), cranial vault width (CVW), cranial vault length (CVL), zygomatic arch width (ZYW), and zygomatic arch length (ZYL).

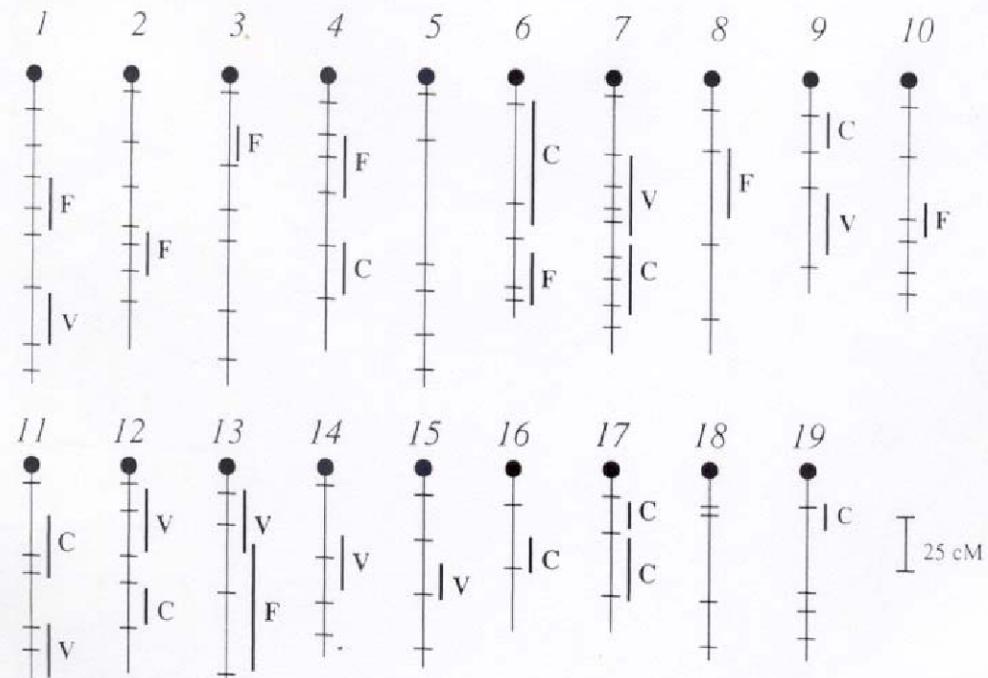


Fig. 7.8.—Genetic map positions of QTLs affecting cranial morphology shown with 95% confidence regions (after Leamy et al. 1999). A 'C' indicates a QTL affecting the whole cranium, 'V' a QTL affecting the cranial vault, and 'F' a QTL affecting the face.

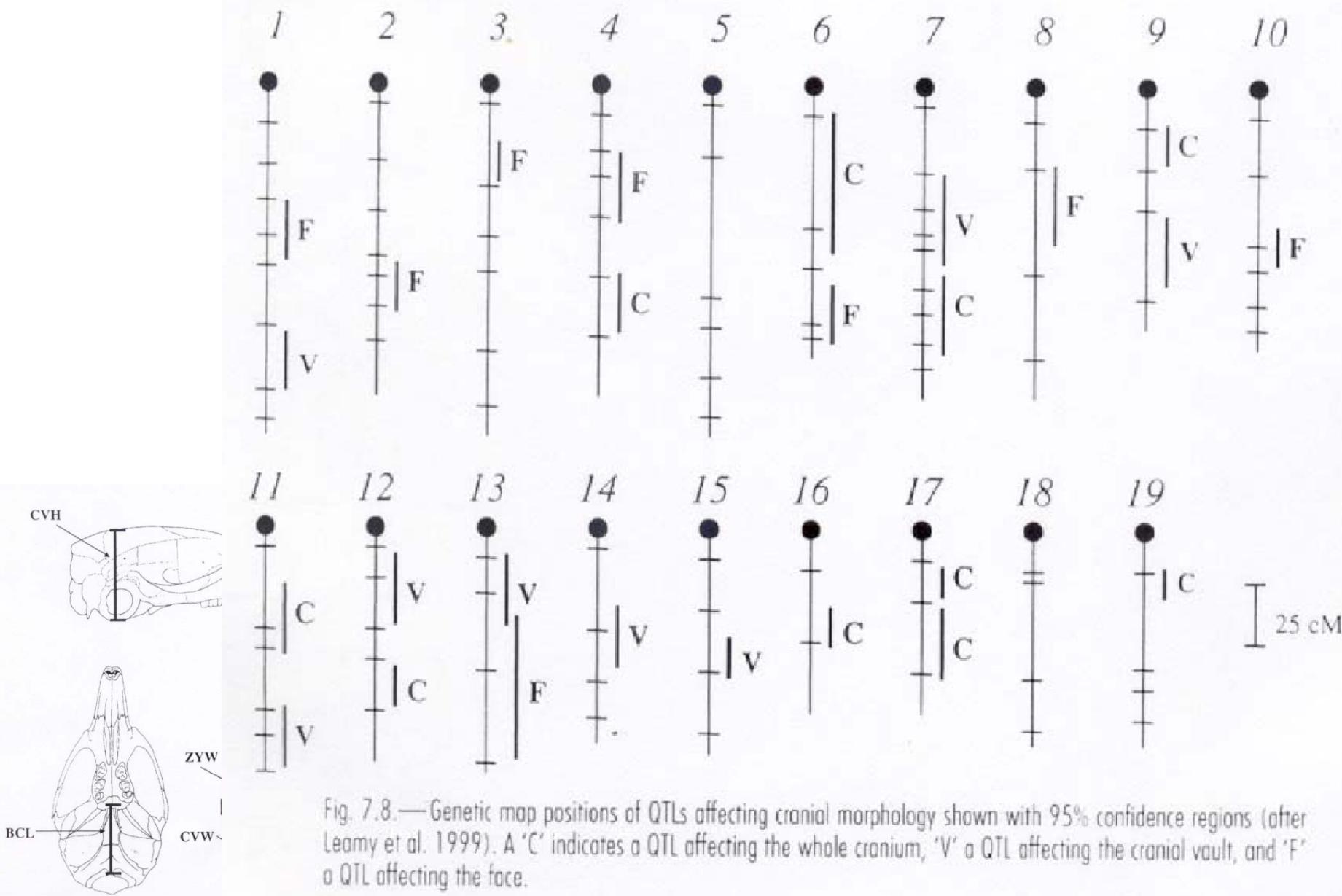


Fig. 7.7.—Measurements taken on the mouse skull (after Leamy et al. 1977). Measurements include cranial vault height (CVH), facial height (FCH), basicranial length (BCL), facial width (FCW), facial length (FL), cranial vault width (CVW), cranial vault length (CVL), zygomatic arch width (ZYW), and zygomatic arch length (ZYL).

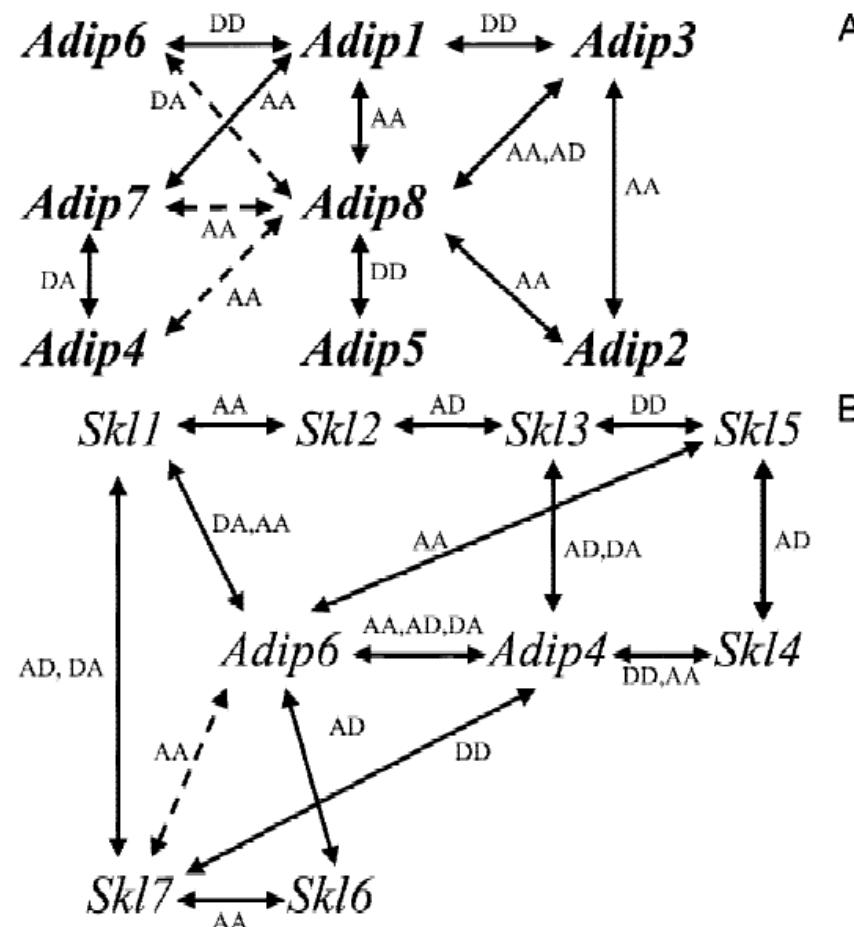


Fig. 2. Epistatic interaction patterns for adiposity (A) and tail length (B). Double-headed arrows indicate epistatic interactions labeled as additive by additive (AA), additive by dominance (AD), dominance by additive (DA), and/or dominance by dominance (DD) epistasis. Dashed lines indicate interactions significant at the 10% level, but not at the 5% level. *Adip4* and *Adip6* also have effects on tail length, and epistasis for these effects is portrayed in 2B.

Quantitative Trait Loci for Maternal Performance for Offspring Survival in Mice

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QTL for Matern

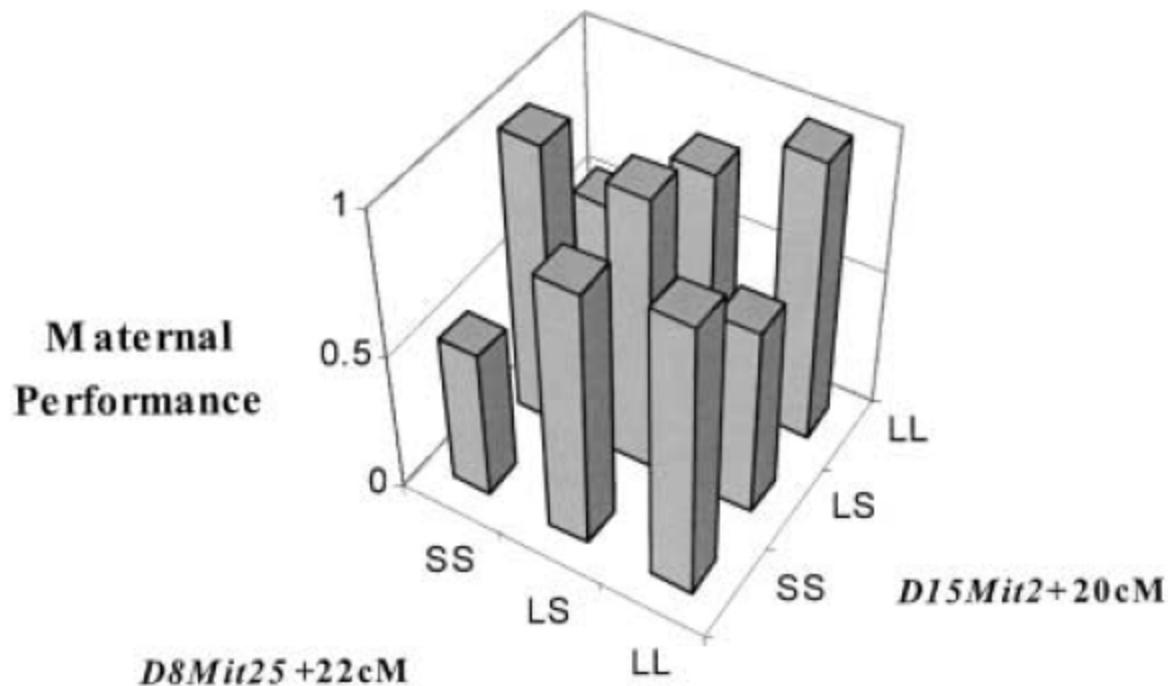


FIGURE 6.—Maternal performance genotypic values for the two-locus genotype at *D8Mit25 + 22 cM* and *D15Mit2 + 20 cM* illustrates additive-by-dominance interaction.

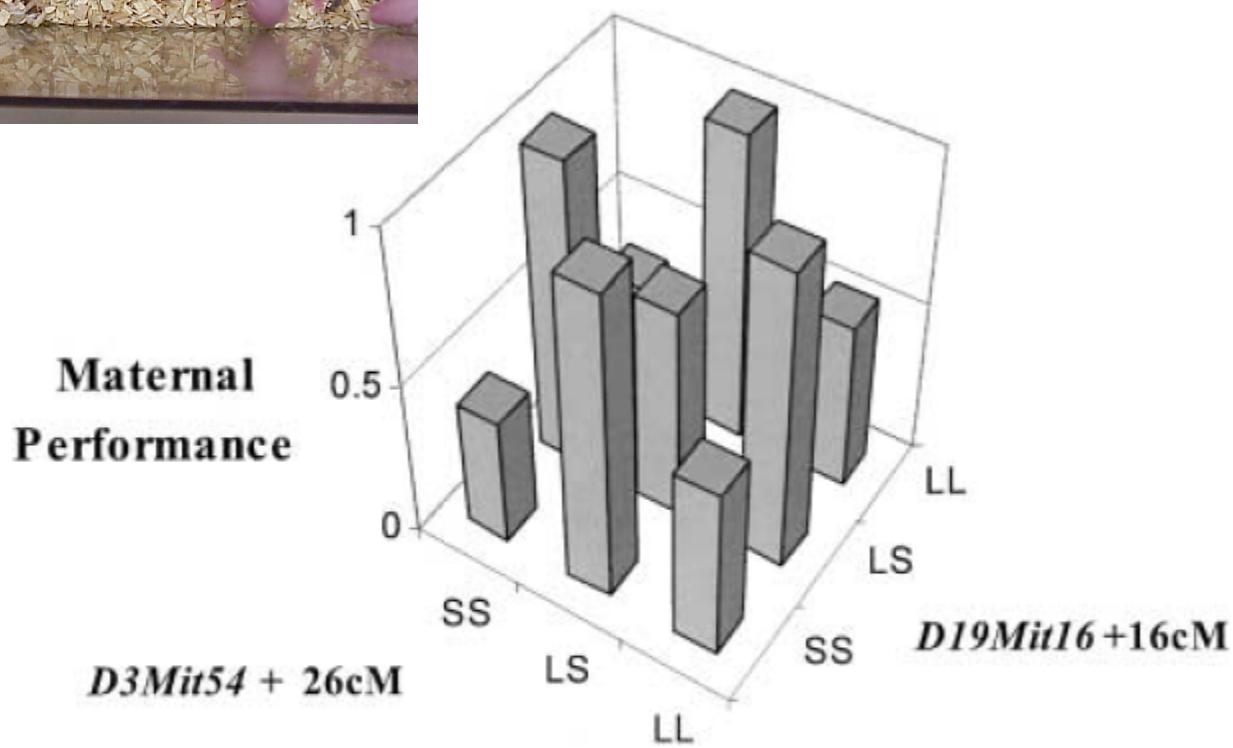


FIGURE 7.—Dominance-by-dominance interaction between *D3Mit54* + 26 cM and *D19Mit16* + 16 cM.

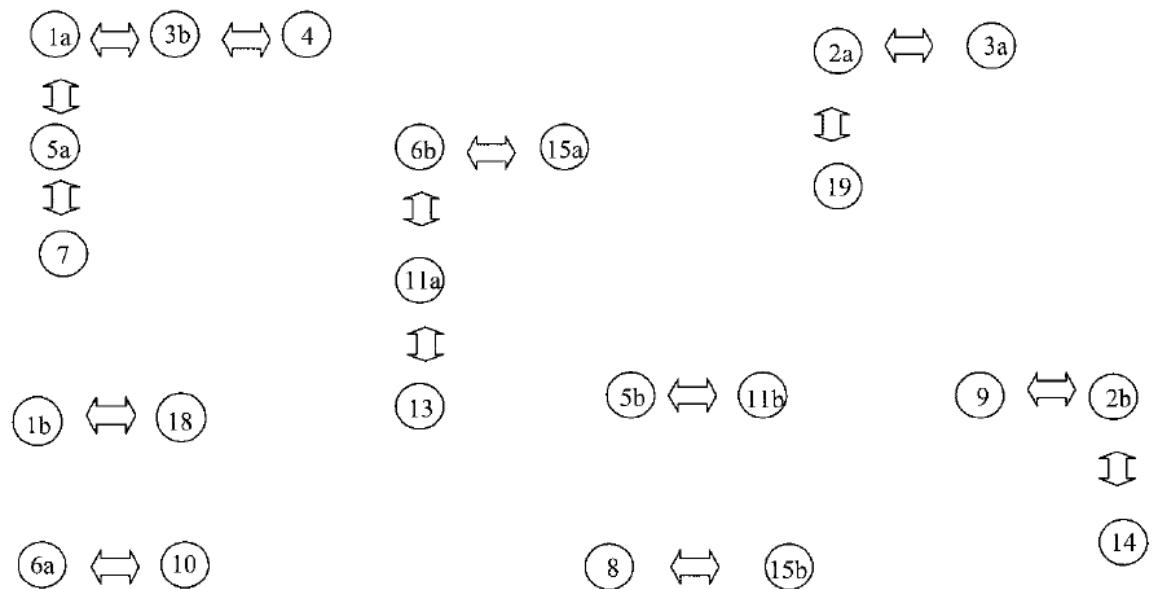


FIGURE 4.—Epistatic interaction patterns for maternal performance. QTL are represented by respective chromosome number or by chromosome number and a letter when more than one QTL occurred in the same chromosome. QTL 1a refers to *D1Mit3*, 1b to *D1Mit14*, 2a to *D2Mit1*, 2b to both *D2Mit38* and *D2Mit17*, 3a to *D3Mit54*, 3b to *D3Mit194*, 5a to *D5Mit61*, 5b to *D5Mit26*, 6a to *D6Mit1*, 6b to both *D6Mit58* and *D6Mit5*, 11a to *D11Mit15*, 11b to *D11Mit333*, 15a to *D15Mit5*, and 15b to *D15Mit2*. For other chromosomes, check Table 2.

Busca de genes candidatos

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TABLE 4
Potential candidate genes for QTL interacting epistatically

QTL	Position (cM)	Candidate gene	Gene name	Position (cM)	Phenotype	References
<i>D1Mit14</i>	78	<i>Htr5b</i>	5-Hydroxytryptamine (serotonin) receptor 5B	63	Anxiety and depression	CLEMENT <i>et al.</i> (1996)
<i>D2Mit380</i>	72	<i>Slc30a4</i>	Solute carrier family 30 (zinc transporter), member 4	69	Lethal milk	DICKIE (1969)
<i>D2Mit1</i>	38	<i>Dbh</i>	Dopamine β -hydroxylase	15.5	Lack of placentophagia/lactation problems	THOMAS and PALMITER (1997)
<i>D3Mit54</i>	0	<i>Crh</i>	Corticotropin-releasing hormone	8	Abnormal maternal behavior	PEDERSEN <i>et al.</i> (1991)
<i>D6Mit1</i>	20	<i>Mest</i>	Mesoderm-specific transcript	7.5	Lack of placentophagia/poor nest	LEFEBVRE <i>et al.</i> (1998)
		<i>Ghrhr</i>	Growth hormone releasing hormone receptor	26	Failure to nurse first litters	EICHER and BEAMER (1976)
<i>D7Nds1</i>	40	<i>Herc2</i>	Hect [homologous to the E6-AP (UBE3A) carboxyl terminus] domain and RCC1 (CHC1)-like domain (RLD) 2	27	Abnormal maternal behavior	LEHMAN <i>et al.</i> (1998)
<i>D8Mit25</i>	44	<i>Slc6a2</i>	Solute carrier family 6 (neurotransmitter transporter, noradrenalin), member 2	45	Complex behavior traits	FRITZ <i>et al.</i> (1998)
<i>D9Mit4</i>	28	<i>Foxb1b</i> (<i>Mf3</i>)	Forkhead box B1b	41	Lactation problems	LABOSKY <i>et al.</i> (1997)
<i>D11Mit15</i>	66	<i>Crhr</i>	Corticotropin-releasing hormone receptor	62	Abnormal maternal behavior	PEDERSEN <i>et al.</i> (1991)
<i>D13Mit115</i>	38	<i>Prl</i>	Prolactin	14	Abnormal maternal behavior	LUCAS <i>et al.</i> (1998)
<i>D15Mit15</i>	22	<i>Prlr</i>	Prolactin receptor	4.6	Abnormal maternal behavior	LUCAS <i>et al.</i> (1998)
<i>D18Mit51</i>	28	<i>CamK2a</i>	Calcium/calmodulin-dependent protein kinase II α	33	Aggressive behavior	CHEN <i>et al.</i> (1994)

Arquitetura genética complexa

Vários genes, a maioria de pequeno efeito (menos ou até 1 desvio padrão)

Muita pleiotropia

Diversos graus de aditividade e dominância

Muita epistasia

Problemas e perspectivas

QTL's são uma subestimativa (2 QTL's próximos contam como 1; + x – cancelam o efeito)

Limite de resolução = 20 cM (ou 20.000.000 bp em humanos ou 40.000.000 em camundongos ou 10.000.000 em Drosophila)

QTL identificado é um segmento do cromossomo (pode conter vários loci) – mapeamento fino chega-se à 3 cM

Genes candidatos e clonagem de posição

Módulos

Mapa Genotípico-Fenotípico

ADAPTATION AND EVOLVABILITY

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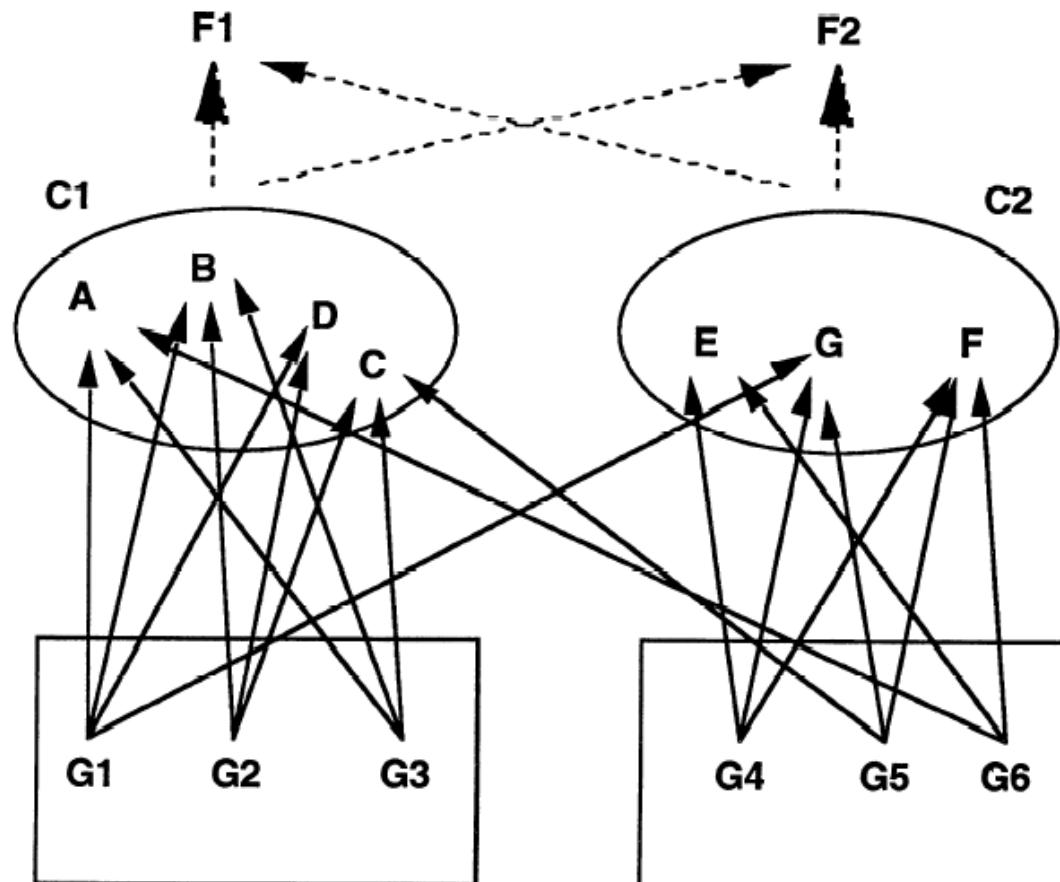


FIG. 1. Example of a modular representation of the character complexes $C_1 = \{A, B, C, D\}$ and $C_2 = \{E, F, G\}$ which serve to functions F_1 and F_2 . Each character complex has a primary function, F_1 for C_1 and F_2 for C_2 . Only weak influences exist of C_1 on F_2 and vice versa. The genetic representation is modular because the pleiotropic effects of the genes $M_1 = \{G_1, G_2, G_3\}$ have primarily pleiotropic effects on the characters in C_1 and $M_2 = \{G_4, G_5, G_6\}$ on the characters in complex C_2 . There are more pleiotropic effects on the characters within each complex than between them.

Evolução da modularidade – Note que o conceito de módulos se aplica a vários níveis na hierarquia biológica (do molecular ao organismal)

ADAPTATION AND EVOLVABILITY

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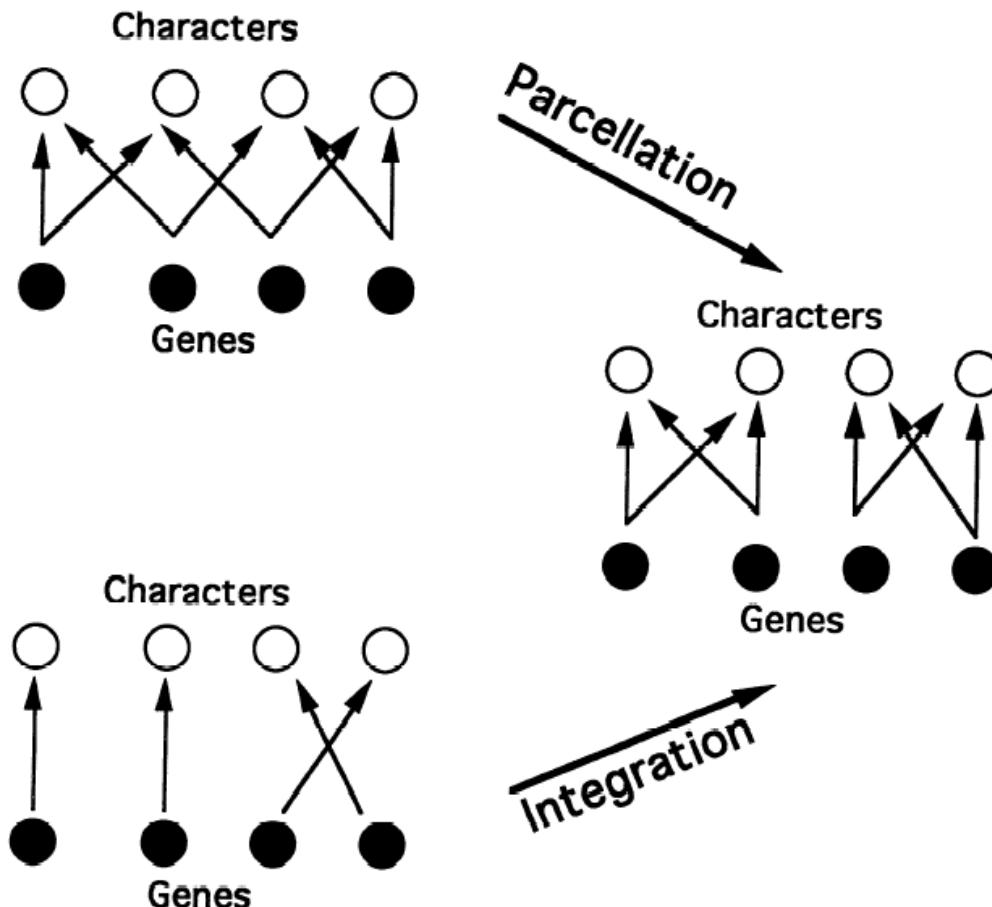
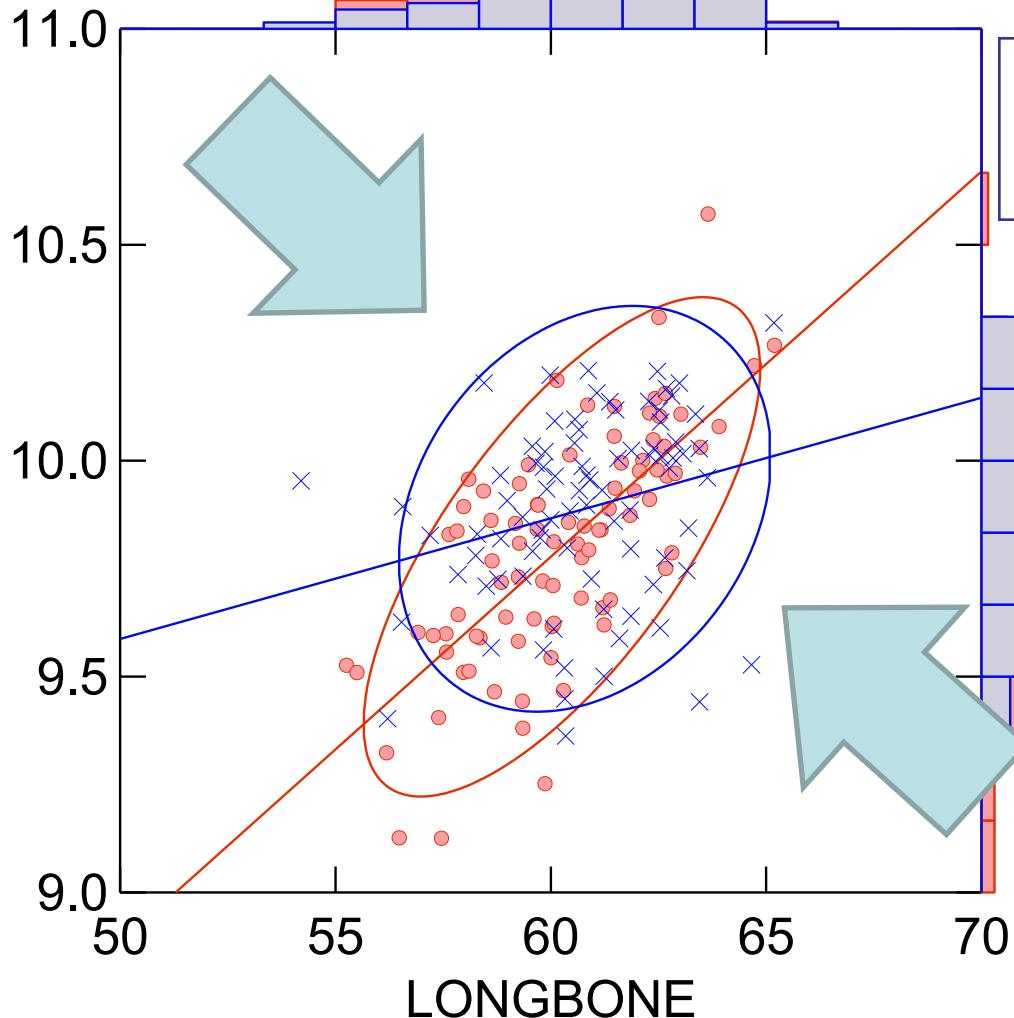


FIG. 2. Two ways of obtaining modularity. Parcellation consists of a differential suppression of pleiotropic effects between groups of characters. Modularity through integration consists in the selective acquisition of pleiotropy among characters from the same group.

C

NEURWDSUP



• $R = 0.711$; 50.5% of all variation in braincase width explained by “body size”

• $R = 0.257$; 6 % of all variation in braincase width explained by “body size”

Chr 2.2 / 3.1 genotype

- LLSS
- SSSL

Equality of variances tests between the two genotypes on Longbone non-significant and for NeurWdSup barely – $P = 0.047$

Offspring height

20

10

0

-10

-20

Mid-parent weight

-30

-20

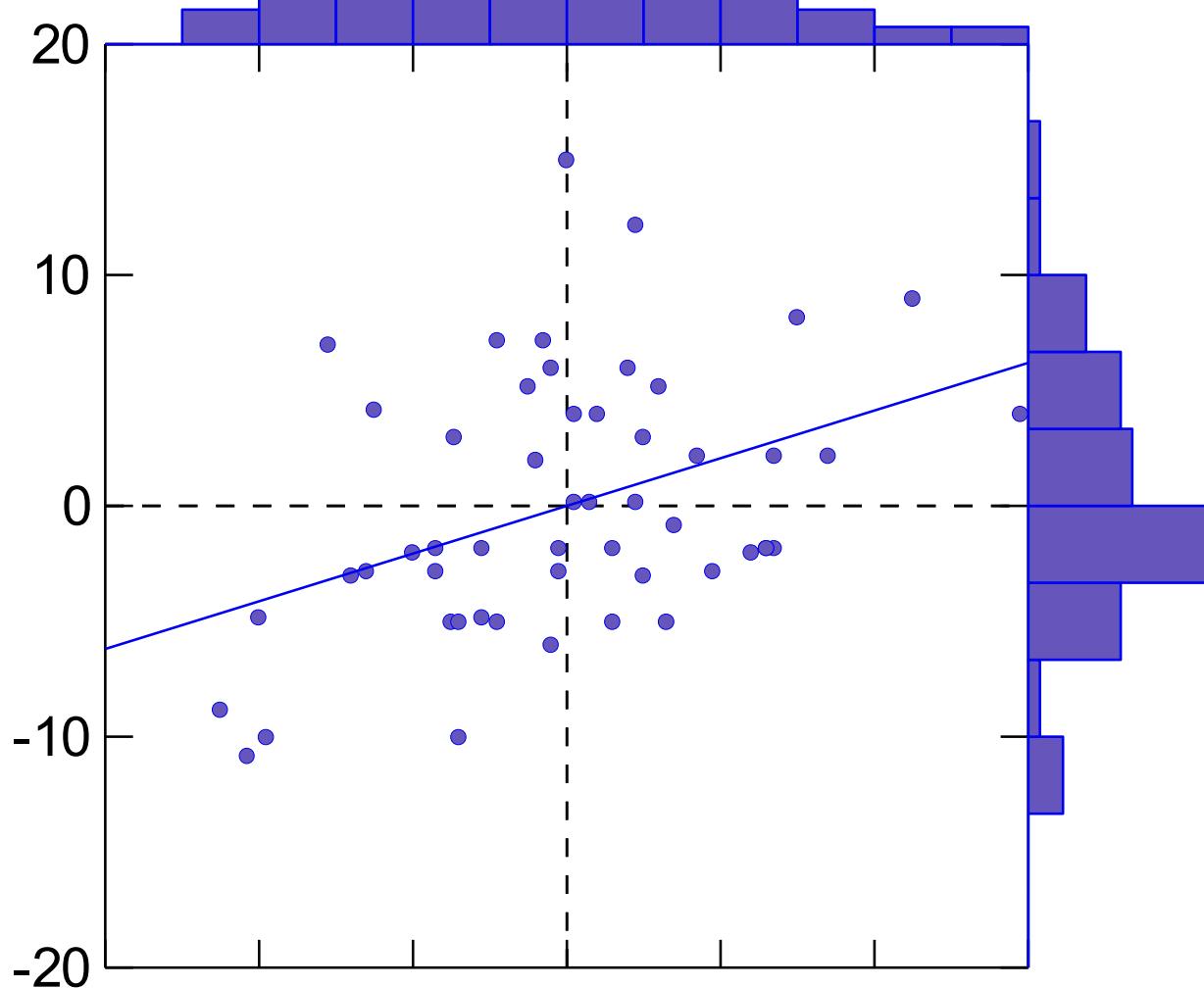
-10

0

10

20

30



Genetic Correlation

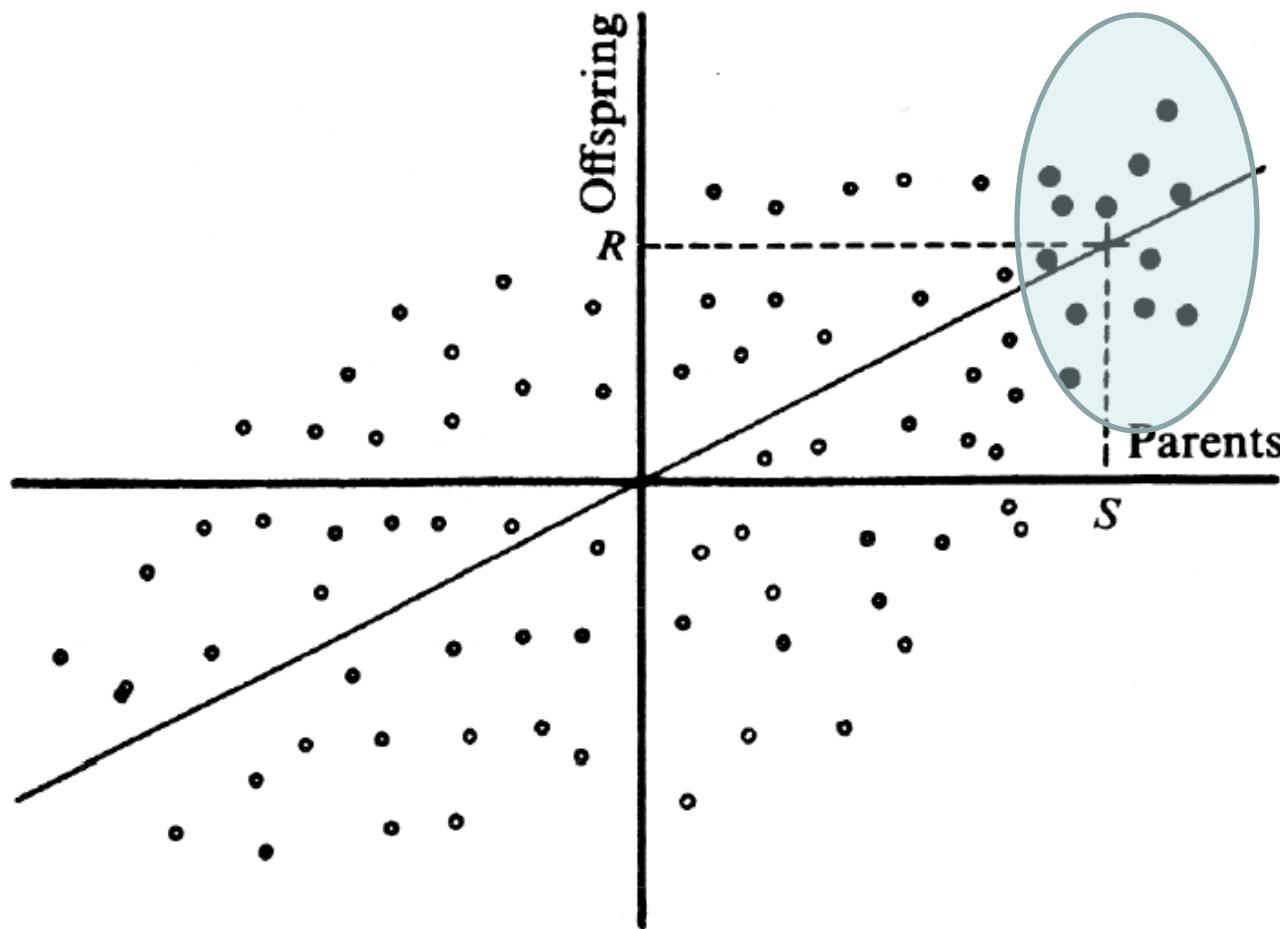


Fig. 11.1. Diagrammatic representation of the mean values of progeny plotted against the mid-parent values, to illustrate the response to selection, as explained in the text.