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Investigations on Inheritance of Quantitative Characters in Animals by Gene Markers I. Methods

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Summary. The method described uses monogenic inherited characters as markers by which the transmission of homologous chromosome sections from parents to progeny can be controlled. The procedure then attributes effects on continuously varying characters to marked chromosome sections. It allows the mapping of effects having a share in quantitative characters in natural or breeding populations.

Many characters of organisms show a continuous variation in the progeny of specific parents. The analysis of these characters, called "metric" or "quantitative", led to the use of biometric methods which assume that the variation is caused by the effects of several gene loci, by environmental influences as well as by genotype-environment interactions. Accordingly, the continuous variation includes individual discontinuities caused by Mendelian genes. In some cases this discontinuous part of the variable can be revealed when segregation of chromosome sections can be observed.

The transmission of chromosomes from parents to progeny can be assessed by means of gene markers (Thoday 1961). The offspring of a diploid parent - considering a heterozygous marker locus - may be subdivided into two classes, one class of progeny receiving one allele while the other class receives the other. If genes for a metric trait are linked to the marker locus and the parent has alleles with differential effects, it is highly probable that the two classes also differ in this trait. When there is no crossing-over between the marker locus and the gene(s) for the metric character, each of the two classes will be homogeneous for that specific character. On the other hand, if within a class of progeny crossing-over occurs between loci for a metric trait and the gene marker, a heterogeneous distribution of the values for the corresponding character is expected within the two classes of progeny.

Assessment of the gene effects of a metric trait linked to individual marker loci therefore allows an evaluation of the number of marked chromosome sections showing different effects in the parents considered. Beyond this, statements can be made on the kind of such effects, on the position of the genes for quantitative characters in the chromosomes, as well as on the frequencies of the alleles concerned. Finally, from the allele combinations of marker genes in an individual, conclusions can be drawn on the combination of gene effects based on a metric character. As soon as polygenic characters can be reduced to the effects of chromosome sections, a valuable instrument is available to solve some problems of quantitative genetics. In this way, a better understanding of the structure of polygenic systems, as well as their ability to be modified in natural or breeding populations, is offered.

The main limitations to judgements on the individual effects of polygenic characters lie in the availability of numerous gene markers and in the description of their phenotypes. Many of the macromolecules in vertebrates appear in qualitatively different forms which are inherited monogenically (review s. Lewontin 1973). However, the number of markers which can be demonstrated at present is seriously restricted by the methodical efforts necessary to identify the corresponding phenotypes in large numbers of individuals. The chemical or serological methods generally used to find these phenotypes require considerable expenditure. A further limitation is the extent of the effect on a metric character, linked to a marker locus, in connection with the size of the random samples which can be included. To what extent the limitations mentioned become effective or can be modified still remains to be investigated.

Selection of the model

Previous models for the analysis of quantitative characters (e.g. Elston and Stewart 1973, Forkmann 1974, Gilmour and Morton 1971a and b, Jana 1972, Jana and

Seyffert 1971, Morton 1973, Seyffert 1966, Stewart 1969, Stewart and Elston 1973) take into account situations involving a considerable number of progeny, a limited number of marker loci or examine the quantitative effect of identified gene loci. The model described here should be used for animals with only small groups of offspring per parent, and should allow the inclusion of several marker loci at the same time. Under these conditions, the model selected should be as simple as possible and, therefore, limited to the main effects. The procedure is based on the following considerations:

a) Quantitative characters are calculated assuming a defined environment.

After measuring the metric characters for many individuals under different influences of environment, corrections are made based on the assumption of a defined environment.

b) The animal data come from families in which several offspring need to be covered for one parent only.

For example there are fathers with several offsprings, whereas there is only one offspring per mother.

c) The degree of linkage among the marker genes themselves should not affect the results.

In case of linkage of two marker genes, the method should be able to distribute ascertained relations of a quantitative character to both loci.

d) A marker allele represents a specific homologous chromosome section during its transfer from parents to progeny.

There is a probability of representation of a chromosome section by a marker locus, which depends on the distance between marker gene and the gene(s) for a metric character.

e) The model should be applicable to minimal numbers of animals.

The smaller the random sample the greater the effect on a quantitative character must be, to verify it as linked to a marker gene. However, considerable effort is involved in finding adequate animals, as well as in determining several marker genes in these animals. As one aim of the analyses is their continuous use in practical animal breeding, it can be expected that large numbers of animals will be obtained later, if the analyses have proved to be advantageous. Larger numbers of animals guarantee a greater efficiency for the method of evaluation.

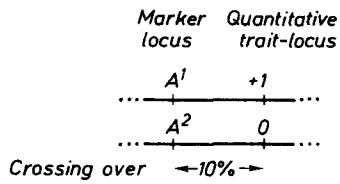

Fig. 1. Hypothetical example for coupling of a marker locus and a character affecting locus. One chromosome contains allele A^1 at the marker locus and an effect +1 at the locus affecting the character, the homologous chromosome contains the allele A^2 coupled with an effect 0

Genetic effects assessable by marked chromosome section

It is assumed that a marker allele represents a section of a chromosome when its transmission from parent to progeny is noted. Then an allele substitution of the marker gene also denotes a substitution of the chromosome section concerned. The aim of this study is to estimate quantitatively the effects of substitution of a chromosome section on the metric phenotypes within a progeny.

Crossing over effects

It can be expected that few of the marker genes themselves influence the metric trait considered. However a marker gene can be linked to one or several loci, the alleles of which influence the development of a distinct quantitative trait. If only one segregating locus for a quantitative trait (quantitative-trait-locus, QTL) is linked to a marker locus, the relations shown in Fig. 1 can be observed for a region of the two homologous chromosomes. In that example, the allele A^1 of the marker gene is coupled to an allele of a QTL which improves the trait value towards +1, opposite to the homologous chromosome section with the allele A^2. Assuming a crossover portion of 10%, 90% of the progeny with the allele A^1 receive the trait value +1, whereas 10% have a trait value of 0. Therefore, assuming additive inheritance, a chromosome section obtains on average a trait value of 0.9 in all progeny with allele A^1, whereas the progeny containing allele A^2 shows a trait average of 0.1. The difference in average trait values between the progeny classes with marker alleles A^1 and A^2, respectively, reduces with increasing crossover frequency between marker locus and QTL. Simultaneously the variance within a progeny class increases (Fig. 2).

If multiple alleles appear at a QTL, or if several QTL's are linked to a marker locus, positively effective alleles at QTL may be placed on both homologous chro-

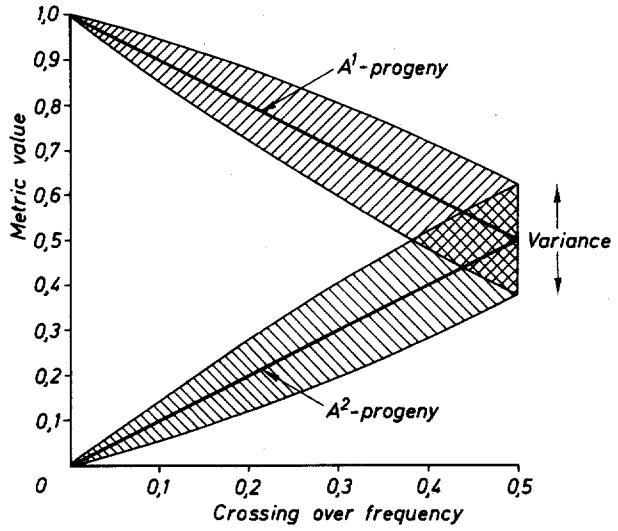

Fig.2. Average trait values and variances of progeny classes with marker alleles A^1 and A^2 as a function of crossing-over between marker locus and quantitative-trait-locus. Conditions from Fig.1 are used with alternating crossover portions. Effects from other loci on the metric trait are neglected

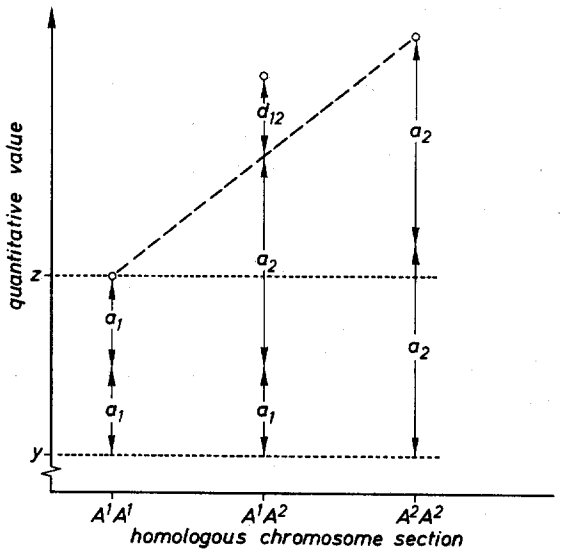

Fig.3. Additive and non-additive effects of a pair of homologous chromosome sections

mosome sections of a parent. Then, measuring the efficiency of individual homologous chromosome sections within the progeny, parts of the effects are neutralized. There remains, as a measurable quantity, the difference of effects between the homologous chromosome sections of a parent ("netto effect").

Intra-action of a chromosome section

The marker gene proceeding described here measures differing effects of homologous chromosome sections of a parent on the development of a quantitative trait within its progeny. It does not identify the loci of quantitative traits, if these are not the marker genes themselves, but attributes all effects on metric traits to the marker loci. Therefore, in the following, the effects of a chromosome section measureable at a marker locus are characterized with the symbol of the marker gene.

Characterizing the effect of a pair of parental homologous chromosome sections, marked with A^1 and A^2, on a quantitative value of a descendant, additive components (a_1 and a_2) can be differentiated from non-additive ones (d_{12}) as shown in Fig.3. If the sections i and j exist, intraactions produce the following phenotype effects:

Genotype	Phenotype value	
	Additive effect (a)	Non-additive effect (d)
A^iA^j	$a_i + a_j$	$i \neq j: d_{ij}$

If one parent, e.g. the father, is heterozygous for the section under consideration, the phenotypes of the offspring can be influenced by the different effects of the two chromosome sections (Table 1). This influence depends on the mothers' genotype. With known maternal genotypes and several descendants per mating type, the average phenotype of A^1- and A^2- progeny within every mating type can be obtained, i.e. within every row of Table 1. Comparing the degree of development of the metric character for the mating types, the variables a_i and d_{ij} can be determined. Where the female genotypes are unknown or there is only one offspring per mother, assumptions from population genetics must be made. As female genotypes for a chromosome section,

$$A^iA^j;\ i = 1,2,\ldots,K;\ j \geqslant i \leqslant K$$

are supposed, with the additive effects a_i, the non-additive genotype effects d_{ij} für $i \neq j$, the section frequencies p_i and genotype frequencies in Hardy-Weinberg equilibrium. K denotes the number of different chromosome sections in the mothers.

Descendants with the chromosome section A^1 from the father show, according to Table 1, if K = 3 and mothers are selected as a random sample, the following average phenotypes:

$$D_1 = 2p_1a_1 + p_2a_1 + p_2a_2 + p_3a_1 + p_3a_3 + p_2d_{12} + p_3d_{13} \quad (1)$$

The offspring with the section A^2 then has

$$D_2 = p_1a_1 + p_1a_2 + 2p_2a_2 + p_3a_2 + p_3a_3 + p_1d_{12} + p_3d_{23} \quad (2)$$

The difference between the average of both groups of offspring is:

$$D = D_1 - D_2 = a_1 - a_2 + d_{12}(p_2 - p_1) + p_3(d_{13} - d_{23}) \quad (3)$$

If K chromosome sections are assumed for mothers that difference becomes:

$$D = a_1 - a_2 + d_{12}(p_2 - p_1) + \sum_{i>2}^{K} p_i(d_{1i} - d_{2i}) \quad (4)$$

An equivalent expression emerges if the differences of phenotypes between the offspring and their mothers are registered for each mating type. In Table 1 the average differences of phenotypes for all offspring with A^1 and A^2, respectively, are calculated, taking 3 different sections as example. The values for the two groups of offspring can be compared and the result is:

$$D = D_1 - D_2 = a_1 - a_2 + d_{12}\left(p_2^2 - p_1^2 + p_2p_3 - p_1p_3\right)$$
$$+ p_1p_3(d_{13} - d_{23}) + p_2p_3(d_{13} - d_{23}) + p_3^2(d_{13} - d_{23})$$
$$= a_1 - a_2 + d_{12}(p_2 - p_1) + p_3(d_{13} - d_{23})$$

This difference corresponds to that of formula (3), and the general formula (4) is also valid in this case.

Interactions between chromosome sections

Interactions between chromosome sections marked by monogenic traits can be similarly calculated as for gene interactions (Deakin 1973, Jana 1971). The effects on a quantitative character caused by the interactions of two chromosome sections can be derived from the gametic types of the parents. If two types appear for each of the two chromosome sections, four different gametes can be formed. Table 2 reproduces the possible interaction coefficients, w_{ij}, combining four gametes in the parents. It can be assumed that

$w_{ij} = w_{ji}$ and

$w_{14} = w_{23}$,

Table 1. Effects of the male

Mothers		
Genotypes	Frequencies	Phenotype values (1)
A^1A^1	p_1^2	$y+2a_1$
A^1A^2	$2p_1p_2$	$y+a_1+a_2+d_{12}$
A^1A^3	$2p_1p_3$	$y+a_1+a_3+d_{13}$
A^2A^2	p_2^2	$y+2a_2$
A^2A^3	$2p_2p_3$	$y+a_2+a_3+d_{23}$
A^3A^3	p_3^2	$y+2a_3$
Total products of frequencies and phenotypes	for 3 chromosome sections	$y + 2p_1a_1 + 2p_2a_2 + 2p_3a_3 + 2p_1p_2d_{12} + 2p_1p_3d_{13} + 2p_2p_3d_{23}$
	for K chromosome sections	$y + 2\sum_{i=1}^{K} p_ia_i + 2\sum_{i<j}^{K} p_ip_jd_{ij}$

homologous chromosome section A^1 or A^2 on additive and dominant phenotype values among the progeny

Offspring with A^1				Offspring with A^2				Difference
Genotypes	Frequencies	Phenotype values (2)	Phenotype difference progeny - mother (3)	Genotypes	Frequencies	Phenotype values (4)	Phenotype difference progeny - mother (5)	(3) - (5) or (4) - (2) (6)
A^1A^1	p_1^2	$y+2a_1$	0	A^1A^2	p_1^2	$y+a_1+a_2+d_{12}$	$a_2-a_1-d_{12}$	$a_1-a_2+d_{12}$
A^1A^1	p_1p_2	$y+2a_1$	$a_1-a_2-d_{12}$	A^1A^2	p_1p_2	$y+a_1+a_2+d_{12}$	0	$a_1-a_2-d_{12}$
A^1A^2	p_1p_2	$y+a_1+a_2+d_{12}$	0	A^2A^2	p_1p_2	$y+2a_2$	$a_2-a_1-d_{12}$	$a_1-a_2+d_{12}$
A^1A^1	p_1p_3	$y+2a_1$	$a_1-a_3-d_{13}$	A^1A^2	p_1p_3	$y+a_1+a_2+d_{12}$	$a_2-a_3+d_{12}-d_{13}$	$a_1-a_2-d_{12}$
A^1A^3	p_1p_3	$y+a_1+a_3+d_{13}$	0	A^2A^3	p_1p_3	$y+a_2+a_3+d_{23}$	$a_2-a_1+d_{23}-d_{13}$	$a_1-a_2+d_{13}-d_{23}$
A^1A^2	p_2^2	$y+a_1+a_2+d_{12}$	$a_1-a_2+d_{12}$	A^2A^2	p_2^2	$y+2a_2$	0	$a_1-a_2+d_{12}$
A^1A^2	p_2p_3	$y+a_1+a_2+d_{12}$	$a_1-a_3+d_{12}-d_{23}$	A^2A^2	p_2p_3	$y+2a_2$	$a_2-a_3-d_{23}$	$a_1-a_2+d_{12}$
A^1A^3	p_2p_3	$y+a_1+a_3+d_{13}$	$a_1-a_2+d_{13}-d_{23}$	A^2A^3	p_2p_3	$y+a_2+a_3+d_{23}$	0	$a_1-a_2+d_{13}-d_{23}$
A^1A^3	p_3^2	$y+a_1+a_3+d_{13}$	$a_1-a_3+d_{13}$	A^2A^3	p_3^2	$y+a_2+a_3+d_{23}$	$a_2-a_3+d_{23}$	$a_1-a_2+d_{13}-d_{23}$

$$y+(1+p_1)a_1+p_2a_2+p_3a_3+p_2d_{12}+p_3d_{13}$$

$$y+a_1+\sum_{i=1}^{K}\left[p_ia_i+\sum_{i\neq 1}^{K}p_id_{1i}\right]$$

$$a_1-p_2a_2-p_3a_3-d_{12}\left(p_1p_2-p_2^2\right)-d_{13}\left(p_1p_3-p_3^2\right)-2p_2p_3d_{23}$$

$$a_1+\sum_{i\neq 1}^{K}\left[p_ia_i+\left(p_i^2-p_1p_i\right)d_{1i}\right]-2\sum_{\substack{i<j\\ i\neq 1}}^{K}p_ip_jd_{ij}$$

$$y+(1+p_2)a_2+p_1a_1+p_3a_3+p_1d_{12}+p_3d_{23}$$

$$y+a_2+\sum_{i=1}^{K}\left[p_ia_i+\sum_{i\neq 2}^{K}p_id_{2i}\right]$$

$$a_2-p_1a_1-p_3a_3-d_{12}\left(p_1p_2-p_1^2\right)-d_{23}\left(p_2p_3-p_3^2\right)-2p_1p_3d_{13}$$

$$a_2+\sum_{i\neq 2}^{K}\left[p_ia_i+\left(p_i^2-p_2p_i\right)d_{2i}\right]-2\sum_{\substack{i<j\\ i\neq 2}}^{K}p_ip_jd_{ij}$$

$$a_1-a_2+d_{12}(p_2-p_1)+d_{13}p_3-d_{23}p_3$$

$$a_1-a_2+d_{12}(p_2-p_1)+\sum_{i\geq 2}^{K}p_i(d_{1i}-d_{2i})$$

Table 2. Coefficients of interaction between chromosome sections p_1, p_2 means frequencies of types A^1 and A^2 of chromosome section A and q_1, q_2 means frequencies of B^1 and B^2 of B

Mothers		Offspring with male gamete types				Difference
Gamete types	Frequencies	A^1B^1 (1)	A^1B^2 (2)	A^2B^1 (3)	A^2B^2 (4)	(1) - (2) - (3) + (4)
A^1B^1	p_1q_1	w_{11}	w_{12}	w_{13}	w_{14}	E_1
A^1B^2	p_1q_2	w_{21}	w_{22}	w_{23}	w_{24}	E_2
A^2B^1	p_2q_1	w_{31}	w_{32}	w_{33}	w_{34}	E_3
A^2B^2	p_2q_2	w_{41}	w_{42}	w_{43}	w_{44}	E_4
Total products of frequencies and coefficients of interaction		w_1	w_2	w_3	w_4	E

i.e., at the most, only 9 of the 16 coefficients are different. The differences E_1, E_2, E_3 and E_4 correspond to the "coefficients of epistasis" first introduced by Fisher (1918). E can be defined as epistasis coefficient between the male chromosome sections A and B in the population of mothers.

Known genotypes of both parents and large numbers of offspring for every mating type allow the estimation of w_{ij}. When the marker genotypes of one parent are unknown, the assessment must be restricted to an estimation of E and w_i.

Basis of comparison for the genetic effects

In accordance with Forkmann (1974), the value of the least active genotype is used as basis for the estimations. As shown in Fig.3, the scale point z represents the contributions of the genetic background y and of the least efficient chromosome section of the sections observed. An estimated value for z is supplied by mothers with the genotype A^1A^1 and their offsprings when they have received the section A^1 from their father.

If the mothers' marker genotypes are unknown, the difference between the double mean phenotype of all offspring with section A^1 (Column (2) in Table 1) and the phenotype mean of the mothers (Column (1) in Table 1) can be formed. With this difference, an approximate basic value z' can be obtained:

$$z' = y + 2a_1 + 2\left(\sum_{j\neq 1}^{K} p_j d_{1j} - \sum_{\substack{i<j \\ j=1}}^{K} p_i p_j d_{ij}\right) \qquad (5)$$

Model for the determination of the estimated values

To assess the effects of allele substitutions for several genes the following model can be used:

$$L(v) = \sum_{i=1}^{M}\left[F(v,i)\cdot S(i) + \sum_{j>i}^{M} F(v,i)\cdot F(v,j)\cdot E(i,j)\right] + \mu + \delta(v) \qquad (6)$$

v : (1,...,N); Number of the offspring

i : (1,...,M); Number of the marker locus

L(v) : Phenotype of the offspring v. As far as possible this value will be corrected for the influences of environment.

F(v,i) : Function for the marker allele transmission from parent to the offspring. The decision on whether one of the two alleles of a diploid genotype is transmitted can be made only for a heterozygous parent. Besides, this decision depends on the genotypes of the offspring and of its opposite parent. For example, in the case of intermediate inheritance, allele transmission can not be ascertained when one parent is heterozygous and when the offspring and the other parent have the same genotype as the first parent.

F(v,i) can show different values:

F(v,i) = 1 : Allele $A^1(i)$ was transmitted from parent to offspring.

F(v,i) = 0 : No transmission of a specific allele can be ascertained at gene locus i.

If probabilities for the transmission of $A^1(i)$ or $A^2(i)$ can be determined in this group, a value $\neq 0$ can be used. This is allowed when the marker locus does not show any intermediate or codominant inheritance or when conditions are known which cause a deviation from 1 : 1 transmission of the alleles $A^1(i)$ and $A^2(i)$ from a parent to the offspring.

$F(v,i) = -1$: Allele $A^2(i)$ was transmitted from parent to offspring.

$S(i)$: The substitution effect of a chromosome section connected to gene locus i.

$E(i,j)$: Coefficient of epistasis between the chromosome sections marked by the gene loci i and j.

: Mean of phenotype values within progeny of the mating types concerned. With unknown genotypes of one parent it can be obtained as arithmetical mean from the column (2) and (4) in Table 1:

$$\frac{1}{2}a_1 + \frac{1}{2}a_2 + \sum_{i=1}^{K} p_i a_i + d_{12}(p_1 + p_2) + \sum_{i>2}^{K} p_i(d_{1i} - d_{2i})$$

$\delta(v)$: Variable which indicates that part of the phenotype value of the offspring v can not be controlled.

Estimation of S(i)

Because of the large number of interaction variables, estimations of $E(i,j)$ can be carried out only when large numbers of animals are involved. Therefore, a preliminary estimation should not consider gene interactions. The approach then becomes

$$L(v) = \sum_{i=1}^{M} F(v,i) \cdot S(i) + \mu + \delta(v)$$

The method of Least Squares can be applied to the above expression; it then has to minimize the following function:

$$Q[S(1),\ldots,S(M);\mu = S(M+1)] = \sum_{v=1}^{N}\left[L(v) - \sum_{i=1}^{M} F(v,i) \cdot S(i) - \mu\right]^2 \qquad (8)$$

This leads to the equations of determination for $S(i)$ and μ (c.f. Appendix A) as follows:

$$\sum_{i=1}^{M+1} A(j,i) \cdot S(i) = B(j); \qquad (9)$$

$j : (1,\ldots,M+1)$

A and B are defined as:

$$A(j,i) = \sum_{v=1}^{N} F(v,j) \cdot F(v,i) = A(i,j);$$

$i,j : (1,\ldots,M)$

$$A(j,M+1) = A(M+1,j) = \sum_{v=1}^{N} F(v,j);$$

$j : (1,\ldots,M)$

$A(M+1,M+1) = N$

$S(M+1) = \mu$

$$B(j) = \sum_{v=1}^{N} L(v) \cdot F(v,j)$$

$$B(M+1) = \sum_{v=1}^{N} L(v)$$

The inverse matrix $A^{-1}(j,i)$ - in case it exists - is determined numerically and the estimated values for $S(i)$ result:

$$S(i) = \sum_{j=1}^{M+1} A^{-1}(i,j) \cdot B(j) \qquad (10)$$

This equation is valid if the mean $S(M+1)$ is determined within progeny of one parent from the animal data covered. However if that mean is known, the indices in matrix A need only run from 1 to M. From this smaller matrix the inversion - if it exists - can also be calculated and again termed $A^{-1}(j,i)$. The estimated values $S(i)$ can emerge as:

$$S(i) = \sum_{j=1}^{M} A^{-}1(j,i) \cdot [B(j) - A(j,M+1) \cdot \mu] \qquad (11)$$

This equation takes into account a potential linkage between marker genes, and does not count twice a quantitative value associated with linked markers.

Calculation of variance for the L(v)

The variance of phenotype values within the progeny of a parent, σ_μ^2, can be determined with relative precision in larger material, N':

$$\sigma_\mu^2 = \sum_{v=1}^{N'} \frac{(L(v) - \mu)^2}{N' - 1} \qquad (12)$$

If only the progeny N, examined for marker genes, is available for the calculation of σ_μ^2, formula (12) is used with N instead of N'.

Test for different assumptions

The significance in the model are tested under the hypothesis that S(i) = 0, i.e. that there are no effects.

S(i) = 0 for a fixed i and for a specific parent

If $\sigma(i)^2$ indicates the variance of S(i), the following emerges:

$$\sigma(i)^2 = \sum_{v=1}^{N} \left[\sum_{j=1}^{M} A^{-1}(i,j) \cdot F(v,j) \right]^2 \qquad (13)$$

This calculation is possible if, in the case of null hypothesis, the estimated values of S(i) are normally distributed. Then a mean of the estimated values S(i) equal 0 is expected and a value of S(i) becomes significant if

$$S(i) > r \cdot \sigma(i). \qquad (14)$$

The value of r depends on the required significance level.

S(i) = 0 for a fixed i and for all parents

Putting a parent index, w, in the criteria S(i) and $\sigma(i)$ yields S(w,i) and $\sigma(w,i)$, respectively. The test criteria are then represented by:

$$Z(i) = \sum_{w=1}^{L} \frac{S(w,i)^2}{\sigma(w,i)^2} \qquad (15)$$

Z(i) is $\chi^2_{(L)}$-distributed where L stands for the number of parents. It should be noted that only a one-tailed significance level for Z(i) is necessary.

S(i) = 0 for all i and for a specific parent

The different estimated values for S(i) are to be understood as functions of the measured values from animals, because any animal involved is the same when evaluating each i under a different aspect. Therefore the S(i) are no longer independent variables. However an equivalent statement can be derived from the following relation:

$$\sum_{i=1}^{M} S(i)^2 = 0 = \sum_{i=1}^{M} S'(i)^2 \qquad (16)$$

Thus a new variable S'(i) is obtained, supposing that the transformation is caused by a real unitary matrix.

First, the vectors are introduced as follows:

$$S = \begin{pmatrix} S(1) \\ \vdots \\ S(M) \end{pmatrix}$$

$$S' = \begin{pmatrix} S'(1) \\ \vdots \\ S'(M) \end{pmatrix}$$

Then the matrices A^{-1} and A are formed. These matrices have to be symmetrical, thus allowing a transformation on main diagonals:

$$U^T A^{-1} U = \begin{pmatrix} e(1) & & 0 \\ & \ddots & \\ 0 & & e(M) \end{pmatrix}$$

$$U^T U = \begin{pmatrix} \frac{1}{e(1)} & & 0 \\ & \ddots & \\ 0 & & \frac{1}{e(M)} \end{pmatrix}$$

U^T : transposition of U : $U^T(i,j) = U(j,i)$

e(i) : characteristic values of A^{-1}

Then

$$S' = U^T \cdot S$$

In Appendix B it is proved that, for $v \neq \xi$, the estimated values of S'_v and S'_ξ are independent variables. Therefore the variation of S'(i) can be calculated analogously to formula (15):

$$\sigma'(i)^2 = \sum_{v=1}^{N} \left[\sum_{j=1}^{M} (U^T A^{-1})(i,j) \cdot F(v,j) \right]^2 \cdot \sigma_\mu^2 \quad (17)$$

Then

$$(U^T A^{-1})(i,j) = \sum_{\varphi=1}^{M} U(\varphi,i) A^{-1}(\varphi,j) \quad (18)$$

The test criterion of significance Z is calculated as

$$Z = \sum_{i=1}^{M} \frac{S'(i)^2}{\sigma'(i)^2} \quad (19)$$

This criterion is $\chi^2_{(M)}$-distributed with M = number of gene loci. Because an upper limit for Z need not be obtained, a one-tailed significance level is sufficient to test the assumption that Z = 0.

S(i) = 0 for all i and all parents

The variables obtained in the previous chapter can be extended to the situation of L different parents. The test criterion is then

$$Z = \sum_{w=1}^{L} \sum_{i=1}^{M} \frac{S'(w,i)^2}{\sigma'(w,i)^2} \quad (20)$$

Its value is $\chi^2_{(L,M)}$-distributed (L = number of parents, M = number of gene loci).

Confidence interval for $\sum|S(i)|$

The F(v,i) can be defined in such a way that the S(i) are all positive. Then

$$\beta = \sum_{i=1}^{M'} |S(i)| \quad (21)$$

is the influence of a metric phenotype of an offspring calculable from the allele transmission in marker loci of the parents. For the estimated value β a variance σ_β^2 can be reckoned. This variance is caused by the fluctuation of influences which can not be controlled. A small value of σ_β^2 is favourable because it expresses an exact knowledge of β. To calculate σ_β^2 the following formula can be used:

$$\sigma_\beta^2 = \sum_{v=1}^{N} \left[\sum_{i=1}^{M'} \sum_{j=1}^{M'} A'^{-1}(i,j) \cdot F(v,j) \right]^2 \cdot \sigma_\mu^2 \quad (22)$$

It is assumed that

$$S(i) = \sum_{j=1}^{M'} A'^{-1}(i,j) \cdot B(j)$$

M' represents the number of relevant effects of allele substitutions and A'^{-1} arises from combined calculation of those effects.

Discussion

Quantitative traits of higher animals are often very complex in their biochemical and physiological aspects and therefore should generally be caused by numerous genes. The continuous variation of these traits is assumed to be brought about by a large number of additive genes whose single contributions are insignificant. The development of a character is subject also to strong influence from the environment. Therefore it is often believed that the effects of genes producing quantitative traits can only be registered in their totality and most biometric methods for analysing continuously varying characters are based on this concept.

Various studies have proved that these assumptions over-simplify the biological facts. For example, the genes involved in the formation of characters can have a variable strong influence (Stewart and Elston 1973), and non-allelic interactions, varying in kind and extent, affect the development of phenotypes (Jana and Seyffert 1971). The genetically caused variation of a quantitative character is often chiefly controlled by a few genes only (Thoday 1961, Law 1967). This is why methods have been developed to decide whether the continuous variation can be attributed to the segregation of one single locus or of two loci (Stewart 1969).

Because of the biological complexity occurring mostly during the development of a quantitative character in higher animals, polygenic systems often appear. It seems necessary to find ways of recognizing the effects of chromosome sections on a polygenic character and the method described here aims to make possible such analyses of polygenic systems in available animal populations (Geldermann 1972). It is based on the following facts:

a) Monogenic variants on the molecular level of animal body are common in populations.

b) Every gene locus marks a chromosome section, as far as the alleles of adjacent gene loci are linked to it.

c) Metric characters are caused by genes within chromosome sections with discernible effects per section.

When a marker gene allele is transmitted from parent to offspring, the simultaneous transmission of a considerable chromosome section of a specific homologous chromosome is assumed. Where one or more genes of a quantitative character are situated on that chromosome section, it is expected that there will be an effect on the formation of the quantitative phenotype concerned. This effect can be demonstrated, as far as measurable, at a marker locus. In a few cases, effects are caused by the marker gene itself. Mainly, they are effects of linked loci which number per marked chromosome section and crossover frequencies between them and the marker locus are unknown. At these loci, specific alleles are transferred to a progeny together with a distinct marker allele at a higher probability than random. The substitution effects of chromosome sections are then functions of the crossover frequencies between marker loci and QTL's, of the quantities of allele effects and of allele arrangements at QTL's within a homologous chromosome. For example, a specific effect can originate either from a closely linked QTL with an effect of determined amount or from a weakly coupled QTL with a greater influence than estimated. In each case the calculated effect of a chromosome section on a metric trait displays the expected average difference by the transfer of the one or the other allele of a marker gene from parent to progeny. The statement, whether an individual descendant has received from its parent a distinct quantitative trait value together with a marker allele, is valid at a probability deduceable from crossover portions between marker loci and QTL's.

Studying in a progeny the distribution of the trait values which are connected with a specific marker allele can give information about the amount of coupled QTL's and their crossover frequencies. However, according to McMillan and Robertson (1974), the quantity of QTL's is often underestimated.

The participation of individual chromosome sections in the development of quantitative characters in samples of animals from natural populations may be advantageous. Then, a sufficient number of marked chromosome sections allows the following analyses:

a) Determination of the specific effect of a marked chromosome section on quantitative traits.

b) Definition of the importance of each of the two homologous chromosome sections in a diploid organism for the development of metric traits.

c) Assessment of the effect of combinations of homologous or different chromosome sections on quantitative traits.

d) Evaluation of the number of chromosome sections bearing alleles of different efficiency for quantitative characters as well as their distribution in the genome, and frequencies in the population.

To help achieve these aims, a model is described which is able to provide relations between single chromosome sections and a metric character. The application of the model postulates individuals with known gene markers and one or several quantitative traits. The procedure permits a continuously varying character to be traced back to a series of effects connected with marked chromosome sections. The test of significance for a small effect of a marked chromosome section on a polygenic character requires relatively large numbers of animals because of the high residual variation expected. However it is possible that important effects are linked to few chromosome sections (Stewart 1969). The consideration of these effects reduces the residual variation and leads to more advantageous test conditions for minor effects.

The analysis described gives a better insight into animal genetic structure and into the consequences of its changes. It can serve to assess how many, and which, effects on a metric character are transmitted to a specific descendant. This could lead to its practical use in animal breeding.

The application of this method to empirical data will be described in the following sections of this paper.

Appendix A

Application of the method of Least Squares. The result of formula (8) is:

$$0 = \frac{\partial}{\partial \cdot S(j)} Q = -2 \sum_{v=1}^{N} \left[L(v) - \sum_{i=1}^{M} F(v,i) \cdot S(i) - \mu \right] \cdot F(v,j)$$

Therefore

$$\sum_{i=1}^{M}\left[\sum_{v=1}^{N} F(v,i)\cdot F(v,j)\right]\cdot S(i)$$

$$=\sum_{v=1}^{N} F(v,j)\cdot L(v)-\sum_{v=1}^{N}\mu\cdot F(v,j)$$

Further from

$$0=\frac{\partial}{\partial\cdot\mu}\cdot Q=-2\cdot\sum_{v=1}^{N}\left[L(v)-\sum_{i=1}^{M}F(v,i)\cdot S(i)-\mu\right]$$

$$\sum_{i=1}^{M}\left[\sum_{v=1}^{N}F(v,i)\right]\cdot S(i)=\left[\sum_{v=1}^{N}L(v)\right]-N\cdot\mu$$

is obtained.

The equations correspond to the equation system (9). If $v = 1,\ldots,N$ and $S(M+1)=\mu$ are replaced by $F(v,M+1)=1$, the two equations given above can be summarized as:

$$\sum_{i=1}^{M+1}\left[\sum_{v=1}^{N}F(v,i)\cdot F(v,j)\right]\cdot S(i)=\sum_{v=1}^{N}F(v,j)\cdot L(v)$$

Appendix B

Proof that $v \neq \xi$ is independent for S'_v and S'_ξ
According to formula (8)

$$S'_v=\sum_{\alpha}\sum_{\rho}\sum_{\zeta}U(\rho,v)\cdot A^{-1}(\rho,\zeta)\cdot F(\alpha,\zeta)\cdot(L(\alpha)-\mu)$$

$$S'_\xi=\sum_{\alpha'}\sum_{\rho'}\sum_{\zeta'}U(\rho',\xi)\cdot A^{-1}(\rho',\zeta')\cdot F(\alpha',\zeta')\cdot(L(\alpha')-\mu)$$

The following equation is equivalent to the interdependence of the variables if $v \neq \xi$:

$$0=\sum_{\alpha}\sum_{\rho}\sum_{\zeta}\sum_{\rho'}\sum_{\zeta'}U(\rho,v)\cdot A^{-1}(\rho,v)\cdot F(\alpha,\zeta')\cdot U(\rho',\xi)\cdot A^{-1}(\rho',\zeta')\cdot F(\alpha,\zeta)$$

That corresponds to:

$$0=\sum_{\rho,\zeta,\rho',\zeta'}U(\rho,v)\cdot A^{-1}(\rho,\zeta)\cdot A(\zeta,\zeta')\cdot A^{-1}(\rho',\zeta')\circ U(\rho',\xi)$$

$$=U^{T}\cdot A^{-1}\cdot A\cdot A^{-1T}\cdot U(v,\xi)$$

$$=U^{T}\cdot A^{-1}\cdot U(v,\xi)=F_v\cdot\varepsilon_{v,\xi}$$

This expression is 0 for $v \neq \xi$. Thereby $\varepsilon_{v,\xi}$ represents the function

$$\varepsilon_{v,\xi}=\begin{cases}1 \text{ for } v=\xi\\ 0 \text{ for } v\neq\xi\end{cases}.$$

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