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# Investigations on Inheritance of Quantitative Characters in Animals by Gene Markers
# II. Expected Effects

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Summary. Monogenic characters mark chromosome sections and therefore allow estimation of the substitution effects of genes located in them for a quantitative character. From assumptions for higher organisms, the expected effects of a quantitative trait are deduced. The derivations aim to produce comparison values for subsequent empirical investigations in domestic mammals.

Chromosome sections can be marked by use of gene loci. The effects of these sections are analysed, as described by Geldermann (1975). Taking into account some conditions of these effects, it is possible to calculate the expected relations between marked chromosomes and a quantitative trait.

## Assumed conditions for estimation of a quantitative trait by gene markers

For the relations between gene markers and quantitative traits, the following simplified conditions are assumed:

a) A parent has M' gene loci linked to chromosome sections with differing influences on a metric character in the two homologous parts. Together with a distinct allele from one of these marker loci, an extended homologous chromosome section is transmitted from a parent to progeny. This progeny produces a quantitative value for a trait which differs when compared with progeny having the other allele with a substitution value $S(i)$.

b) The effects measurable at a marker gene arise from a gene locus for the quantitative trait (quantitative trait locus = QTL) within the linked chromosome section. The substitution effect of the QTL is termed $\alpha(i)$.

c) All $\alpha(i)$ in a genome make up the variance $\sigma^2_G$ of a metric trait caused by additive genetic effects. Within the progeny of a parent we obtain:

$$\sigma^2_G = \sum_{i=1}^{M'} \left[\frac{\alpha(i)}{2}\right]^2 \qquad (1)$$

if M' is the number of all QTL's with substitution effects.

d) Linkage between marker locus and QTL is interrupted by crossing over. Therefore, only parts of the effects of QTL are recordable at a marker gene locus. The relation between $S(i)$ and $\alpha(i)$ can be expressed by

$$S(i) = \alpha(i) - 2 \cdot c(i) \cdot \alpha(i), \qquad (2)$$

where $c(i)$ is the crossing over frequency between marker gene i and QTL i. A variance $c(i) \cdot (1-c(i)) \cdot \alpha(i)^2$ remain within a progeny class with the same marker allele. From this, inserting $S(i)$ into formula (1), we obtain:

$$\sigma^2_G = \sum_{i=1}^{M'} \left[\frac{S(i)}{2(1-2 \cdot c(i))}\right]^2 \qquad (3)$$

$$= \sum_{i=1}^{M'} \left[\frac{S(i)^2}{4} + c(i) \cdot (1-c(i)) \cdot \alpha(i)\right]^2 \qquad (4)$$

e) Sometimes the $S(i)$ of only one parent can be estimated. If father and mother contribute equally to variance $\sigma^2_G$, both parents cause the same variance $\sigma'^2_G$ in their progeny:

$$2 \cdot \sigma'^2_G = \sigma^2_G \qquad (5)$$

f) The $S(i)$ have different values which are normally distributed, with $\bar{S}$ as mean and $\sigma_S$ as standard deviation. Including a limited sample, the estimated $S(i)$ become significant if their values rise above $\bar{S} - r\sigma_S$. Consideration of the significant $S(i)$ for evaluating a metric trait gives:

$$\sum_{i=1}^{M'} \left[\frac{S(i)}{2(1-2c(i))}\right]^2 = \sigma_G^2 \cdot \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{r} e^{-\frac{x^2}{2}} dx \qquad (6)$$

Thus the maximal share registerable of $\sigma_G^2$ depends on the values of r.

g) Transmission of a homologous chromosome section from a parent to a distinct descendant is registered by tracing a marker allele from parent to progeny. Allele transfer can be identified if the marker genotypes of the parent concerned are heterozygous. Even in this case the allele transfer is not discernible for every offspring. The share of provable transfer for a gene with intermediate or codominant allele effects, and under the hypothesis of genetic equilibrium, is obtained as follows:

$$P(i) = \sum_{j<m}^{K(i)} [2p(i,j) \cdot p(i,m)\{1-p(i,j) \cdot p(i,m)\}] \qquad (7)$$

Thereby,

P(i) : Frequency of detectable allele transfers from parents to offspring

p(i,j), p(i,m) : Allele frequencies; j, m = 1, ..., K(i)

K(i) : Number of alleles of the gene locus i

Consideration of the recordable part of allele transfers is necessary if the average estimation for a single descendant is to be calculated. By observing metric traits within samples of animals the recordable part reduces the number of useable offspring but in the expression above P(i) equals 1.

h) To establish phenotypes with monogenic inheritance, special criteria of proteins or enzymes are often used. Molecules are selected which appear continuously in large amounts during almost the whole postnatal development of the animals. In selecting the macromolecular substances, it is possible to take into consideration those criteria concerned with the metabolism of the quantitative character, or those which have been proved to exercise other influences on the quantitative character (Reviews s. Harris 1971, Matoušek 1970, McKusick and Chase 1973, Mitscherlich 1965). Therefore, it is possible that the selected genes affect a polygenic character to a larger extent than the average of the remaining gene loci.

A direct influence of a monogenic trait on a metric character allows an assessment of effects in all cases where the phenotype of that monogenic trait is known for an individual; thereby the value of P(i) increases to 1. Moreover no crossing over occurs, so that c(i) becomes 0.

i) In general not all chromosome sections with substitution effects can be marked. If the marked chromosome sections are representative for the non-marked sections, i.e. they have the same distribution of the S(i), formula (3) extends to

$$\sum_{i=1}^{M} \left[\frac{S(i)}{2(1-2c(i))}\right]^2 = \frac{M}{M'} \cdot \sigma_G^2 , \qquad (8)$$

where

M: Number of marked chromosome sections with a value of $S(i) \neq 0$.

Expected relations between number of marker genes and estimable variance of a quantitative trait

From the conditions mentioned follow relations between the number of marked chromosome sections and the estimated genetic additive variance of a metric trait. If marker genes with $S(i) > \bar{S} + r \cdot \sigma_S$ are considered we can express

$$\sum_{i=1}^{M} \frac{1}{P(i)} \cdot \left[\frac{S(i)}{2(1-2c(i))}\right]^2 = \sigma_G^2 \cdot \frac{ME}{2M'} \cdot \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{r} e^{\frac{-x^2}{2}} dx$$

with

E: Number of parents per offspring included in the estimations; E = 1 or 2.

When P(i) and c(i) are used without subscripts a transformed equation results:

$$\sum_{i=1}^{M} S(i)^2 = \sigma_G^2 \frac{MPE \cdot [2(1-2c)]^2}{2 \cdot M'} \cdot \frac{1}{\sqrt{2\pi}} \cdot \int_{-\infty}^{r} e^{\frac{-x^2}{2}} dx \qquad (10)$$

If we insert c = 0.1, P = 0.3, r = 1, and M' = 10 into this formula, the graphically represented function for number of marker genes can be obtained, as in Fig. 1. Assuming known marker genes for all 10 relevant chromosome sections, but varying values of c and P, leads to the graph in Fig. 2.

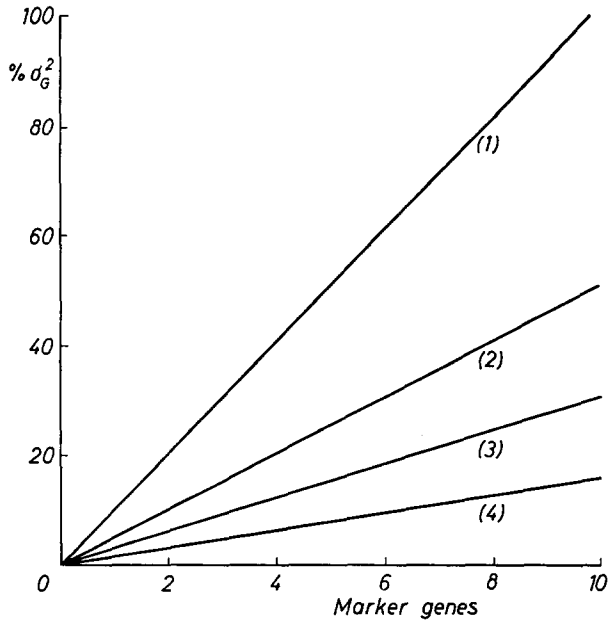


Fig. 1. Estimable part of genetical additive variance as function of marker gene number
(1) Function for a sample of animals and E equal 2
(2) Function for a sample of animals and E equal 1
(3) Function for one descendant and E equal 2
(4) Function for one descendant and E equal 1.
Further assumptions are explained in text

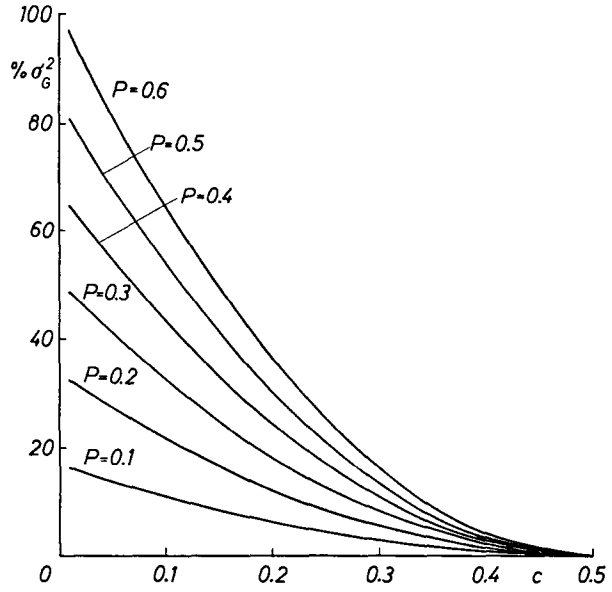


Fig. 2. Estimable part of genetical additive variance as function of recordable allele transfers and crossing over between marker genes and genes for the metric trait. Assumptions are explained in text

## Discussion

The derivation started from the assumption that many traits with allelic forms can be found which are traceable by observing their transmission. Phenotypes of monogenic origin can be frequently demonstrated in "primary" gene products such as soluble proteins or enzymes (Review s. Lewontin 1973).

If the alleles of two or several genes are considered simultaneously, parent-offspring studies give information about the locality of the genes in the chromosomes. The frequency of crossing over between two genes serves as a unit of the distance of the loci (Renwich 1971, Weitkamp et al. 1971). In man and mouse, which have been extensively investigated mammals, the crossing over ratio per chromosome is estimated to be between 50 and 150. The occurrence of crossing over depends on the chromosome regions (Bridges 1935, Whitehouse 1969), on genes (Chinnici 1971a and b, Pandey 1972, Valentin 1973a and b), on sex (Renwich 1971, Weitkamp et al., 1971, 1973), on age (Henderson and Edwards 1968) and on other influences (Bodmer and Parsons 1962). Levitan (1973a and b) inferred that there are selective advantages for certain combinations of the alleles within a chromosome. The combinations are forced by minimizing recombination pressure on the one hand, and by favouring certain allele arrangements on a chromatid on the other hand. The relations of several loci within a chromatid were reviewed by Lewontin (1973). The stated influences on the recombination processes can be useful for the assessment of quantitative character by gene markers.

Further advantages emerge if few chromosome sections exert substitution effects on a certain metric character. Estimations of the numbers of gene loci participating in the continuous variation of a metric character in higher organisms show (Reviews s. Bodmer and Parsons 1962, and Stewart 1969) that there are probably very few genes with greater effects ("oligogenes"), but many genes with smaller effects ("modifier genes"). This means that a small share of the chromosome sections can be assumed to have stronger relations to a quantitative character, leading to a reduced number of selected marker genes for assessing a fixed genetically determined variance of a quantitative trait (Figs. 1 and 2).

Restrictions on the estimation of metric traits with marked chromosome sections originate in the limited

parts of detectable allele transmission from parents to offspring. These parts become smaller when fewer alleles of a marker gene can be differentiated and higher when the frequency of one allele increases. Within a sample the ratio of recognizable allele transmissions determines the frequency of animals which are available for the estimation of the substitutions S(i). But for the evaluation of allele transmission from a parent to a particular descendant the fraction gives the frequency of useable marker genes. To reduce restrictions from the identification of allele transmissions all differing alleles should be represented as far as possible. It is also desirable to mark important chromosome section with more than one gene locus.

The restrictions on the identification of allele transmissions are not valid for those relations which arise directly from recordable alleles or allele combinations in the development of a quantitative trait. Therefore, efforts should be made to find genes with direct effects on the quantitative trait concerned if estimation of single descendants is desired. In animal populations, genes with direct effects are relatively difficult to detect, so one of the aims of the marker gene method can be to offer information for such studies.

To verify whether quantitative characters can be explored in animals of existing populations by using gene markers needs several investigations based on empirical data. An evaluation made with domestic cattle will be presented in the third part of this paper.

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