THE RELATIONSHIP BETWEEN GENIC AND GENOTYPIC FITNESSES IN DIPLOID POPULATIONS

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ABSTRACT.   After a short discussion of the desirable properties that should be exhibited by genetic fitness concepts, an attempt is made to derive a particular fitness concept which is based upon the individual gene as the unit of genetic transmission. It is demonstrated that this definition accords well with common usage as well as with intuitive understanding of the term fitness. The applicability of the concept to discrete and continuous time models of population genetics is verified by stating the basic equations for gene frequency change. In this context, the fundamental significance of studying one-locus-two-allele models is emphasized, and the mode according to which genotypic fitnesses and frequencies determine allelic fitnesses and thus the change in allelic frequencies is discussed. Herewith, an as general as possible characterization of the effects of overdominance, underdominance, etc. for regular Mendelian segregation and the degree to which these effects could possibly be neutralized under the action of segregation distortion is given. The necessity of considering genotypic fitnesses to be, in general, frequency dependent is pointed out by referring to a model of viability-fecundity selection for animal populations.

1. INTRODUCTION

Unfortunately, fitness, as one of the most fundamental concepts of population genetics, is still used with a great variety of meanings, even within specific subject areas. There seems to be general agreement only in that it should describe quantitatively the extent to which biologically definable units reproduce themselves. Herewith, the outcome of reproduction is taken to be characterized by the genetic similarity between the producer and its product. At this point, however, conceptual difficulties already arise. While for vegetatively propagating organisms the parent and offspring are genetically identical, sexually reproducing individuals pass on only a part of their genetic information to their descendants. In the first case, the fitness of an individual could unambiguously be defined as the total number of its offspring. In the second case, it is not so easy to see how the requirement of genetic similarity between parent and offspring could be interpreted in order to specify meaningfully a fitness value for a single individual. This difficulty can be partially overcome by considering gametes as carriers of at least part of an individual's genetic information such that the number of successful gametes (those entering into zygotes) an

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individual produces measures the degree to which it transmits
its information (which is termed 'realized individual fitness'
by Gregorius and Ross (1981)). Despite the fact that, for sexu-
ally reproducing organisms, this fitness concept appears to be
quite obvious in its basic statement, it does not after all pro-
vide any information about how successful an individual is in
producing identical copies of its genotype. However, most of our
intuitive understanding of the plan according to which genetic
selection acts relies on this very property (for instance, cf.
Denniston 1978).

In order to find a way out of this dilemma, it might be use-
ful to begin by referring back to the unit of heredity which is
also necessarily the basic unit of evolutionary processes, the
gene. In this sense, the gene (for reasons of distinction from
other gene concepts sometimes also called the 'Mendelian gene')
is defined to be a set of genetic information which, if it is
transmitted from parent to offspring, has a high probability of
remaining unchanged. Any changes in information which do occur
are classified as mutational events, whether they result from
point mutation, chromosomal mutation or rare so-called intra-
genic recombination. Thus, in exclusively vegetatively repro-
ducing species, the whole genotype of an individual has to be
considered as a single gene. In particular, this statement indi-
cates clearly that, in the last consequence, the biologically
evolutionary relevance of each genetic fitness concept should be
evaluated with respect to the precision with which it allows for
conclusions to be drawn concerning the chances of individual
genes to produce identical copies.

Therefore, the best one could probably do is to define fit-
ness as a property of individual (Mendelian) genes and use this
definition to derive fitness concepts applicable to more complex
genetic units such as diploid multilocus genotypes. This way of
proceeding would also have the advantage of facilitating the
biological interpretation of phenomena, such as allelic effects,
by merely considering them to be the result of interaction of
a gene with its genotypic and ecological environment.

That is, the gene is considered to be the unit of reproduc-
tion, and its capacity to multiply is influenced by other genes
present in the complex genotype. From this point of view, the
fitness of a genotype should reflect the reproductive activities
(realized fitnesses) of all the genes of which it is made up.
This differs from common practice, where genotypic fitnesses
are assumed to be given and genic (allelic) fitnesses are ex-
tracted from these with the help of more or less purely mathe-
matical methods, not referring explicitly to their intrinsically
biological meaning.

In the present paper, an attempt will be made to give a defi-
nition of genic fitness which is assumed to be relevant in an
evolutionary sense and to relate this to an established concept
of genotypic fitness as applied to a single diploid gene locus.
With the help of a few classical selection models of population
genetics, the close correspondence of the two fitness concepts
to those used in the construction of these models will be
exemplified. Since allelic fitnesses directly determine the
change in allelic frequencies from one generation to the next,
main emphasis will be put on considering the conditions which
should be met by genotypic fitnesses and frequencies to ensure

that one allele is superior (inferior, equal) to a second allele with respect to its fitness value.

2. DEFINITION OF ALLELIC AND GENOTYPIC FITNESS

Considering a particular gene as an integral part of the complete genotype of an individual means that this individual is conceived of as a unit with respect to its reactions to ecological factors, while the gene is a subunit involved in the creation of these reactions. Consequently, all of the copies of a gene present in the cells of an individual organism should be counted as one single gene. Based on this idea, it is meaningful to consider only those copies which appear in the reproductive cells (gametes) produced by an individual. Among these, in turn, there might be only a few which are 'successful' in the sense that they take part in the initiation of new individuals (zygotes). Hence a definition of genic fitness which is in complete agreement with the basic requirements stated in the introduction to this paper could be given as follows:

> The (realized) fitness of an individual gene is equal to the number of successful copies it produces.

However, this definition of genic fitness does not reflect the fact that the copies may be produced at different ages of the individual containing the gene in question. But this is an indispensable piece of information needed in population genetic models dealing with iteroparous organisms and therefore concerned with the description of the dynamics of genetic structures depending on age class structures. To take this aspect into account, one could conceive of genic fitness as an age dependent cumulative function specifying for each instant of time the number of successful copies produced by a gene from birth up to that time. Therefore the following more specific definition appears to make sense:

> The cumulative (realized) fitness of an individual gene is a time dependent function specifying for each age the number of successful copies produced by this gene from birth up to that age.

Thus the fitness of an individual gene is equal to its cumulative fitness measured at its age of death, i.e. the age of death of the individual carrying this gene.

As was argued previously, a purely vegetatively reproducing organism should be considered as possessing only a single (Mendelian) gene, such that the fitness of this individual is equal to the fitness of its gene. For sexually reproducing organisms this correspondence between gene and individual is not realized in general, since individuals might carry more than one gene. We have already seen that the fitness of an individual gene is measured by the number of 'successful' gametes which contain copies of this gene produced by the individual carrying the gene. Consequently, the fitness of an individual, when viewed as the result of the interaction of all of its single genes, is expressed simply as the number of successful gametes it produces.

> The (realized) fitness of an individual organism is equal to the number of successful gametes it produces.

The same reasoning leading to the concept of cumulative genic fitness can be applied to define:

> The cumulative (realized) fitness of an individual organism is a time dependent function specifying for each age the number of successful gametes it produces from birth up to that age.

These definitions imply that, given a diploid sexually re-producing organism, for example, its fitness is exactly equal to the sum of the genic fitnesses for the two homologous genes (alleles) present at any of the organism's gene loci.

So far, fitness has been treated as a variable the expressions of which are measured at individual genes or organisms and not at classes or groups within which these individual expressions could vary. The classes of primary interest in population genetics are those formed for example by the sets of individual genes exhibiting certain allelic states or sets of individual organisms having certain genotypes. The usual method of characterizing such a class with respect to fitness is to consider the fitness averages over the individual members belonging to the class. This is also the basis of the definition of allelic and genotypic fitnesses. However, it is not sufficient, in general, to characterize individuals only by their alleles or genotypes, since fitness may change with the population structure, the mating system and the environmental conditions. Therefore, averages should be taken only over individuals born at the same instant of time (a cohort), and it should be made clear that they refer only to a particular population including all the factors governing the living and reproductive conditions of the members of this population as it evolves. In favor of brevity, it is tacitly assumed in the following that the term population comprises in substance all these aspects. The first requirement (individuals born at the same time instant) seems to be evident, when considering discrete, non-overlapping generations. But for overlapping generations erroneous conclusions might be made if it is not explicitly taken into account. Of course, in practice we actually mean a relatively short interval of time when speaking of an 'instant of time' at which individuals are born. In other words, allelic and genotypic fitness should be considered primarily as a cohort property.

> The (realized) fitness (cumulative fitness) of a certain allele in a particular population at a given instant of time is equal to the population average over the fitnesses (cumulative fitnesses) of all individual genes 'born' at this instant and exhibiting this allelic state.

In an analogous manner, one arrives at the definition of genotypic fitness.

> The (realized) fitness (cumulative fitness) of a certain genotype in a particular population at a given instant of time is equal to the population average over the fitnesses (cumulative fitnesses) of all individual organisms born at this instant and having this genotype.

Building upon this definitional groundwork, it is now an easy task to derive the formal relationship between allelic and genotypic fitnesses. This will be done for a population of di-

ploid, sexually reproducing organisms. It suffices to restrict the considerations to fitnesses only, since cumulative fitnesses result in the same representations with the only difference that an age index has to be added. Furthermore, being concerned with the fitnesses of homologous genes, it does not make sense to consider genotypic fitnesses of multilocus genotypes, since they contain non-homologous genes. For notational convenience, we also omit subscripts indicating the instant of time to which the fitnesses refer.

A necessary precondition for relating allelic to genotypic fitness is to specify allelic fitnesses within their respective 'genotypic environments'. Therefore we denote by $a_{ij}(k)$ the fitness of the k-th allele within a genotype composed of the i-th and j-th allele; clearly k is equal to i or j. The overall population fitnesses of the i-th allele and the (i,j)-genotype are denoted by a_i and w_{ij}, respectively. It follows that $w_{ij} = a_{ij}(i) + a_{ij}(j)$ for all i and j, such that, in particular, $w_{ii} = 2 \cdot a_{ii}(i)$ for homozygotes. The case $a_{ij}(i) \neq a_{ij}(j)$ for a heterozygote ($i \neq j$) is commonly termed 'segregation distortion', and for $a_{ij}(i) = a_{ij}(j)$, i.e. $a_{ij}(i) = 1/2 \cdot w_{ij} = a_{ij}(j)$, one speaks of regular Mendelian segregation.

Moreover, for some given instant of time, let N_{ij} be the number of individuals at the zygotic stage which have the (i,j)-genotype (considered to be an unordered pair of alleles) and let $N := \sum\limits_{i \leq j} N_{ij}$ be the total number of zygotes at this instant. Then the number of individual genes having the i-th allele equals $N_{ii} + \sum\limits_{j} N_{ij}$ among the zygotes, and it is equal to $a_{ii}(i) \cdot N_{ii} + \sum\limits_{j} a_{ij}(i) \cdot N_{ij}$ among the successful gametes produced by the cohort. Consequently, the allelic fitness a_i turns out to be

$$a_i = \frac{a_{ii}(i) \cdot N_{ii} + \sum\limits_{j} a_{ij}(i) \cdot N_{ij}}{N_{ii} + \sum\limits_{j} N_{ij}} \, .$$

To translate this expression into relative frequencies, we introduce $P_{ij} := N_{ij}/N$ for genotypic frequencies and

$$p_i := \frac{N_{ii} + \sum\limits_{j} N_{ij}}{2 \cdot N} = P_{ii} + \frac{1}{2} \sum\limits_{\substack{j \\ j \neq i}} P_{ij} \quad \text{for allelic frequencies.}$$

Hence

$$a_i = \frac{1}{2} \cdot \frac{a_{ii}(i) \cdot P_{ii} + \sum\limits_{j} a_{ij}(i) \cdot P_{ij}}{p_i} \, .$$

This can be written in a more compact and probably more comprehensible manner if one makes use of the quantities

$$q_i(j) := \begin{cases} P_{ii}/p_i & \text{for } i=j \\ \\ \frac{1}{2}P_{ij}/p_i & \text{for } i \neq j \end{cases}$$

for which it holds that $\sum\limits_{j} q_i(j) = 1$. Expressed in words, $q_i(j)$ is the portion of the individual genes exhibiting the i-th allelic state which is contributed by individual organisms having the (i,j)-genotype. Thus $q_i(\cdot)$ specifies the distribution of individual genes exhibiting the i-th allelic state over their 'genotypic environments'. Note that by assumption, the distributions $q_i(\cdot)$ depend on the allelic frequencies p_i according to the identity

$$q_i(j) \cdot p_i = q_j(i) \cdot p_j.$$

Thus

$$a_i = \sum\limits_{j} a_{ij}(i) \cdot q_i(j). \tag{1a}$$

Under the particular situation of regular Mendelian segregation ($a_{ij}(i) = a_{ij}(j) = \frac{1}{2}w_{ij}$ for all $i \neq j$) this equation has the representation

$$a_i = \frac{1}{2} \cdot \sum\limits_{j} w_{ij} \cdot q_i(j) \tag{1b}$$

Apart from the factor 1/2, Gregorius and Ziehe (1982) arrived at exactly the same expression for allelic fitness in a model for non-overlapping generations, random-mating and viability-fecundity selection. More specifically, assuming Hardy-Weinberg proportions for the P_{ij}'s, i.e. $P_{ii} = p_i^2$ and $P_{ij} = 2 \cdot p_i \cdot p_j$ for $i \neq j$, (1b) reads $a_i = \frac{1}{2} \cdot \sum\limits_{j} w_{ij} \cdot p_j$, which, again apart from the factor 1/2, is the well-known representation of allelic fitness in the classical viability selection model. Hence, the concepts of allelic and genotypic fitness considered here reflect as special cases the pertinent fitness functions known from standard viability selection theory (cf. e.g. Crow and Kimura 1970, p. 180, Equations 5.2.5 and 5.2.8). However, as mentioned earlier, viability is only one component of selection and must not necessarily be a major component of fitness. This, together with the fact that other components may determine fitness in a more complex and non-obvious manner is demonstrated with the help of a particular example presented in Section 5.

Equation (1a) as opposed to (1b) demonstrates that, in general, the information available from genotypic fitnesses does not uniquely determine allelic fitness. This deficiency is due to the effect of segregation distortion, in a global sense. Basing their considerations on the classical viability selection model, Liberman and Feldman (1980) recently discussed the significance of this effect with respect to attractivity properties of equilibrium states for the diallelic case (also cf. Hiraizumi et al. 1960). The assumptions of this model imply that genotypic fitnesses are constant over time, genotypic frequencies are in Hardy-Weinberg proportions after the first generation and segre-

gation distortion is measured by a constant $s(0 \leq s \leq 1)$ such that, in our notation, $s = a_{12}(1)/w_{12}$. Thus

$$a_1 = \tfrac{1}{2}w_{11} \cdot p_1 + s \cdot w_{12} \cdot p_2, \quad a_2 = \tfrac{1}{2}w_{22} \cdot p_2 + (1-s) \cdot w_{12} \cdot p_1.$$

To close these primarily terminological considerations, a brief remark on the relationship between the population (cohort) averages for allelic and genotypic fitnesses seems appropriate. Denote these averages by $\bar{a}$ and $\bar{w}$. Then it follows that

$$\bar{a} = \sum_i p_i \cdot a_i \text{ and } \bar{w} = \sum_{i \leq j} w_{ij} \cdot P_{ij}, \text{ and it is easily seen that}$$

$\bar{a} = \tfrac{1}{2} \cdot \bar{w}$. This is an expected result, since in effect $\bar{a}$ and $\bar{w}$ are the average numbers of successful copies per individual gene at a single locus and successful gametes per individual organism, respectively. In particular, for discrete, nonoverlapping generations a cohort comprises all members of the population, and therefore $\bar{a}$ is equal to the average number of offspring per member of the cohort, irrespective of whether the cohort consists of bisexual or unisexual organisms or a mixture of sexual types.

3. THE INFLUENCE OF ALLELIC FITNESSES ON THE CHANGE IN ALLELIC FREQUENCIES

In the preceding two sections, an attempt was made to explain why genotypic fitnesses should merely be thought of as specifying the conditions under which the single alleles realize their fitnesses. Therefore, before analyzing how genotypic fitnesses affect allelic ones, the population genetic relevance of the latter should be characterized more explicitly. This relevance undoubtedly lies in the mode according to which allelic fitnesses determine allelic frequency changes. In order to arrive at a formulation which is as widely applicable as possible, the model parameters will be chosen such that they can be applied to nonoverlapping as well as to overlapping generations and allow for a direct population biological interpretation. The following notation is recommended for this purpose:

$N(t,\delta)$:= number of successful gametes produced in the time interval ranging from t to $t+\delta$ by individual organisms born before time t.

$p_i(t,\delta)$:= allelic frequency of the i-th allele among the successful gametes produced in the time interval ranging from t to $t+\delta$ by individual organisms born before time t.

$a_i(\varepsilon;t,\delta)$:= cumulative allelic fitness of the i-th allele, based on the set of successful gametes produced in the time interval from t to $t+\delta$ by individual organisms born before time t and evaluated at time $t+\delta+\varepsilon$. Thus, at time $t+\delta+\varepsilon$, individual genes produced by the cohort range in age from 0 to $\delta+\varepsilon$. For given t and δ, $a_i(\varepsilon;t,\delta)$ is assumed to remain constant for all ε such that $\delta+\varepsilon$ exceeds some maximum attainable age α.

With the help of this notation, it is quite easy to see the way in which the allelic frequency $p_i(t,\delta)$ depends on states realized in the population prior to t. First, divide the maximum life expectancy, α, into m equally spaced intervals of length $\beta = \frac{\alpha}{m} \leq \delta$ and consider the set of individual genes 'born' in the time interval $t-\beta \cdot k$ to $t-\beta \cdot k+\beta$, where $1 \leq k \leq m$. This set contains $N(t-\beta \cdot k,\beta) \cdot p_i(t-\beta \cdot k,\beta)$ individual genes exhibiting the i-th allelic state. In the time interval t to $t+\delta$ each of these individual genes produces, on the average, a number of successful copies which is given by $a_i(\beta \cdot (k-1)+\delta;t-\beta \cdot k,\beta) - a_i(\beta \cdot (k-1);t-\beta \cdot k,\beta)$.

Consequently,

$$p_i(t,\delta) = \sum_{k=1}^{m} \left[a_i(\beta \cdot (k-1)+\delta;t-\beta \cdot k,\beta) - a_i(\beta \cdot (k-1);t-\beta \cdot k,\beta) \right] \cdot$$
$$\cdot p_i(t-\beta \cdot k,\beta) \cdot N(t-\beta \cdot k,\beta) / D \tag{2}$$

where the normalizing denominator D is equal to

$$D = \sum_{k=1}^{m} \left[\bar{a}(\beta \cdot (k-1)+\delta;t-\beta \cdot k,\beta) - \bar{a}(\beta \cdot (k-1);t-\beta \cdot k,\beta) \right] \cdot$$
$$\cdot N(t-\beta \cdot k,\beta) = N(t,\delta),$$

with the population average of the cumulative allelic fitnesses given by
$$\bar{a}(\varepsilon;t,\delta) = \sum_i a_i(\varepsilon;t,\delta) \cdot p_i(t,\delta).$$

For iteroparous populations reproducing in distinct breeding seasons, it is common usage to choose β such that the length of each breeding season is an integer multiple of β, and δ is set equal to β. Moreover, since newborns cannot reproduce, $a_i(0;t-\beta,\beta) = 0$ for all i. The situation of non-overlapping generations can be considered as a special case, for which $\alpha = \beta = \delta$ and thus m=1. Consequently, in this case (2) reads

$$p_i(t,\alpha) = p_i(t-\alpha,\alpha) \cdot \frac{a_i(\alpha;t-\alpha,\alpha)}{\bar{a}(\alpha;t-\alpha,\alpha)} .$$

Omitting the time and age parameters and denoting the allelic frequencies in the next generation with primes, p_i', this equation attains the familiar form

$$p_i' = p_i \cdot \frac{a_i}{\bar{a}} . \tag{3}$$

On the other hand, since the choice of δ and β in (2) is arbitrary, equation (2) can always be considered in the form of (3), i.e. with m=1 and $\alpha = \beta = \delta$, however with the restriction that $a_i(0;t-\alpha,\alpha)$ need not be zero. Hence, a_i in (3) should then read $a_i(\alpha;t-\alpha,\alpha) - a_i(0;t-\alpha,\alpha)$, which is the

allelic fitness averaged over, so to say, the set of successful gametes produced by one generation, i.e. produced in the time interval from $t-\alpha$ to t by individual organisms born before time $t-\alpha$. The considerations of the next section, treating the kind of dependence of allelic on genotypic fitnesses will therefore be based on the simplified version (3) of the general equation (2).

Before closing the present section, a remark will be made on how (2) should be applied to arrive at a correct continuous time (integral) representation of the change in allelic frequencies. For this purpose let $\delta=\beta$ approach zero (i.e. m tends to infinity for fixed α). Furthermore, suppose that

$$\lim_{\delta \to 0} p_i(t,\delta) =: p_i(t), \quad \lim_{\delta \to 0} \frac{N(t,\delta)}{\delta} =: B(t) \text{ and}$$

$$\lim_{\delta \to 0} \frac{\partial a_i(\varepsilon;t,\delta)}{\partial \varepsilon} =: a_i^*(\varepsilon;t) \text{ exist, where } a_i^*(\varepsilon;t) \text{ is the}$$

allelic fitness density and $B(t)$ is commonly referred to as the birth rate. Then it is readily seen that, as β tends to zero, (2) attains the integral representation

$$p_i(t) = \int_0^\alpha a_i^*(\varepsilon;t-\varepsilon) \cdot p_i(t-\varepsilon) \cdot B(t-\varepsilon) \cdot d\varepsilon \ / \ B(t)$$

with

$$B(t) = \int_0^\alpha \overline{a^*}(\varepsilon;t-\varepsilon) \cdot B(t-\varepsilon) \cdot d\varepsilon, \quad \text{where}$$

$\overline{a^*}(\varepsilon;t) := \sum_i a_i^*(\varepsilon,t) \cdot p_i(t)$. This result corresponds to those of Charlesworth (1970) contained in his equations (2.9) and (2.10) and the equation preceding (3.5) as well as Charlesworth (1973) Equations (1) and (2). It has also been used to derive necessary and sufficient conditions under which Fisher's famous continuous-time model of gene frequency change is correct (Gregorius and Ziehe 1981).

4. THE INFLUENCE OF GENOTYPIC FITNESSES ON THE CHANGE IN ALLELIC FREQUENCIES

It was shown that genotypic fitnesses in connection with the effects of segregation distortion are the fundamental determinants of allelic fitnesses, which, in turn, are the fundamental determinants of changes in allelic frequencies. Furthermore, it was reasoned in the last section why the representation stated in (3) is suitable for studying on a rather general basis the effect of allelic fitnesses on the change in allelic frequencies. With the help of this equation, the problem in question reduces to finding the conditions under which the frequency of the i-th allele decreases, remains the same, or increases, i.e. under which $a_i < \bar{a}$, $a_i = \bar{a}$, or $a_i > \bar{a}$. This can be done most conveniently and without loss of generality by opposing the effect of the i-th allele to the summarized effects of all other alleles, which are then treated as a single allele indexed k.

To keep the number of symbols used at a low level, the fitness and frequency of this compound allele will again be denoted by a_k and p_k, respectively, such that

$p_k = 1-p_i$ and $a_k = \sum\limits_{\substack{j \\ j \neq i}} a_j \cdot p_j/(1-p_i)$. Hence, in effect, one is

concerned with a diallelic case, where all other possibly existing alleles are considered as being 'hidden' behind at least one of the two alleles i and k.

For two alleles, $\bar{a}$ can be written as $\bar{a} = a_i + p_k \cdot (a_k - a_i)$ and, consequently, the cases $a_i < \bar{a}, a_i = \bar{a}$ and $a_i > \bar{a}$ are equivalent to $a_k > a_i$, $a_k = a_i$ and $a_k < a_i$, respectively, where it is always assumed that $0 < p_i < 1$. Moreover, setting $q_i(i) =: q_i$ and $q_k(k) =: q_k$ for simplicity, (1a) reads

$a_i = a_{ii}(i) \cdot q_i + a_{ik}(i) \cdot (1-q_i)$ and $a_k = a_{kk}(k) \cdot q_k + a_{ik}(k) \cdot (1-q_k)$, thus relating allelic fitnesses to their 'genotypic environments' and hereby to genotypic fitnesses. Consequently, the basic concern is to study the sign of the difference $a_i - a_k$, which can be written as

$$a_i - a_k = \frac{1}{2}(w_{ii} - w_{ik}) \cdot q_i + \frac{1}{2}(w_{ik} - w_{kk}) \cdot q_k +$$
$$+ (a_{ik}(i) - a_{ik}(k)) \cdot (1 - \frac{1}{2}(q_i + q_k)) \ . \tag{4}$$

Herein, the first two summands describe the effect of genotypic fitnesses, and the last summand refers to the effect of segregation distortion, which vanishes for $a_{ik}(i) = a_{ik}(k)$ $(= \frac{1}{2} w_{ik})$ or $q_i = q_k = 1$, whereas the latter refers to the trivial case that there are no heterozygotes in the population.

Equation (4) demonstrates that the sign of $a_i - a_k$, for given genotypic fitnesses and q_i and q_k, can, in general, depend on the magnitude of segregation distortion measured by $a_{ik}(i) - a_{ik}(k)$. This requires, as a first step, separate characterizations of the modes of action of genotypic fitnesses and segregation distortion. It is therefore reasonable to begin with the situation $a_{ik}(i) = a_{ik}(k)$, and, after this, seek for conditions under which segregation distortion does not change the sign of $a_i - a_k$.

Before doing so, it is advisable to point out more clearly the relationship between genotypic as well as allelic frequencies and the q's. For this purpose we shall make use of the well-known representation of genotypic frequencies as points in an equilateral triangle. The coordinate system is illustrated in Fig. 1 (with i=1 and k=2, for instance). In the opinion of the present author, this system has an advantage over the DeFinetti system, in that coordinates can be measured directly along the triangle sides, which have unit length.

Fig. 1
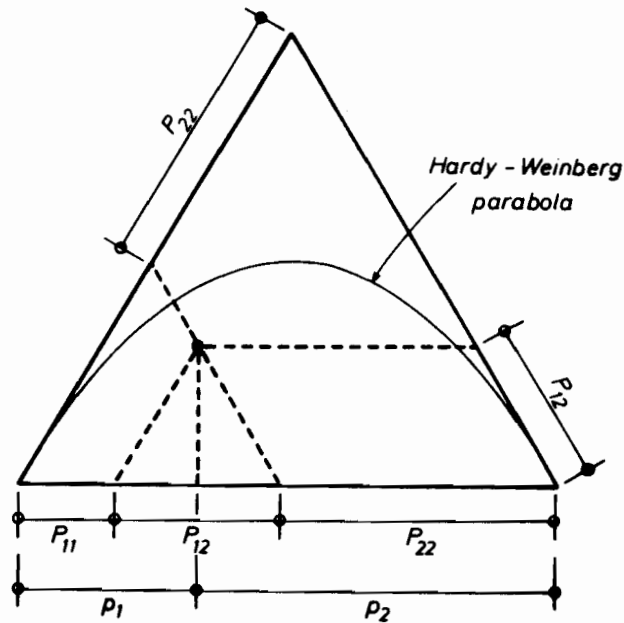
Since it is always assumed that $0 < p_i, p_k < 1$, genotypic and allelic frequencies are uniquely determined by q_i and q_k when $q_i, q_k < 1$, and the following identities are easily verified:

$$P_{ii} = \frac{q_i(1-q_k)}{2-q_i-q_k} \quad, \quad P_{ik} = \frac{2(1-q_i)(1-q_k)}{2-q_i-q_k} \quad, \quad p_i = \frac{1-q_k}{2-q_i-q_k} \quad.$$

Hence, in this case, $q_i < q_k$, $q_i > q_k$ and $q_i = q_k$ if and only if $p_i < p_k$, $p_i > p_k$ and $p_i = p_k = \frac{1}{2}$, respectively.

The significance of q_i and q_k in relation to Hardy-Weinberg proportions for the genotypic frequencies can be demonstrated by comparing p_i to q_i. If $p_i < q_i$, then $p_i^2 < P_{ii}$ and thus $p_k^2 < P_{kk}$, $2 \cdot p_i \cdot p_k > P_{ik}$, which, in turn, implies that $p_k < q_k$. Adding both inequalities for the p's and q's yields $1 < q_i + q_k$. Analogously, $p_i > q_i$ implies $2p_i p_k < P_{ik}$, $p_k > q_k$ and $q_i + q_k < 1$, and $p_i = q_i$ implies $2p_i p_k = P_{ik}$, $p_k = q_k$ and $q_i + q_k = 1$. These implications hold, of course, also in the reverse directions and are therefore equivalence relationships. The representation of these results in the frequency diagram of Fig. 1 shows that genotypic

frequencies characterized by $p_i > q_i$ ($q_i + q_k < 1$),
$p_i < q_i$ ($q_i + q_k > 1$) and $p_i = q_i$ ($q_i + q_k = 1$) are placed above,
below and on the Hardy-Weinberg parabola, respectively.

These representations will prove to be helpful in illustrating the subsequent considerations.

(a) No segregation distortion, $a_{ik}(i) = a_{ik}(k)$

In this case equation (4) reduces to

$$a_i - a_k = \frac{1}{2}(w_{ii} - w_{ik}) \cdot q_i + \frac{1}{2}(w_{ik} - w_{kk}) \cdot q_k.$$

The influence of the heterozygote on $a_i - a_k$ vanishes if
$q_i = q_k$, which requires that either $p_i = p_k = \frac{1}{2}$ or $P_{ik} = 0$,
and the sign of $a_i - a_k$ is identical to that of $w_{ii} - w_{kk}$.
The same statement holds, but irrespective of the values for
q_i and q_k, if the heterozygote fitness is located between the
two homozygote fitnesses, including equality with one of the
homozygote fitnesses (dominance). The only exception to this
rule is to be found in the case of complete dominance and zero
frequency for the genotype homozygous with respect to the
recessive allele, in which case $a_i = a_k$.

The remaining rankings between genotypic fitnesses are those
commonly denoted as overdominance (heterozygote superiority)
and underdominance (heterozygote inferiority), i.e. $w_{ik} > w_{ii}, w_{kk}$
and $w_{ik} < w_{ii}, w_{kk}$. Excluding the trivial cases in which
q_i or q_k is equal to zero, a simple reformulation of the above
equation shows that the sign of

$\dfrac{w_{ik} - w_{kk}}{w_{ik} - w_{ii}} - \dfrac{q_i}{q_k}$ equals that of $a_i - a_k$ for overdominance, and it is

equal to the sign of $a_k - a_i$ for underdominance. This result
demonstrates that, for each given genotypic structure and
absolute values of the deviations in genotypic fitnesses of both
homozygotes from the heterozygote, overdominance and underdominance have opposite effects on the direction of change in allelic
frequencies. Again there is an immediate correspondence to the
findings from classical viability selection. But it should also
again be emphasized that the above generalization comprises all
kinds of selection (such as fertility, fecundity, sexual selection, selection through assortative mating, etc.) and deviations
from Hardy-Weinberg-proportions (caused by inbreeding, mating
preferences, etc.), and that the formulation of the result is
rendered possible by the particular concept of fitness applied
here. Furthermore, if certain ranking relationships between
the homozygote fitnesses are realized, the above result can be
applied to show that the sign of $a_k - a_i$ does not depend on the
concrete values for q_i and q_k.

To see this, recall that $p_i < \frac{1}{2}$ if and only if $q_i < q_k$.

Consequently, provided $p_i < \frac{1}{2}$, $w_{kk} \leq w_{ii}$ implies $a_i > a_k$ in the case of overdominance, and $w_{ii} \leq w_{kk}$ implies $a_k > a_i$ in the case of underdominance. Hence, the only situations in which one expects the sign of $a_i - a_k$ to depend explicitly on the genotypic frequencies are those for which $p_i < \frac{1}{2}$ and $w_{ii} < w_{kk} < w_{ik}$ or $w_{ik} < w_{kk} < w_{ii}$, i.e. where the homozygous expression of the more frequent allele (k) is intermediate with respect to the other homozygote and the heterozygote. A comprehensible treatment of these situations can be achieved if one proceeds from the idea that, if $\frac{w_{ik} - w_{kk}}{w_{ik} - w_{ii}}$ is given by some value γ, the sign of $a_i - a_k$ is equal to that of $\gamma - \frac{q_i}{q_k}$ and $\frac{q_i}{q_k} - \gamma$ for over- and underdominance, respectively, where q_i / q_k varies with the genotypic frequencies.

Note that by assumption $0 < \gamma < 1$. For this purpose it is advantageous to look at the contour lines for q_i / q_k and use these for the interpretation of the sign of $a_i - a_k$.

Equating q_i / q_k to γ, one obtains $P_{ii} \cdot p_k = \gamma \cdot P_{kk} \cdot p_i$ and from this $p_i \cdot p_k - \frac{1}{2} P_{ik} \cdot p_k = \gamma \cdot p_i \cdot p_k - \gamma \cdot \frac{1}{2} P_{ik} \cdot p_i$. Thus

$$P_{ik} = \frac{2 \cdot p_i \cdot p_k \cdot (1-\gamma)}{p_k - \gamma \cdot p_i} = \frac{2 \cdot p_i \cdot (1-p_i) \cdot (1-\gamma)}{1 - p_i (1+\gamma)} ,$$

so that P_{ik} can be conceived of as a function of γ and p_i, i.e. $P_{ik} = P_{ik}(\gamma, p_i)$, which can be applied to draw for each γ the contour lines $q_i / q_k = \gamma$ given in Fig. 2. Assuming, without loss of generality, that i=1 and, therefore, considering the left half of the frequency triangle in Fig. 2, one arrives, for a given value of

$\gamma = \frac{w_{ik} - w_{kk}}{w_{ik} - w_{ii}}$, at the following result: If γ is realized in

the domain of genotypic frequencies located above (left of) or below (right of) the γ-contour line for q_i / q_k then

$a_i > a_k$ or $a_i < a_k$, respectively, for overdominance. For underdominance, the reverse relationships hold. If γ is realized on the γ-contour line, then $a_i = a_k$.

In order to demonstrate briefly the significance of these results for population genetics, consider the following situation: Suppose that the breeding system of a population implies $q_i + q_k \leq 1$, which signifies that genotypic frequencies are located on or above the Hardy-Weinberg parabola as was shown previously. Furthermore, suppose that there exists γ_o,

Fig 2

contour lines for $\frac{q_1}{q_2} = \gamma$ contour lines for $\frac{q_2}{q_1} = \gamma$
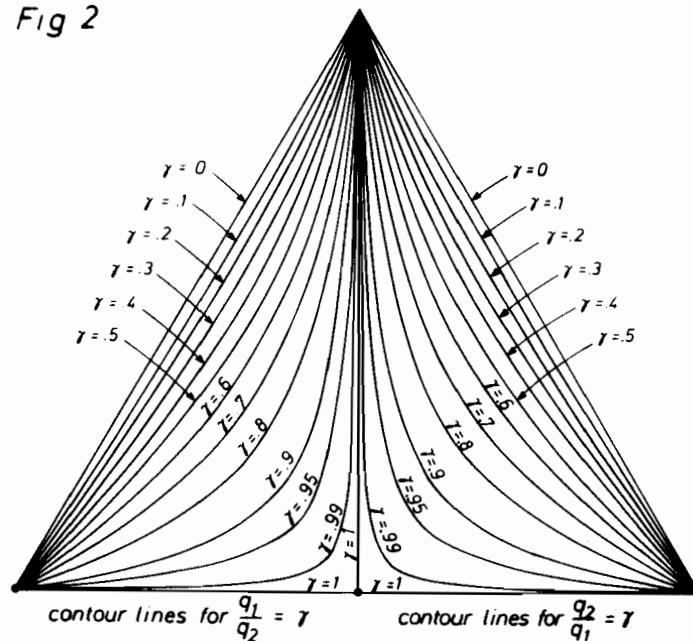
$0 < \gamma_0 < 1$ such that for all genotypic structures with $q_i + q_k \leq 1$ and $q_i/q_k \leq \gamma_0$ the genotypic fitnesses obey the conditions $w_{kk} < w_{ik}$ and $\dfrac{w_{ik} - w_{kk}}{w_{ik} - w_{ii}} \geq \gamma_0$ in case $w_{ii} < w_{ik}$.

Hence, we allow for $w_{ii} \geq w_{ik}$ but exclude underdominance, and in the case of overdominance $\dfrac{w_{ik} - w_{kk}}{w_{ik} - w_{ii}}$ is not allowed to approach arbitrarily close to the value of 0. Consulting Fig. 2, it is immediately seen that the frequency of the i-th allele increases at the latest when the trajectory of genotypic frequencies enters the region to the left of the γ_0-contour line for q_i/q_k (and on or above the Hardy-Weinberg parabola). This implies that the i-th allele is protected in such a system.

(b) The limits set to the effect of segregation distortion by genotypic fitnesses

As before, the aim is to find conditions under which $a_i - a_k$ is positive or negative. Segregation distortion is considered as a force that causes deviations from the results to be expected under the action of regular Mendelian segregation as they are presented in the preceding subsection. This necessi-

tates a study of the effect of segregation distortion within the frame set by the genotypic fitnesses. In accordance with common usage, the amount of segregation distortion will be defined as the average proportion of the i-th allele, say, among the successful gametes produced by heterozygotic individuals and will be denoted by σ_i. Hence, $a_{ik}(i) = \sigma_i \cdot w_{ik}$ and therefore $a_{ik}(i) - a_{ik}(k) = w_{ik} \cdot (2 \cdot \sigma_i - 1)$, which must be inserted into (4). The problem, as it now appears, is to consider $a_i - a_k$ as a function of σ_i for each given set of genotypic fitnesses and frequencies and observe whether this function changes its sign as σ_i varies between 0 and 1.

Clearly, $a_i - a_k$ assumes its smallest and largest value for $\sigma_i = 0$ and $\sigma_i = 1$, respectively. Consequently, if $a_i - a_k$ is negative for $\sigma_i = 0$ and positive for $\sigma_i = 1$, the results expected for regular Mendelian segregation could be reversed in the presence of segregation distortion, while otherwise they are maintained. Because of this, interest will be focused on specifying the conditions for genotypic fitnesses and frequencies under which $a_i - a_k$ is negative and positive according to the extreme values $\sigma_i = 0$ and $\sigma_i = 1$. In terms of equation (4), these conditions require that

$$\tfrac{1}{2}(w_{ii} - w_{ik}) \cdot q_i + \tfrac{1}{2}(w_{ik} - w_{kk}) \cdot q_k - w_{ik}(1 - \tfrac{1}{2}(q_i + q_k)) \leq$$

$$\leq 0 \leq \tfrac{1}{2}(w_{ii} - w_{ik}) \cdot q_i + \tfrac{1}{2}(w_{ik} - w_{kk}) \cdot q_k + w_{ik}(1 - \tfrac{1}{2}(q_i + q_k))$$

holds, which can be written more conveniently as

$$- 2 \cdot w_{ik} \cdot (1 - q_i) \leq w_{ii} q_i - w_{kk} \cdot q_k \leq 2 \cdot w_{ik} \cdot (1 - q_k). \tag{5}$$

The case $w_{ik} = 0$ or $q_i = q_k = 1$ can be excluded from the considerations since in both these cases the influence of heterozygotes on $a_i - a_k$ is eliminated.

If, in particular, $q_i = q_k =: q > 0$ (and thus $p_i = p_k = \tfrac{1}{2}$), then (5) reduces to $|w_{ii} - w_{kk}| \leq 2 \cdot w_{ik} \cdot \dfrac{1-q}{q}$ (note that for q=0 (5) is always realized). One expects this inequality not to be realized and, therefore, the sign of $a_i - a_k$ not to be affected by the influence of segregation distortion if w_{ik} but not q is small and the homozygotes differ markedly in fitness. In general, assuming that both q_i and q_k are not small, the same speculation applies when $q_i \neq q_k$. A more precise representation of this aspect, however, requires the explicit formulation of a question that allows for a meaningful answer. For the present purpose, the probably most comprehensive characterization would be to delimit the region of genotypic frequencies within which a given set of genotypic fitnesses must be realized in order to satisfy (5). In the complement of this region, the sign

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of a_i-a_k would then not be influenced by segregation distortion.

Division of (5) by w_{ik} yields

$$-2(1-q_i) \leq h_i \cdot q_i - h_k \cdot q_k \leq 2(1-q_k) \tag{5a}$$

where $h_i = w_{ii}/w_{ik}$ and $h_k = w_{kk}/w_{ik}$ could be conceived of as measuring the deviation of both homozygotes from the hetero-zygote with respect to fitness and are kept fixed in accordance with the above reasoning.

In order to achieve comparability of the present results with those of the previous subsection, it is advisable to investigate the validity of (5a) along q_i/q_k-contour lines. Again, considerations are restricted to one-half of the frequency triangle (Fig. 2) by assuming that $q_i/q_k \leq 1$. Hence, setting $\gamma := q_i/q_k$ as before, with the restriction that $0 \leq \gamma \leq 1$ and $0 < q_k < 1$, (5a) reads

$$-2(1-q_k \cdot \gamma) \leq q_k(h_i \cdot \gamma - h_k) \leq 2(1-q_k). \tag{5b}$$

It is immediately clear that (5b) holds for small values of q_k, i.e. in the vicinity of the top of the triangle (Fig. 2), as was to be expected. The following statements are easily proven:
If $h_i \cdot \gamma - h_k > 0$ then (5b) is satisfied exactly for all positive q_k not exceeding a value of $\dfrac{2}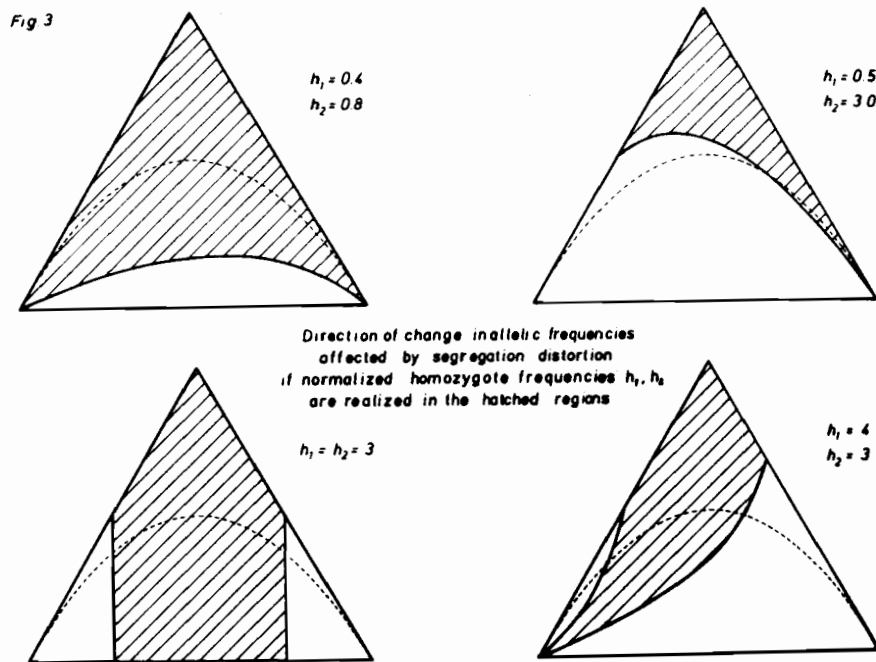{2 + h_i \cdot \gamma - h_k}$; if $h_i \cdot \gamma - h_k < -2(1-\gamma)$ then (5b) is satisfied exactly for all positive q_k not exceeding a value of $\dfrac{2}{h_k - \gamma(h_i - 2)}$; (5b) is satisfied for all q_k, $0 < q_k < 1$ if and only if

$$-2(1-\gamma) \leq h_i \cdot \gamma - h_k \leq 0.$$

The most significant conclusion that can be drawn from these findings is that (5a) holds for all genotypic frequencies (with $P_{ik} > 0$) if and only if $h_i = h_k \leq 2$. Therefore, only if this condition is not met by a set of genotypic fitnesses does there exist a region of genotypic frequencies such that, provided the fitnesses are realized in this region, the sign of a_i-a_k does not depend on the amount of segregation distortion. Several examples for this are given in Fig. 3.

An exhaustive discussion of the precise conditions under which the regions shown in this figure take on their characteristic shapes would grow too lengthy to be justified by the nature of this paper. However, the examples presented here have been selected as demonstrating typical relationships that may occur between genotypic fitnesses. In particular, the triangle with $h_1 = 0.5$ and $h_2 = 3.0$, indicating selective disadvantage of allele 1 refers to the frequent observation that an allele (allele 1) inducing segregation distortion also lowers fitness (cf. e.g. Crow 1979).

Fig 3

$h_1 = 0.4$
$h_2 = 0.8$

$h_1 = 0.5$
$h_2 = 30$

Direction of change in allelic frequencies
affected by segregation distortion
if normalized homozygote frequencies h_1, h_2
are realized in the hatched regions

$h_1 = h_2 = 3$

$h_1 = 4$
$h_2 = 3$

5. AN EXAMPLE OF HOW TO OBTAIN GENOTYPIC FITNESSES

Consider an effectively infinite dioecious population of
diploid animals reproducing in discrete, non-overlapping gene-
rations. All females mate exactly once and at random; males
also mate at random and do not differ with respect to mating
propensity. For a single, autosomal locus, let
$N_{ij}^{\female}$ and $N_{ij}^{\male}$ be the number of females and males, respectively,
having the (unordered) (i,j)-genotype at the zygotic stage.
Furthermore, let $s_{ij}^{\female}$, $s_{ij}^{\male}$ be the probability of survival from
the zygotic to the reproductive stage of female and male
(i,j)-genotypes, and denote by $b_{ij;kl}$ the average number of
offspring of a mating between an (i,j)-female and (k,l)-male.

According to the definition in Section 2, the fitness of
an (i,j)-female is obtained by computing the average number
of successful gametes (ovules) produced per (i,j)-female over
its whole life span. The number of (i,j)-female zygotes sur-
viving to the reproductive stage equals
$N_{ij}^{\female} \cdot s_{ij}^{\female}$ and, at that stage, the relative frequency of (k,l)-

males equals $\dfrac{P_{kl}^{\male} \cdot s_{kl}^{\male}}{\bar{s}^{\male}}$ where $P_{kl}^{\male} := N_{kl}^{\male}/N^{\male}$, $N^{\male} := \sum\limits_{i \leq j} N_{ij}^{\male}$ and

$\bar{s}^{\male} := \sum\limits_{i \leq j} s_{ij}^{\male} \cdot P_{ij}^{\male}$. Consequently, a fraction $P_{kl}^{\male} \cdot s_{kl}^{\male} / \bar{s}^{\male}$

of the $N^{\female}_{ij} \cdot s^{\female}_{ij}$ females produce $b_{ij;kl}$ zygotes, and therefore the total number of zygotes (successful ovules) produced per (i,j)-female equals

$$\frac{N^{\female}_{ij} \cdot s^{\female}_{ij}}{N^{\female}_{ij}} \cdot \sum_{\substack{k,l \\ k \leq l}} b_{ij;kl} \cdot s^{\male}_{kl} \cdot P^{\male}_{kl} / \bar{s}^{\male}. \text{ Hence, the fitness } w^{\female}_{ij} \text{ of an}$$

(i,j)-female genotype is given by

$$w^{\female}_{ij} = \sum_{\substack{k,l \\ k \leq l}} c_{ij;kl} \cdot P^{\male}_{kl} / \bar{s}^{\male}$$

with $c_{ij;kl} = s^{\female}_{ij} \cdot b_{ij;kl} \cdot s^{\male}_{kl}$.

To obtain the male genotypic fitnesses, note that the number of matings performed by (k,l)-males with (i,j)-females equals

$$N^{\female}_{ij} \cdot s^{\female}_{ij} \cdot \frac{s^{\male}_{kl} \cdot P^{\male}_{kl}}{\bar{s}^{\male}} , \text{ where each such mating yields } b_{ij;kl}$$

offspring (successful male gametes). Therefore, the total number of zygotes initiated per (k,l)-male equals

$$\sum_{\substack{i,j \\ i \leq j}} N^{\female}_{ij} \cdot s^{\female}_{ij} \cdot \frac{s^{\male}_{kl} \cdot P^{\male}_{kl}}{\bar{s}^{\male}} \cdot b_{ij;kl} / N^{\male}_{kl}, \text{ which can be written as}$$

$$\sum_{\substack{i,j \\ i \leq j}} N^{\female} \cdot P^{\female}_{ij} \cdot s^{\female}_{ij} \cdot b_{ij;kl} \cdot s^{\male}_{kl} / (N^{\male} \cdot \bar{s}^{\male}), \text{ where } P^{\female}_{ij} = N^{\female}_{ij} / N^{\female} \quad \text{and}$$

$N^{\female} = \sum_{i \leq j} N^{\female}_{ij}$. Hence, the fitness $w^{\male}_{kl}$ of a (k,l)-male genotype is given by

$$w^{\male}_{kl} = \frac{N^{\female}}{N^{\male}} \cdot \sum_{\substack{i,j \\ i \leq j}} c_{ij;kl} \cdot P^{\female}_{ij} / \bar{s}^{\male}.$$

Setting $N_{ij} := N^{\female}_{ij} + N^{\male}_{ij}$, it follows that the fitness w_{ij} of the (i,j)-genotype (i.e. averaged over (i,j)-males and females in the population) equals $\dfrac{N^{\female}_{ij}}{N_{ij}} \cdot w^{\female}_{ij} + \dfrac{N^{\male}_{ij}}{N_{ij}} \cdot w^{\male}_{ij}$,

which can be reformulated in terms of genotypic frequencies:

$$w_{ij} = \frac{N^{\female} \cdot P^{\female}_{ij}}{N^{\female} \cdot P^{\female}_{ij} + N^{\male} \cdot P^{\male}_{ij}} \cdot w^{\female}_{ij} + \frac{N^{\male} \cdot P^{\male}_{ij}}{N^{\female} \cdot P^{\female}_{ij} + N^{\male} \cdot P^{\male}_{ij}} \cdot w^{\male}_{ij}.$$

This representation is simplified considerably if any form of sex distortion among the zygotes can be excluded, such that

$N^{\female} = N^{\male}$ and $P^{\male}_{ij} = P^{\female}_{ij} =: P_{ij}$ for all genotypes. In this case

$$w_{ij} = \frac{1}{2}(w^{\female}_{ij} + w^{\male}_{ij}) = \sum_{\substack{k,l \\ k \leq l}} \frac{1}{2}(c_{ij;kl} + c_{kl;ij}) \cdot P_{kl} / \bar{s}^{\male} \qquad (6)$$

which, apart from the denominator, coincides with the representation derived by Gregorius and Ziehe (1982) for a fecundity selection model introduced by Roux (1977). It is seen that, even if the selection coefficients $s^{\female}_{ij}$, $s^{\male}_{ij}$ and $b_{ij;kl}$ are constant, genotypic fitnesses are, in general, frequency dependent, so that ranking relationships such as overdominance, underdominance, etc. could be realized in certain regions of the state space of genotypic frequencies but not in others. This frequency dependence vanishes if there are no fecundity differences between the mating pairs, i.e. $b_{ij;kl} \equiv b$, and if viability selection takes place symmetrically in the sexes, i.e. $s^{\female}_{ij} = s^{\male}_{ij} = s_{ij}$, since then (6) reads $w_{ij} = b \cdot s_{ij}$. This is the situation of the 'classical' viability-selection model, and it is probably the only selection model based on random-mating for which frequency dependence of genotypic fitnesses vanishes. A detailed discussion of this problem for a general model for plant populations consisting of several sexual types can be found in Gregorius and Ross (1981).

An attempt to give an even extremely condensed survey of the range of applicability of the ideas presented here would by far exceed the limits reasonably set to a single paper. Nevertheless, the present author hopes that at least some of his considerations could help to achieve a higher level of precision concerning our intuitive understanding of genetic fitness concepts with regard to their population and evolutionary genetic relevance. For example, many population geneticists still feel confused by the arguments exerted in connection with the selectionist-neutralist controversy which, essentially, seems to be due to the interpretation of fitnesses as being multiplicative, additive, etc. and constant. Biologically intelligible justifications for such mathematically technical assumptions can hardly be found. However, as is demonstrated by the above example, even for constant selection coefficients of biologically justifiable structure, fitnesses may easily show frequency dependence and are therefore more liable to maintain multiple allelic polymorphisms. This touches also very basically on the question of the conditions under which it is reasonable to consider the gene, the gamete or the genotype as the unit of selection (cf. e.g. Franklin and Lewontin (1970)).

It may be that many results from theoretical population genetics could be classified much more easily with respect to their underlying ecological and evolutionary principles if they were given an interpretation in terms of fitness properties rather than properties of selection parameters.

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