CHROMATID SEGREGATION OF TETRAPLOIDS AND HEXAPLOIDS[1]

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INTRODUCTION

IN an earlier paper (GEIRINGER 1948) the author has investigated the mathematical genetics of autopolyploids if one locus is considered and chromosome segregation is assumed. A paper on the linkage theory of autopolyploids (m loci), under the same assumption, is in press (GEIRINGER 1949). However, while chromosome segregation might be assumed as an approximation theory, the study of polyploids should actually be based on the consideration of chromatid segregation. In the case of one locus this theory can be worked out and is presented in this paper as far as random mating is concerned. This study, for $m=1$, as well as the approximation theory for general m, may serve as a necessary preparation for a general linkage theory of polyploids under chromatid segregation.

A basic paper by J. B. S. HALDANE (1930) is mainly concerned with the chromosome segregation theory of polyploids; "random chromatid segregation" of tetraploids is briefly discussed too and a limit formula (our formula (24)) follows. In a paper of a more recent date R. A. FISHER (1947) deals with the linkage theory of polyploids under chromatid segregation. The paper uses important earlier investigations by the same author (1941, 1944) as well as a paper by FISHER and MATHER (1943) and papers by MATHER (1935, 1936).

As in previous papers it is our aim to consider a heredity problem like the one in question as a probability problem. From certain basic probability distributions which must be known other genetical distributions are derived by means of probability calculus. The fate of these distributions, from generation to generation, is the main subject of the mathematical investigation.

If we assume distinct, non overlapping generations, numbered 0, 1, $\cdots$ n, $\cdots$ we may denote by $w^{(n)}(x; y)$ the *distribution of genotypes* in the n^{th} generation. Here x denotes the genetic material the individual has received from its mother and y designates the paternal heritage. We assume that there is no genotypic difference between an individual of type (x; y) and one of type (y; x); that is: $(x; y)=(y; x)$. Accordingly $w^{(n)}(x; y)=w^{(n)}(y; x)$; and $\sum_x\sum_y w^{(n)}(x; y)=1$. We may assume that at the beginning, for $n=0$, the distributions of genotypes are the same for males and females; if they are not the same, that is, if $w^{(0)}(x; y)$ is the genotype for females and $\overline{w}^{(0)}(x; y)$ the one for males, they will be the same after one generation of random breeding.

In the formation of a new individual a parent transmits to the offspring one set of genes, the other set coming from the other parent. The kinds of gametes which an organism may produce correspond to the possible combinations of the genetic material it has inherited. This segregation takes place according to a

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probability law which we call *segregation distribution* (s.d., see section 2). It is one of the main tasks of biological theory to suggest, in accordance with observations and other theoretical (for instance cytological) evidence, the s.d. which corresponds to a biological situation. If we assume random breeding, it is possible to derive from the *distribution of genotypes* (d.ge.) and the s.d. the third important distribution, the *distribution of gametes* (d.ga.), $p^{(n)}(z)$. Finally, under random mating, $w^{(n+1)}(x; y)$ follows from $p^{(n)}(z)$ since a new genotype is formed by the fusion of two gametes. A complete cycle of inheritance is thus described.

So far we have been faced with the following problems: a) Complete enumeration of the possible genotypes and gametes corresponding to a biological situation; b) definition of the s.d.; c) derivation of the d.ga. from the d.ge. by means of the s.d. These problems are of course not new: for example, FISHER's statement "The laws of inheritance obtained by genetic studies are the rules whereby, given the constitution of an organism, the kinds of gametes it can produce and their relative frequencies can be predicted" (1947, p. 55) corresponds to our problems b) and c). While in all these instances the basic suggestions must come from the biologist—from his observations and their interpretation—the mathematician may be able to help in clarifying and simplifying the concepts.

A few further problems are of a more theoretical nature: d) It is essential to derive direct *recurrence relations* between subsequent distributions of gametes, that is, relations by means of which we know $p^{(n+1)}(z)$ if $p^{(n)}(z)$, or perhaps several $p^{(\gamma)}(z)$ where $\gamma \leqq n$, are known. Such a recurrence formula will be simpler than the corresponding one for $w^{(n+1)}(x; y)$. The recurrence problem constitutes the basic problem of the theory. e) It is desired to *integrate* these recurrence relations, that is, to determine $p^{(n)}(z)$ in terms of $p^{(0)}(z)$, of "n," and of the parameters introduced. f) We want to know whether, and if so, under what conditions an *equilibrium status* is reached for $p^{(n)}(z)$, and, consequently, for $w^{(n)}(x; y)$. In connection with this question we must study the *limit distribution* of $p^{(n)}(z)$ and of $w^{(n)}(x; y)$ as $n \to \infty$.

Those last problems seem to be of a rather theoretical character. They are, however, of practical value as well, since they allow qualitative and quantitative predictions which, in turn, may be checked by means of observations. In particular, the equilibrium distribution is of interest, since we may often be entitled to assume that a population has actually reached the equilibrium status.

In the present paper all these problems have been studied for autopolyploids with *one locus*, for an *arbitrary number of alleles*, r, assuming *chromatid segregation*. The result is that we find an entirely *new type of recurrence relations* as compared with those in GEIRINGER (1944, 1948) which are characteristic for chromosome segregation; we likewise arrive at a *new type of limit distribution* (see sections 3 and 5). The case of tetraploids and hexaploids has been investigated completely and octoploids have been considered in some detail. Let us now, briefly, describe the approach.

The main characteristic of a polyploid organism is that (with respect to one locus) a gamete consists not of one but of $s > 1$ genes. An orthopolyploid has $2s$ genes, or $2s$ chromosomes. More specifically, the organism possesses two sets

of s chromosomes each, each chromosome being represented by one of the numbers $a_1, \cdots, a_r$, the r alleles, where r may be less than, greater than, or equal to s. Accordingly, the d.ge. and the d.ga. are discrete probability distributions in 2s and s variables respectively. In the formation of a new individual each parent transmits to the offspring one set of s genes. The selection of those transmitted genes happens according to the s.d. Of this s.d. we assume: 1) that it is the same for males and females, 2) that it does not depend on "n" and hence remains the same throughout the generations, 3) that it does not depend on the specific genotype of the parent.

There are 4s chromatids (2s chromosomes) and out of these 4s chromatids,

$$S = \binom{4s}{s} = \frac{(4s)!}{s!(3s)!}$$

sets of s can be selected. For $s = 2, 3, 4$, $S = 28, 220, 1820$. (See page 671 for comparison with chromosome segregation theory.) A set of s selected genes may be derived from $(s-\rho)$ different chromosomes where ρ may take on the values $0, 1, \cdots, \mu$ if $s = 2\mu$ or $2\mu+1$ respectively; such a set contains ρ pairs of sister chromatids. Hence there are from this point of view $(\mu+1)$ different modes of segregation. A gamete may be called "normal" for the moment if it is derived from s chromosomes ($\rho = 0$) and hence does not contain any pair of sister chromatids. There exist obviously $S_1 = 2^s \cdot \binom{2s}{s}$ "normal" gametes and $S - S_1$ gametes which contain at least one pair of sister chromatids (due to "double reduction"). If the consequences of occasional double reduction are neglected, that is, if in the definition of the s.d. all probabilities of non-normal gametes are assumed to be zero, then chromatid s.d. and chromosome s.d. amount to the same. Such an assumption may be regarded as an approximation to reality. According to the $(\mu+1)$ values of ρ, FISHER and MATHER introduce $(\mu+1)$ parameters in the s.d. (section 2).

The present author considers a more general s.d. Besides the above explained differentiation, which refers to the values of ρ, we take into account the *proportion of paternal and of maternal genes* in a gamete. This idea has been used to great advantage in the author's previous papers (1944, 1948, 1949). In fact, this more differentiated segregation distribution is needed in order to establish the recurrence relations and to understand their structure. In these recurrence formulas which form the main aim of the mathematical theory and which express biological facts, the values of the s.d. act as separators between meaningful groups of probabilities. This fact suggests that these parameters may have a biological meaning; this, of course, can be checked by counting the results of observations and evaluating the resulting figures in the usual statistical way. On the other hand, it is very easy to forget about those parameters after having established the recurrence relations. If, for example, we accept FISHER and MATHER'S segregation theory we merely have to put all our segregation probabilities which correspond to the same ρ equal to each other, reducing thus the number of parameters to $(\mu+1)$. Other s.d.'s contained as particular cases in our s.d. represent *the general chromosome s.d.* of the author's earlier paper (1948), *random chromatid segregation* (HALDANE 1930), etc.

In section 2 of this paper the three basic distributions, the distributions of genotypes and of gametes, and the segregation distribution are defined. In section 3 we derive the recurrence relations (problem (d)) for $s=2, 3, 4$. They differ in an essential way from the recurrence relations under chromosome segregation. Section 4 contains, by way of illustration, a simple numerical example. Finally, in section 5 corresponding to problems e) and f), the recurrence relations are integrated and the equilibrium status is determined.

THE DISTRIBUTION OF GAMETES, THE DISTRIBUTION OF GENOTYPES, AND THE SEGREGATION DISTRIBUTION

The enumeration of the possible types of gametes and of genotypes is simple. In the case of $m=1$ locus there exist, for a 2s-ploid and r alleles, $R=\binom{r+s-1}{s}$ possible gametes; that is, if $s=2$, $r=3$: $R=6$ and the gametes are a_1^2, a_2^2, a_3^2, a_1a_2, a_2a_3, a_3a_1; or if $s=4$, $r=5$: $R=70$ possible gametes: $a_1^4, \cdots a_5^4$, $a_1^3a_2, \cdots, a_4^3a_5, \cdots, a_2a_3a_4a_5$. If one wants to enumerate the possible *types* of gametes, the number of *partitions* is to be considered as R. A. FISHER remarks. Denote by $\pi_\rho(s)$, $(\rho \geqq 1)$ the number of different ways in which the integer s can be resolved into the sum of ρ positive integers; clearly $\pi_\rho(s)=0$, if $\rho > s$. Next put $P_r(s)=\sum_{\rho=1}^{r}\pi_\rho(s)$. There are obviously $P_r(s)$ different types of gametes for a 2s-ploid and r alleles. Consider for instance $s=2$, $r=3$ $\pi_1(2)=1$, $(2=2)$, $\pi_2(2)=1$, $(2=1+1)$, $\pi_\rho(2)=0$, $\rho \geqq 3$; $P_3(2)=1+1+0=2$ and the two types are, in fact: a_1^2 and a_1a_2. Or if $s=4$, $r=3$: $\pi_1(4)=1$, $(4=4)$, $\pi_2(4)=2$, $(4=3+1=2+2)$, $\pi_3(4)=1$, $(4=2+1+1)$, $\pi_4(4)=1$, $(4=1+1+1+1)$, $\pi_\rho(4)=0$, $\rho \geqq 5$; and $P_3(4)=1+2+1=4$. In fact the types are: a_1^4, $a_1^3a_2$, $a_1^2a_2^2$, $a_1^2a_2a_3$.

Similar remarks hold for the genotypes. If (like most authors) one does not distinguish between maternal and paternal heritage there are $R'=\binom{r+2s-1}{2s}$ possible genotypes. If, however, this distinction *is* made, (as we do), then, with $R=\binom{r+s-1}{s}$ there are $R(R+1)/2$ possible genotypes.

For example for $2s=4$, $r=4$ these two numbers are 35 and 55 respectively with 5 or 7 different types respectively. These are in the first conception: a_1^4, $a_1^3a_2$, $a_1^2a_2^2$, $a_1^2a_2a_3$, $a_1a_2a_3a_4$, and in the second: $(a_1^2; a_1^2)$, $(a_1^2; a_1a_2)$, $(a_1^2; a_2^2)$, $(a_1a_2; a_1a_2)$, $(a_1^2; a_2a_3)$, $(a_1a_2; a_1a_3)$, $(a_1a_2; a_3a_4)$.

Let us review a few of the definitions given in the author's previous paper (1948), particularly those dealing with the *distribution of gametes* and the *marginal distributions* derived from it. For $s=2$ the d.ga. is given by $p(z_1, z_2)$, (we may omit the upper script) where each of the two z_i may take on each of the r values $a_1, \cdots, a_r$. We assume that there is no difference between the gametes (a_ia_k) and (a_ka_i) and consequently, $p(a_ia_k)=p(a_ka_i)$. Hence there is one value $p(a_i^2)$ but two values $p(a_ia_k)$, $(a_i \neq a_k)$ and

$$\sum_{i}^{1\cdots r}\ \sum_{k}^{1\cdots r} p(a_i a_k) = 1.$$

From $p(z_1 z_2)$ we derive the marginal distributions of order one:

$$p_1(a_j) = \sum_{z}^{a_1\cdots a_r} p(a_j, z) \quad \text{and} \quad p_2(a_j) = \sum_{z}^{a_1\cdots a_r} p(z, a_j), \quad (j = 1, 2, \cdots, r).$$

It follows from $p(a_i a_k) = p(a_k a_i)$ that $p_1(a_j) = p_2(a_j) = p(a_j)$; these are the *marginal distributions of order one* and

$$\sum_{i}^{1\cdots r} p(a_i) = 1.$$

If $s = 3$ the d.ga. is $p(z_1 z_2 z_3)$ where each z_i equals a_1, or a_2, $\cdots$, or a_r and we derive from it

$$p_{12}(a_i a_k) = \sum_{z}^{a_1\cdots a_r} p(a_i, a_k, z), \qquad p_{13}(a_i a_k) = \sum_{z}^{a_1\cdots a_r} p(a_i, z, a_k)$$

and $p_{23}(a_i a_k)$. Again $p_{12}(a_i a_k) = p_{13}(a_i a_k) = p_{23}(a_i a_k) = p(a_i a_k)$. This *marginal distribution of order two* denotes the probability that of the existing three genes two (specific) genes have the values a_i and a_k. In the same way $p_1(a_i) = p_2(a_i) = p_3(a_i) = p(a_i)$ is derived from $p(z_1, z_2, z_3)$ and

$$\sum\sum\sum p(a_i, a_j, a_k) = 1, \qquad \sum\sum p(a_i a_j) = 1, \qquad \sum p(a_i) = 1.$$

For any s (see GEIRINGER 1948, 271ff) the d.ga. may be denoted either by $p(z_1 \cdots z_s)$, $(z_i = a_1 \cdots, a_r,\ i = 1, 2, \cdots, s)$, or by $p(a_1^{x_1} a_2^{x_2} \cdots a_r^{x_r})$, $(x_j = 0, 1, 2, \cdots; x_1 + x_2 + \cdots + x_r = s)$ and marginal distributions of orders, $1, 2, \cdots, s-1$ may be derived; for instance with

$$s = 7, r = 5, p(a_1^2 a_2) = \sum_{z_1}\sum_{z_2}\sum_{z_3}\sum_{z_4} p(a_1 a_1 a_2 z_1 z_2 z_3 z_4)$$

(the summations are from a_1 to a_5), and there are $\binom{7}{3}\cdot\binom{3}{2} = 105$ such probabilities; here $p(a_1^2 a_2)$ denotes the probability that of the existing 7 genes, 3 specified ones have the values a_1, a_1, a_2.

All this is independent of the distinction between chromosome and chromatid segregation.

Let us now consider *the s.d.* In a 2s-ploid of one locus, there are 2s chromosomes and 4s chromatids; in a diploid organism there are 2 chromosomes and 4 chromatids. *For the diploid with any number of loci, chromatid segregation and chromosome segregation amounts to the same.* In fact denote a diploid with m loci by $(x; y) = (x_1 \cdots x_m; y_1 \cdots y_m)$ where x_i, (y_i) constitutes the maternal (paternal) heritage with respect to the i^{th} character. Consider chromosome segregation. There are 2^m possible gametes. We denote (GEIRINGER 1944) for instance by $l(11000 \cdots 10)$ the probability that $(x_1 x_2 y_3 y_4 y_5 \cdots x_{m-1}, y_m)$ be transmitted—with certain symmetry relations for these $l(\epsilon_1 \epsilon_2 \cdots \epsilon_m)$. Next

consider chromatid segregation and denote by x_i, x_i' or by y_i, y_i' corresponding sister chromatids. There are now $2^m \cdot 2^m = 2^{2m}$ possible gametes. Denote by $2^m l'(11 \cdots 1)$ the probability that the gamete contains x-values only (for example, $(x_1 x_2 \cdots x_m)$, or $(x_1' x_2 \cdots x_m)$, etc.) by $2^m l'(11000 \cdots 10)$ the probability that the first, second $\cdots$ and $(m-1)^{st}$ value is an x, the third, fourth, fifth $\cdots$ and last a y-value, etc. Then, with $2^m l'(\epsilon_1 \epsilon_2 \cdots \epsilon_m) = l(\epsilon_1 \epsilon_2 \cdots \epsilon_m)$, $(\epsilon_i = 0, 1; i = 1, 2, \cdots, m)$ we obtain again the same s.d. as before. The reason is of course that, if $s = 1$, with respect to each character, one gene only is transmitted, hence x_i, x_i' can not be found in the same gamete. In particular, *there is no difference between* "random chromosome segregation" ("independent assortment") and "random chromatid segregation." The former amounts to

$$l(\epsilon_1 \epsilon_2 \cdots \epsilon_m) = \frac{1}{2^m}$$

for all ϵ-combinations, the second to

$$l'(\epsilon_1 \epsilon_2 \cdots \epsilon_m) = \frac{1}{2^{2m}}$$

and

$$2^m l'(\epsilon_1 \cdots \epsilon_m) = \frac{1}{2^{2m}} \cdot 2^m = \frac{1}{2^m} = l(\epsilon_1 \epsilon_2 \cdots \epsilon_m).$$

This is quite different if $s > 1$. Assume $m = 1$ (one locus), and denote an organism by $(x_1 \cdots x_s; y_1 \cdots y_s)$ where each x_i and each y_i may be equal to one of the r alleles $a_1, \cdots, a_r$. If we want a notation to show the 4s chromatids we write:

$$(1) \qquad (x_1 \cdots x_s, x_1' \cdots x_s'; y_1 \cdots y_s, y_1' \cdots y_s')$$

or rather:

$$(1') \qquad \begin{pmatrix} x_1 \cdots x_s & y_1 \cdots y_s \\ x_1 \cdots x_s & y_1 \cdots y_s \end{pmatrix}.$$

Denote by μ_α the probability that a specified set of α maternal and a specified set of $(s-\alpha)$ paternal genes be transmitted, but such that the resulting gamete does not contain a single pair of sister chromatids. There are, corresponding to each α, $2^\alpha \binom{s}{\alpha} \cdot 2^{s-\alpha} \binom{s}{s-\alpha} = 2^\alpha \left[\binom{s}{\alpha}\right]^2$ such probabilities and we assume *that they be all equal to each other;* moreover we assume

$$(2) \qquad \mu_\alpha = \mu_{s-\alpha}.$$

Next *denote by μ_α'* (by μ_α'', by μ_α''', $\cdots$,) *the probability that a specified set of α maternal and $(s-\alpha)$ paternal genes be transmitted such that the resulting gamete contains exactly one pair (exactly two pairs, exactly three pairs, $\cdots$) of corresponding sister chromatids.* In other words: The gamete is derived from $s-\rho$ different chromosomes where $\rho = 1, 2, \cdots, \mu$, if $s = 2\mu$ or $2\mu+1$ respec-

tively. Assume that all μ_α' for the same α, equal each other; all μ_α'' for the same α, equal each other; etc. and

$$\mu_\alpha' = \mu'_{s-\alpha},\ \mu_\alpha'' = \mu''_{s-\alpha},\ \text{etc.} \tag{3}$$

With these notations we have for s=2, 3, 4:

$$\text{s} = 2: \quad 4(\mu_0 + 4\mu_1 + \mu_2) + 2(\mu_0' + \mu_2') = 1 \tag{4}$$

or, using (2), (3):

$$\text{s} = 2: \quad 4\cdot 2(\mu_0 + 2\mu_1) + 4\mu_0' = 1 \tag{4'}$$

$$\text{s} = 3: \quad 8\cdot 2(\mu_0 + 9\mu_1) + 2(12\mu'_0 + 18\mu_1') = 1 \tag{5}$$

$$\text{s} = 4: \quad 16\cdot 2(\mu_0 + 16\mu_1 + 18\mu_2) + 2(48\mu_0' + 192\mu_1' + 96\mu_2') + 2(6\mu_0'' + 8\mu_2'') = 1. \tag{6}$$

We see that for s=2, 3, 4 we have respectively 2, 3, and 7 parameters. According to FISHER and MATHER (1943) we would put for each s, all μ equal to each other, all μ' equal to each other, etc. and this would amount to:

$$\text{s} = 2: \quad 24\mu + 4\mu' = 1, \quad 4\mu' = \alpha \tag{4''}$$

$$\text{s} = 3: \quad 160\mu + 60\mu' = 1, \quad 60\mu' = \beta \tag{5''}$$

$$\text{s} = 4: \quad 1120\mu + 672\mu' + 28\mu'' = 1, \quad 28\mu' = \gamma, \quad 28\mu'' = \delta. \tag{6''}$$

If the s.d. is known, the "gametic output" that corresponds to any particular genotype follows very easily. As an example consider the genotype

$$(a_1a_2^2;\ a_1^2a_3) \quad \text{or} \quad \begin{pmatrix} a_1a_2a_2 & a_1a_1a_3 \\ a_1a_2a_2 & a_1a_1a_3 \end{pmatrix}$$

where the following ten gametes and their corresponding probabilities may originate:

gamete	probability
a_1^3	$4\mu_2' + 8\mu_1 + 4\mu_1' + 4\mu_0'$
a_2^3	$4\mu_3'$
a_3^3	0
$a_1^2a_2$	$4\mu_3' + 32\mu_2 + 16\mu_1 + 8\mu_1$
$a_1^2a_3$	$2\mu_2' + 16\mu_1 + 8\mu_0 + 4\mu_0'$
$a_2^2a_1$	$4\mu_3 + 4\mu_3' + 16\mu_2 + 8\mu_2'$
$a_2^2a_3$	$8\mu_2 + 4\mu_2'$
$a_3^2a_1$	$2\mu_1' + 4\mu_0'$
$a_3^2a_2$	$4\mu_1'$
$a_1a_2a_3$	$16\mu_2 + 32\mu_1$

To illustrate the computation of each of these ten probabilities consider for instance $a_1^2a_2$: Firstly, three maternal values may be transmitted, namely the two a_1-values and one of the four a_2-values; that can happen in $1 \cdot 4 = 4$ ways and since in such a gamete one pair of sister chromatids occurs the probability is $4\mu_3'$. Next, two maternal values and one paternal value may be used; there are to the left of the semicolon two a_1-chromatids and four a_2-chromatids, hence a_1a_2 may be selected in eight ways while the last a_1-value may be selected from the four values to the right in four ways, hence the term $32\mu_2$. Next one maternal value is used; since a_2 occurs to the left only this value must be a_2, which can be selected in four ways; it is combined with a pair out of the four a_1-values to the right. Among the six possible pairs of such values two correspond to sister-chromatids while four pairs are "normal"; hence the two terms $4 \times 4\mu_1 + 4 \times 2\mu_1'$. In the same way all other gametes and their probabilities may be discussed.

If the genotype in question is considered as: $(a_1^3a_2^2a_3)$ and accordingly all μ-values are equal to each other and all μ'-values equal to each other, the probability of the gamete $a_1^2a_2$ becomes

$$48\mu + 12\mu' + \frac{18 - 6\beta}{60}$$

which appears in FISHER, 1947, p. 58, second table, second line, third column. (Our a_1, a_2, a_3 are denoted by Fisher by a, A', A).

Consider on the other hand the genotype $(a_1a_2a_3;\ a_1^2a_2)$ which, in my conception is different from $(a_1a_2^2;\ a_1^2a_3)$. The probability that the organism $(a_1a_2a_3;\ a_1^2\,a_2)$ transmits the gamete $a_1^2a_2$ is: $2\mu_3' + 16\mu_2 + 2\mu_2' + 16\mu_3 + 8\mu_1 + 4\mu_1' + 8\mu_0 + 4\mu_0'$ and this is quite different from the previously found value $4\mu_3' + 32\mu_2 + 16\mu_1 + 8\mu_1'$ which corresponds to the same gamete $(a_1^2a_2)$ derived from $(a_1a_2^2;\ a_1^2a_3)$. If however, $\mu_3 = \mu_2 = \mu_1 = \mu_0$, $\mu_3' = \mu_2' = \mu_1' = \mu_0'$ the preceding probability reduces again to $48\mu + 12\mu'$, as before. These examples should suffice. (See also beginning of sec. 4.)

As stated before, *our* s.d. *reduces to* FISHER *and* MATHER'S *assumption by equating all* μ *to each other, all* μ' *to* each other, all μ'' to each other, etc. It *reduces to the general chromosome segregation distribution* introduced in GEIRINGER (1948) if all μ', all μ'', $\cdots$ *are equal to zero.* In particular, *random chromosome* segregation follows if, *in addition all* μ_α *are equal to* each other. We have *random chromatid segregation* if *all* parameters, that is all μ_i, μ_j', μ_k'', $\cdots$, are equal to each other.

RECURRENCE FORMULAS IN CASE OF S = 2, 3, 4

An important formal justification for the introduction of our more complicated s.d. may be found in the role which this s.d. plays in the recurrence formulas which, in the author's opinion, constitute the main result of the mathematical theory. These recurrence formulas, based on the consideration of chromatid segregation, are essentially different from the ones that hold for polyploids with one or several loci if chromosome segregation is assumed. The

new recurrence formulas are *no longer homogeneous*, in a sense we shall explain presently. Nevertheless they are still quite clear-cut and understandable.

We know that if all μ_i', μ_k'', $\cdots$ are equal to zero, chromatid segregation reduces to chromosome segregation. Hence in this case the new recurrence formulas must reduce to the known recurrence formulas for chromosome segregation (GEIRINGER 1948). Hence we actually knowthese new formulas as far as the coefficients of the μ_i are concerned and we are interested in the other terms only.

Let us start with $s=2$. Use $v(x; y)=w(x; y)+w(y; x)=2w\ (x; y)$, $(x\neq y)$, $v(x; x)=w(x; x)$. In terms of these v we have $v(a_1^2; a_1^2)+2v(a_1^2; a_1a_2)+v(a_1^2; a_2^2)+4v(a_1a_2; a_1a_2)+2v(a_1a_2; a_2^2)+v(a_2^2; a_2^2)+\cdots=1$. Here the points at the end of the left side indicate terms corresponding to other alleles. We write $p^{(n)}=p$, $v^{(n)}=v$, $p^{(n+1)}=p'$, $v^{(n+1)}=v'$. We assume now two alleles and compute in the same way as in the example page 671, the probability of the gamete (a_1^2) as derived from various genotypes:

$$\begin{aligned} p(a_1^2) &= v(a_1^2; a_1^2)\cdot 1 + 2v(a_1^2; a_1a_2)(\mu_2' + 8\mu_1 + 4\mu_0 + 2\mu_0') \\ &\quad + v(a_1^2; a_2^2)(4\mu_0 + 2\mu_0') + 4v(a_1a_2; a_1a_2)(\mu_2' + 4\mu_1 + \mu_0') \\ &\quad + 2v(a_1a_2; a_2^2)\mu_0'. \end{aligned} \tag{7}$$

Next we write the same formula (7) for the $(n+1)^{st}$ generation and consider:

$$w^{(n+1)}(x; y) = p^{(n)}(x)p^{(n)}(y) \tag{8}$$

we get, using (2) and (3):

$$\begin{aligned} p'(a_1^2) &= p(a_1^2)^2 + p(a_1^2)p(a_1a_2)(12\mu_0' + 16\mu_0 + 32\mu_1) \\ &\quad + p(a_1^2)p(a_2^2)(8\mu_0 + 4\mu_0') + p(a_1a_2)^2(16\mu_1 + 8\mu_0') \\ &\quad + p(a_1a_2)p(a_2^2)\cdot 4\mu_0' \\ &= 8\mu_0\cdot[p(a_1^2)^2 + 2p(a_1^2)p(a_1a_2) + p(a_1^2)p(a_2^2)] \\ &\quad + 16\mu_1[p(a_1^2)^2 + 2p(a_1^2)p(a_1a_2) + p(a_1a_2)^2] \\ &\quad + 4\mu_0'[p(a_1^2)^2 + 3p(a_1^2)p(a_1a_2) + p(a_1^2)p(a_2^2) \\ &\quad + 2p(a_1a_2)^2 + p(a_1a_2)p(a_2^2)]. \end{aligned}$$

The expressions in brackets are respectively:

$$\begin{aligned} &p(a_1^2)\cdot[p(a_1^2) + 2p(a_1a_2) + p(a_2^2)] = p(a_1^2)\cdot 1 = p(a_1^2) \\ &[p(a_1^2) + p(a_1a_2)]^2 = [p(a_1)]^2 \\ &[p(a_1^2) + 2p(a_1a_2) + p(a_2^2)]\cdot[p(a_1^2) + p(a_1a_2)] = 1\cdot p(a_1) = p(a_1). \end{aligned}$$

Thus we get:

$$p^{(n+1)}(a_1^2) = 8\mu_0 p^{(n)}(a_1^2) + 16\mu_1[p^{(n)}(a_1)]^2 + 4\mu_0' p^{(n)}(a_1). \tag{9}$$

We find the same formula (9) without any change if we assume, more generally, $r>2$ alleles.

This formula (9) reduces to my formula for chromosome segregation if

$\mu_0'=0$, $4\mu_0=\lambda_0$, $4\mu_1=\lambda_1$. If, however, $\mu_0'\neq 0$, (9) is a *non-homogeneous* recurrence formula in contrast to all recurrence formulas established (in GEIRINGER 1944, 1948) under the assumption of chromosome segregation. In fact $p^{(n+1)}(a_1^2)$, $p^{(n)}(a_1^2)$, and $[p^{(n)}(a_1)]^2$ are "of second degree" while $\mu_0' p^{(n)}(a_1)$ is "of first degree." The occurrence of such a term in the recurrence formula can easily be interpreted. This will be done later, together with the consideration of the cases $s=3$, and $s=4$.

Next we compute $p^{(n+1)}(a_1a_2)$ and find:

$$p^{(n+1)}(a_1a_2) = 8\mu_0 p^{(n)}(a_1a_2) + 16\mu_1 p^{(n)}(a_1)p^{(n)}(a_2). \tag{9'}$$

Upon addition of (9) and (9') we obtain:

$$p^{(n+1)}(a_1) = 8\mu_0 p^{(n)}(a_1) + 16\mu_1 p^{(n)}(a_1) + 4\mu_0' p^{(n)}(a_1) = p^{(n)}(a_1).$$

Hence, just as in case of chromosome segregation:

$$p^{(n+1)}(a_i) = p^{(n)}(a_i) = p^{(0)}(a_i) \qquad \begin{matrix}(n = 1, 2, \cdots)\\ (i = 1, 2, \cdots r)\end{matrix} \tag{10}$$

The frequency of each allele remains constant throughout the generations. None of these results changes in case of any number r of alleles. Thus the recurrence formulas for $s=2$ become (with $p^{(0)}(a_i)\equiv p(a_i)$):

$$\begin{aligned} p^{(n+1)}(a_i^2) &= 8\mu_0 p^{(n)}(a_i^2) + 16\mu_1[p(a_i)]^2 + 4\mu_0' p(a_i) \\ p^{(n+1)}(a_ia_k) &= 8\mu_0 p^{(n)}(a_ia_k) + 16\mu_1 p(a_i)p(a_k) \qquad (i, k = 1, 2, \cdots, r). \end{aligned} \tag{9''}$$

For *random chromatid segregation* $\mu_1=\mu_0=\mu_0'=\frac{1}{28}$ these become:

$$\begin{aligned} p^{(n+1)}(a_i^2) &= \frac{2}{7} p^{(n)}(a_i^2) + \frac{4}{7}[p(a_i)]^2 + \frac{1}{7} p(a_i) \\ p^{(n+1)}(a_ia_k) &= \frac{2}{7} p^{(n)}(a_ia_k) + \frac{4}{7} p(a_i)p(a_k) \end{aligned} \tag{9'''}$$

To "complete *equational separation*" (MATHER 1936) $\mu_0=\mu_1=\frac{5}{144}$, $\mu_0'=\frac{6}{144}$ correspond the formulas:

$$\begin{aligned} p^{(n+1)}(a_i^2) &= \frac{5}{18} p^{(n)}(a_i^2) + \frac{10}{18}[p(a_i)]^2 + \frac{3}{18} p(a_i) \\ p^{(n+1)}(a_ia_k) &= \frac{5}{18} p^{(n)}(a_ia_k) + \frac{10}{18} p(a_i)p(a_k). \end{aligned} \tag{9IV}$$

Under FISHER-MATHER's theory where $24\mu+4\mu'\equiv 24\mu+\alpha=1$ we find

$$\begin{aligned} p^{(n+1)}(a_i^2) &= \frac{1-\alpha}{3} p^{(n)}(a_i^2) + \frac{2}{3}(1-\alpha)[p(a_i)]^2 + \alpha p(a_i) \\ p^{(n+1)}(a_ia_k) &= \frac{1-\alpha}{3} p^{(n)}(a_ia_k) + \frac{2}{3}(1-\alpha)p(a_i)p(a_k). \end{aligned} \tag{11}$$

Next consider the case s=3. Computing in the same way as before we find the result:

$$(12)\qquad \begin{aligned} p^{(n+1)}(a_1^3) &= 16\mu_0 p^{(n)}(a_1^3) + 144\mu_1 p^{(n)}(a_1^2)p(a_1) \\ &\quad + 24\mu_0' p^{(n)}(a_1^2) + 36\mu_1'[p(a_1)]^2. \end{aligned}$$

We shall now interpret formula (12) and similar formulas. First let us consider the analogous formula for chromosome segregation (GEIRINGER 1948, p. 259):

$$(12')\qquad \begin{aligned} p^{(n+1)}(A^3) &= \lambda_0 p^{(n)}(A^3) + 9\lambda_1 p(A)p^{(n)}(A^2) \\ &\quad + 9\lambda_2 p^{(n)}(A^2)p(A) + \lambda_3 p^{(n)}(A^3). \end{aligned}$$

We want to analyze it in some detail and consider, for example, the term $9\lambda_2 p^{(n)}(A^2)p(A)$, assuming, for the sake of simplicity, two alleles A and a. Here $p^{(n)}(A^2)=p_{12}^{(n)}(A^2)=p^{(n)}(A^3)+p^{(n)}(A^2a)$ is the probability of a gamete for which the first two of the three genes equal A. In the same way $p_1(A)=p(A)=p^{(n)}(A^3)+p^{(n)}(AAa)+p^{(n)}(AaA)+p^{(n)}(Aaa)$ is the probability of a gamete for which the first of the three genes equals A. We know that $p_{12}^{(n)}(A^2)=p_{13}^{(n)}(A^2)=p_{23}^{(n)}(A^2)=p^{(n)}(A^2)$ and $p_1^{(n)}(A)=p_2^{(n)}(A)=p_3^{(n)}(A)=p^{(n)}(A)=p(A)$. Next consider:

$$\begin{aligned} p^{(n)}(A^2)p(A) &= [p^{(n)}(A^3) + p^{(n)}(A^2a)]\cdot[p^{(n)}(A^3) + 2p^{(n)}(A^2a) + p^{(n)}(Aa)^2)] \\ &= p^{(n)}(A^3)\cdot p^{(n)}(A^3) + p^{(n)}(A^2a)p^{(n)}(A^3) + \cdots \\ &= w^{(n+1)}(A^3; A^3) + w^{(n+1)}(A^2a; A^3) + \cdots + w^{(n+1)}(A^2a; Aa^2) \\ &= \sum_x \sum_y \sum_z w^{(n+1)}(AAx; Ayz). \end{aligned}$$

Consider any of the six $w^{(n+1)}$-terms. For example $9\lambda_2 w^{(n+1)}(A^3; A^3)$ is the probability that, in the $(n+1)^{st}$ generation a genotype be of type $(A^3; A^3)$ and transmits two of its three maternal A-alleles (can happen in three ways) and one of its three paternal alleles (in three ways). In the same way:

$$\begin{aligned} &9\lambda_2 w^{(n+1)}(A^2a; A^3) \\ &\qquad = 3\lambda_2[w^{(n+1)}(AAa; A^3) + w^{(n+1)}(AaA; A^3) + w^{(n+1)}(aAA; A^3)]. \end{aligned}$$

Here $3\lambda_2 w^{(n+1)}(AAa; A^3)$ is the probability of this genotype times the probability that it transmits its two maternal A-genes and (in three ways) one of its three paternal A-genes. Hence, on the whole, $9\lambda_2 p^{(n)}(A)p^{(n)}(A)$ *is the probability of a zygote in the* $(n+1)^{st}$ *generation, which possesses at least two maternal and, at least, one paternal A-alleles and which transmits a gamete consisting of two maternal and one paternal A-alleles.* It is clear from this analysis that the sum of the four terms to the right of (12′) gives the probability of a gamete of type (A^3) in the $(n+1)^{st}$ generation.

In case of chromatid segregation the discussion of the terms to the right of (12) which contain μ_0 or μ_1 is exactly the same. Of course $72\mu_1$ plays the role of $9\lambda_1$, etc.

Next consider the "*non-homogeneous*" *terms* in (12) namely

$$36\mu_1'p(A)^2 + 24\mu_0'p^{(n)}(A^2) = 12\mu_3'p^{(n)}(A^2) + 18\mu_2'p(A)^2 + 18\mu_1'p(A)^2 + 12\mu_0'p^{(n)}(A^2).$$

Such terms are due to a double-counting pair of sister chromatids. Consider for instance, $18\mu_2'[p(A)]^2$. Here, as before $[p(A)]^2 = \sum w^{(n+1)}(A\cdot\cdot\,;\,A\cdot\cdot)$, where the summation is four-fold, the empty places being filled with all combinations of A and a. Consider, as before, one of these terms, for example

$$18\mu_2'w^{(n+1)}(AAA;\,Aaa) = 6\mu_2'[w^{(n+1)}(AAA;\,Aaa) + w^{(n+1)}(AAA;\,aAa) + w^{(n+1)}(AAA;\,aaA)].$$

Here $6\mu_2'w^{(n+1)}(A^3;\,Aaa)$ is the probability of a zygote of type $(A^3;\,Aaa)$ times the probability that this zygote transmits one maternal pair of sister chromatids A (in three ways), and one paternal A-chromatid (in two ways). Hence, on the whole $18\mu_2'p(A)^2$ *is the probability of a zygote of the* $(n+1)^{st}$ *generation which possesses at least one maternal and at least one paternal* A*-chromosome and transmits one pair of maternal sister chromatids,* A, A, *and one paternal* A*-chromatid.*

In an analogous way $p^{(n)}(A^2)\times 1 = \sum w^{(n+1)}(AA\cdot\,;\,\cdot\cdot\cdot)$ where the empty places are to be filled with the 16 possible combinations of A and a. Consider such a term, as for instance $12\mu_3'w^{(n+1)}(A^2a;\,Aa^2) = 4\mu_3'[w^{(n+1)}(AAa;\,a^2A) + w^{(n+1)}(AaA;\,a^2A) + \cdot]$. Out of the four maternal A-chromatids a triple (containing necessarily a pair of sister chromatids) can be chosen in 4 ways; hence $w^{(n+1)}(AAa;\,a^2A)\cdot 4\mu_3'$ is the probability of this genotype, times the probability that it transmits (in four ways) a maternal triple of A-chromatids. Thus it is seen that the sum of all these "non-homogeneous" terms plus the homogeneous terms to the right of (12) gives just the probability of the gamete (A^3) in the $(n+1)^{st}$ generation (if A stands for a_1).

Analogous considerations hold, of course, for (9).

In addition to (12) we may for $s=3$ derive a recurrence formula for $p^{(n+1)}(a_1^2a_2)$ and $p^{(n+1)}(a_1a_2a_3)$:

$$\begin{aligned}
p^{(n+1)}(a_i^3) &= 16\mu_0p^{(n)}(a_i^3) + 144\mu_1p^{(n)}(a_i^2)p(a_i) + 24\mu_0'p^{(n)}(a_i^2) + 36\mu_1'[p(a_i)]^2 \\
p^{(n+1)}(a_i^2a_j) &= 16\mu_0p^{(n)}(a_i^2a_j) + 48\mu_1p^{(n)}(a_i^2)p(a_j) + 96\mu_1p^{(n)}(a_ia_j)p(a_i) \\
&\quad + 8\mu_0'p^{(n)}(a_ia_j) + 12\mu_1'p(a_i)p(a_j) \qquad (13)\\
p^{(n+1)}(a_ia_ja_k) &= 16\{\mu_0p^{(n)}(a_ia_ja_k) + 3\mu_1[p(a_i)p^{(n)}(a_ja_k) + \cdot + \cdot]\}.
\end{aligned}$$

For the interpretation of the terms to the right of (13) similar considerations hold as before.

Upon addition of $p^{(n+1)}(a_i^3) + p^{(n+1)}(a_1^2a_2) + \cdots$ in (13) we get a recurrence formula for $p^{(n+1)}(a_1^2)$, and, in a similar way, one for $p^{(n+1)}(a_1a_2)$. The result is:

$$\begin{aligned}
p^{(n+1)}(a_i^2) &= (16\mu_0 + 48\mu_1 + 16\mu_0')p^{(n)}(a_i^2) + (96\mu_1 + 24\mu_1')p(a_i)^2 + (8\mu_0' + 12\mu_1')p(a_i) \\
p^{(n+1)}(a_ia_j) &= (16\mu_0 + 48\mu_1 + 16\mu_0')p^{(n)}(a_ia_j) + (96\mu_1 + 24\mu_1')p(a_i)p(a_j). \qquad (14)
\end{aligned}$$

Addition of these two formulas shows, as in (10) as anticipated in our notation:

$$p^{(n)}(a_i) = p^{(0)}(a_i) \qquad (n = 1, 2, \cdots; i = 1, 2, \cdots, r).$$

Again, we may consider particular cases of these formulas by specifying the s.d.:

Random chromatid segregation correspond to $\mu_0=\mu_1=\mu_0'=\mu_1'=\frac{1}{220}$. We have in this case

$$p^{(n+1)}(a_i^3) = \frac{4}{55}p^{(n)}(a_i^3) + \frac{36}{55}p^{(n)}(a_i^2)p(a_i) + \frac{6}{55}p^{(n)}(a_i^2) + \frac{9}{55}p(a_i)^2. \tag{15}$$

For FISHER-MATHER'S theory with $\mu_0=\mu_1=\mu$, $\mu_0'=\mu_1'=\mu'$, $60\mu'=\beta$:

$$p^{(n+1)}(a_i^3) = \frac{1-\beta}{10}p^{(n)}(a_i^3) + \frac{9}{10}(1-\beta)p^{(n)}(a_i^2)p(a_i) + \frac{4\beta}{10}p(a_i^2) + \frac{6\beta}{10}p(a_i)^2$$

$$p^{(n+1)}(a_i^2a_j) = \frac{1-\beta}{10}p^{(n)}(a_i^2a_j) + \frac{3(1-\beta)}{10}p^{(n)}(a_i^2)p(a_j) + \frac{6(1-\beta)}{10}p^{(n)}(a_ia_j)p(a_i) + \frac{2\beta}{15}p^{(n)}(a_ia_j) + \frac{3\beta}{15}p(a_i)p(a_j). \tag{16}$$

We shall now finish this section with the *recurrence formulae* for $s=4$. We find:

$$\begin{aligned} p^{(n+1)}(a_i^4) = {} & 16[2\mu_0 p^{(n)}(a_i^4) + 2\cdot 16\mu_1 p^{(n)}(a_i^3)p(a_i) + 36\mu_2 p(a_i)^2] \\ & + 96[\mu_0' p^{(n)}(a_i^3) + 4\mu_1' p^{(n)}(a_i^2)p(a_i) \\ & + 2\mu_2' p^{(n)}(a_i^2)p(a_i)] + 4[3\mu_0'' p^{(n)}(a_i^2) + 4\mu_2'' p(a_i)^2]. \end{aligned} \tag{17}$$

To understand the non-homogeneous terms we need (6). Consider for example, $48\mu_4'p^{(n)}(a_i^3)$ or, (with two alleles to fix the ideas) $48\mu_4'p^{(n)}(A^3)\cdot 1 = 48\mu_4'\sum w^{(n+1)}(AAA\cdot, \cdots\cdot)$. Now four A-chromatids belonging to three chromosomes can be selected from eight A-chromatids in $4\cdot 12=48$ ways. Next the term $192\mu_3'p^{(n)}(A^2)p(A)$ corresponds to combining three maternal chromatids from two maternal chromosomes with one paternal chromatid. This can happen in $(4\cdot 6)\cdot 8=192$ ways. The term $96\mu_2'p^{(n)}(A^2)p(A) = (28-4)\cdot 4\mu_2'p^{(n)}(A^2)p(A)$ corresponds to the combination of two maternal chromatids (from two chromosomes) with two paternal sister-chromatids (from one chromosome), or vice versa; etc. etc.

In a similar way we may derive and interpret the formula

$$\begin{aligned} p^{(n+1)}(a_i^3a_j) = {} & 16\{2\mu_0 p^{(n)}(a_i^3a_j) + 8\mu_1[p^{(n)}(a_i^3)p(a_j) + 3p^{(n)}(a_i^2a_j)p(a_i)] \\ & + 36\mu_2 p^{(n)}(a_i^2)p^{(n)}(a_ia_j)\} \\ & + 48\{\mu_0' p^{(n)}(a_i^2a_j) + 2\mu_1' p^{(n)}(a_i^2)p(a_j) \\ & + (2\mu_1' + 2\mu_2')p^{(n)}(a_ia_j)p(a_i)\}. \end{aligned} \tag{18}$$

AN EXAMPLE

We shall illustrate the recurrence formulas by an example where $s=3$. In order to be able to apply our recurrence formulas we must first derive $p^{(0)}(z)$ from $w^{(0)}(x; y)$ the way it was done in (7) for $s=2$. The formula corresponding to (7), if $s=3$, is:

$$
\begin{aligned}
p(A^3) = {} & v(A^3; A^3)\cdot 1 + 3v(A^3; A^2a)[8\mu_0 + 72\mu_1 + 16\mu_0' + 24\mu_1'] \\
& + 3v(A^3; Aa^2)[8\mu_0 + 24\mu_1 + 12\mu_0' + 12\mu_1'] \\
& + v(A^3; a^2)(8\mu_0 + 12\mu_0') + 9v(A^2a; A^2a)(16\mu_1 + 4\mu_0' + 8\mu_1') \\
& + 9v(A^2a; Aa^2)(8\mu_1 + 4\mu_0' + 8\mu_1') + 3v(A^2a; a^3)\cdot 4\mu_0' \\
& + 9v(Aa^2; Aa^2)\cdot 4\mu_1'
\end{aligned} \tag{19}
$$

and similar formulas for $p(A\ a)$, etc. In most applications in the given distribution the probabilities of a few types only will be different from zero so that for the derivation of $p^{(0)}(z)$ a general formula like (19) is not needed.

Now consider the *following* simple *example:* A female organism of type $(A^3; A^3)$ is mated to $(a^3; a^3)$. Assuming continued random mating we should like to know the distribution of genotypes in the third filial generation if FISHER'S theory of four strand segregation is considered. According to the data we have

$$
\begin{aligned}
& v^{(0)}(A^3; A^3) = 1 \text{ (females)}, \qquad \bar{v}^{(1)}(a^3; a^3) = 1 \text{ (males)} \\
& p^{(0)}(A^3) = 1, \text{ all others zero}, \qquad \bar{p}^{(1)}(a^3) = 1 \text{ (all others zero)}.
\end{aligned}
$$

In the next generation, for males and for females: $v^{(1)}(A^3; a^3) = 1$, all others zero.

It follows that

$$
\begin{aligned}
p^{(1)}(A^3) &= v^{(1)}(A^3; a^3)(8\mu_0 + 12\mu_0') = 8\mu_0 + 12\mu_0' \\
3p^{(1)}(A^2a) &= v^{(1)}(A^3; a^3)(72\mu_2 + 18\mu_2') = 72\mu_1 + 18\mu_1' \\
3p^{(1)}(Aa^2) &= v^{(1)}(A^3; a^3)(72\mu_1 + 18\mu_1') = 72\mu_1 + 18\mu_1' \\
p^{(1)}(Aa^3) &= v^{(1)}(A^3; a^3)(8\mu_0 + 12\mu_0 P') = 8\mu_0 + 12\mu_0'.
\end{aligned}
$$

Now with FISHER-MATHER'S assumptions:

$$
\begin{aligned}
p^{(1)}(A^3) = p^{(1)}(a^3) &= \frac{1-\beta}{20} + \frac{\beta}{5} = \frac{1+3\beta}{20} \\
3p^{(1)}(A^2a) = 3p^{(1)}(Aa^2) &= \frac{9}{20}(1-\beta) + \frac{3\beta}{20} = \frac{9-3\beta}{20} \\
p^{(1)}(A^2) = p^{(1)}(a^2) &= \frac{2+\beta}{10} \\
p^{(1)}(Aa) &= \frac{3-\beta}{10} \\
p^{(1)}(A) = p^{(1)}(a) &= \frac{1}{2}.
\end{aligned}
$$

Next we use the recurrence formulas and find:

$$\begin{aligned}
p^{(2)}(A^3) &= \frac{1-\beta}{10}p^{(1)}(A^3) + \frac{9}{10}(1-\beta)p^{(1)}(A^2)p(A) + \frac{4\beta}{10}p^{(1)}(A^2) + \frac{6\beta}{10}p(A)^2 \\
&= \frac{1-\beta}{10}\,\frac{1+3\beta}{20} + \frac{9}{10}(1-\beta)\,\frac{2+\beta}{10}\cdot\frac{1}{2} + \frac{4\beta}{10}\,\frac{2+\beta}{10} + \frac{6\beta}{10}\cdot\frac{1}{4} \\
&= \frac{19+39\beta-4\beta^2}{200} = p^{(2)}(a^3),
\end{aligned}$$

$$\begin{aligned}
p^{(2)}(A^2a) &= \frac{1-\beta}{10}p^{(1)}(A^2a) = \frac{3(1-\beta)}{10}p^{(1)}(A^2)p(a) + \frac{6(1-\beta)}{10}\,p^{(1)}(Aa)\cdot\frac{1}{2} \\
&\quad + \frac{2\beta}{15}p^{(1)}(Aa) + \frac{3\beta}{15}p(A)p(a) \\
&= \frac{(1-\beta)(3-\beta)}{200} + \frac{3(1-\beta)(2+\beta)}{200} + \frac{6(1-\beta)(3-\beta)}{200} \\
&\quad + \frac{2\beta}{15}\,\frac{3-\beta}{10} + \frac{3\beta}{15}\cdot\frac{1}{4} \\
&= \frac{1}{3}\,\frac{81-39\beta+4\beta^2}{200} = p^{(2)}(Aa^2).
\end{aligned}$$

Also:

$$p^{(2)}(A^2) = p^{(2)}(a^2) = \frac{69+39\beta-4\beta^2}{300}$$

$$p^{(2)}(Aa) = \frac{81-39\beta+4\beta^2}{300}.$$

In order to estimate the order of magnitude of the various terms introduce $\beta=0.117$ (FISHER and MATHER 1943, p. 17). We find:

$$\frac{19+39\beta-4\beta^2}{200} = .118 \qquad \frac{81-39\beta+4\beta^2}{200} = .382$$

and finally by (8) for the third generation:

$$\begin{aligned}
v^{(3)}(A^3;\,A^3) &= v^{(3)}(a^3;\,a^3) = \tfrac{1}{2}v^{(3)}(A^3;\,a^3) = .014 \\
3v(A^3;\,A^2a) &= 3v(A^3;\,Aa^2) = 3v(a^3;\,A^2a) \\
&= 3v(a^3;\,Aa^2) = .090 \\
9v(A^2a;\,A^2a) &= 9v(Aa^2;\,Aa^2) = \tfrac{1}{2}\cdot 9v(A^2a;\,Aa^2) = .146
\end{aligned}$$

and

$$4\cdot(.014 + .090 + .146) = 1.000.$$

INTEGRATION OF THE RECURRENCE FORMULAS AND LIMIT THEOREMS

We start integrating the formulas for $s=2$. We find immediately:

$$
\begin{aligned}
p^{(n)}(a_i^2) &= (8\mu_0)^n p^{(0)}(a_i^2) \\
&\quad + [1-(8\mu_0)^n]\cdot\left[\frac{4\mu_1}{4\mu_1+\mu_0'}\,p(a_i)^2+\frac{\mu_0'}{4\mu_1+\mu_0}\,p(a_i)^2\right] \\
p^{(n)}(a_ia_k) &= (8\mu_0)^n p^{(0)}(a_ia_k) \\
&\quad + [1-(8\mu_0)^n]\,\frac{4\mu_1}{4\mu_1+\mu_0'}\,p(a_i)p(a_k)
\end{aligned}
\tag{20}
$$

or, in FISHER'S theory:

$$
\begin{aligned}
p^{(n)}(a_i^2) &= \left(\frac{1-\alpha}{3}\right)^n p^{(0)}(a_i^2) \\
&\quad + \left[1-\left(\frac{1-\alpha}{3}\right)^n\right]\cdot\left[\frac{2-2\alpha}{2+\alpha}\,p(a_i)^2+\frac{3\alpha}{2+\alpha}\,p(a_i)\right] \\
p^{(n)}(a_ia_k) &= \left(\frac{1-\alpha}{3}\right)^n p^{(0)}(a_ia_k) \\
&\quad + \left[1-\left(\frac{1-\alpha}{3}\right)^n\right]\frac{2-2\alpha}{2+\alpha}\,p(a_i)p(a_k).
\end{aligned}
\tag{21}
$$

We see from these formula that the *rate of approach to equilibrium* is $(8\mu_0)^n$ *or* $(1-\alpha/3)^n$ *respectively*$_n$ it is $(\frac{2}{7})^n$ *for random chromatid segregation,* $(\frac{5}{18})^n$ *for complete equational* and $(\frac{1}{3})^n$ *for chromosome segregation.* These figures differ but little from each other.

From (20) we find, *if* $8\mu_0<1$, *the limit formulas*:

$$
\begin{aligned}
\lim_{n\to\infty} p^{(n)}(a_i)^2 &= \frac{4\mu_1}{4\mu_1+\mu_0'}\,p(a_i)^2+\frac{\mu_0'}{4\mu_1+\mu_0'}\,p(a_i) \\
\lim_{n\to\infty} p^{(n)}(a_ia_k) &= \frac{4\mu_1}{4\mu_1+\mu_0'}\,p(a_i)p(a_k)
\end{aligned}
\tag{22}
$$

If, however, $8\mu_0=1$, that is, $\mu_1=\mu_0'=0$, we see that (see Geiringer 1948, p. 277)

$$
p^{(n)}(a_i^2)=p^{(0)}(a_i^2),\quad p^{(n)}(a_ia_k)=p^{(0)}(a_ia_k),\qquad (n=1,2,\cdots).
\tag{22'}
$$

Under FISHER'S *assumptions* we get the limit formula:

$$
\begin{aligned}
\lim_{n\to\infty} p^{(n)}(a_i^2) &= \frac{2-2\alpha}{2+\alpha}\,p(a_i)^2+\frac{3\alpha}{2+\alpha}\,p(a_i) \\
\lim_{n\to\infty} p^{(n)}(a_ia_k) &= \frac{2-2\alpha}{2+\alpha}\,p(a_i)p(a_k)
\end{aligned}
\tag{23}
$$

and for *random chromatid segregation*

$$\begin{aligned}\lim_{n\to\infty} p^{(n)}(a_i^2) &= \frac{4}{5}\,p(a_i)^2 + \frac{1}{5}\,p(a_i)\\ \lim_{n\to\infty} p^{(n)}(a_i a_k) &= \frac{4}{5}\,p(a_i)p(a_k).\end{aligned} \tag{24}$$

The results (24), for $s=2$, have been given by HALDANE (1930, p. 370). The recurrence formulas (9''), the explicit solutions (20), (21) as well as the limit results (22), (23) are new. All results are new in the case $s=3$, which we now shall consider.

We have already found the recurrence formulas (13) and (14). Here (13) can be integrated too. First we find the explicit result for $p^{(n)}(a_i^2)$ which corresponds to (14) and is of form (20). Introducing this into the right side of the first formula (13) this right side becomes a known function, f_n, of n. Denoting $p^{(n)}(a_i^3)$ by x_n and $16\mu_0 = a$, we have the equation $x_{n+1} - a x_n = f_n$ which has the solution

$$x_n = a^n x_0 + \sum_{\gamma=0}^{n-1} f_\gamma a^{n-1-\gamma}.$$

This can be computed for every given s.d.

Let us consider the limit of the $p^{(n)}$ as $n\to\infty$. Assume $16\mu_0 < 1$. It then follows that in (14), $16\mu_0 + 48\mu_1 + 16\mu_0' < 1$. If this would not be so we could conclude that $\mu_1 = \mu_1' = \mu_0' = 0$ hence $16\mu_0 = 1$. We get from (14)

$$\lim_{n\to\infty} p^{(n)}(a_i^2) = \frac{(24\mu_1 + 6\mu_1')p(a_i)^2 + (2\mu_0' + 3\mu_1')p(a_i)}{24\mu_1 + 9\mu_1' + 2\mu_0'}. \tag{25}$$

Hence in (13) which is of the form $x_{n+1} - a x_n = f_n$ we know the $\lim_{n\to\infty} f_n = f$. It follows from a lemma (GEIRINGER 1948, p. 262) that, if

$$|a| < 1, \qquad \lim x_n = \frac{f}{1-a}.$$

In our case we have:

$$\begin{aligned} f = {} & [144\mu_1 p(a_i) + 24\mu_0']\cdot\frac{(24\mu_1 + 6\mu_1')p(a_i)^2 + (2\mu_0' + 3\mu_1')p(a_i)}{24\mu_1 + 9\mu_1' + 2\mu_0'} \\ & + 36\mu_1' p(a_i)^2. \end{aligned}$$

Our result is, if

$16\mu_0 < 1$ and $(12\mu_1 + 3\mu_1' + 2\mu_0')(24\mu_1 + 9\mu_1' + 2\mu_0') = M$:

$$\begin{aligned} \lim_{n\to\infty} p^{(n)}(a_i^3) = {} & \frac{1}{M}\cdot\{(288\mu_1^2 + 72\mu_1\mu_1')p(a_i)^3 + (72\mu_1\mu_0' + 108\mu_1\mu_1' \\ & 18\mu_0'\mu_1' + 27\mu_1'^2)p(a_i)^2 + (4\mu_0'^2 + 6\mu_0'\mu_1')p(a_i)\}. \end{aligned} \tag{26}$$

If $16\mu_0 = 1$:

$$p^{(n)}(a_i^3) = p^{(0)}(a_i^3).$$

In case of *random chromatid segregation* (26) gives:

$$\lim_{n\to\infty} p^{(n)}(a_i^3) = \frac{72}{7\cdot 17} p(a_i)^3 + \frac{45}{7\cdot 17} p(a_i)^2 + \frac{2}{7\cdot 17} p(a_i). \tag{27}$$

We may derive similar results for $p^{(n)}(a_i^2 a_k)$. First we have a second formula (25):

$$\lim_{n\to\infty} p^{(n)}(a_i a_k) = \frac{24\mu_1 + 6\mu_1'}{24\mu_1 + 2\mu_0' + 9\mu_1'} p(a_i)p(a_k). \tag{25}$$

Now we proceed with the second formula (13) exactly as with the first. In fact, if we substitute on the right side of this formula the values (14) for $p^{(n)}(a_i^2)$ and $p^{(n)}(a_i a_k)$ this right side becomes a known function of n, say z_n, such that $\lim_{n\to\infty} z_n = z$ exists and

$$\lim_{n\to\infty} p^{(n)}(a_i^2 a_k) = \frac{z}{1 - 16\mu_0}.$$

The result is:

$$\begin{aligned} \lim_{n\to\infty} p^{(n)}(a_i^2 a_k) &= \frac{1}{M}\cdot\{(288\mu_1^2 + 72\mu_1\mu_1')p(a_i^2)p(a_k) \\ &\quad + (24\mu_1\mu_0' + 36\mu_1\mu_1' + 6\mu_1'\mu_0' + 9\mu_1'^2)p(a_i)p(a_k)\}, \\ \lim_{n\to\infty} p^{(n)}(a_i a_j a_k) &= \frac{1}{M} 12\mu_1(24\mu_1 + 6\mu_1')p(a_i)p(a_j)p(a_k). \end{aligned} \tag{26}$$

For random chromatid segregation this becomes:

$$\begin{aligned} \lim_{n\to\infty} p^{(n)}(a_i^2 a_k) &= \frac{72}{7\cdot 17} p(a_i^2)p(a_k) + \frac{15}{7\cdot 17} p(a_i)p(a_k), \\ \lim_{n\to\infty} p^{(n)}(a_i a_j a_k) &= \frac{72}{7\cdot 17} p(a_i)p(a_j)p(a_k). \end{aligned} \tag{27}$$

Finally, with FISHER's and MATHER's assumption; where

$160\mu + 60\mu' = 160\mu + \beta = 1$:

$$\begin{aligned} \lim_{n\to\infty} p^{(n)}(a_i^3) &= \frac{27(1-\beta)(3-\beta)}{(9+\beta)(9+2\beta)} p(a_i)^3 + \frac{45\beta(3-\beta)}{(9+\beta)(9+2\beta)} p(a_i)^2 \\ &\quad + \frac{20\beta^2}{(9+\beta)(9+2\beta)} p(a_i), \\ \lim_{n\to\infty} p^{(n)}(a_i^2 a_k) &= \frac{27(1-\beta)(3-\beta)}{(9+\beta)(9+2\beta)} p(a_i)^2 p(a_k) \end{aligned} \tag{28}$$

$$+\frac{15\beta(3-\beta)}{(9+\beta)(9+2\beta)}p(a_i)p(a_k),$$

$$\lim_{n\to\infty} p^{(n)}(a_ia_ja_k) = \frac{27(1-\beta)(3-\beta)}{(9+\beta)(9+2\beta)}p(a_i)p(a_j)p(a_k).$$

The *rate of approach to equilibrium* is $(16\mu_0+48\mu_1+16\mu_0')^n$ This is $\left(\frac{6-2\beta}{15}\right)^n$ under FISHER'S assumption, and $\left(\frac{4}{11}\right)^n$ for random chromatid segregation, compared to $\left(\frac{4}{10}\right)^n$ for random chromosome segregation.

In order to compute the limit status for the example in the preceding section we merely have to put in (28): $p(a_1)=p(a_2)=\frac{1}{2}$, $\beta=.1176$.

Similar results may be established for $s=4$, using (17) and (18).

We see that the limit results under the assumption of chromatid segregation are essentially different from the ones for chromosome segregation where, in the limit, the alleles were independently distributed. By multiplication of the limit expressions (26) or (27) or (28) we get the respective limit-distributions of genotypes.

SUMMARY

The mathematical genetics of autopolyploids under chromatid segregation, is dealt with, in particular for tetraploids, hexaploids, and octoploids. The segregation-distribution introduced by R. A. FISHER and K. MATHER [1943] has been generalized so as to contain as particular cases this segregation distribution as well as HALDANE'S "random chromatid segregation" [1930] and the author's [1948] general chromosome segregation distribution. The possible kinds of gametes and of genotypes are enumerated, recurrence relations for their distributions are established and "integrated," and limit results as, n, the number of discrete non-overlapping generations tends to infinity, are investigated. The recurrence relations as well as the limit theorems are essentially different from the analogous results under chromosome segregation and seem to present a new type of statistical-biological law.

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