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JUNCTIONS IN INBREEDING

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INTRODUCTION

For a regular system of inbreeding, the genetic consequences of primary importance are embodied in the generation matrix which may be constructed for matings relative to a single locus. In considering the heterogeneity of the germ plasm, the initial state at each locus may be taken to be that of greatest complexity. It follows that if the probability of a mating being heterogeneous at any locus in a given generation is p and is the same for all loci, then for k loci, with any linkage relations, the expected number in the heterogeneous condition is kp. However, closely linked loci are more likely to be in the same state, either heterogeneous or homogeneous, than loci showing loose linkage and it is of some little interest to consider the number and typical length of the separate heterogeneous tracts after many generations. Such a discussion has been given for the sib-mating of disomic organisms by FISHER (1949). As the approach through junctions constitutes an important advance in inbreeding theory, further discussions of the method seem desirable.

JUNCTIONS AND SELF-FERTILISATION

Three steps are to be distinguished in the junction approach. In the first place, we determine for gametogenesis from each generation, the rate of production of junctions between segments of the germ plasm of unlike origin. We then calculate the probability

that any such junction will survive until some later generation without its having become homogeneous, i.e. it must not be bounded by two homogeneous segments. As not every heterogeneous junction marks the end of a heterogeneous tract, we must then allow for internal junctions, i.e. junctions bounded by two heterogeneous segments.

With self-fertilisation, the rate of production of junctions between segments of unlike origin is, in gametogenesis from the r-th generation,

$$2L(\tfrac{1}{2})^r$$

where L is the total map length of the species. Since the probability of a mating being heterozygous for a given junction is halved in each generation, the probability of a junction formed in gametogenesis from the r-th generation being heterozygous in the n-th generation is

$$(\tfrac{1}{2})^{n-r-1}$$

With self-fertilisation, internal junctions do not arise and so the total number of heterozygous junctions accumulated in the n-th generation is

$$2L \sum_{r=0}^{n-1} (\tfrac{1}{2})^{n-r-1}(\tfrac{1}{2})^r = 2nL(\tfrac{1}{2})^{n-1}$$

If there are ν pairs of homologous chromosomes, the number of heterozygous chromosome ends in the n-th generation is

$$\nu(\tfrac{1}{2})^{n-1}.$$

Counting these as heterozygous junctions and allowing two such junctions to each tract, the average number of tracts per unit crossover length of the heterogeneous portion of the germ plasm is

$$2n + \frac{\nu}{L}.$$

The typical length of a heterogeneous tract after n generations of self-fertilisation is therefore

$$\frac{100}{2n + \frac{\nu}{L}} \text{ centimorgans.}$$

A similar approach can be used to determine the typical length

of homogeneous tracts of the same origin. The probability of a junction formed in gametogenesis from the r-th generation being homozygous in the n-th generation is

$$\tfrac{1}{4}\left(1 + \tfrac{1}{2} + \frac{1}{2^2} + \ldots + \frac{1}{2^{n-r-2}}\right) \qquad n \geqslant r+2$$

i.e. $\tfrac{1}{2}[1 - (\tfrac{1}{2})^{n-r-1}]$.

Since the rate of junction production in gametogenesis from the r-th generation is

$$2L(\tfrac{1}{2})^r,$$

the total number of homozygous junctions accumulated in the n-th generation is, for $n \geqslant 2$,

$$2L \sum_{r=0}^{n-2} (\tfrac{1}{2})^{r+1} [1 - (\tfrac{1}{2})^{n-r-1}] = 2L[1 - (n+1)(\tfrac{1}{2})^n].$$

As a heterozygous junction marks the end of a heterogeneous tract and the beginning of a homogeneous one, whereas a homozygous junction separates two different homogeneous tracts, it follows that the number of different homogeneous tracts is equal to the number of homozygous junctions plus one half of the sum of heterozygous junctions and homozygous chromosome ends. In the n-th generation this is

$$(2L + \nu)\,[1 - (\tfrac{1}{2})^n] \qquad n \geqslant 2.$$

As the total map length which is homogeneous in the n-th generation is

$$L[1 - (\tfrac{1}{2})^n],$$

the typical length of a homogeneous tract of given origin is, in any generation after the first,

$$\frac{100}{2 + \frac{\nu}{L}} \text{ centimorgans.}$$

JUNCTIONS IN PARENT-OFFSPRING INBREEDING

With a single locus and parent-offspring inbreeding, only four heterogenic mating types need be distinguished. The λ-matrix is as follows (FISHER, 1949, pp. 67).

TABLE 1

	Offspring	Parent	u_0	u_0'	v_0	x_0
u_1	aa	ab	-2λ	1	1	1
u_1'	ab	aa	1	-2λ	.	.
v_1	ab	ab	.	1	$1-2\lambda$	1
x_1	ab	ac	.	.	.	$2-4\lambda$

Putting ε equal to $\frac{1}{4}(1 + \sqrt{5})$, the latent roots and the corresponding principal components of frequency are as shown in Table 2.

TABLE 2

Root	Principal Components of Frequency
$\frac{1}{2}$	x
0	$P = u - v$
ε	$Q = 2u + 4\varepsilon u' + 4\varepsilon v + (4\varepsilon + 1)x$
$\frac{1}{2} - \varepsilon$	$R = 2u + (2 - 4\varepsilon)u' + (2 - 4\varepsilon)v + (3 - 4\varepsilon)x$

If L is the total map length of the species, the length still heterogeneous in the n-th generation is the coefficient of x_0 in

$$L(u_n + u_n' + v_n + x_n).$$

This coefficient is

$$L[\tfrac{1}{5}(2 + 7\varepsilon)\varepsilon^n + \tfrac{1}{10}(19 - 26\varepsilon)\,(\tfrac{1}{2} - \varepsilon)^n - \tfrac{1}{2}(\tfrac{1}{2})^n]$$

in which the leading term is

$$LZ'\varepsilon^n$$

where $Z' = \frac{1}{5}(2 + 7\varepsilon)$ is the maximum complexity of a parent-offspring mating.

As one genotype is common to each of two successive matings each mating contributes only two new chromosomes to the next. It follows that in gametogenesis from the r-th generation, the rate of production of junctions between segments of unlike origin is the coefficient of x_0 in

$$L(u_r + u_r' + 2v_r + 2x_r),$$

or

$$\tfrac{1}{2}L[(1 + 4\varepsilon)\varepsilon^r + (3 - 4\varepsilon)\,(\tfrac{1}{2} - \varepsilon)^r].$$

When a junction occurs in gametogenesis from the r-th generation the (r + 1)-th mating will be of type u′ in respect of this junction. The coefficient of u_0' in

$$u_{n-r-1} + u_{n-r-1}' + v_{n-r-1}$$

is the probability of junctions formed in gametogenesis from the r-th generation being still heterogeneous in the n-th generation. This is

$$\tfrac{4}{5}(1 + \varepsilon)\varepsilon^{n-r} + \tfrac{2}{5}(7 + 2\varepsilon)\,(\tfrac{1}{2} - \varepsilon)^{n-r}.$$

The total number of such heterogeneous junctions accumulated in the n-th generation is therefore

$$\tfrac{1}{2}L \sum_{r=0}^{n-1} [(1+4\varepsilon)\varepsilon^r + (3-4\varepsilon)\,(\tfrac{1}{2}-\varepsilon)^r][\tfrac{4}{5}(1+\varepsilon)\,\varepsilon^{n-r} + \tfrac{2}{5}(7+2\varepsilon)(\tfrac{1}{2}-\varepsilon)^{n-r}]$$
$$= L\{2Z'\varepsilon^n[n - \tfrac{1}{5}(31 - 34\varepsilon)] + \tfrac{1}{5}[1 + 12\varepsilon + n(19 - 26\varepsilon)]\,(\tfrac{1}{2} - \varepsilon)^n\}.$$

Hence subject to correction for internal junctions and by terms of lower order, the average number of tracts per unit crossover length of the heterogeneous portion of the germ plasm in the n-th generation is

$$n - \tfrac{1}{5}(31 - 34\varepsilon) = n - 0.69868.$$

In order to allow for internal junctions, we must distinguish those matings which besides being heterogeneous for a junction involve chromosomes of two or more different kinds in the neighbourhood of the junction. A mating with an internal junction which involves only two kinds of chromosomes will be of type x. Hence the probability that an internal junction of this kind formed in gametogenesis from the r-th generation is still present as an internal junction in the n-th generation is the coefficient of x_0 in x_{n-r-1}, i.e. $(\tfrac{1}{2})^{n-r-1}$. The rate of production of such internal junctions in gametogenesis from the r-th generation is the coefficient of x_0 in

$$L(u_r' + 2v_r + \tfrac{1}{2}x_r),$$

As the leading term in this coefficient is $LZ'\varepsilon^r$, it follows that the total number of internal junctions of this kind present in the n-th generation is

$$\sum_{r=0}^{n-1} LZ'\varepsilon^r(\tfrac{1}{2})^{n-r-1}$$

in which the leading term is $4\varepsilon LZ'\varepsilon^n$. FISHER (personal communication)

has pointed out that the contribution from internal junctions with more than two kinds of chromosomes is of the same order of magnitude. Considering those matings which involve a heterogeneous junction with three kinds of chromosomes, we shall suppose that a, b and c represent three different sources of germ plasm in the neighbourhood of the junction and that j denotes a junction between a and b. The following are the matings of this kind that are produced at gametogenesis.

i) aj = ac
ii) cj = ac
iii) cj = ab.

The rate of production of each of these in gametogenesis from the r-th generation is $L(\frac{1}{2})^{r+1}$. As the absolute complexities are $(1 + \varepsilon)/5$, ε and $(-1 + 4\varepsilon)/5$ respectively, it follows that the probability of an internal junction of this kind formed in gametogenesis from the r-th generation being still present as an internal junction in the n-th generation is, correct as far as terms in ε^{n-r-1},

$$\frac{\varepsilon^{n-r-1}}{5}[(1 + \varepsilon) + 5\varepsilon + (-1 + 4\varepsilon)] = 2\varepsilon^{n-r}$$

Hence the total number of internal junctions of this kind present in the n-th generation is

$$\sum_{r=0}^{n-1} 2L(\tfrac{1}{2})^{r+1}\varepsilon^{n-r}$$

in which the leading term is $4(-2 + 3\varepsilon)LZ'\varepsilon^n$. The total number of internal junctions in the n-th generation is therefore, to this degree of approximation,

$$4(-2 + 4\varepsilon)LZ'\varepsilon^n.$$

The total number of external junctions in the n-th generation is therefore

$$2[n - \tfrac{1}{5}(11 + 6\varepsilon)]LZ'\varepsilon^n.$$

It follows that the average number of separate heterogeneous tracts is

$$\left[n - \tfrac{1}{5}(11 + 6\varepsilon) + \frac{\nu}{L}\right]LZ'\varepsilon^n.$$

The typical length of a heterogeneous tract is therefore

$$\frac{100}{n - 3.17082 + \frac{\nu}{L}} \text{ centimorgans.}$$

For sib-mating, the corresponding length is

$$\frac{100}{1.44721\left(n - 3.18622\right) + \frac{\nu}{L}} \text{ centimorgans.}$$

If m_n is the expected number of heterogeneous tracts in the n-th generation, the probability of the germ plasm being completely homogeneous in a mating of this generation is exp $(-m_n)$. Values of this probability after many generations of sib and parent-offspring matings have been plotted in figure 1. In constructing these graphs, the values $L = 25$, $\nu = 20$, which are appropriate to mice, have been used. It is seen that parent-offspring matings have an advantage over sib-matings of approximately three generations.

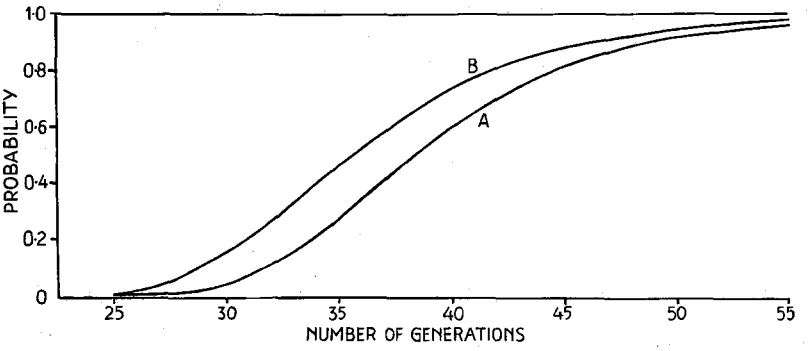

Fig. 1. Probability of the germ plasm being completely homogeneous after many generations of A. sib and B. parent-offspring matings

Summing the rate of formation of junctions in parent-offspring matings over all generations, we obtain 11 L. As only one third of these junctions survive, the average number of unbroken segments when the whole of the germ plasm has become homogeneous is

$$3\tfrac{2}{3}L + \nu.$$

For sib-mating, the average number of unbroken segments is

$$6L + \nu.$$

JUNCTIONS IN THE SELF-FERTILISATION OF TETRASOMIC ORGANISMS

Tetrasomic organisms which are heterogenic at a single locus may be classified in respect of the genic content of this locus into four types corresponding with those partitions of the number four which have more than one part. The generation matrix for self-fertilisation has been given by FISHER (1949, p. 82). If α denotes the amount of double reduction at the given locus, the latent roots and the principal components of frequency are as follows.

TABLE 3

Root	Principal components of frequency
$\frac{1}{6}(1-\alpha)^2$	$M = f(1^4)$
$\frac{1}{6}(1-\alpha)^2$	$N = (2-10\alpha+17\alpha^2)\,f(21^2) - 8(1+\alpha-2\alpha^2)\,f(2^2) + 3(2-2\alpha+3\alpha^2)\,f(31)$
$\frac{1}{2}(1-\alpha)$	$P = 2f(1^4) + f(21^2)$
$\frac{1}{6}(5-2\alpha)$	$Q = 6f(1^4) + 5f(21^2) + 4f(2^2) + 3f(31).$

It follows that

$$f(1^4) = M$$

$$f(21^2) = -2M + P$$

$$f(2^2) = \frac{1}{4(4-\alpha^2)}[2(2+6\alpha-11\alpha^2)M - N - 2(4-\alpha^2)P + (2-2\alpha+3\alpha^2)Q]$$

$$f(31) = \frac{1}{3(4-\alpha^2)}[6(2-2\alpha+3\alpha^2)M + N - 3(4-\alpha^2)P + (2+2\alpha-4\alpha^2)Q]$$

The dominant root is $\frac{1}{6}(5-2\alpha)$ with the maximum value of $\frac{5}{6}$ when $\alpha = 0$.

Considering a small region of the germ plasm of map length dx, the expected length of that part which is heterogeneous in the n-th generation is the coefficient of $f_0(1^4)$ in

$$[f_n(31) + f_n(2^2) + f_n(21^2) + f_n(1^4)]\,dx.$$

This coefficient has as its leading term,

$$Z(\alpha)\left(\frac{5-2\alpha}{6}\right)^n dx$$

where $Z(\alpha) = \dfrac{14 + 2\alpha - 7\alpha^2}{2(4 - \alpha^2)}$ is the maximum complexity of a selfing.

Now consider the formation of junctions in this region. In an individual of genotype (1^4) for this region, the four homologous chromosomes can be assorted into heterogeneous pairs in six ways. In an individual of genotype (21^2), such a pairing can be made in five ways, whilst in one of genotype (2^2) this can be done in four ways and in one of genotype (31) in three ways. These numbers are the products of the parts of the corresponding partitions taken two at a time. When multiplied by $\frac{4}{6}$, they tell us how many of the four new chromosomes formed we can expect to have been derived from pairs of chromosomes which were heterogeneous for this region. Thus, for example, on selfing an individual of genotype (1^4), each of the four new chromosomes must be derived from a heterogeneous pair, whereas on selfing an individual of genotype (31) only two of the four new chromosomes are expected to have been derived from such a parental pair. It follows that for this region of the germ plasm, the rate of formation of junctions in gametogenesis from the r-th generation is the coefficient of $f_0(1^4)$ in

$$\tfrac{4}{6}[6f_r(1^4) + 5f_r(21^2) + 4f_r(2^2) + 3f_r(31)]\,dx.$$

As the latter expression is

$$\tfrac{2}{3}Q_r\,dx,$$

the rate of formation is

$$4\left(\frac{5 - 2\alpha}{6}\right)^r dx.$$

Several new features are encountered with junctions in tetrasomic organisms. In particular, internal junctions may now arise in the gametes. In the present discussion, however, we shall suppose that all junctions are external. In respect of a junction that has occurred in gametogenesis from the r-th generation, the $(r + 1)$-th selfing may then be taken to be of the type (31). The coefficient of $f_0(31)$ in

$$f_{n-r-1}(31) + f_{n-r-1}(2^2)$$

is the probability of such a junction being heterogeneous in the n-th generation. The total number of heterogeneous junctions accumulated in the region dx in the n-th generation is therefore

$$\frac{4}{12(4-\alpha^2)}\sum_{r=0}^{n-1}\left(\frac{5-2\alpha}{6}\right)^r\left\{3(14+2\alpha-7\alpha^2)\left(\frac{5-2\alpha}{6}\right)^{n-r-1}+\right.$$
$$\left.+(2-2\alpha+3\alpha^2)\left[\frac{(1-\alpha)^2}{6}\right]^{n-r-1}\right\}dx$$

in which the leading term is

$$2n\,Z(\alpha)\left(\frac{5-2\alpha}{6}\right)^{n-1}dx.$$

Hence the average number of tracts per unit crossover length of the heterogeneous portion of the germ plasm in any region where the amount of double reduction is α, is for large n

$$\frac{6n}{5-2\alpha}.$$

The typical length of a separate heterogeneous tract in such a region is therefore

$$\frac{50(5-2\alpha)}{3n}\text{ centimorgans.}$$

Heterogeneous tracts in those regions of the germ plasm for which $\alpha = 0$ are on the average longer than those elsewhere. (see Table 4).

TABLE 4

Expected heterogeneity on selfing tetrasomic organisms

Generations	Expected proportion of heterogeneous germ plasm		Expected length of heterogeneous tracts, cM.	
	$\alpha = 0$	$\alpha = \frac{1}{7}$	$\alpha = 0$	$\alpha = \frac{1}{7}$
10	0.28263	0.15934	8.33333	7.85714
15	0.11358	0.04771	5.55556	5.23810
20	0.04565	0.01429	4.16667	3.92857
25	0.01834	0.00428	3.33333	3.14286
30	0.00737	0.00128	2.77778	2.61905
35	0.00296	0.00038	2.38095	2.24490
40	0.00119	0.00011	2.08333	1.96429
45	0.00048	0.00003	1.85185	1.74603
50	0.00019	0.00001	1.66667	1.57143

Neglecting double reduction, if L is the total map length of the tetrasomic species, the map length heterogeneous in the n-th generation has as its leading term

$$1.75L(\tfrac{5}{6})^n.$$

With double reduction, there will be somewhat less heterogeneous germ plasm. In a chromosome arm of length l and with a high frequency of quadrivalent formation q, the germ plasm still heterogeneous after many generations n is concentrated near the centromere and has the length

$$1.75(\tfrac{5}{6})^n \int_0^l \exp(-\tfrac{2}{5}n\alpha)dx.$$

If we assume that the probability is $\frac{1}{3}$ that at the first division of meiosis any two centromeres of a quadrivalent go to the same interphase nucleus, then for any locus at a small map distance x from the centromere, the amount of double reduction may be equated to $\frac{1}{3}qx$. It follows that the length of the heterogeneous germ plasm (in this chromosome) has as its leading term,

$$\frac{105}{4nq}(\tfrac{5}{6})^n.$$

Irrespective of its position on the chromosome, each junction that is formed has a survival probability of $\frac{1}{4}$. Since

$$4\left(\frac{5-2\alpha}{6}\right)^r dx$$

is the rate of production of junctions in dx in gametogenesis from the r-th generation, the total number of junctions remaining in the region dx when the whole of the germ plasm has become homogeneous is

$$\sum_{r=0}^{\infty}\left(\frac{5-2\alpha}{6}\right)^r dx = \frac{6}{1+2\alpha}dx.$$

For $\alpha = 0$, the expected density of unbroken segments is the same as that for sib-mating disomic organisms. The total number of junctions remaining in a given chromosome when complete homogeneity has been attained is

$$\int \frac{6}{1+2\alpha}dx$$

where the integral is to be taken over all possible values of x for this chromosome. To evaluate this integral we require some knowledge of the relationship between the amount of double reduction α and the map distance x from the centromere. If q is the frequency of quadrivalent formation for this set of homologous chromosomes and y is the recombination fraction between the centromere and a given locus, the following terminal conditions must be satisfied.

$$y = 0,\ \alpha = 0;$$
$$y = \tfrac{1}{2},\ \alpha = \tfrac{1}{7}q.$$

Further, if it is assumed that the probability is $\frac{1}{3}$ that at the first division of meiosis, any two centromeres of a quadrivalent go to the same interphase nucleus, there is the additional terminal condition,

$$y = 0, \frac{\partial \alpha}{\partial y} = \tfrac{1}{3}q.$$

A simple monotonic relation connecting α and y which satisfies these conditions is

$$\alpha = \frac{yq}{3 + y}$$

Data on linkage in a tetrasomic organism have been givin by FISHER (1949a) for the short versus non-short styles and purple versus rosy in *Lythrum salicaria*. From the absence of the two modes of gamete formation involving double reduction at both loci, it was concluded that the centromere lies between the two loci. On the assumption of no genetical interference across the centromere, the above relation leads to a value of 65 per cent for the frequency of quadrivalent formation for this chromosome. A comparable frequency of quadrivalent formation for the chromosome containing the mid locus is demanded by the large body of data which gives the frequency of double reduction at this locus as 8 per cent. (FISHER, 1944, p. 169). These values are much larger than those which cytologists have been led to accept. Assuming the Kosambi relation to obtain between y and x, i.e. $2y = \tanh 2x$, the integral expression for the total number of junctions remaining in a chromosome arm of length l for which the frequency of quadrivalent formation is q, is

$$6\int_0^l \frac{6 + \tanh 2x}{6 + (1 + 2q)\tanh 2x}\,dx$$

This has the value

$$\frac{42l}{7+2q} - \frac{36q}{(7+2q)(5-2q)} \log_e \{\tfrac{1}{12}[7+2q+(5-2q)\exp(-4l)]\}.$$

DISTRIBUTION OF THE GENERATION NUMBER AT WHICH COMPLETE HOMOGENEITY IS ATTAINED

From a consideration of the formation and fate of junctions on inbreeding, we can determine the probability of the germ plasm being completely homogeneous in any generation. Figure 2 shows the distributions of generation number at which complete homogeneity

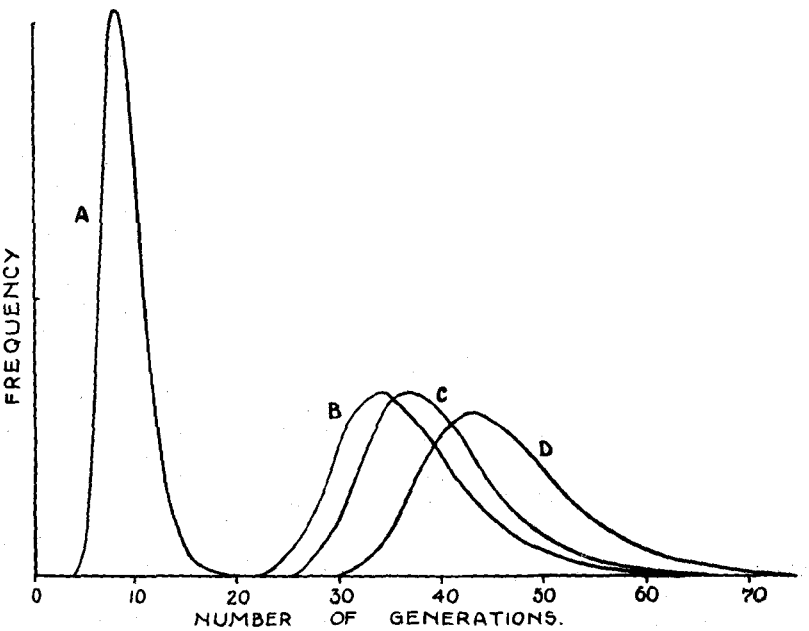

Fig. 2. Distribution of the generation number at which complete homogeneity is attained in a species with a total map length of 2500 centimorgans.

A. Self-fertilisation

B. Parent-offspring mating

C. Sib-mating

D. Self-fertilisation of tetrasomic organisms, neglecting double reduction.

These distributions depend to a small extent on the average chromosome length which has been taken to be 125 centimorgans

is attained by self-fertilisation, sib and parent-offspring matings of disomic organisms and the self-fertilisation of tetrasomic organisms, neglecting double reduction, in a species whose total map length is 2500 centimorgans. The average chromosome length which is a factor of minor importance in the calculations has been taken to be 125 centimorgans.

SUMMARY

An examination is made of the formation and fate of junctions in the self-fertilisation and parent-offspring mating of disomic organisms. If ν is the haploid number of chromosomes and L is the total map length of the species, the typical length of a heterogeneous tract in the n-th generation of self-fertilisation is $\frac{100}{2n + \frac{\nu}{L}}$ centimorgans. In any generation after the first, the typical length of an unbroken homogeneous tract is $\frac{100}{2 + \frac{\nu}{L}}$ centimorgans.

With parent-offspring mating, the typical length of an heterogeneous tract after a large number of generations is $\frac{100}{n - 3.17082 + \frac{\nu}{L}}$ centimorgans, whilst the average number of unbroken segments when the whole of the germ plasm has become homogeneous is $3\frac{2}{3}L + \nu$. These values should be compared with those for sib mating. For this system of inbreeding, FISHER has shown that the typical length of an heterogeneous tract after many generations is $\frac{100}{1.44721\left(n - 3.18622\right) + \frac{\nu}{L}}$ centimorgans and that the average number of unbroken segments when the whole of the germ plasm has become homogeneous is $6L + \nu$. Hence with sib mating, the heterogeneous germ plasm is spread over a larger number of shorter tracts and the homogeneous segments of given origin are also shorter than in the case of parent-offspring mating.

Junctions are also considered in the self-fertilisation of tetrasomic organisms. Neglecting double reduction, the map length heterogeneous in the n-th generation has as its leading term $1.75L(\frac{5}{6})^n$. With double reduction, there is less heterogeneous germ plasm. In a chromosome with a high frequency of quadrivalent formation q, the germ plasm heterogeneous after many generations n is concentrated about the centromere and has the length $\frac{105}{4nq}(\frac{5}{6})^n$ which is independent of the chromosome length. The monotonic relation $\alpha = \frac{yq}{3+y}$ is suggested for the amount of double reduction α at any locus and the recombination fraction y between the locus and its centromere. Expressions are given for the average number of unbroken segments when the whole of the germ plasm has become homogeneous.

An important consequence of the junction approach is that it enables the determination of the probability of the germ plasm being completely homogeneous in any generation. A comparison is given of the distributions of generation number at which complete homogeneity is attained by self-fertilisation, sib and parent-offspring matings of disomic organisms and the self-fertilisation of tetrasomic organisms, neglecting double reduction.

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