THE AVERAGE RECOMBINATION FREQUENCY PER CHROMOSOME¹

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THE concept of a recombination frequency averaged over all possible pairs of loci for a given chromosome was introduced by GRIFFING (1960). He indicated that the average recombination frequency must lie between upper and lower limits given by his "index" and "modified noninterference" models respectively. More recently HANSON (1962) has given an analysis which is claimed to estimate directly the average recombination frequency, and has extended the analysis to estimate a parameter denoted as the average recombination frequency for a mating system. This analysis is based on assumptions of noninterference, similar to those of GRIFFING's lower-limit model. The calculations however are based on a chromatid method, whereas those of GRIFFING utilize a chromosome method.

The purpose of this paper is to compare the results of these two analyses. The comparison will be made by deriving the average recombination frequency by both chromosome and chromatid methods, when the assumptions of complete noninterference are used. Since the concept of average recombination frequency has utility principally when a large number of loci are involved, the comparison will be made for the limiting case where the number of loci becomes infinite.

Noninterference model utilizing the chromosome method: With this method both chromosomes, or four strands, of a bivalent are considered during meiosis, and the average recombination is derived in terms of the number of chiasmata per bivalent, assuming that each chiasma is associated with a genetic crossing over. The calculations are made assuming a number of loci to be distributed at random throughout the chromosome pair.

The complete noninterference model requires that: (1) There is no chiasma interference; i.e. the number of chiasmata follows a Poisson distribution; (2) There is no chromatid interference.

The noninterference model used by GRIFFING has two modifications to these assumptions: (1) At least one chiasma is obligatory for the survival of the bivalent; (2) There cannot be more than one chiasma in any segment between two consecutive loci.

Assumption (2) takes account of positive chiasma interference to a certain extent when the products of one meiotic division and small numbers of loci are considered, but becomes trivial as the number of loci increases. Since the comparison is to be made considering an infinite number of loci, the assumption is

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of no consequence in this case except to facilitate the calculation of the recombination fraction.

Using the above assumptions, GRIFFING (1960) has found the mean recombination frequency to be:

$$\bar{r}_1 = \frac{1}{2} - \frac{1}{\lambda} + \frac{2(\lambda-1)}{\lambda^3} + \frac{2}{\lambda^3 e^\lambda} \quad (1)$$

where $\lambda = (\text{average number of chiasmata}) - 1$.

This value was considered to provide a lower limit to the average frequency of recombination expected in practice since the occurrence of positive chiasma interference would lead to a spreading out of chiasmata, which it was shown would tend to increase this value. The assumption of the obligatory chiasma was used in these calculations to give a closer approximation to the generally accepted cytological facts than is given by a complete noninterference model, and as will be shown later, can be expected to lead to a more accurate lower limit.

For comparison with the results utilizing the chromatid method, the average recombination frequency has been recalculated in a similar fashion using the assumptions of complete noninterference, i.e. neglecting the obligatory chiasma, giving

$$\bar{r}_2 = \frac{1}{2} - \frac{1}{\lambda_1} + \frac{1}{\lambda_1^2} - \frac{1}{\lambda_1^2 e^{\lambda_1}} \quad (2)$$

where $\lambda_1 = \text{average number of chiasmata}$.

Noninterference model utilizing the chromatid method: Using the chromatid method, the linkage phases of loci on a single reconstituted strand are enumerated in terms of the number of points of recombination per chromatid. HANSON (1962) in calculating the average recombination frequency has assumed that any number of recombination points may occur in a segment between two loci. Under these assumptions the general formula for the average recombination frequency has been given by HANSON and HAYMAN (1963). However, as pointed out earlier, as the number of loci becomes infinite, the restriction to zero or one recombination points per segment does not affect the value of the average recombination frequency. With a small number of loci and one meiotic division this restriction appears to be realistic, but with a mating system consisting of a large number of generations, multiple crossing over within a segment will tend to invalidate the formulae derived. Nevertheless since the restriction leads to useful formulae for the limiting case which is being considered here it will be used in deriving $\bar{r}$.

Let the number of loci be $N+1$. Consider first the case of an even number of recombination points, say $2x$. In the reconstituted strand, a certain number of loci will be in the same phase as the first locus, and the remaining loci will be in the opposite phase. The number of loci in the first phase may be represented as $x+i+1$, and the number in the second phase as $N-x-i$, where i takes all integral values from 0 to $N-2x$. The total number of pairs of loci in the same phase for this particular configuration will then be

$$\binom{x+i+1}{2} + \binom{N-x-i}{2}.$$

The number of configurations having $x+i+1$ loci in the first phase and $N-x-i$ in the second may now be shown to be

$$S_{x-1}^{N-2x-i+1} \times S_x^{i+1}, \text{ where } S_b^a = \binom{a+b-1}{b}.$$

The average recombination frequency for $2x$ points of recombination then becomes:

$$\frac{(\text{Total number of pairs of loci}) - (\text{Total number of pairs of loci in the same phase})}{(\text{Total number of pairs of loci})}$$

which in algebraic terms is equal to:

$$\frac{\frac{1}{2}N(N+1) \sum_{i=0}^{N-2x} \binom{N-x-i-1}{x-1} \binom{x+i}{x} - \sum_{i=0}^{N-2x} [\binom{x+i+1}{2} + \binom{N-x-i}{2}] \binom{N-x-i-1}{x-1} \binom{x+i}{x}}{\frac{1}{2}N(N+1) \sum_{i=0}^{N-2x} \binom{N-x-i-1}{x-1} \binom{x+i}{x}}$$

By using related forms of the identity

$$\sum_{i=0}^{N-2x} \binom{N-x-i-1}{x-1} \binom{x+i}{x} = \binom{N}{2x}$$

this expression can be simplified to $\frac{(N+2)x}{N(2x+1)}$. As N becomes infinite this value

approaches $\frac{x}{2x+1}$, which is equivalent to the value given by HANSON for the limiting case.

The calculations may be repeated for an odd number of loci, $2x-1$, and the result is again $\frac{(N+2)x}{N(2x+1)}$.

The number of points of recombination is now assumed to follow the Poisson distribution with mean s . Then the average recombination frequency (for an infinite number of loci) becomes

$$\sum_{x=0}^{\infty} e^{-s} \cdot \frac{s^{2x}}{(2x)!} \cdot \frac{x}{2x+1} + \sum_{x=0}^{\infty} e^{-s} \cdot \frac{s^{2x-1}}{(2x-1)!} \cdot \frac{x}{2x+1}$$

$$\text{which equals } \frac{1}{2} - \frac{1}{2s} + \frac{1}{4s^2} - \frac{1}{4s^2 e^{2s}} \quad (3)$$

Since each chiasma involves only two of the four strands, the mean chiasma frequency per bivalent must be twice the mean frequency of recombination points per strand, i.e. $\lambda_1 = 2s$. With this substitution it may be seen that expressions (2) and (3) are equal. Thus the average recombination frequencies as

calculated by the chromosome and chromatid methods respectively are equal if the assumptions of noninterference are used.

DISCUSSION

In order to compare the results of the analyses of GRIFFING and HANSON, it is necessary to assess the effect on the recombination frequency of the obligatory chiasma assumption. It may be argued, analogously to GRIFFING (1960), that since this assumption postulates a departure from noninterference of the same type as caused by positive chiasma interference, it will lead to a higher recombination frequency than that calculated without using the assumption. This result may be confirmed algebraically by showing that $\bar{y}_1 - \bar{y}_2 =$

$$-\frac{1}{\lambda} + \frac{2(\lambda-1)}{\lambda^3} + \frac{2}{\lambda^3 e^\lambda} + \frac{1}{\lambda+1} - \frac{1}{(\lambda+1)^2} + \frac{1}{e^{(\lambda+1)} (\lambda+1)^2}$$

is positive for all values of λ in the range $(0, \infty)$.

It seems unlikely that the obligatory chiasma assumption would lead to an overcorrection to the lower limit, i.e. give a recombination fraction greater than that which would actually be found. Therefore, for a single meiotic division, the lower limit calculated using these assumptions must usually lie closer to the true frequency than does the limit calculated using the assumptions of noninterference. For a mating system of n generations, the obligatory chiasma model may again be introduced, but in a modified form. For example, consider a population synthesized by intermating a selected group of individuals; in the gametes of individuals after n generations of random mating, the equivalent of $n+1$ chiasmata would be obligatory, and the number of additional chiasmata would be specified by the Poisson distribution. In general, however, the application of the obligatory chiasma model to specified mating systems, while possible in principle, appears to be mathematically intractable.

HANSON (1962) has given numerical comparisons of the results of the two analyses, which show his estimates as lying between the upper and lower limits given by GRIFFING. In view of the above result this is evidently not possible. It appears that it has been incorrectly suggested that the chiasma frequencies considered by GRIFFING must be doubled to make them correspond with cytological observation. The comparison should be made on the basis of $\lambda = 2s-1$ and not $\lambda = s-1$. With the correct substitutions the above-mentioned estimates are found to lie below the range defined by the lower and upper limits given by GRIFFING's analysis.

In conclusion, for a single meiotic division, there is apparently no reason for considering the value derived from the chromatid method as giving a better approximation than that derived by the chromosome method, nor is there justification for using the former as an estimate of the average recombination value rather than as a lower limit for this parameter. These conclusions apply also in the estimation of the average recombination frequency for a mating system, although in this case the lower limits calculated may be expected to approximate more closely to the true value.

Parenthetically, it is interesting to note the equivalence of several formulae derived from the chromosome and chromatid methods. If the number of chiasmata is Poisson distributed with mean λ , and there is no chromatid interference, then the probability of x recombination points on one strand is

$$\sum_{y=x}^{\infty} (\text{Probability of } y \text{ chiasmata}) \times (\text{Probability that } x \text{ of these involve one strand})$$

$$= \sum_{y=x}^{\infty} \left[\frac{e^{-\lambda} \cdot \lambda^y}{y!} \cdot \binom{y}{x} \left(\frac{1}{2}\right)^x \cdot \left(\frac{1}{2}\right)^{y-x} \right] = \frac{e^{-\lambda/2} (\lambda/2)^x}{x!}$$

Thus the number of points of recombination per strand is also Poisson distributed with the parameter $\lambda/2$. Secondly, the recombination fraction for $2x$ recombination points, $x/(2x+1)$ in the limit, is equivalent to the recombination frequency for K chiasmata, $K/2(K+2)$, when $2(2x)$ is substituted for K . The equality, however, does not hold for an odd number of recombination points. Finally the equality of the average recombination frequencies given by the two methods has been demonstrated by the equivalence of formulae (2) and (3).

SUMMARY

A comparison has been made of the average recombination frequency per chromosome as derived by the noninterference models of GRIFFING (1960) and HANSON (1962). It is shown that with a slightly less realistic assumption than that considered by GRIFFING, the two models lead to identical results. This value cannot be regarded as an estimate, but only as a lower limit, of the average recombination frequency.

LITERATURE CITED

- GRIFFING, B., 1960 Accommodation of linkage in mass selection theory. *Australian J. Biol. Sci.* **13**: 501-526.
- HANSON, W. D., 1962 Average recombination per chromosome. *Genetics* **47**: 407-415.
- HANSON, W. D., and B. I. HAYMAN, 1963 Linkage effects on additive genetic variance among homozygous lines arising from a cross between two homozygous parents. *Genetics* **48**: 755-766.