THE THEORY OF GENETICAL RECOMBINATION: EFFECT OF CHANGING THE $\frac{1}{4}\chi^2_4$ INTERCEPT LENGTH DISTRIBUTION

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1. INTRODUCTION

The modern conception of the hereditary process, or the "chromosome theory of inheritance" as it is sometimes referred to, rests essentially on two broadly based facts. First, hereditary factors are readily classifiable into well-defined groups (known as linkage groups) according as they segregate independently or not; and secondly, the number of these groups in any species corresponds exactly to the haploid complement of chromosomes characteristic of the species in question. In terms of this conception the precise specification of the genetic constitution of an organism is achieved by assigning to each of its genes a certain location on a linkage map. The unit of measure in terms of which this might best be achieved is by no means obvious and it is only in the last few years in fact that a satisfactory metric has been put forward. Before describing this it is perhaps worthwhile recalling in very brief outline the attempts to develop a consistent theory of genetical recombination. Morgan propounded the cross-over theory in 1911. On the basis of this theory the segregation ratios of genetic factors belonging to the same linkage group were attributed to the exchange of chromosomal material during the meiotic process, and it was conjectured that the proportion of recombinants was in some way related to the distance apart of the genes on the chromosome. Subsequent research showed this to be an excellent first approximation where the recombination fractions were small, but that its effectiveness diminished as the recombination fraction increased. The recombination fraction could not therefore be regarded as a satisfactory metric and was eventually superseded by the map distance. Defined as the average number of cross-overs in an interval this was clearly additive, but it had the disadvantage of being unobservable, so that necessarily therefrom attention was focused on clarifying the precise relation between it and the observable recombination fractions. The difference between the map distance, x say, and the recombination fraction, y say, is due to two causes, multiple crossing-over and genetic interference, and it was the second of these which presented the main obstacle to progress. It was perhaps not very surprising therefore that the first relation to be established (Haldane, 1919) was based on the simplifying assumption of no interference; namely,

$$y(x) = \tfrac{1}{2}(1 - e^{-2x}).$$

The attempts to establish relations of wider applicability have been more numerous. Perhaps the best of them is Kosambi's empirical relation,

$$y(x) = \tfrac{1}{2} \tanh 2x.$$

In many organisms, particularly for describing gene loci on median segments in long arms, this is a very useful relation ; so much so that one feature to be expected of any theory of genetical recombination is that it should agree with Kosambi's relation over median ranges. Even so in other respects it has many serious shortcomings (see section 5) and this rather unsatisfactory state of affairs remained until the combined work of Fisher *et al.* (1947) and Owen (1949). Their theory is not dependent on any particular conception of the meiotic process ; it is simply formulated in terms of the probabilities of cross-overs occurring, and allows the observed recombination fractions themselves to provide the criterion as to whether a given probability distribution is well chosen or whether it should be altered so as to describe more accurately what has been observed.

2. THE GENERAL THEORY OF GENETICAL RECOMBINATION

This theory starts from the point of view that recombination between two loci takes place when, in terms of a single strand, an odd number of exchange points occurs between them during meiosis. The recombination fraction therefore is the probability that 1, or 3, or 5, or in general an odd number of interchanges has taken place, so that denoting the recombination fraction by y and using an obvious notation for the probabilities,

$$y = p_1+p_3+p_5+\ldots = \sum_r p_{2r+1} \quad . \quad . \quad . \quad (1)$$

On the other hand the map distance, defined as the average number of exchange points,

$$x = 0p_0+1p_1+2p_2+3p_3+\ldots = \sum_r rp_r \quad . \quad . \quad (2)$$

adequately supplies a consistent measure of location on the linkage map.

In a more general way, for the case of several loci on a finite arm, if we let $p_{r_1r_2\ldots r_n}$ denote the joint probability of just r_1, r_2, ..., r_n exchange points in each of say n genetically distinguishable segments then for the kth segment, the map distance,

$$x_k = \sum_{allr_k} r_k p_{r_1\ldots r_k\ldots r_n}$$

= the expected number of exchange points in the kth segment, and the recombination fraction,

$$y_k = \sum_{oddr_k} p_{r_1\ldots r_k\ldots r_n}$$

= the probability of an odd number of exchange points in the kth segment.

This simple and direct approach is the basis of the theory of genetical recombination developed in recent years by Fisher and Owen. It requires only the specification of the probability distribution of the exchange points on a single strand after meiosis, and is not dependent in any way on the particular manner in which a single exchange point occurs. Since the detail of this process is unobservable, this is an advantage as the theory would otherwise contain a formal aspect, *i.e.* one not testable by observation. Like many recent advances in biology during the past few decades it recognises variability and treats it as a whole, realising that what may happen in a particular instance depends on a large number of factors, which are either unknown or too complex to be treated individually even if they were known, while all that is necessary very often is the statistical regularity

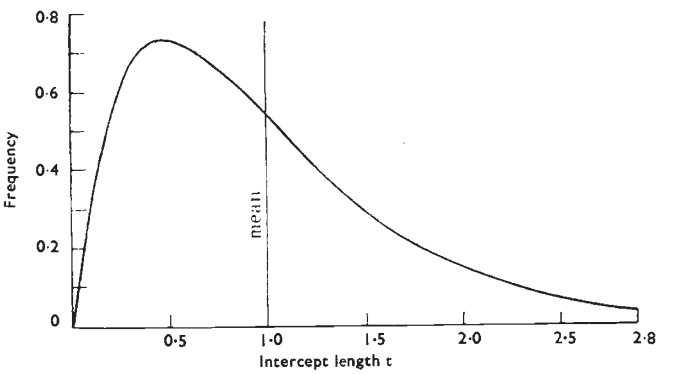


FIG. 1.—The intercept length distribution, $\frac{1}{4}\chi^2_4(t)dt = 4te^{-2t}dt$ having a variance $= \frac{1}{2}$.

which can be *observed* and *measured.* Evidently, therefore, the only essential requirement of this theory is a specification of the intercept length distribution between successive exchange points on a single strand ; from this the probabilities used in (1) and (2) can be inferred. In this feature lies the great flexibility of the theory ; one has only to find a distribution consistent with the observed recombination fractions and this will automatically subsume the composite effect of genetic interference. Furthermore the existence of a satisfactorily postulated form for the intercept distribution embodies the entire observational record of recombination fractions in an organised form and therefore provides an empirically established piece of knowledge for which future, more detailed investigation of genetic interference must account. Therefore, apart from allowing a consistent description of observed recombinations, which it does without prejudging the mechanism of genetic interference, it summarises in a compact way the observational experience with which any possible postulated mode of interference must accord.

To set up the requisite probabilities used in (1) and (2) Fisher recognised that there is nothing sacrosanct about the map distance.

(As Owen (1950) has demonstrated, there are an infinite number of possible additive metrics.) He chose, therefore, to define the intercept length distribution in terms of a metric in which it was supposed that the interference was uniform ; mathematically there is everything to be gained by adopting this procedure. If we denote this metric by t then the postulated form he chose,* is given by the $\frac{1}{4}\chi^2_4$ distribution,

$$\tfrac{1}{4}\chi^2_4(t)dt = 4te^{-2t}dt \quad . \quad . \quad . \quad . \quad (3)$$

This is shown graphically in fig. 1.

In terms of the auxiliary metric t one may express the probabilities p_r, and hence x and y, for

$$y = p_1(t) + p_3(t) + p_5(t) + \ldots = y(t)$$

and similarly $x = x(t)$.

Perhaps the first reaction of the reader is that the $\frac{1}{4}\chi^2_4(t)$ distribution is rather arbitrary, but it is the purpose of this paper to show in a summary fashion † that if only a small departure from the essential form of the $\frac{1}{4}\chi^2_4(t)$ distribution is made, then this leads to results which are directly at variance with current genetical experience, and that therefore the $\frac{1}{4}\chi^2_4(t)$ distribution must simulate the actual intercept distribution rather closely.

3. THE $\frac{1}{4}\chi^2_4(t)$ THEORY

In 1951 Fisher showed that the frequencies of all recombination classes among any number of marked loci on a finite arm can be expressed in terms of the following four functions,

$$\left.\begin{aligned}
\alpha(t) &= 1 + \frac{t^4}{4!} + \frac{t^9}{8!} + \ldots . \\
\beta(t) &= t + \frac{t^5}{5!} + \frac{t^9}{9!} + \ldots . \\
\underline{\alpha}(t) &= \frac{t^2}{2!} + \frac{t^6}{6!} + \frac{t^{10}}{10!} + \ldots . \\
\underline{\beta}(t) &= \frac{t^3}{3!} + \frac{t^7}{7!} + \frac{t^{11}}{11!} + \ldots .
\end{aligned}\right\} \quad . \quad . \quad (4)$$

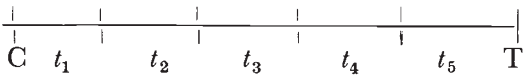
Note that in this notation t represents *twice* the metrical length. If products of these are formed in a certain combinatorial way (Fisher, 1951) then the frequency of each recombination class is readily deduced. However, for the purpose of this paper, it is more convenient to adopt a slightly different procedure. Suppose we have an arm of

* The $\frac{1}{4}\chi^2_4$ distribution was suggested by Owen (1949) as a mathematically more convenient mimic of the $\frac{\pi}{2}\tanh(\frac{1}{2}\pi s)\operatorname{sech}(\frac{1}{2}\pi s)ds$ distribution originally proposed by Fisher (1947).

† For the detailed analysis the reader is referred to Payne (1956).

five segments defined by four internal markers between the centromere and terminus ; in addition consider the 2×2 matrix.

$$\begin{pmatrix} \alpha & \beta \\ \underline{\beta} & \underline{\alpha} \end{pmatrix} \quad . \quad . \quad . \quad . \quad . \quad (5)$$



To form the frequency of non-recombinants in all five segments we write down the matrix product,

$$\overset{\leftarrow t_1 \rightarrow}{\begin{pmatrix} \alpha & \beta \\ o & o \end{pmatrix}} \overset{\leftarrow t_2 \rightarrow}{\begin{pmatrix} \alpha & \beta \\ \underline{\beta} & \underline{\alpha} \end{pmatrix}} \overset{\leftarrow t_3 \rightarrow}{\begin{pmatrix} \alpha & \beta \\ \underline{\beta} & \underline{\alpha} \end{pmatrix}} \overset{\leftarrow t_4 \rightarrow}{\begin{pmatrix} \alpha & \beta \\ \underline{\beta} & \underline{\alpha} \end{pmatrix}} \overset{\leftarrow t_5 \rightarrow}{\begin{pmatrix} \alpha & o \\ \underline{\beta} & o \end{pmatrix}}$$

that is, we associate the matrix $\begin{pmatrix} \alpha & \beta \\ \underline{\beta} & \underline{\alpha} \end{pmatrix}$ with each *internal* segment, its first *row* with the segment proximal to the centromere, and its first *column* with the terminal segment. If recombination occurs in any segment, *e.g.* in the second, the appropriate frequency for that particular class is given by exchanging $\begin{pmatrix} \underline{\alpha} & \underline{\beta} \\ \beta & \underline{\alpha} \end{pmatrix}$ for $\begin{pmatrix} \alpha & \beta \\ \underline{\beta} & \underline{\alpha} \end{pmatrix}$ in the second segment (*i.e.* we merely interchange the elements of the matrix according to whether they are underlined or not). Thus we may regard,

$\begin{pmatrix} \alpha & \beta \\ \underline{\beta} & \underline{\alpha} \end{pmatrix}$ as the " non-recombination matrix "

and $\begin{pmatrix} \underline{\alpha} & \underline{\beta} \\ \beta & \underline{\alpha} \end{pmatrix}$ as the " recombination matrix ".

According as we use one or the other in each segment we thus obtain in a straightforward way the full set of 2^5 frequencies ($2^5 - 1$ recombinant, 1 non-recombinant) appropriate to there being recombination or non-recombination in each of the five segments. Incidentally we note that the sum of recombinants and non-recombinants in a given segment is found by adding,

$$\overset{\leftarrow t \rightarrow}{\begin{pmatrix} \alpha & \beta \\ \underline{\beta} & \underline{\alpha} \end{pmatrix}} + \overset{\leftarrow t \rightarrow}{\begin{pmatrix} \underline{\alpha} & \underline{\beta} \\ \beta & \underline{\alpha} \end{pmatrix}} = \overset{\leftarrow\!\!-\!\!- t \!\!-\!\!-\rightarrow}{\begin{pmatrix} \alpha+\underline{\alpha} & \beta+\underline{\beta} \\ \underline{\beta}+\beta & \alpha+\underline{\alpha} \end{pmatrix}} = \begin{pmatrix} \cosh t & \sinh t \\ \sinh t & \cosh t \end{pmatrix}$$

so that the sum of all recombination frequencies is just,

$$\overset{\leftarrow\!\!-\!\!- t_1 \!\!-\!\!-\rightarrow}{\begin{pmatrix} \cosh & \sinh \\ o & o \end{pmatrix}} \overset{\leftarrow\!\!-\!\!- t_2 \!\!-\!\!-\rightarrow}{\begin{pmatrix} \cosh & \sinh \\ \sinh & \cosh \end{pmatrix}} \cdots\cdots \overset{\leftarrow t_5 \rightarrow}{\begin{pmatrix} \cosh & o \\ \sinh & o \end{pmatrix}} = \cosh(t_1+t_2+\ldots+t_5)$$

or simply cosh T, where T is twice the total metrical length of the arm. This will therefore be a constant divisor for finding absolute frequencies.

In the same way that the expressions are built up for the recombination frequencies from the " recombination " and " non-recombination " matrices, so we can build up the expression for the map distance from the following " map distance matrix."

$$\tfrac{1}{2}\begin{pmatrix} t\sinh t & t\cosh t-\sinh t \\ t\cosh t+\sinh t & t\sinh t \end{pmatrix}$$

4. THE $\frac{1}{6}\chi^2_6$ THEORY

The above summary of a method for quickly finding $y(t)$ and $x(t)$ in the $\frac{1}{4}\chi^2_4$ case can readily be extended to other metrics. Since we are anxious to determine the genetic consequences implicit upon a slight change in the $\frac{1}{4}\chi^2_4$ distribution of intercept length we now investigate the case of the $\frac{1}{6}\chi^2_6$ distribution. Explicitly,

$$\tfrac{1}{6}\chi^2_6(t)dt = \frac{27}{2}\,t^2e^{-3t}dt.$$

This is compared graphically with the $\frac{1}{4}\chi^2_4$ distribution in fig. 2.

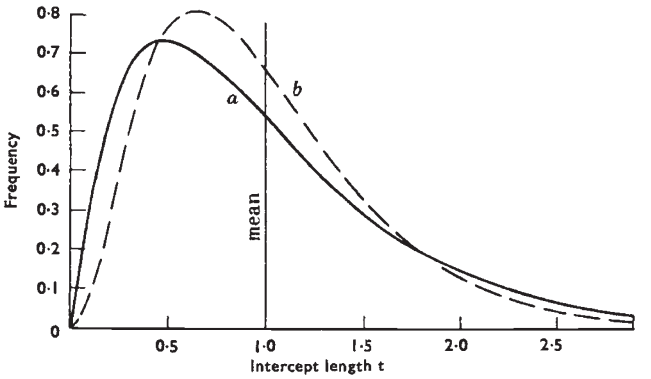


FIG. 2.—Curve (a) $\frac{1}{4}\chi^2_4(t) = 4te^{-2t}$ (variance $= \frac{1}{2}$).
Curve (b) $\frac{1}{6}\chi^2_6(t) = \frac{27}{2}t^2e^{-3t}$ (variance $= \frac{1}{3}$).

The expressions for $x(t)$ and $y(t)$ in this case can be formulated in terms of the following six functions,

$$\left.\begin{aligned}
\alpha(t) &= 1 + \frac{t^6}{6!} + \frac{t^{12}}{12!} + \ldots. \\
\beta(t) &= \frac{t}{1!} + \frac{t^7}{7!} + \frac{t^{13}}{13!} + \ldots. \\
\gamma(t) &= \frac{t^2}{2!} + \frac{t^8}{8!} + \frac{t^{14}}{14!} + \ldots. \\
\underline{\alpha}(t) &= \frac{t^3}{3!} + \frac{t^9}{9!} + \frac{t^{15}}{15!} + \ldots. \\
\underline{\beta}(t) &= \frac{t^4}{4!} + \frac{t^{10}}{10!} + \frac{t^{16}}{11!} + \ldots. \\
\underline{\gamma}(t) &= \frac{t^5}{5!} + \frac{t^{11}}{11!} + \frac{t^{17}}{17!} + \ldots.
\end{aligned}\right\} \quad . \quad . \quad (6)$$

Note that in this notation t represents *thrice* the metrical length. The expressions for $x(t)$ and $y(t)$ can now be formed in exactly the same way as for the $\frac{1}{4}\chi^2_4$ case, but using instead the following matrices,

$$\begin{pmatrix} \alpha & \beta & \gamma \\ \underline{\gamma} & \alpha & \beta \\ \underline{\beta} & \underline{\gamma} & \alpha \end{pmatrix}$$ is the " non-recombination matrix "

$$\begin{pmatrix} \underline{\alpha} & \underline{\beta} & \underline{\gamma} \\ \gamma & \underline{\alpha} & \beta \\ \beta & \gamma & \underline{\alpha} \end{pmatrix}$$ is the " recombination matrix "

and $\frac{1}{3}\begin{pmatrix} t\phi & t\delta-\epsilon & t\epsilon-2\phi \\ t\epsilon+\phi & t\phi & t\delta-\epsilon \\ t\delta+2\epsilon & t\epsilon+\phi & t\phi \end{pmatrix}$ is the " map distance matrix ",

where, $\delta \equiv \alpha+\underline{\alpha}$, $\epsilon \equiv \beta+\underline{\beta}$ and $\phi \equiv \gamma+\underline{\gamma}$.

By associating one or other of the first two matrices with each internal segment and the first row and column with the segments proximal to the centromere and terminus respectively, the full set of recombination frequencies can be obtained. Similarly the map distances are obtainable from the third matrix.

We note that each matrix is of order 3×3 ; for this reason no confusion is likely to arise from the notation adopted for the sets of functions (4) and (6), and something is perhaps gained by observing the natural extension of the way in which the matrices can be built up. Finally we note that in this case the sum of all possible frequency classes is just $\delta(\tau)$; this is therefore the constant divisor required to obtain absolute frequencies.

5. COMPARISON OF THE TWO DISTRIBUTIONS

With the above summary of how, within the framework of the general theory of genetical recombination, the required relation between x and y can be found, ($x = x(t)$, $y = y(t)$ expresses it parametric form), in the cases of the two assumed forms for the intercept distribution (which we note subsumes the effects of multiple crossing-over and genetic interference) we can now pass on to compare the implicit genetic consequences.

To do this we adopt a suitable convention for representing the level of interference induced over a finite arm already used by Fisher.* Taking an arm length of 90 cM. between centromere and terminus we mark off segments at distances such that the recombination fraction for each segment is 10 per cent. The Kosambi coefficient † is then

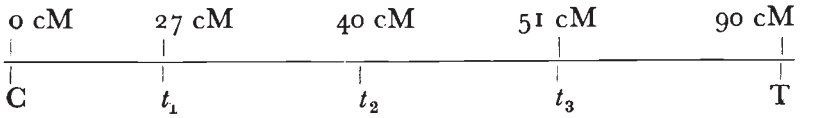
* A chart, based on an arm length of 60 cM. is exhibited as a wall diagram in the Dept. of Genetics, Cambridge.

† The Kosambi coefficient of interference is given by

$$K_{12} = \frac{y_1+y_2-y_{1+2}}{4y_1y_2y_{1+2}} = \frac{C}{2y_{1+2}}$$

where C is the coefficient of coincidence between segments 1 and 2.

calculated for each adjacent pair of segments and plotted against the central marker as abscissæ. The matrix method of the previous sections facilitates the calculation of the necessary recombination fractions and map distances. To illustrate the method consider the calculation of a single point on the graph. Let two segments, 1 and 2 say, be specified by $t_1 = 27$, $t_2 = 40$ and $t_3 = 51$ cM. (these points refer to the standardised metric ; *i.e.* put $2t$ for t in the formulæ of the previous sections).



For the $\frac{1}{4}\chi^2_4$ case the appropriate expression for the recombination fraction $y(t_1t_2)$ is as follows.

$$y(t_1t_2) = (\cosh \sinh) \overset{\leftarrow 2t \rightarrow}{\begin{pmatrix} \alpha & \beta \\ \beta & \alpha \end{pmatrix}} \overset{\leftarrow 2(t_2-t_1) \rightarrow}{\begin{pmatrix} \cosh \\ \sinh \end{pmatrix}} \Big/ \cosh 2T \overset{\leftarrow 2(T-t_3) \rightarrow}{=} \frac{A.B.C.}{\cosh 2T}, \text{ say.}$$

Hence if y_1 and y_2 refer to the respective recombination fractions of segments 1 and 2 then we have (simply substituting in the above for the appropriate t_1 and t_2) that,

$$y_1(27, 40) = \begin{Bmatrix} 1\cdot1494 \\ 0\cdot5666 \end{Bmatrix} \overset{\leftarrow A \rightarrow}{\begin{Bmatrix} 0\cdot1861178 \\ 0\cdot0225182 \end{Bmatrix}} \overset{\leftarrow B \rightarrow}{\begin{Bmatrix} 1\cdot6685 \\ 1\cdot3356 \end{Bmatrix}} \overset{\leftarrow C \rightarrow}{=} 0\cdot0997$$

$$y_2(40, 51) = \begin{Bmatrix} 1\cdot3374 \\ 0\cdot8881 \end{Bmatrix} \begin{Bmatrix} 0\cdot2277512 \\ 0\cdot0238657 \end{Bmatrix} \begin{Bmatrix} 1\cdot4128 \\ 0\cdot9981 \end{Bmatrix} = 0\cdot1011$$

These are as near to 10 per cent. as the tables* permit.

whilst $$y_{1+2}(27, 51) = \begin{Bmatrix} 1\cdot1494 \\ 0\cdot5666 \end{Bmatrix} \begin{Bmatrix} 0\cdot4045187 \\ 0\cdot0864691 \end{Bmatrix} \begin{Bmatrix} 1\cdot4128 \\ 0\cdot9981 \end{Bmatrix} = 0\cdot1925.$$

Thus the Kosambi coefficient K_{12} is,

$$K_{12} = \frac{y_1+y_2-y_{1+2}}{4y_1y_2y_{1+2}} = 1\cdot070.$$

This is therefore plotted against the central marker $t_2 = 40$ cM as abscissa ; but this point corresponds to a map distance of,

$$x(t) = \tfrac{1}{2}\begin{pmatrix} 2t \sinh 2t & 2t \cosh 2t - \sinh 2t \\ 0 & 0 \end{pmatrix}\begin{pmatrix} \cosh 2(T-t) & 0 \\ \sinh 2(T-t) & 0 \end{pmatrix} \Big/ \cosh 2T$$

$$= (2t \sinh 2t - \sinh 2t \sinh 2(T-t))_{/2 \cosh 2T}$$

which for $t = 0\cdot40$ gives,

$$x(0\cdot40) = \{0\cdot8 \sinh (1\cdot9) - \sinh (0\cdot8) \sinh (1\cdot1)\}_{/3\cdot4177}$$

$$= 20\cdot90 \text{ cM.}$$

$K = 1\cdot07$ is therefore plotted against $x = 20\cdot9$ cM as abscissa. The

* The segmental functions (4) are tabulated in Fisher and Yates' *Statistical Tables* (1953).

entire set of results obtained in the above manner are given in table I. The ordinate value $K_0 = 2{\cdot}78$ for $x = 0$ is derived on the assumption

TABLE 1

t . .	00·00	27·00	40·00	51·00	61·00	70·00	78·00	85·00	91·00
$x(t)$.	00·00	10·73	20·90	31·15	41·74	52·42	63·06	73·49	83·50
K . .	2·78	1·61	1·07	0·85	0·69	0·57	0·47	0·38	...

that there is no interference across the centromere so that the corresponding y_{1+2} refers to segments on either side of the centromere, and is therefore given by,

$$\begin{aligned} y_{1+2} &= y_1 + y_2 - 2y_1y_2 \\ &= 0{\cdot}1 + 0{\cdot}1 - 2(0{\cdot}1 \times 0{\cdot}1) \\ &= 0{\cdot}18, \end{aligned}$$

whence $K_0 = 2{\cdot}78$.

TABLE 2

t . .	00·00	36·67	49·33	58·67	66·00	72·33	77·67	82·00	86·00
$x(t)$.	00·00	10·27	20·29	30·18	39·88	50·04	60·21	69·87	80·05
K . .	2·78	0·88	0·34	0·18	0·11	0·07	0·04	0·03	...

A similar calculation applies to the $\frac{1}{6}\chi^2_6$ case ; the only difference is that $x(t)$ and $y(t)$ are built up from the 3×3 matrices instead of the

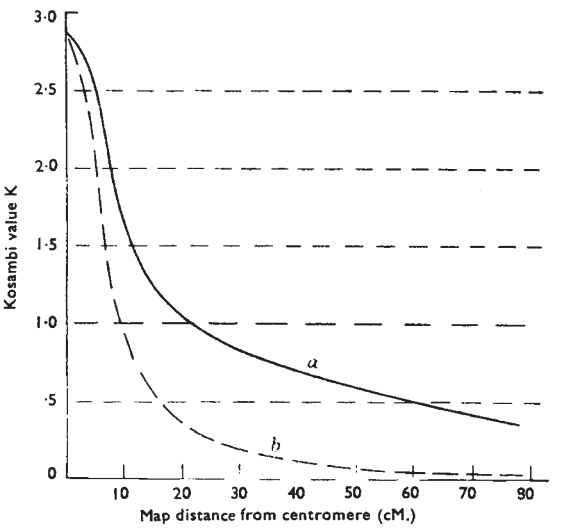


FIG. 3.—Values of K for pairs of segments, each with 10 per cent. recombination, plotted against the position of the central marker. Curve (*a*) corresponds to the $\frac{1}{4}\chi^2_4$ intercept distribution and curve (*b*) to the $\frac{1}{6}\chi^2_6$ distribution.

2×2. (Tables for the six functions (6) have been calculated by the author.) The results for the $\frac{1}{6}\chi^2_6$ case are summarised in table 2.

A graphical illustration of tables 1 and 2 is given in fig. 3.

One notices that the range of values predicted by the $\frac{1}{4}\chi^2_4$ theory is consistent with current genetical evidence, whilst those predicted by the $\frac{1}{6}\chi^2_6$ theory are of a much lower order. The fact that only a relatively slight departure from the $\frac{1}{4}\chi^2_4$ distribution (see fig. 2) is sufficient to imply very different K values from those which have been observed suggests that the $\frac{1}{4}\chi^2_4$ distribution simulates the actual intercept distribution rather closely.

6. RELATION TO KOSAMBI'S THEORY

Kosambi's empirically derived relation between the map distance and the recombination fraction is of the form,

$$y(x) = \tfrac{1}{2}\tanh 2x$$

from which it may be verified that the Kosambi coefficient is unity throughout the arm. This follows from the implicit addition formula,

$$y_{1+2} = \frac{y_1+y_2}{1+4y_1y_2}.$$

It also follows from this that for n loci only the recombination fractions between $\frac{1}{2}n(n-1)$ pairs of points can be derived, whilst there actually exist 2^n-1 recombination classes. Therefore this relation does not provide an adequate basis from which to infer all the gametic frequencies in the cases of four or more loci. Further, it requires that y be a monotonic function of x, sets an upper limit of 50 per cent. to the recombination fraction for any segment and implies uniform properties for a chromosome arm throughout its length. However, it is known to give good agreement in many cases for segments distal from the centromere on long arms, and it will be expected therefore of any theory (such as that based on the $\frac{1}{4}\chi^2_4$ or $\frac{1}{6}\chi^2_6$ distribution) that apart from overcoming the weaknesses of the Kosambi relation, it will agree closely with it over median ranges (where K is approximately unity). One may observe in fig. 3 that there is a range of values of x over which, for the $\frac{1}{4}\chi^2_4$ curve, K is near unity, *i.e.* the value given by Kosambi's relation. For this range one may therefore expect there to be good agreement between these theories, and correspondingly less good agreement between Kosambi's relation and the $\frac{1}{6}\chi^2_6$ theory. The relevant approximations are * given by the following expressions.

$$\tfrac{1}{4}\chi^2_4 : y(x) = \tfrac{1}{2}(1-e^{-2x}\cos 2x)$$
$$\tfrac{1}{6}\chi^2_6 : y(x) = \tfrac{1}{3}e^{-3x}\cdot\{3\alpha(3x)+2\beta(3x)+2\gamma(3x)+2\gamma(3x)+\beta(3x)\}$$

These are compared with Kosambi's relation in table 3. Both approximations agree fairly well with Kosambi over this range, though as we anticipated from fig. 3 the agreement is rather better in the $\frac{1}{4}\chi^2_4$ case.

In other respects the $\frac{1}{6}\chi^2_6$ analysis enjoys qualitative advantages similar to the $\frac{1}{4}\chi^2_4$ theory, in that it does not confine all recombination

* See Owen (1951), Payne (1956).

fractions below 50 per cent., nor ascribe uniform properties throughout the length of a finite arm, but does allow us to calculate any required recombination class frequency and provide a consistent measure of location in an additive metric. It will be interesting to see if there are any species where the theory of recombination based on the $\frac{1}{6}\chi^2_6$ distribution of intercept length, corresponding to more severe genetic interference, gives better agreement than that based on the $\frac{1}{4}\chi^2_4$ distribution. The simple experimental criterion suggested by fig. 3 should assist such investigation.

TABLE 3

x (cM)	Kosambi	$\frac{1}{4}\chi^2_4$	$\frac{1}{6}\chi^2_6$
0	0·000	0·000	0·000
4	0·040	0·040	0·040
8	0·079	0·079	0·080
12	0·118	0·118	0·120
16	0·155	0·155	0·159
20	0·190	0·191	0·198
24	0·223	0·226	0·235
28	0·254	0·258	0·272
32	0·283	0·289	0·307
36	0·308	0·317	0·340

7. SUMMARY

A simple algebraic method is given for obtaining the relation between the map distance x and the recombination fraction y in the cases of two assumed distributions for the intercept length between successive exchange points on a single strand (the $\frac{1}{4}\chi^2_4$ and $\frac{1}{6}\chi^2_6$ distributions). Since these correspond to different levels of genetic interference the interference levels are calculated in either case. It is clear from this that whereas the $\frac{1}{4}\chi^2_4$ distribution yields results in good agreement with current genetical evidence, the $\frac{1}{6}\chi^2_6$ distribution does not, and as the difference between these distributions is slight one is led to infer that the $\frac{1}{4}\chi^2_4$ distribution (due to Fisher and Owen) simulates the actual intercept length distribution rather closely.

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