INTERFERENCE IN GENETIC CROSSING OVER AND CHROMOSOME MAPPING

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ABSTRACT

This paper proposes a general model for interference in genetic crossing over. The model assumes serial occurrence of chiasmata, visualized as a renewal process along the paired (or pairing) chromosomes. This process is described as an underlying Poisson process in which the 1st, $n + 1$th, $2n + 1$th, etc., events are to be interpreted as realized chiasmata. Chromatid interference is described in terms of the probabilities that two successive chiasmata involve two, three or four different chromatids. Several characteristics of this model, *e.g.*, the cytological and genetic mapping function and the density of chiasmata along the chromosomes, are discussed. Some aspects of other interference models are briefly discussed.

TWO types of interference are to be distinguished in genetic crossing over. (1) *Chiasma interference* refers to the influence of a given chiasma on the probability of occurrence of another one in its neighborhood. Positive chiasma interference reduces this probability. In the absence of chiasma interference, the formation of chiasmata can be visualized as a Poisson process along the chromosome. A powerful approach to interference theory is indeed by describing chiasma occurrence as a renewal process that starts at a fixed point on the chromosome. Chiasma interference is then incorporated by assuming a distribution of intercept lengths that is different from the negative exponential distribution (as it is in the Poisson process). (2) *Chromatid interference* refers to the configuration of pairs of successive chiasmata. Pairs of successive chiasmata may be of three types, *i.e.*, two-strand doubles, three-strand doubles and four-strand doubles (see Figure 1). If the involvement of chromatids in any chiasma is a matter of pure chance, the frequencies of the two-, three- and four-strand doubles are 0.25, 0.5 and 0.25, respectively. Any deviation from these relative frequencies can be referred to as chromatid interference.

Most of the presently existing interference models deal with a renewal process along a given chromatid. The nature of such a process is determined by both chiasma and chromatid interference. Thus, if the probability density function (pdf) of intercept lengths along a given chromatid contains a single parameter, the model does not distinguish between the two types of interference. The theory developed by OWEN (1950) is based on such a model.

The idea of chiasma formation as a serial process (a renewal process) is from

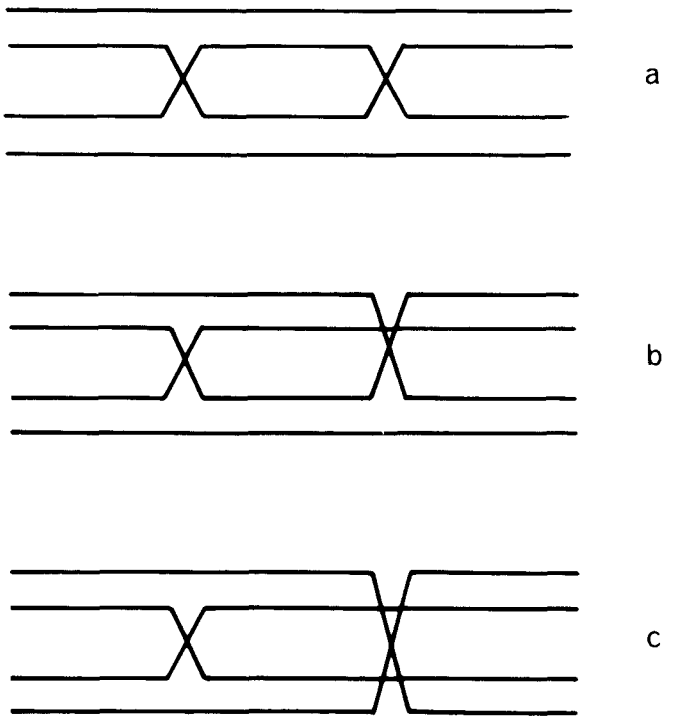

FIGURE 1.—The three types of pairs of chiasmata: (a) two-strand double; (b) three-strand double; (c) four-strand double.

MATHER (1936), who also introduced the concept of a "differential distance" (see below). The theory of renewal processes was applied by OWEN only to the process along a given chromatid probably because at that time virtually no reliable data were available on chiasma densities. Correctness of OWEN's (1950) model could at that time be tested only by means of comparing crossover data obtained from multiple backcross experiments. Although the chiasma density can readily be obtained from OWEN's theory, there was apparently no need for doing so. During the last decade, however, data on chiasma densities along chromosomes have become available (HENDERSON 1963; FOX 1973; HULTÈN 1974). Since the pattern of chiasma density is affected only by chiasma interference, there is now need for a model that incorporates both types of interference in such a way that they are "separable". With such a model, the chiasma density and the prediction of genetic map distances between gene loci from recombination frequencies can be separately analyzed.

The aim of this paper is to analyze a model that accounts for both types of interference, each described by its own parameter. The approach is to consider first the process of occurrence of chiasmata as such, *i.e.*, without considering the involvement of chromatids. Chiasma interference is reflected by the characteristics of this process. The process along a given chromatid is connected to the

"main process" by means of a simple probability law that describes the degree of chromatid interference. This permits a separation of the two types of interference.

ASSUMPTIONS AND DEFINITIONS

Considering the occurrence of chiasmata as such, the following assumptions are made: (1) The process of chiasma occurrence starts at a fixed point (the centromeric or telomeric end of a chromosome arm). (2) The distance, X_1, between this starting point and the first chiasma (the differential distance) has pdf, $f_1(x)$. (3) The distances between subsequent chiasmata, X_2, X_3, etc., (the interference distances) are independent and identically distributed with pdf, $f(x)$.

The independence of subsequent intercept lengths implies that we are considering single chiasma interference.

Positive chiasma interference operates such that the probability of occurrence of a chiasma is reduced in the neighborhood of a given one. With sequential formation of chiasmata, this means that only the first chiasma to be formed is not subject to interference; it is formed without restriction. Therefore, if chiasma interference exists, the differential distance and the interference distance will not be identically distributed [$f_1(x) \neq f(x)$].

We further introduce the following variables:

$F_1(t) = \int_0^t f_1(x)\,dx$, the cumulative distribution function (cdf) of the differential distance;

$F(t) = \int_0^t f(x)\,dx$, the cdf of the interference distance;

$\gamma(t_0,t)$, the probability of at least one chiasma in the interval (t_0, t_0+t)

$x(t_0,t)$, the mean number of chiasmata in the interval (t_0,t_0+t)

$r(t_0,t)$, the recombination fraction between two gene loci at t_0 and t_0+t

$z(t_0,t)$, the mean number of crossovers between these two loci; z refers to crossovers involving a given chromatid.

The quantity z will be referred to as genetic map distance, whereas x will be called cytological map distance. The (parametric) relation between $r(t_0,t)$ and $z(t_0,t)$ is known as the genetic mapping function (gmf). The relation between $\gamma(t_0,t)$ and $x(t_0,t)$ will be called the cytological mapping function (cmf). Absence of chromatid interference means that a given chromatid has probability 0.5 of being involved in any chiasma, irrespective of involvement in preceding ones. Therefore, in the absence of chromatid interference we have

$$r(t_0,t) = \gamma(t_0,t)/2.$$

Since a chiasma involves one of the two chromatids per homologue,

$$z(t_0,t) = x(t_0,t)/2, \tag{1}$$

irrespective of the degree of chromatid interference. Thus, if a cmf reads

$$\gamma = \psi(x), \tag{2}$$

the transformation into the gmf, gives (assuming absence of chromatid interference)

$$r = \psi(2z)/2. \tag{3}$$

In HALDANE's classical model (*i.e.*, a Poisson process along the chromosome, we have

$$y = 1 - e^{-x} ,$$

so that

$$r = (1 - e^{-2z})/2 .$$

A renewal process that started long before it is first observed is approximately stationary. Stationary processes have a number of useful characteristics, some of which will be used below. For a stationary process, we will write

$$x_s(t) = \lim_{t_0 \to \infty} x(t_0,t) , \text{ and}$$

$$y_s(t) = \lim_{t_0 \to \infty} y(t_0,t) .$$

The variable

$$h(t) = \frac{d}{dt} x(0,t) \tag{4}$$

is known as the renewal density, or, in our terminology the chiasma density.

Referring to a textbook on (continuous time) stochastic processes, the following results will be used (*cf.* Cox 1962 for a monograph on the subject).

$$\lim_{t \to \infty} h(t) = 1/\mu, \tag{5}$$

where μ is the mean interference distance, *i.e.*,

$$\mu = \int_0^\infty t f(t)\, dt .$$

Since

$$x_s(0) = 0, \text{ (5) leads, via (4), to}$$

$$x_s(t) = t/\mu. \tag{6}$$

The distance to the first event in a stationary process has the pdf

$$[1 - F(t)]/\mu .$$

This pdf directly leads to

$$y_s(t) = \mu^{-1} \int_0^t \{1 - F(u)\}\, du . \tag{7}$$

If we standardize the pdf $f(t)$, such that $\mu=1$, the cmf (7) becomes

$$y_s(x) = \int_0^x \{1 - F(u)\}\, du . \tag{8}$$

We will write

$$f^*(s) = \mathcal{L}\{f(x)\} = \int_0^\infty e^{-sx} f(x)\, dx$$

for the Laplace transform of the function $f(x)$ with respect to the argument x. The usefulness of Laplace transforms in renewal theory is obvious because the transform of the pdf of the sum of n-intercept lengths simply is the n-fold convolution of the transform of the pdf of a single intercept length with itself. We will use the following results.

$$\mathcal{L}\{h(t)\} = h^*(s) = \frac{f_1^*(s)}{1 - f^*(s)} \tag{9}$$

$$\mathcal{L}\{x(0,t)\} = x^*(s) = \frac{f_1^*(s)}{s\{1-f^*(s)\}} \tag{10}$$

$$\mathcal{L}\{E(N_t(N_t+1))\} = \mathcal{L}\{\psi(t)\} = \psi^*(s) = \frac{2f_1^*(s)}{s\{1-f^*(s)\}^2} . \tag{11}$$

In (11), N_t is the number of events in the interval $(0,t)$. Formal inversions of expressions (9) to (11) yields explicit expressions for $h(t)$, $x(0,t)$ and $\psi(t)$. We will use $\psi(t)$ for calculation of the variance of the number of chiasmata in $(0,t)$.

CHIASMA INTERFERENCE

Absence of chiasma interference corresponds to a Poisson process along the chromosome, or, alternatively, a negative exponential pdf for the interference distance. Chiasma interference can be described by means of the instantaneous rate of occurrence, $\phi(t)$ (the "age-specific failure rate" in terms of general renewal theory), as a function of the distance to the last chiasma. In a Poisson process $\phi(t)$ is constant; when $\phi(t)$ is increasing (decreasing) chiasmata are inhibited (enhanced) near a given one. The relation between $\phi(t)$ and the pdf of intercept lengths, $f(t)$, is

$$f(t) = \phi(t) \exp\{-\int_0^t \phi(u)du\} .$$

Thus, $\phi(t)$ uniquely determines $f(t)$. One way to formulate a model of chiasma interference is to start from a given function, $\phi(t)$. This approach was first applied by FISHER, LYON and OWEN (1947). In general, a more-or-less arbitrary choice of $\phi(t)$, such as hyperbolic or exponential curve, leads to a complicated pdf. Since $f(t)$ and $\phi(t)$ are mathematically equivalent, one can equivalently set up a model by choosing an adequate form of the pdf, preferably a family that represents some generality and yet is relatively simple, so that it allows further analysis of the model. Such a pdf is the gamma density

$$f(t) = \lambda^n t^{n-1} e^{-\lambda t} / (n-1)! , \; t > 0 \tag{12}$$

For integer values of n, this is the pdf of the distance to the nth event in a Poisson process with intensity λ. For $n=1$, there is no chiasma interference; for $n > 1$ (< 1) interference is positive (negative). For integer values of n, the analysis of the model is greatly simplified because the process can then be visualized as an underlying Poisson process in which after an event the next $n-1$ events are suppressed; every nth event in the underlying "silent" process is counted as a realization. The disadvantage of the restriction (n taking only integer values) is that negative chiasma interference is then not covered by the model. However, negative chiasma interference seems to be rare in nature. Only in the mold Aspergillus has it been demonstrated in a limited number of crosses; *cf.* FINCHAM and DAY 1963. Notice that chiasma interference as such can be inferred only from either direct cytological observations or from tetrad analysis.) Therefore we can use the pdf (12) with the restriction of n being an integer, without great loss of generality.

The most important characteristic of the distribution of intercept lengths is its variance relative to the mean; the smaller the ratio variance : mean, the stronger the interference is. Standardization of (12) to $\mu=1$ is achieved by putting $\lambda=n$. Then, the variance equals $1/n$, so that, by varying n, almost any variance can be obtained.

Since we assume that the first chiasma is formed without restriction, we put $n=1$ (no interference) for the pdf of the differential distance. We then have as our model

$$f_1(t) = \lambda e^{-\lambda t} \qquad t > 0 \ .$$
$$f(t) = \lambda^n t^{n-1} e^{-\lambda t} / (n-1)!$$

or, after standardizing the mean interference distance to unity,

$$f_1(t) = ne^{-nt} \qquad t > 0 \ . \tag{13}$$
$$f(t) = n^n t^{n-1} e^{-nt} / (n-1)!$$

We now have a model with a single parameter (n) that describes the degree of chiasma interference. With this model the occurrence of chiasmata can be visualized as an underlying Poisson process in which the events with index numbers 1, $n+1$, $2n+1$, etc., are to be interpreted as chiasma. Further considerations are based on this simple model.

Analysis of the model

With the model (13) we have

$$f_1^*(s) = \int_0^\infty e^{-st} n e^{-nt} dt = \frac{n}{s+n} \ , \tag{14}$$

and

$$f^*(s) = \int_0^\infty \{e^{-st} n^n t^{n-1} e^{-nt} / (n-1)!\} dt = \left(\frac{n}{s+n}\right)^n \ . \tag{15}$$

Inversion of the Laplace transforms (9) to (11) is straightforward, because they are easily written as partial fraction expansions. The probability of at least one chiasma, $y(t_0,t)$, is most easily obtained by a direct method.

The chiasma density

Since

$$h^*(s) = \frac{f_1^*(s)}{1-f^*(s)} \quad [cf., (9)] \ ,$$

the partial fraction expansion is of the form

$$h^*(s) = \sum_{k=0}^{n-1} \frac{A_k}{s - s_k} \ . \tag{16}$$

where the s_k are the roots of the equation $f^*(s) = 1$; *i.e.*, the s_k satisfy

$$\left(\frac{n}{s_k+n}\right)^n = 1 \ . \tag{17}$$

For the coefficients A_k in (16), we find

$$A_k = \frac{f_1^*(s_k)}{-f^{*\prime}(s_k)} = \frac{\frac{n}{s_k+n}}{\left(\frac{n}{s_k+n}\right)^{n+1}} = 1 \quad \text{[by (17)]} \ .$$

Inversion of (16) thus yields

$$h(t) = \sum_{k=0}^{n-1} \exp(ts_k) \ . \tag{18}$$

The roots s_k are found from (17):

$$\frac{s_k+n}{n} = \exp(\pm 2\pi ki/n) \ , \ (i^2=-1) \ , \ k = 0,1, \ldots ,n-1 \ .$$

or

$$\begin{aligned} s_k &= n \exp(2\pi ki/n) - n \\ &= n \cos(2\pi k/n) - n + in \sin(2\pi k/n) \ , \ k = 0,1, \ldots ,n-1 \ . \end{aligned} \tag{19}$$

It is seen that complex roots occur in conjugate pairs. Writing $s_k = a+ib$, $\bar{s}_k = a-ib$ for such a pair, we find that the contribution of a pair of complex conjugates in (18) equals

$$\begin{aligned} & e^{(a+ib)t} + e^{(a-ib)t} \\ &= e^{at}\,(e^{ibt} + e^{-ibt}) \\ &= 2\,e^{at} \cos bt \ . \end{aligned} \tag{20}$$

Here

$$a = Re(s_k) = n \cos(2\pi k/n) - n \ ,$$

and

$$b = Im(s_k) = n \sin(2\pi k/n) \ . \tag{21}$$

As an example, consider the case n=6. Equation (17) then has roots

$$\begin{aligned} s_0 &= 0 \\ s_{1,5} &= -3 \pm i3\sqrt{3} \ , \\ s_{2,4} &= -9 \pm i3\sqrt{3} \ , \\ s_3 &= -12 \ . \end{aligned} \tag{21a}$$

Substitution into (18), taking into account (20), yields

$$h(t) = 1 + 2\,(e^{-3t} + e^{-9t}) \cos 3t\sqrt{3} + e^{-12t} \ .$$

The chiasma density, $h(t)$, has been plotted for several values of n in Figure 2. It is seen that chiasma density has a peak [$h(0) = n$] at the starting point and that, in general, it shows a damped oscillation towards its stationary value of unity. A wavy pattern of chiasma density, with a peak at one end of the chromosome arm has been observed in several organisms: Trillium (NEWCOMBE 1941), a locust (HENDERSON 1963; FOX 1973), man (HULTÈN 1974) and the mouse (DE BOER and STAM, in preparation). It probably is a widespread characteristic of chiasma occurrence.

It should be noted here that even in the absence of interference, chiasmata might occur in clusters, in the sense that the chiasma density is not uniform. Such a nonuniformity, then, merely is the reflection of "hot" and "cool" regions along the chromosome. In the model we use here it is assumed that the instan-

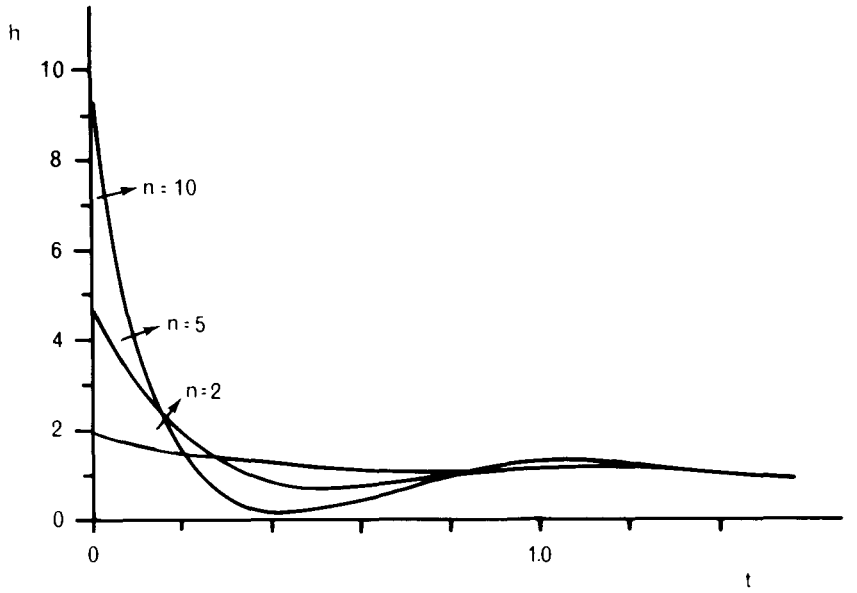

FIGURE 2.—Chiasma densities (h) along the chromosome for different intensities of chiasma interference (n).

taneous rate of occurrence depends only on the distance to the previous chiasma; it does not depend on the position on the chromosome. Notice that the existence of "hot" and "cool" regions does not alter the mapping functions, if we think of a "hot spot" as being a region where the axis along which the process proceeds is contracted. (I owe this point to an anonymous reviewer.)

The mean number of chiasmata

For the mean number of chiasmata (the cytological map distance), $x(t_0,t)$, in the interval (t_0, t_0+t) we simply have

$$x(t_0,t) = x(0,t_0+t) - x(0,t_0) \tag{21b}$$

because means are additive. Thus, knowledge of $x(0,t)$ suffices for the calculation of $x(t_0,t)$.

We have [*cf.* (10)]

$$x^*(s) = \frac{f_1^*(s)}{s\{1-f^*(s)\}} \ . \tag{22}$$

Here $s=0$ is a double root of the equation $s\{1-f^*(s)\} = 0$.
The partial fraction expansion of (22) takes the form

$$x^*(s) = \frac{A_2}{s^2} + \frac{A_1}{s} + \sum_{k=1}^{n-1} \frac{B_k}{s-s_k} \ , \tag{23}$$

where the s_k are the non-zero roots of $f^*(s) = 1$.
Substituting (14) and (15) it is found that

$$A_2 = 2 \ , \text{ and}$$
$$A_1 = (n-1)/2n \ .$$

The coefficients B_k are found to be

$$B_k = \frac{f_1^*(s_k)}{-s_k f^{*\prime}(s_k)}$$
$$= s_k^{-1} \left(\frac{n}{s_k + n}\right)^{-n} = s_k^{-1}, \quad k = 1,2, \ldots, n-1 .$$

Inversion of (23) thus yields

$$x(0,t) = t + (n-1)(2n)^{-1} + \sum_{k=1}^{n-1} \frac{\exp(s_k t)}{s_k} \tag{24}$$

where the s_k are given by (19). Writing, as before, $s_k = a + ib$, $\bar{s}_k = a - ib$ for a pair of complex conjugate roots, the contribution to (24) of such a pair equals

$$\frac{e^{(a+ib)t}}{a+ib} + \frac{e^{(a-ib)t}}{a-ib} = \frac{e^{at}}{a^2+b^2}\{a(e^{ibt} + e^{-ibt}) - ib(e^{ibt} - e^{-ibt})\}$$
$$= \frac{2e^{at}}{a^2+b^2}(a \cos bt + b \sin bt) . \tag{25}$$

As an example, consider again the case $n = 6$; substitution of (21a) into (24), and taking into account the contribution of a complex conjugate pair (25), one obtains

$$x(0,t) = t + \frac{5}{12} - \frac{1}{12}e^{-12t} + \frac{1}{6}e^{-3t}(\cos 3t\sqrt{3} + \sqrt{3} \sin 3t\sqrt{3})$$
$$+ \frac{1}{18}e^{-9t}(3 \cos 3t\sqrt{3} + \sqrt{3} \sin 3t\sqrt{3}).$$

The distribution of the number of chiasmata

Let $p_{.k}(t_0,t)$ be the probability of k chiasmata in the interval (t_0, t_0+t). Let further $q_l(t)$ be the probability of l events in the underlying Poisson process in an interval of length t, *i.e.*,

$$q_l(t) = e^{-nt}(nt)^l / l! \tag{26}$$

We now define ${}_j\theta_k(t)$ as the probability of k chiasmata in $(0,t_0)$, such that after the k-th chiasma j unrealized events have occurred in the underlying process. This state of affairs corresponds to a number of $1 + (k-1)n + j$ events in the underlying process (see diagram below).

Events in Poisson process,	1	2	3	. .	$n+1$	. . .	$2n+1$	. .	$(k-1)n+1$	. . .	$(k-1)n+1+j$
Chiasmata			1			2			3				k				

Thus, $${}_j\theta_k(t) = q_{1+(k-1)n+j}(t) . \tag{27}$$

Notice that $${}_j\theta_0(t) = \begin{cases} q_0(t) , & j = 0 \\ 0 , & j > 0 \end{cases}$$

because with no chiasmata in $(0,t)$ there can be no unrealized events in the underlying Poisson process. Now suppose that j unrealized events have occurred after the lth chiasma in $(0,t_0)$ $(l>0)$. Then k chiasmata occur in (t_0, t_0+t) if the number of events in the underlying process in (t_0, t_0+t) equals one of the values $n-j+(k-1)n$, $n-j+(k-1)n+1$, . . . $n-j+(k-1)n+n-1$. The total probability

of k chiasmata in (t_0, t_0+t), together with l chiasmata ($l>0$) in $(0, t_0)$ thus equals

$$\sum_{j=0}^{n-1} {}_j\theta_l(t_0) \sum_{\substack{m=n-j+(k-1)n \\ m \geq 0}}^{(k+1)n-j-1} q_m(t) \ .$$

If $l=0$, this becomes

$${}_0\theta_0(t_0) \sum_{\substack{m=1+(k-1)n \\ m \geq 0}}^{kn} q_m(t) \ .$$

Summing over all possible values of l, one obtains

$$p_{.k}(t_0,t) = {}_0\theta_0(t_0) \sum_{\substack{m=1+(k-1)n \\ m \geq 0}}^{kn} q_m(t) + \sum_{l=1}^{\infty} \sum_{j=0}^{n-1} {}_j\theta_l(t_0) \sum_{\substack{m=n-j+(k-1)n \\ m \geq 0}}^{(k+1)n-j-1} q_m(t) \quad (28)$$

where $q_l(t)$ and ${}_j\theta_l(t)$ are given by (26) and (27), respectively. In particular, the probability of no chiasmata in (t_0, t_0+t) is

$$p_{.0}(t_0,t) = q_0(t_0+t) + \sum_{l=1}^{\infty} \sum_{j=0}^{n-1} {}_j\theta_l(t_0) \sum_{m=0}^{n-j-1} q_m(t) \ . \quad (29)$$

Expressions (28) and (29) are useful for numerical evaluation.

The cytological mapping function

Equations (21b), (24) and (29) enable tabulation of $x(t_0,t)$ and $y(t_0,t)$ $[=1-p_{.0}(t_0,t)]$ for a given value of n. The relation between x and y, *i.e.*, the cytological mapping function, has been plotted in Figure 3 for several values of n and t_0. For each value of n, two different values of t_0 were chosen, *i.e.*, $t_0 = 0$ and a value corresponding approximately to $x(0,t_0) = 0.5$. In the latter case, segments are measured from a point where cytological map distance (measured from the starting point) approximately equals 0.5. It is seen that, especially for large values of n, the cmf may seriously depend on the value of t_0. In other words, the relation between cytological map distance and probability of being "bound" (*i.e.*, having at least one chiasma) varies with the position of the segment.

Models for chiasma interference that do not take into account this position dependency have been formulated by BARRAT *et al.* (1954) and STURT (1976). In these models the occurrence of chiasmata can be regarded as a stationary renewal process. It is therefore worthwhile to consider here also the cmf of the process in stationary phase; these can then be compared with the cmf's corresponding to BARRAT's and STURT's models. Application of (8) directly leads to

$$y_s(x) = 1 - \frac{e^{-nx}}{n} \sum_{k=0}^{n-1} \frac{(n-k)(nx)^k}{k!} \ , \quad (30)$$

(*cf.*, Cox 1962, p. 39). This function has been plotted for several values of n in Figure 4.

The variance of the number of chiasmata

In cytogenetics the ratio, R, of the mean to the variance of the number of chiasmata is often used as a measure of interference (see SYBENGA 1975 for several examples). In the absence of chiasma interference ($n = 1$ in our model),

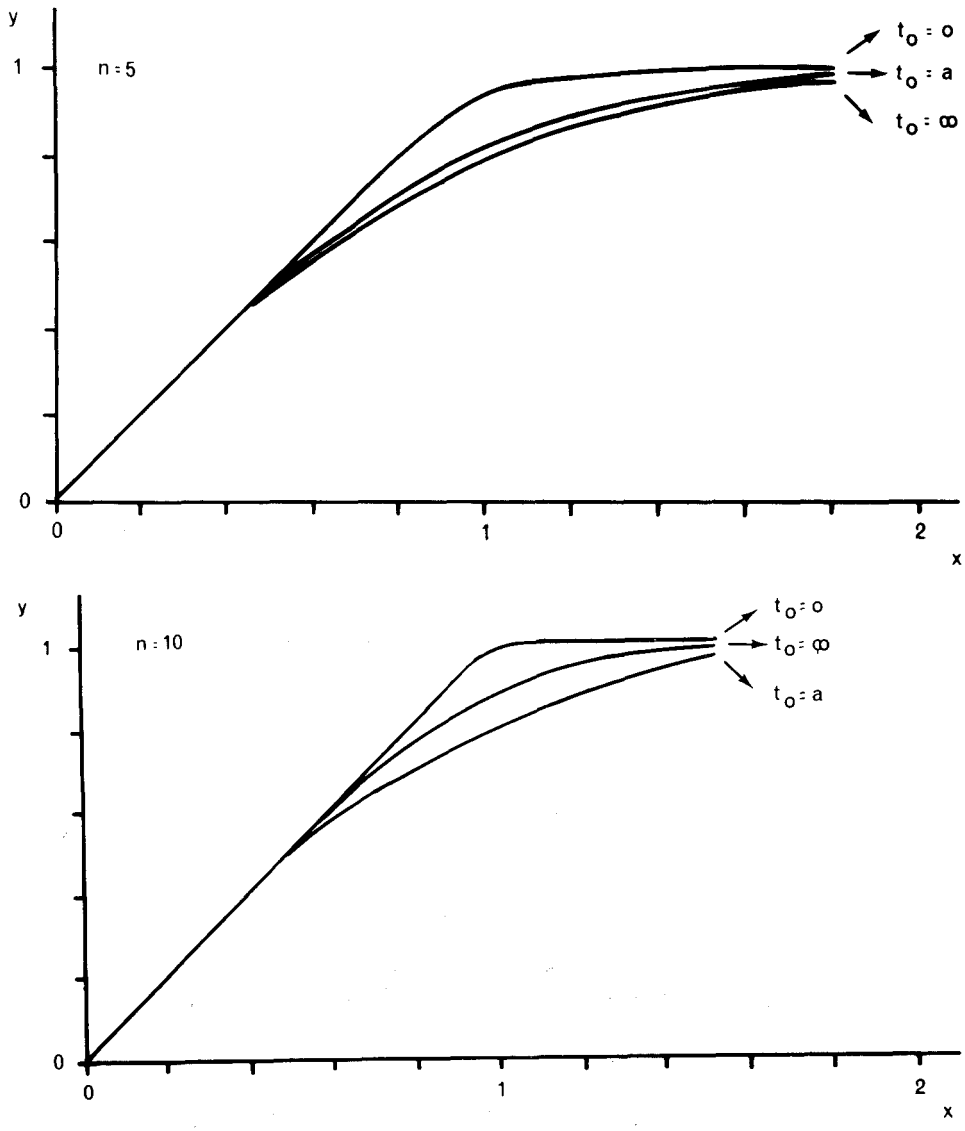

FIGURE 3.—Cytological mapping functions for nonstationary processes. t_0 is the point from which segments ar measured. $t_0 = a$ corresponds to a point where the average number of chiasmata, measured from $t = 0$, approximately equals 0.5. (n = parameter of chiasma interference; x = mean number of chiasmata; y = probability of at least one chiasma.)

the number of chiasmata in any segment is Poisson distributed; thus, R equals unity in that case. With positive interference, chiasmata are more evenly distributed over single chromosomes, resulting in a decrease of the variance relative to the mean, *i.e.*, $R>1$. In order to have an impression of the value that R may take in our model, we calculate

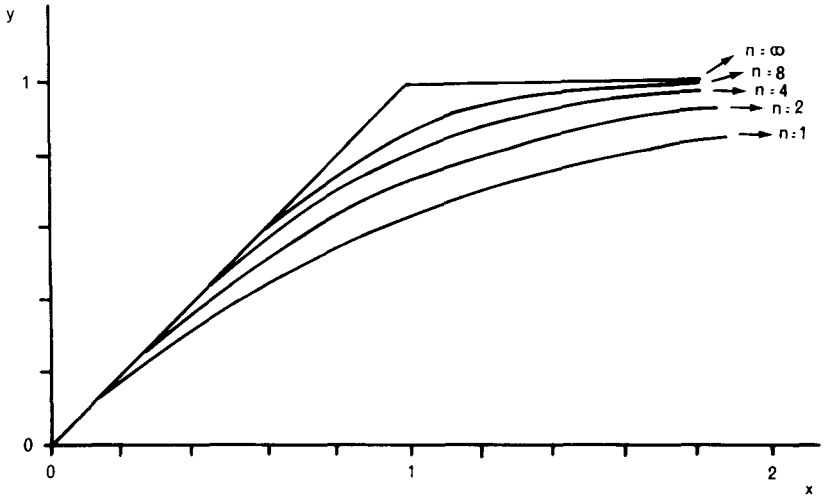

FIGURE 4.—Cytological mapping functions for stationary processes. n = parameter of chiasma interference; x = mean number of chiasmata; y = probability of at least one chiasma.)

$$\sigma^2(t) = \psi(t) - x(0,t) - \{x(0,t)\}^2 \ . \tag{31}$$

From this

$$R = x(0,t) \ / \ \sigma^2(t)$$

is calculated.

The Laplace transform of $\psi\ (t)$ is [*cf.* (11)]

$$\psi^*(s) = \frac{2 f_1^*(s)}{s\{1-f^*(s)\}^2} \ . \tag{32}$$

The equation $s\{1-f^*(s)\}^2 = 0$ has roots $s=0$ of multiplicity 3 and $n-1$ roots of multiplicity 2 that satisfy (17), so that the partial fraction expansion of (32) takes the form

$$\psi^*(s) = \frac{A}{s^3} + \frac{B}{s^2} + \frac{C}{s} + \sum_{k=1}^{n-1} \left\{ \frac{D_k}{(s-s_k)^2} + \frac{E_k}{s-s_k} \right\} \ . \tag{33}$$

Inversion of (33) gives

$$\psi(t) = \frac{1}{2} At^2 + Bt + C + \sum_{k=1}^{n-1} \exp(s_k t)\ (t D_k + E_k) \ . \tag{34}$$

Straightforward application of the rules for determining the coefficients in a partial fraction expansion yields

$$\begin{aligned} A &= 2 \\ B &= 2 \\ C &= (n-1)(5n-1) \ / \ 6n^2 \\ D_k &= 2\left(\frac{1}{n} + \frac{1}{s_k}\right) \\ E_k &= \frac{2}{s_k}\left(1 - \frac{1}{n} - \frac{1}{s_k}\right) \end{aligned} \tag{35}$$

The contribution of a pair of complex conjugate roots to (34) is found to be

$$4\,t\,e^{at}\left\{\frac{a\cos bt + b\sin bt}{a^2+b^2} + \frac{\cos bt}{n}\right\}$$
$$-\frac{4\,e^{at}}{a^2+b^2}\left\{\frac{(a^2-b^2)\cos bt + 2ab\sin bt}{a^2+b^2} - \frac{a\cos bt + b\sin bt}{n}\right\} \qquad (36)$$

where a and b are given by (21). Using (24) and (34) to (36), I have produced graphs of the ratio R against the mean in Figure 5. It is seen that R may vary abruptly when n is large. Variance estimates from cytological observations are usually inefficient, and, besides, they often contain an unknown between-chromosome component. Taken together with the fact that R may vary widely with the mean, estimates of R must be considered of little value as to the information they provide on chiasma interference.

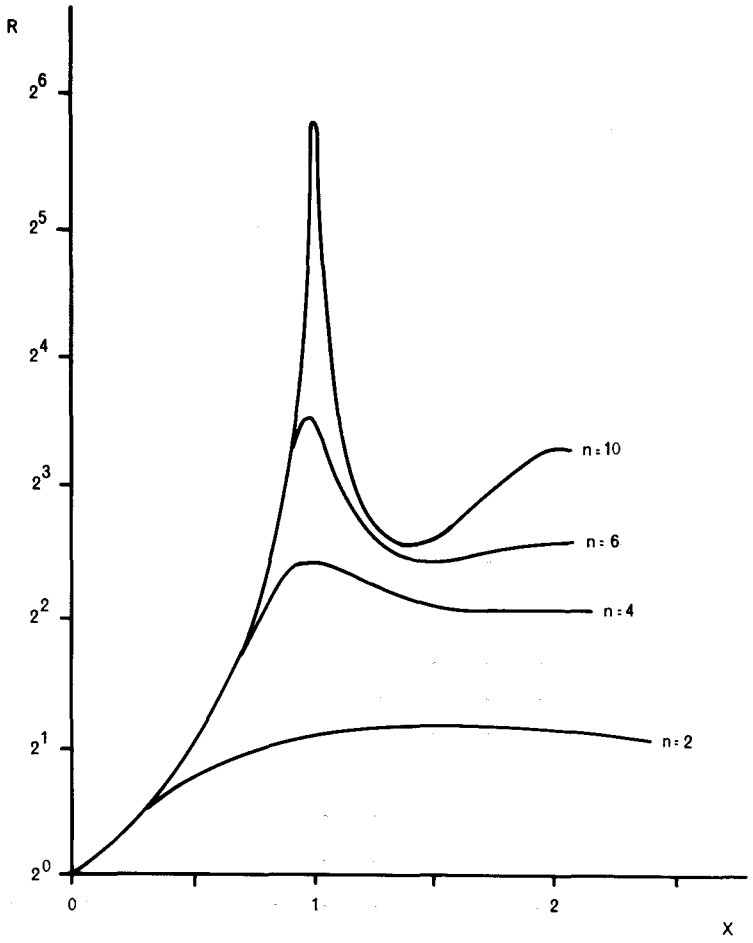

FIGURE 5.—The ratio mean : variance (R) plotted against the mean (x) for different values of n.

The segmental calculus

In this section I will indicate how the probability distribution $p_{k_1,..,k_r}(t_1,..,t_r)$, *i.e.*, the probability that $k_1,..,k_r$ chiasmata occur in subsequent segments of lengths $t_1,..,t_r$, can be obtained.

Analogously to ${}_j\theta_{k_1}(t_1)$ we define ${}_j\theta_{k_1,k_2}(t_1,t_2)$ as the probability that in the adjoint segments $(0,t_1)$ and (t_1,t_1+t_2) k_1 and k_2 chiasmata occur, such that after the k_2-th chiasma j unrealized events occur in the underlying Poisson process. Then, obviously,

$$p_{k_1,\ldots,k_r}(t_1,..,t_r) = \sum_{j=0}^{n-1} {}_j\theta_{k_1,\ldots,k_r}(t_1,..,t_r) \ . \tag{37}$$

We will call the (column) vector with elements ${}_0\theta_{k_1}(t_1), {}_1\theta_{k_1}(t_1), \ldots, {}_{n-1}\theta_{k_1}(t_1)$ the state vector of order 1, denoted by $\theta^{(1)}$. Similarly the state vector of order 2, $\theta^{(2)}$ has elements ${}_0\theta_{k_1,k_2}(t_1,t_2), \ldots, {}_{n-1}\theta_{k_1,k_2}(t_1,t_2)$. The state vectors of increasing order can be obtained recursively as follows. First suppose $k_1>0$; then

$$\begin{bmatrix} {}_0\theta_{k_1,k_2}(t_1,t_2) \\ {}_1\theta_{k_1,k_2}(t_1,t_2) \\ . \\ . \\ {}_{n-1}\theta_{k_1,k_2}(t_1,t_2) \end{bmatrix} = \begin{bmatrix} q_{nk_2}(t_2) & q_{nk_2-1}(t_2) & . & . & q_{nk_2-n+1}(t_2) \\ q_{nk_2+1}(t_2) & q_{nk_2}(t_2) & . & . & q_{nk_2-n+2}(t_2) \\ . & . & . & . & \\ . & . & . & . & \\ q_{nk_2+n-1}(t_2) & q_{nk_2+n-2}(t_2) & . & . & q_{nk_2}(t_2) \end{bmatrix} \begin{bmatrix} {}_0\theta_{k_1}(t_1) \\ {}_1\theta_{k_1}(t_1) \\ . \\ . \\ {}_{n-1}\theta_{k_1}(t_1) \end{bmatrix} \tag{38}$$

or, in shorthand notation

$$\theta^{(2)} = {}_{k_2}C_{t_2} \cdot \theta^{(1)} \ .$$

Similarly,

$$\theta^{(3)} = {}_{k_3}C_{t_3} \cdot \theta^{(2)} = {}_{k_3}C_{t_3} \cdot {}_{k_2}C_{t_2} \cdot \theta^{(1)} \ .$$

The matrix to be inserted for the ith segment, ${}_{k_i}C_{t_i}$, is called the "segmental matrix" (*cf.* BAILEY 1961). Evidently, elements $q_l(t)$ with $l<0$ must be taken identically zero. Next, consider the case $k_1=0$, $k_2>0$. Then, the right-hand side of (38) takes the form

$$\begin{bmatrix} q_{1+(k_2-1)n}(t_2) & 0 & . & . & 0 \\ q_{1+(k_2-1)n+1}(t_2) & 0 & . & . & 0 \\ . & . & . & . & . \\ . & . & . & . & . \\ q_{nk_2}(t_2) & 0 & . & . & 0 \end{bmatrix} \begin{bmatrix} {}_0\theta_0(t_1) \\ 0 \\ . \\ . \\ 0 \end{bmatrix} \ . \tag{39}$$

When $k_1=0$, $k_2=0$ this becomes

$$\begin{bmatrix} q_0(t_2) & 0 & . & . & 0 \\ 0 & 0 & . & . & 0 \\ . & . & . & . & . \\ . & . & . & . & . \\ 0 & 0 & . & . & 0 \end{bmatrix} \begin{bmatrix} {}_0\theta_0(t_1) \\ 0 \\ . \\ . \\ 0 \end{bmatrix} \ . \tag{40}$$

Denoting the three types of segmental matrices in (38), (39) and (40) by ${}_{k_i}C_{t_i}$, ${}_{k_i}D_{t_i}$ and E_{t_i}, respectively, we have the following rule. The matrix ${}_{k_i}C_{t_i}$ is inserted if the first chiasma occurs before the i-th segment; ${}_{k_i}D_{t_i}$ is inserted if the first chiasma occurs in the i-th segment and E_{t_i} is inserted if the first chiasma occurs after the i-th segment. The first segment can be considered as being preceded by a segment with no chiasmata, which corresponds to the state vector $V' = (1,0,\ldots,0)$. So if we post-multiply by V, the appropriate segmental matrix for the first segment can be inserted (being either ${}_{k_1}D_{t_1}$ or E_{t_1}).

Chromatid interference

Chromatid interference can be described by considering pairs of subsequent chiasmata, which may be of three possible types, *viz.*, two-, three- and four-strand doubles (*cf.*, (Figure 1). Let the probabilities of these types be u, v and w, respectively. For simplicity we will assume that these values do not depend on the distance between the successive chiasmata of a pair. (This assumption may be an oversimplification; the effect of dependency of u, v and w on the distance is discussed later on). It can be shown (WEINSTEIN 1958) that the probability, r, of a given chromatid being involved in an odd number of chiasmata (r is the recombination frequency) is given by

$$r(t_0,t) = \{1 - p_{.0}(t_0,t) - \sum_{k=1}^{\infty} \alpha^k \, p_{.2k}(t_0,t)\} \,/\, 2 \ . \tag{41}$$

where $\alpha = u - w$ and $p_{.j}(t_0,t)$ is the probability that the interval (t_0,t_0+t) contains j chiasmata as such. (Expression (41) has recently been derived anew by STURT and SMITH 1976). Equation (41) shows that recombination is affected by chromatid interference only if the latter is such that $u \neq w$. For this reason we will call $\alpha = u - w$ the parameter of chromatid interference. The distribution $p_{.k}(t_0,t)$ is given by (28). The genetic map distance simply equals half the cytological map distance:

$$z(t_0,t) = x(t_0,t) \,/\, 2 \ . \tag{42}$$

The genetic mapping function is given by the (doubly) parametric relation between $r(t_0,t)$ and $z(t_0,t)$. Using (24), (28), (41) and (42), $r(t_0,t)$ and $z(t_0,t)$ can be tabulated for any combination of n and α (*i.e.*, chiasma and chromatid interference). Before considering the behavior of the gmf in the general case (arbitrary values of n and α), it is worth paying attention to a few specific combinations of the two types of interference.

Absence of both chiasma and chromatid interference (n=*1*; α=*0*)

This is Haldane's classical model with

$$p_{.k}(t_0,t) = e^{-t} \, t^k \,/\, k! \quad \text{and}$$
$$x(t_0,t) = t \ .$$

Substitution into (41) leads to Haldane's gmf:

$$r(z;t_0) = (1 - e^{-2z}) \,/\, 2 \ .$$

Absence of chromatid interference (n>1; $\alpha=0$)

In this case (41) reduces to

$$r(t_0,t) = \{1 - p_{.0}(t_0,t)\} / 2 ,$$

whereas $z(t_0,t)$ must be evaluated as indicated above.

Absence of chiasma interference (n=1; $-1 \leq \alpha \leq 1$; $\alpha \neq 0$)

With $n=1$, we again have

$$p_{.k}(t_0,t) = e^{-t} t^k / k! .$$

Substitution into (41), and remembering $z(t) = \frac{1}{2}t$ for this case, yields

$$r(t_0,t) = \left\{ 1 - e^{-t} \sum_{k=0}^{\infty} \frac{\alpha^k t^{2k}}{(2k)!} \right\} /2 \tag{43a}$$

$$z(t_0,t) = t/2 \tag{43b}$$

For $\alpha<0$, (43a) can be written as

$$r(t_0,t) = \{1 - e^{-t} \cos (t|\alpha|^{\frac{1}{2}})\} / 2 ,$$

so that the gmf becomes

$$r(z;t_0) = \{1 - e^{-2z} \cos (2z|\alpha|^{\frac{1}{2}})\} / 2 . \tag{44}$$

For $\alpha>0$, the gmf can be written as

$$r(z;t_0) = \{1 - e^{-2z} \cosh (2z\alpha^{\frac{1}{2}})\} / 2 . \tag{45}$$

For any value of α, except $\alpha=1$, the limiting value of r (as z tends to infinity) equals 0.5. With $\alpha=1$ (corresponding to the hypothetical case that all chiasmata of a chromosome pair involve the same pair of chromatids), (45) becomes

$$r(z;t_0) = (1 - e^{-4z}) / 4 .$$

The limiting value of r then equals 0.25.

For $\alpha<0$ (*i.e.*, more four-strand doubles than two-strand doubles), the recombination fraction rises above 0.5; there is a damped oscillation towards the limiting value 0.5.

Both chiasma and chromatid interference (n > 1 ; $\alpha \neq 0$)

For this general case, I applied numerical evaluation of (41) and (42) to produce graphs of the gmf. These are shown in Figure 6 (all distances measured from $t_0=0$). It is seen that a negative value of α always predicts a recombination frequency of over 50% for certain chromosome regions. Since these have only rarely been found in genetic experiments (see OWEN 1950 for a classic example), this type of chromatid interference probably plays a minor role in nature. With positive values of α, recombination frequency never exceeds 50%, but it does not necessarily always increase with map distance. Crossover data that are inconsistent with respect to gene order (as has been found in fungi) could possibly result from this type of chromatid interference. Another important feature of positive α values is that recombination frequency may hardly increase over large map distances at a level well below 50%.

Other interference models

The approach to interference theory followed by OWEN (1950) (see also BAILEY 1961 for a detailed description) is to consider the process of chiasma

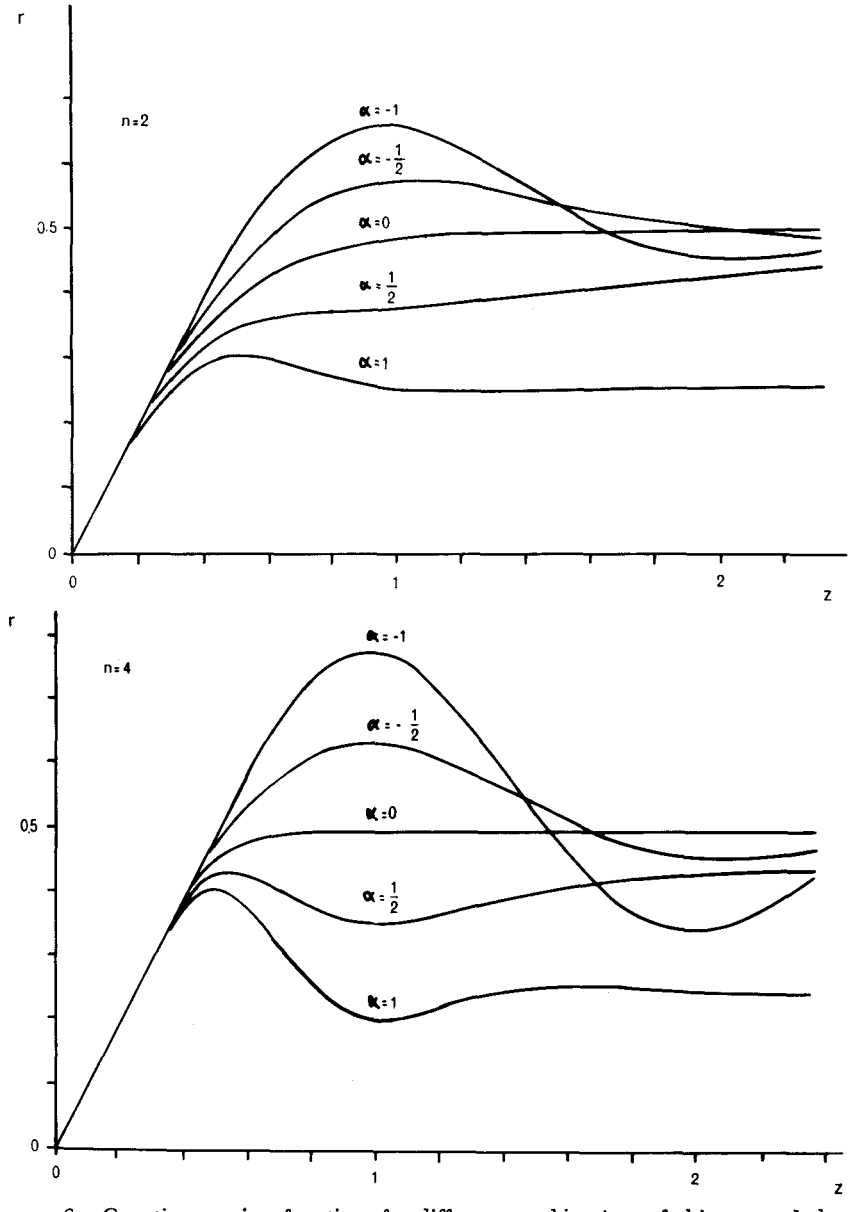

FIGURE 6.—Genetic mapping functions for different combinations of chiasma and chromatid interference. (z = genetic map distance; r = recombination frequency; n = parameter of chiasma interference; α = parameter of chromatid interference. Segments measured from $t_0 = 0$.)

determination along a given chromatid as a renewal process. As mentioned earlier such a model does not distinguish between the two types of interference. It is worth considering here some aspects of OWEN's (1950) model and see how these fit into the model presented in this paper.

Let, as before, $f_1(t)$ be the pdf of differential and interference distance, respectively. Further, let $g_1(t)$ and $g(t)$ be the pdf of the first and subsequent intercept lengths along a given chromatid. [OWEN's (1950) analysis starts from a given $g_1(t)$ and $g(t)$.] Assuming as before, that α is constant, we can express $g_1^*(s) = \mathcal{L}\{g_1(t)\}$ and $g^*(s) = \mathcal{L}\{g(t)\}$ in terms of $f_1^*(s)$ and $f^*(s)$ (see APPENDIX for a derivation):

$$g_1^*(s) = f_1^*(s)\,\frac{1-\alpha f^*(s)}{2-(1+\alpha)f^*(s)}\,, \text{ and} \tag{46a}$$

$$g^*(s) = f^*(s)\,\frac{1+\alpha-2\alpha f^*(s)}{2-(1+\alpha)f^*(s)}\,. \tag{46b}$$

Both OWEN (1950) and BAILEY (1961) for simplicity assume identity of $g_1(t)$ and $g(t)$ (all intercept lengths identically distributed, included the first one), though their general theory covers other situations as well. They pay special attention to the case that all intercept lengths (along a given chromatid) follow a gamma distribution. In that case, the model always predicts recombination frequencies of over 50% for certain regions (*cf.*, BAILEY 1961). It is interesting to verify what conditions are to be imposed on the main process in my model for $g_1(t)$ and $g(t)$ to be identical. Since $g_1^*(s)$ and $g^*(s)$ uniquely determine $g_1(t)$ and $g(t)$, identity of $g_1(t)$ and $g(t)$ requires identity of $g_1^*(s)$ and $g^*(s)$, or equivalently, from (46)

$$f_1^*(s) = f^*(s)\,\frac{1+\alpha-2\alpha f^*(s)}{1-\alpha f^*(s)}\,.$$

Taking the first moment [$f_1^{*\prime}(0) = -\mu_1$, $f^{*\prime}(0) = -\mu$, etc.] this leads to the condition

$$\mu_1 = \mu\,\frac{1-2\alpha}{1-\alpha}\,. \tag{47}$$

We have seen that recombination frequencies of over 50% can occur only when $\alpha<0$. This in turn implies the condition $\mu_1>\mu$ (47). Thus, the simplifying assumption that $g_1(t)$ and $g(t)$ are identical requires that for the "main" process the mean differential distance be larger than the mean interference distance. This is in conflict with the concept of a differential distance (MATHER 1936).

An entirely different approach to chiasma interference is to disregard the sequential nature of chiasma formation, but to regard only the probability distribution of the number of chiasmata in a segment of given length. This distribution is assumed to be independent of the position of the segment. In the absence of chiasma interference, this distribution is Poissonian. Several authors have formulated interference by means of a distribution which, in some way, deviates from the Poisson distribution. BARRATT *et al.* (1954) used the following modification of the Poisson distribution.

$$p_k(t) = \begin{cases} e^{-\lambda t} & , \ k=0 \\ \dfrac{1-e^{-\lambda t}}{e^{\lambda tc}-1}\ \dfrac{(\lambda tc)^k}{k!} & , \ k>0 \end{cases}\,, \tag{47}$$

where λ is a dummy variable and c is the interference parameter. For $c=1$, the distribution is Poissonian. STURT (1976) considered a model in which a chromosome (or chromosome arm) always has one obligatory chiasma, while the number of "extra" chiasma is Poisson-distributed. With this formulation the total arm length, T, enters into the distribution

$$p_k(t;T) = \begin{cases} \left(1-\frac{t}{T}\right)e^{-\lambda t} & k=0 \\ \frac{t}{T}e^{-\lambda t}\frac{(\lambda t)^{k-1}}{(k-1)!}+\left(1-\frac{t}{T}\right)e^{-\lambda t}\frac{(\lambda t)^k}{k!}\ , & k>0 \end{cases} \tag{48}$$

In this model, the degree of interference decreases as the chromosome length increases; as T tends to infinity, the distribution (48) approaches the Poisson distribution. It is straightforward to verify that the BARRATT *et al.* (1954) model leads to the following inverse cmf.

$$x(y;c) = \{-yc \ln (1-y)\} / \{1-(1-y)^c\}\ . \tag{49}$$

Sturt's model leads to the c.m.f.

$$y(x;T) = 1-\left(1-\frac{x}{1+\lambda T}\right)\exp\left(-\frac{\lambda T x}{1+\lambda T}\right)\ , \tag{50}$$

where $1+\lambda T$ is the mean number of chiasmata in the whole chromosome (arm). The functions (49) and (50) are in general appearance very similar to the cmf in stationary phase in my model (30).

Still another approach is to search for a gmf that satisfies two conditions; (1) monotonically increasing and (2) asymptotically approaching the value 0.5. The criterion for such a gmf is its general applicability. Such functions have been designed by KOSAMBI (1944) and CARTER and FALCONER (1951). With this approach the nature of the process of chiasma formation is almost completely disregarded. Although a gmf developed along these lines may indeed fit fairly well to many actual crossover data, it hardly contributes to a better understanding of the processes during meiosis.

DISCUSSION

Describing chromatid interference I have, for simplicity, assumed that the difference, α, between frequencies of two- and four-strand doubles does not depend on the distance between the two chiasmata. A more natural assumption would be that α decreases with increasing distance, resulting in absence of chromatid interference over long distances. This could for example, be accounted for by assuming a relationship of the form

$$\alpha(t) = \alpha(0)\ e^{-ct}\ , \tag{51}$$

c being a positive constant. Since such a relationship cannot be incorporated into the model in a simple way, I resorted to a Monte Carlo simulation of the process, accounting for (51). From the results of 2000 replicate runs, genetic mapping functions were plotted (segments measured from $t_0=0$). Figure 7 shows these

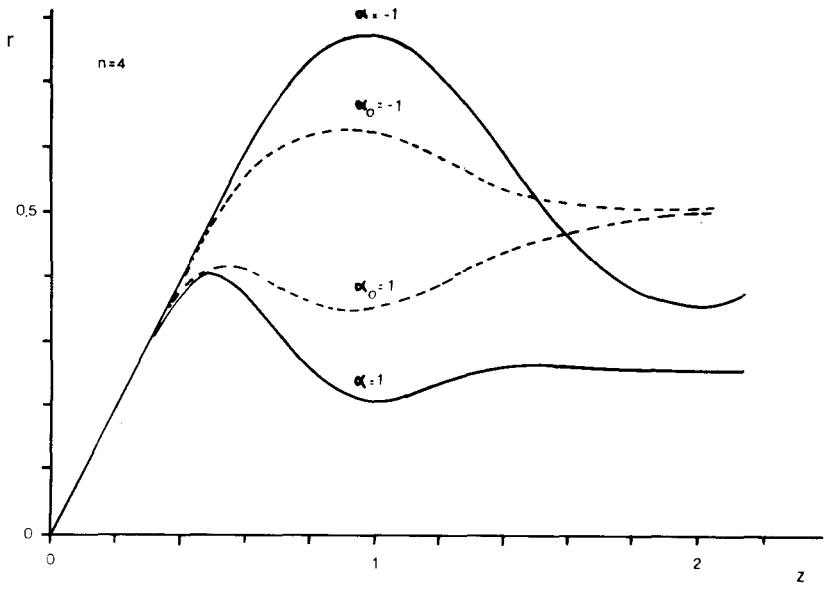

FIGURE 7.—Genetic mapping functions when chromatid interference (α) decreases with distance. (Solid lines = constant values of α. Segments measured from $t_0 = 0$.)

graphs for $c = \ln 2$ (*i.e.*, $\alpha(1) = \alpha(0)/2$) and two different values of $\alpha(0)$, *viz.*, $\alpha(0) = 1$ and $\alpha(0) = -1$; the chiasma interference parameter (n) here equals 4. The gmf for constant α is also shown for comparison. It is seen (*cf.*, Figure 6) that, roughly speaking, the effect of decreasing chromatid interference with distance is similar to the effect of constant chromatid interference at a lower level. Similar results were obtained for other combinations of $\alpha(0)$ and n.

So far I have described chiasma interference solely in terms of a mathematical model. The pdf of intercept lengths was intentionally chosen to reflect the well-known phenomenon that an existing chiasma reduces the rate of occurrence in its neighborhood relative to the overall rate of occurrence. How can this effect be brought about by the biological (biochemical) process of chiasma formation? Fox (1973) proposed the following model. A "chiasma determining mechanism" (CDM) moves along the chromosome at constant speed. For a chiasma to be formed, the CDM must be triggered in some way. Fox (1973) considers the following alternatives for the triggering mechanism: (1) trigger signals reach the CDM from outside the chromosome; (2) triggers are located on the chromosome, switching on the CDM as it passes. In the latter case, the chiasma density merely reflects the density of triggers. Neither possibility satisfactorily explains the great similarity between chiasma densities of all chromosomes of *Schistocerca gregaria* studied by Fox. (In all chromosomes, chiasma density has a wavy pattern with a peak near the telomeric end.) On the one hand, a similar distribution of triggers over all chromosomes seems highly improbable. The great similarity between chromosomes of different length can, on the other hand, not be explained by signals arriving from outside. This would mean that the rate of

arrival changes with time, but the rate of change is different for chromosomes of different length. If the rate of change were the same for all chromosomes, short chromosomes would be too short to have the second peak that occurs in long ones.

The following slight modification of the Fox model partially explains the great similarity between all chromosomes. The CDM is an (enzyme) complex that remains "occupied" for a variable period (the busy period) to finish a chiasma. The process of chromosome pairing proceeds along the chromosome at constant rate and the CDM can only be triggered as long as pairing has not yet been completed. After completing a chiasma the CDM jumps forwards to the site of pairing where the probability of being triggered per unit length is constant. Then the distance between two successive chiasmata is the sum of two random variables: (1) the "jump distance" over which pairing proceeds during the busy period, and (2) the distance over which the free CDM moves before it is triggered again. This model explains the high density near the starting point; for the first chiasma there is no preceding busy period. The similarity between chromosomes of different length could be due to an adjustment of the rate of the whole process (*i.e.*, pairing and chiasma formation) to the chromosomal length. Different chromatin concentrations might be responsible for the latter. This model closely parallels the formulation that I used for my mathematical model. The "busy period" corresponds to the $n-1$ unrealized chiasmata in the underlying Poisson process. Chromatid interference ($\alpha>0$) could be due to the tendency of the CDM to remain associated with the same pair of chromatids.

The model described above is a speculative one. It does not account for the possibility that the process of pairing and chiasma determination may start simultaneously at several sites and proceed in both directions. Nevertheless the general framework allows the formulation of a mathematical model, the analysis of which contributes to a better understanding of the control of chiasma determination and its consequences for chromosome mapping.

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LITERATURE CITED

BAILEY, N. T. J., 1961 *Introduction to the Mathematical Theory of Genetic Linkage.* Oxford Press, London.

BARRATT, R. W., D. NEWMEYER, D. D. PERKINS and L. GARNJOBST, 1954 Map construction in *Neurospora crassa.* Advan. Genet. **6:** 1–93.

CARTER, T. C. and D. S. FALCONER, 1951 Stocks for detecting linkage in mouse, and the theory of their design. J. Genet. **50:** 307–323.

COX, D. R., 1962 *Renewal Theory.* Methuen & Co., London.

FINCHAM, J. R. S. and P. R. DAY, 1963 *Fungal Genetics.* Blackwell, Oxford.

FISHER, R. A., M. F. LYON and A. R. G. OWEN, 1947 The sex chromosome in the mouse. Heredity **1:** 355–365.

FOX, D. P., 1973. The control of chiasmata distribution in the locust *Schistocerca gregaria* (Forskål). Chromosoma (Berl.) **43:** 289–328.

HENDERSON, S. A., 1963 Chiasma distribution at diplotene in a locust. Heredity **18**: 173–190.

HULTÈN, M., 1974 Chiasma distribution at diakinesis in the normal human male. Hereditas **76**: 55–78.

KOSAMBI, D. D., 1944 The estimation of map distance from recombination values. Ann. Eugen. **12**: 172–175.

MATHER, K., 1936 The determination of position in crossing over. J. Genet. **32**: 207–235.

NEWCOMBE, H. B., 1941 Chiasma interference in *Trillium erectum*. Genetics **26**: 128–136.

OWEN, A. R. G., 1950 The theory of genetical recombination. Advan. Genet. **3**: 117–157. ——, 1953 Super recombination in the sex chromosome of the mouse. Heredity **7**: 103–110.

STURT, E., 1976 A mapping function for human chromosomes. Ann. Human Genet. **40**: 147–163.

STURT, E. and C. A. B. SMITH, 1976 The relation between chromatid interference and the mapping function. Cytogenet. Cell Genet. **17**: 212–220.

SYBENGA, J., 1975 *Meiotic Configurations*. Springer-Verlag, Berlin, Heidelberg, New York.

WEINSTEIN, A., 1958 The geometry and mechanics of crossing over. Cold Spring Harbor Symp. Quant. Biol. **23**: 177–196.

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APPENDIX

Let p be the probability that a given chromatid is involved in a chiasma, given that it was also involved in the preceding one. Then p is also the probability that a given chromatid is not involved in a chiasma, given that it was not involved in the preceding one. If u, v and w are the probabilities of two-, three- and four-strand doubles, then $p = u + \frac{1}{2}v$ and $q = 1 - p = \frac{1}{2}v + w$. With $u - w = \alpha$, we have $p = \frac{1}{2}(1 + \alpha)$. Let $\phi_1(s)$ and $\phi(s)$ be the Laplace transforms of $f_1(t)$ and $f(t)$, respectively. Now consider the distance to the first chiasma involving a given chromatid and denote the Laplace transform of its pdf by $\Psi_1(s)$. Then, by the rules for a compound distribution (and dropping the argument), we have

$$\Psi_1 = \tfrac{1}{2}\phi_1 + \tfrac{1}{2}q\,\phi_1\,\phi + \tfrac{1}{2}qp\,\phi_1\,\phi^2 + \ldots\ \tfrac{1}{2}qp^n\,\phi_1\,\phi^{n+1} + \ldots \tag{A1}$$

The first term in this expression arises from the fact that a given chromatid is involved in the first chiasma with probability 0.5. The terms of the form $0.5\,qp^n\,\phi_1\,\phi^{n+1}$ state that with probability $0.5\,qp^n$ the distance to the first chiasma involved equals the sum of the distance to the first one, plus $n + 1$ subsequent intercept lengths. Expression (A1) reduces to

$$\Psi_1 = \phi_1 \frac{1 - \alpha\phi}{2 - (1 + \alpha)\,\phi}. \tag{A2}$$

Next consider the distance between two successive chiasmata involving a given chromatid. Analogous to the above reasoning we can write

$$\begin{aligned}\Psi &= p\,\phi + q^2\,\phi^2 + q^2\,p\,\phi^3 + \ldots + q^2\,p^n\,\phi^{n+2} + \ldots \\ &= \phi \frac{1 + \alpha - 2\alpha\phi}{2 - (1 + \alpha)\phi}.\end{aligned} \tag{A3}$$

(A2) and (A3) are the required Laplace transforms.