Revista Chilena de Historia Natural
74: 99-105, 2001

A critical view to explanations for the maximal value of 50 % of genetic recombination

Críticas a las explicaciones del máximo de 50 % de recombinación genética

CARLOS Y. VALENZUELA[1], PATRICIA PÉREZ-ALZOLA[2], & MANUEL J. SANTOS[2]

[1]Programa de Genética Humana, Instituto de Ciencias Biomédicas, Facultad de Medicina, Universidad de Chile, Independencia 1027, Casilla 70061, Santiago 7, Chile, e-mail: cvalenzu@machi.med.uchile.cl
[2]Departamento de Biología Celular y Molecular, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Avenida Bernardo O'Higgins 340, Casilla 114-D, Santiago 1, Chile

ABSTRACT

The maximal value of 50 % of genetic recombination (RF = recombination fraction) between two linked gene loci has been explained by two models: (i) the restriction of crossovers to only two of the four chromatids of a tetrad (tetrad model); (ii) the limit of the occurrence of an odd number of crossovers between two loci, when the expected number of crossovers tends to infinite (odd-even model). This article shows that (i) is wrong. If tetrads were responsible for the maximal 50 % RF, sister chromatid exchanges (SCE) should display a maximal 100 % RF. In mammalian CHO cells we found that SCE yield a maximal 50 % recombination. Also, we demonstrated that the maximal 50 % RF for tetrads occurs because the sum of odd order coefficients in the binomial distribution is equal to the sum of even order coefficients. At the end of meiosis the two chromatids of a chromosome that receives K crossovers are separated. Then K breaks should distribute into two chromatids. Thus, the expected number of breaks per chromatid distributes, when K is large, in 50 % of chromatids having an even number of breaks (RF = 0) and 50 % having an odd number (RF = 1), irrespective of tetrads, hexads, octads or more complex meiotic chromosome configurations.

Key words: 50 % recombination, tetrads, odd-even crossovers, SCE.

RESUMEN

El máximo de 50 % de recombinación genética (RF) entre dos loci ligados ha sido explicado por dos modelos. (i) la restricción de los entrecruzamientos a dos de las cuatro cromátidas de una tétrada (modelo de tétrada); (ii) el límite de la ocurrencia de un número impar de entrecruzamientos entre los dos loci, cuando el número esperado de entrecruzamientos tiende a infinito (modelo par-impar). Este artículo muestra que (i) es erróneo, ya que, si la tétrada fuera responsable del máximo de 50 % de RF, el intercambio de cromátidas hermanas (SCE) debería alcazar el 100 % de recombinación y esto no se da en células CHO, en las que encontramos un máximo de 50 %. Además, demostramos que el máximo de 50 % RF para las tétradas ocurre porque la suma de los coeficientes de orden impar, en una distribución binomial, es igual a la suma de los de orden par. Al final de la meiosis las dos cromátidas de un cromosoma que recibe K entrecruzamientos se separan. Entonces, K roturas se distribuyen en dos cromátidas y, así el numero esperado de roturas por cromátida se distribuye, si K es grande, en 50 % de cromátidas con un número par de roturas (RF = 0) y 50 % con un número impar de roturas (RF = 1), con independencia de si se trata de tétradas, héxadas, óctadas o configuraciones meióticas de órdenes superiores.

Palabras clave: 50 % de recombinación, tétradas, entrecruzamientos par-impar, SCE.

INTRODUCTION

The maximal value of 50 % of genetic recombination, between two linked genetic loci found in eucaryotes, has been explained as the result of the restriction of crossing-overs to only one pair of chromatids in the tetrad at meiosis (tetrad model). Also, it has been explained as the result of the limit of odd numbers of crossover (odd-even model) between two loci (Haldane 1919, Fisher et al. 1947, Owen 1950, Griffiths et al. 1993, Russell 1996). If both explanations were true and since they are completely independent processes, a maximal value of 25 % of recombination should be expected. The purpose of this article is to demonstrate that the explanation based on the tetrad model is wrong, at least, as it is described in most of textbooks on genetics. We took advantage of the occurrence of sister chromatids exchanges (SCE), where there are chromatid exchanges but not in tetrads, in CHO chromosomes, to test the tetrad hypothesis, instead of using meiotic paired chromosomes.

FORMAL DEMONSTRATIONS

Odd-even number of crossovers analyses (odd-even model)

Let us remember the demonstration that the limit for the probability (or frequency) of an odd number of crossovers between two loci, A and B, (the event that yields an ascertainable recombinant) grows from 0 to 1/2, as the number of crossovers increases. We define a site for a crossover as a DNA segment where a crossover can occur (the DNA involved in a recombination nodule, Alberts et al. 1994). The occurrence of crossovers between A and B follows a binomial distribution with parameters q (the probability of a crossover in a nucleotide site) and k (the number of sites for crossovers in the segment A-B). Let p be the probability that there is not a crossover in a site; $q + p = 1$ ($1 > q > 0$, $1 > p > 0$, $q << p$). The expected number of crossovers between these two loci [E(x)] is kq and their variance [Var (x)] is kpq. The series of crossovers occurring between two loci is described by the binomial $(p + q)^k$, where

$$(p + q)^k = p^k + kp^{k-1}q + [k(k - 1)/2]p^{k-2}q^2 + \ldots kpq^{k-1} + q^k = \sum\{k!/[(k - i)!\, i!]\}p^{(k-i)}q^i,\ i \text{ going from 0 to } k \quad (1).$$

A chromatid yields recombination if q has odd exponent. Even numbers of crossovers do not yield visible recombinants (0 is even; p^k implies q^0). To obtain the limit of the sum of the terms with odd exponents for q (Sodd - q), or the probability for the occurrence of an odd number of crossovers (P_o), in (1) when k increases, we subtract $(p - q)^k$ from $(p + q)^k$:

$$(p + q)^k = p^k + kp^{k-1}q + \ldots\ldots\ldots\ldots kpq^{k-1} + q^k$$
$$-(p - q)^k = -(p^k - kp^{k-1}q + \ldots\ldots\ldots\ldots (-1)^{k-1}kpq^{k-1} + (-1)^k q^k)$$

$$(p + q)^k - (p - q)^k = 2\,(\text{Sodd-q}) \qquad (2);$$

Because terms with even exponents for q vanish. Since $p + q = 1$ and $0 < p - q < 1$, the limit of the difference of binomials is 1 as k increases, thus, Sodd-q (P_o), approaches 1/2, as k increases. P_o is equivalent to the recombination fraction or frequency (RF). When both loci are very close kq is small and no crossover is the most probable outcome. Since q is very small and k very large, the binomial approximates a Poisson distribution, in which, the probability of occurrence of 0, 1, 2,...j crossovers between two loci is given by the general term $(e^{-m})(m^j)/(j!)$; where m is the mean numbers of crossovers occurring in the segment (m is kq, the expected number of crossovers). To obtain the probability of occurrence of an odd number of crossovers (P_o or RF) we subtract e^{-m} from e^m (developed as the limit of an infinite series) to obtain the sum of the terms $(m^j)/(j!)$ when j is odd (Sodd):

$$e^m = (m^0/0! + m^1/1! + m^2/2! + m^3/3! + \ldots + m^{(j-1)}/(j - 1)! + m^j/j! + \ldots)$$
$$-e^{-m} = (-m^0/0! + m^1/1! - m^2/2! + m^3/3! + \ldots\_m^{(j-1)}/(j - 1)! + mJ/j! + \ldots)$$

$$e^m - e^{-m} = 2\text{Sodd}$$

$\text{Sodd} = (e^m - e^{-m})/2$. P_o is Sodd times e^{-m}; $P_o = e^{-m}(e^m - e^{-m})/2 = (1 - e^{-2m})/2$ (3), which goes from 0 to 1/2 as m goes from 0 to infinite. Since odd numbers of crossovers yield RF = 1.0, the expected mean of RF or E(x) is also equal to $(1 - e^{-2m})/2$. This result was found by Haldane (1919), when any information about DNA, tetrad structure, synaptonemal complex was not yet known. This result is valid for a single chromatid or for sister chromatid exchanges (SCE). It is straightforward that the expected square RF [$E(x^2)$], is also $(1 - e^{-2m})/2$, because, odd and even numbers associate with RF = 1 ($1^2 = 1$) and RF = 0 ($0^2 = 0$), respectively. The variance is $E(x^2) - [E(x)]^2 = [(1 - e^{-2m})/2] - [(1 - e^{-2m})^2/4] = (1 - e^{-4m})/4$. Hereafter, to give an abstract and general approach for all type of chromatid interchanges, crossovers, chromatid interchanges or breaks, and chromosome break points will be taken as synonymous. The particular context will point out the precise meaning in each situation.

Tetrad analysis

Figure 1 shows a tetrad analysis for 0, 1, 2 and 3 crossovers. Loci A-a and B-b and 4 crossover sites (S1, S2, S3, S4) are considered. M1, M2, P1 and P2 are maternal and paternal (left and right going from centromere to telomere) chromatids, respectively; m_1, m_2, p_1 and p_2 are the number of chromatid breaks from crossovers in M1, M2, P1 and P2, respectively. There is only one alternative for 0 crossover (I), with 0 % of recombination. There are four alternatives for 1 crossover per site (16 for the four sites) (II): M1 - P1, M1 - P2, M2 - P1, M2 - P2; it yields 50 % of recombination because it implies necessarily one break in only one maternal chromatid and one break in only one paternal chromatid. Two crossovers (six possibilities for the four sites) occur in three configurations according to the number of strands (chromatids) involved: two-strand double crossover (2S, III) causing four alternatives and 0 % of recombination; three-strand double crossover (3S, IV and V) with eight alternatives producing 50 % of recombinant strands; four-strand double cross-

over (4S, VI) with four alternatives bringing about 100 % of recombination. Thus, the maximal 50 % of recombination is explained because one crossover yields 50 % of recombination (II). Two crossovers produce 0 % (III), 50 % (IV), 50 % (V) and 100 % (VI) recombination. Since III, IV, V and VI are in the proportion 1:1:1:1, the average is 50 %.

Then, the tetrad model for the maximal 50 % of recombination is constructed as follows: (i) It assumes that only one crossover is possible in a site, two of the four chromatids are involved; (ii) 0 crossover yields 0 % of recombination; (iii) According to (i) 1, 2, 3, ... n crossovers yield 50 % recombination as shown in Fig. 1. In conclusion, as the expected number of crossovers increases the expected proportion of recombination approaches 1/2, because zero crossover is less and less frequent. It is important to remark that the model depends completely on (i), because if two crossovers could be produced in a site the expected recombination fraction should be different from 1/2. With 2 crossovers (and two sites) configurations as XII (Fig. 1) which yield 100 % of recombination, should be produced as frequently as III, IV, V or VI. Since two of such

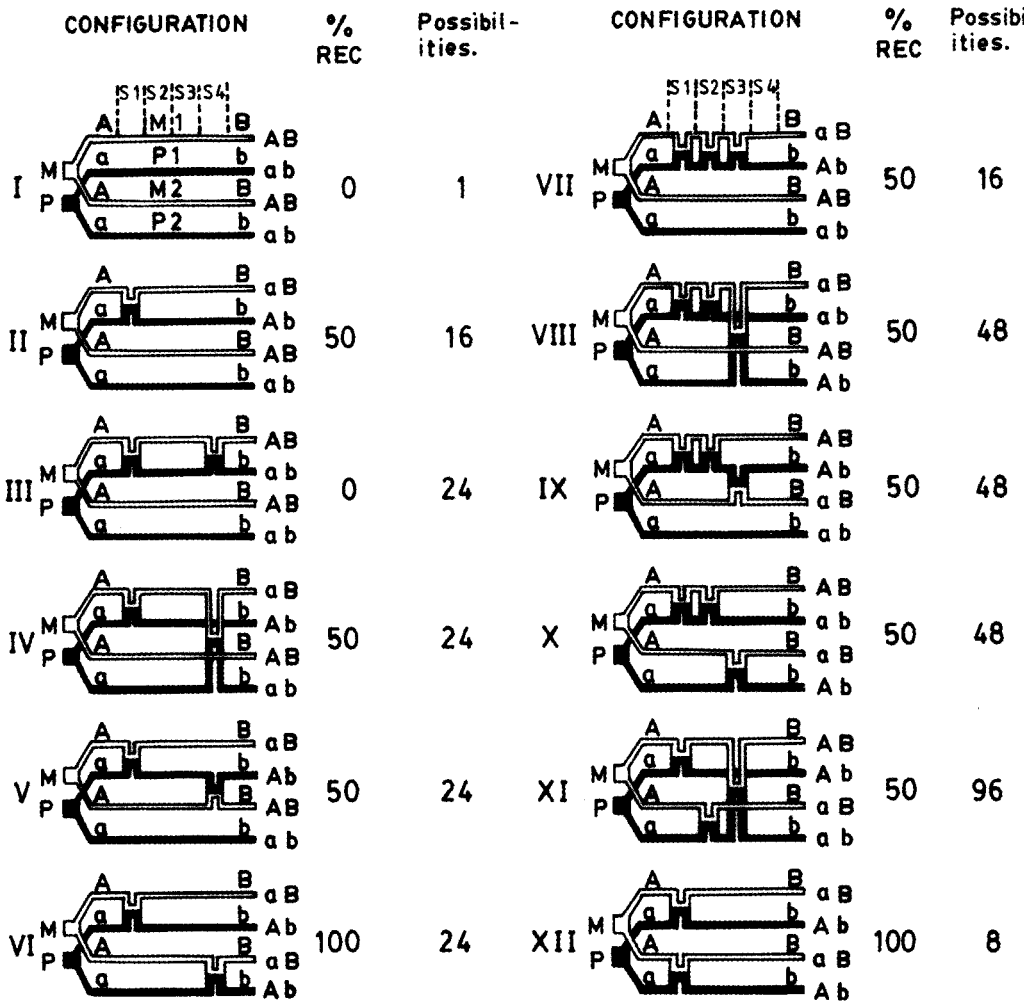

Fig. 1. Zero, one, two and three crossovers configurations in a tetrad. S1, S2, S3 and S4 are sites for crossovers; M = maternal chromosome; P = paternal chromosome; M1 = left maternal chromatid; M2 = right maternal chromatid; P1 = left paternal chromatid; P2 = right paternal chromatid. A, a and B, b are segregating alleles of loci A-a and B-b, respectively. % REC is the percentage of genetic recombination (RF) for each configuration.

Configuraciones con cero, uno, dos y tres entrecruzamientos en una tétrada. S1, S2, S3 y S4 son sitios de entrecruzamiento; M = cromosoma materno, P = cromosoma paterno; M1 = cromátida materna izquierda; M2 = cromátida materna derecha, P1 = cromátida paterna izquierda, P2 = cromátida paterna derecha. A, a y B, b son alelos que segregan en los loci A-a y B-b respectivamente. % REC es el porcentaje de recombinación genética (RF) para cada configuración.

configurations are possible (in S1 and S4), the overall expected recombination fraction for 2 crossovers (allowing for two crossovers in a site) should be 2/3 = 66.67 % (not 50 %). The probabilities of the occurrence of 0, 1, 2, ... n ... crossovers complete the model. If the Poisson distribution is accepted, the probability for zero crossover with zero recombination frequency is e^{-m} and the probability for 1, 2,...n...cross-overs with 1/2 recombination frequency is $(1 - e^{-m})$, where m is the parameter of the distribution. So, the expected mean [E(x) = E(RF)] for the recombination fraction (RF) is:

$$\begin{matrix} & \text{RF (Prob)} & & \text{RF (Prob)} \\ E(x) = (0)(e^{-m}) & + & (1/2)(1 - e^{-m}) & = (1 - e^{-m})/2, \quad (4) \end{matrix}$$

As Griffiths et al. (1993) proposed, RF tends to 1/2 and 0 as m increases or decreases, respectively. It is evident the exponential difference from the one chromatid or SCE analysis where P_o = RF = E(x) = $(1 - e^{-2m})/2$, and not $(1 - e^{-m})/2$. Somewhere there is a hidden different step between Haldane (1919)'s and Griffiths et al. (1993)'s analyses. Naturally, the aforementioned analysis showed that the Haldane (1919)'s formula can be applied only to one chromatid or SCE, and the Griffiths et al. (1993)'s one to tetrads. A restriction or possible error in the Griffiths et al. (1993)'s presentation can be demonstrated when calculating the variance {Var(x) = $E(x^2) - [E(x)]^2$} of RF.

$$E(x) = (0)(e^{-m}) + (1/2)(1 - e^{-m}) = (1 - e^{-m})/2, \quad (4)$$

$$E(x^2) = (0)^2(e^{-m}) + (1/2)^2(1 - e^{-m}) = (1 - e^{-m})/4, \quad (5)$$

$$Var(x) = E(x^2) - [E(x)]^2 = (1 - e^{-m})/4 - (1 - e^{-m})^2/4 = [(1 - e^{-m})e^{-m}]/4, \quad (6)$$

Since e^{-m} tends to zero as m increases, the limit of Var(x) also does. This is an absurd result. The origin of this inconsistency is found by analysing the difference between the chromatid or SCE and tetrad (hexads, octads, etc.) processes. We remarked that recombination is seen when an odd number of exchanges or crossovers occurred between two loci. This is only valid for chromatid or SCE analyses. It is not valid for tetrads. As Fig. 1 shows, an even number of cross-overs can yield chromatids with an even or an odd number of exchanges. Figure 1 and most such figures in textbooks of genetics attribute to the tetrads, and restriction of crossovers to only one pair of homologous chromatids in a site, the production of 50 % of chromatids either with an even or an odd number of exchanges. This explanation is wrong.

Finding the error and solution

At last, meiosis yields chromatids with an even or odd number of exchanges. The maximal 50 % of recombination is true, if and only if, among all the chromatids, issued from meiosis, there are 50 % with odd and 50 % with even number of exchanges or breaks. Since a crossover implies two breaks, one in a paternal and one in a maternal chromatid, K crossovers determine K breaks on the maternal and K breaks on the paternal pair of chromatids. At the end of meiosis, both paternal or maternal chromatids are separated, so, the problem is to partition K breaks in those two chromatids, either paternal or maternal. As we described previously K crossovers occur with probability $(e^{-m})(m^K)/(K!)$, m being the expected number of crossovers in the chromosome segment. Then, we need the analysis once K crossovers have occurred. Let us choose the maternal set. K is either odd or even.

(I) K is odd. The only possibility for the partition of K in the two maternal (or paternal) chromatids is one (for example, left M1) with an odd and the other (right M2) with an even number of exchanges. Thus, an odd number of crossovers yields, always, 50 % of chromatids with RF = 1.0 (100 % recombination) and 50 % of chromatids with RF = 0.0 (0 % recombination), no matter tetrads or restrictions for the number of crossover per site (Fig. 1, K = 3, VII, VIII, IX, X and XI). If K = 3, M1 can have zero, one, two and three while M2 has three, two, one, and zero breaks respectively. The probabilities for these configurations are given by the binomial distribution [b (3, 1/2)], as we shall show.

(II) K is even. There are two possibilities for the distribution of K breaks in the two maternal (or paternal) chromatids. (i) An even number of exchanges in M1 and in M2; yielding 100 % of chromatids with RF = 0.0. (ii) An odd number of breaks in both chromatids, yielding 100 % of chromatids with RF = 1.0. We need to demonstrate that the probability for (i) and (ii) are equal (1/2). The tetrad allows only the possibility for an even number of crossovers to yield chromatids with an even or an odd number of crossovers (and this is the difference with SCE), but it cannot determine that the probability for both is 0.5. Again the demonstration comes from the binomial distribution. Let K = 4, and number of crossover sites = 4 also. In M1 there can be zero, one, two, three and four breaks, while M2 should have four, three, two, one, and zero breaks, respectively. There is only one possibility {K!/[(K - 0)!0!]} for the (M1 = 0, M2 = 4) configuration; 4 possibilities {K!/[(K - 1)!1!]} for (M1 = 1, M2 =

3), 6 possibilities {K!/[(K-2)!2!]} for (M1 = 2, M2 = 2), 4 {K!/[(K - 3)!3!]} for (M1 = 3, M2 = 1) and 1 {K!/[(K - 4)!4!]} for (M1 = 4, M2 = 0) configurations. If we assume that any site can be touched randomly the respective probabilities are 1/16, 4/16, 6/16, 4/16, 1/16. It is evident the binomial distribution and its coefficients with parameters p = 0.5 (any site in both chromatids can be touched with an equal probability) and K (number of crossovers). Thus the demonstration is obtained by demonstrating that the sum of odd order binomial coefficients is equal to the sum of even order binomial coefficients. This demonstration is found in textbooks of algebra. Also, it is obtained by making p = q = 1/2 in (2). In fact, $(p + q)^k - (p - q)^k = 2(Sodd - q)$; $(1/2+1/2)^k - (1/2-1/2)^k = 2(Sodd-q)$; 1 - 0 = 2(Sodd - q). Then, Sodd-q = 1/2 and Seven - q = 1/2 for any k, (in this opportunity). Thus, the probability for i) and ii) is 1/2 no matter the tetrad structure and the restriction to only one crossover per site. If the probabilities for odd and even order binomial coefficients were not 1/2 and 1/2 respectively, the expected maximal recombination frequency should not be 0.5, again, independently of the tetrad structure. This completes the demonstration that for an even K it is expected 50 % of chromatids with an odd number of breaks (RF = 1.0) and 50 % of chromatids with an even number of breaks (RF = 0.0).

Now, we recalculate (4), (5) and (6)

$$E(x) = (0)(e^{-m}) + (1)(1 - e^{-m})(1/2) + (0)(1 - e^{-m})(1/2) = (1 - e^{-m})/2, \quad (7)$$

$$E(x^2) = (0)^2(e^{-m}) + (1)^2(1 - e^{-m})(1/2) + (0)^2(1 - e^{-m})(1/2) = (1 - e^{-m})/2, \quad (8)$$

$$Var(x) = E(x^2) - [E(x)]^2 = (1 - e^{-m})/2 - (1 - e^{-m})^2/4 = (1 - e^{-2m})/4 \quad (9)$$

This variance tends to 1/4 as m increases, and to zero as m decreases. The mean RF (7) is equal to that of (4), but it was obtained by a different way. It is very important to remark that in the preceding demonstrations we have assumed that a crossover or a point of exchange occur by only one event both in tetrads or sister chromatid exchanges. In tetrads, this could not be the case, and a pair of events could be necessary to produce a crossover. If this latter was the case a square Poisson distribution would be necessary to describe crossovers. Experimental designs measuring the kinetics and variances of crossovers and recombination are needed to decide between both models.

We demonstrated that the expected proportion of chromatids with odd or even breaks is 0.5 for odd or even number of crossovers (K). This is valid for K > 0. This is not valid for K = 0 (even). Now, we need the probabilities for an odd or an even K. The sum of probabilities for odd crossovers, including that for K = 0, is $(1 - e^{-2m})/2$. If we exclude e^{-m} (the probability for K = 0), the new probability for an odd number of crrossovers is $(1 - e^{-2m})/[2(1 - e^{-m})] = (1 + e^{-m})/2$; m > 0. This function of m approaches 1 as m tends to 0 and to 1/2 as m grows. Then, the probability for the occurrence of an even number (without zero) of crossovers is $(1 - e^{-m})/2$, which goes from zero to 1/2 as m grows from a little more than zero to infinite. This last analysis shows that the tetrad model is only valid once excluding the possibility of zero crossover. Otherwise, it needs the Poisson (or binomial) distribution to demonstrate that the probability for one or more crossovers tends to one as m increases (then RF tends to 1/2). It is very important to make a difference. SCE or the number of crossovers yielding recombination follow the equation RF = $(1 - e^{-2m})/2$; but, once a set of crossovers (not applicable to SCE) has occurred their breaks distribute on chromatids according to a binomial distribution, which warrants 50 % as maximal RF.

A short consideration of hexads, octads, or more complex configurations. If more than two homologous chromosomes participate in meiosis, the expected RF should have a maximum in 50 %, but the kinetics to reach this maximal value should be different. In hexads zero crossover shall yield RF = 0. In one crossover, RF = 1/3. In two crossovers, the maximal RF = 2/3 (not 1) and the minimal is zero. The possibility to reach a mean RF = 0.5 appears with three crossovers. As m increases RF approaches 1/2 because in any chromatid there can be an odd or even number of exchanges with equal probability (1/2). This is due to the two chromatids condition of each chromosome and because any site can be touched with equal chance. This is not due to tetrads, hexads, octads or more complex structures. Moreover, an odd or even number of crossovers can yield configurations with RF 0 % or 100 %, and others where intermediate RF values are possible.

Biological test in sister chromatid exchanges

If the tetrad explanation was true, we should expect that hexads and octads (octals) should have 0.333 and 0.250 as maximal proportion of recombination (RF), respectively. Unfortunately there are not hexads or octads in nature. Fortunately there are biads (doublets) in nature. They are two chromatid (of a duplicated mitotic chromosome) «crossovers» known as sister chromatids exchanges (SCE). In SCEs, it is expected, according to the tetrad explanation, a maximal RF equals 100 %. In the odd-even explanation RF is $(1 - e^{-2m})/2$ with maximum 50 %. We measured RF

TABLE 1

Concordance (C) and discordance (D) in sister chromatid exchanges in the chromosome 1 of CHO cells

Concordancia (C) y no concordancia (D) en el intercambio de cromátidas hermanas en el cromosoma 1 de las células CHO

Breaks	p arm			q arm			Chromatid		
	Obs	Exp	χ^2 Co	Obs	Exp	χ^2 Co	Obs	Exp	χ^2 Co
0	195	204.2	0.41	159	176.2	1.67	75	89.9	2.48
1	154	137.3	2.03	167	144.5	3.52	145	134.2	0.87
2	39	46.2	1.11	62	59.2	0.13	113	100.2	1.65
3	11	10.4	0.04	11	16.2	1.66	47	49.8	0.16
4	1	1.7	0.31	1	3.3	1.62	16	18.6	0.36
5	0	0.2	0.23	0	0.5	0.54	3	5.6	1.17
6	0	0.0	0.02	0	0.1	0.07	1	1.4	0.10
Total	400	400.0	4.15	400	400.0	9.21	400	399.6	6.79
m	269/400 = 0.6725			328/400 = 0.8200			597/400 = 1.4925		
C	235/400 = 0.5875			222/400 = 0.5550			205/400 = 0.5125		
D	165/400 = 0.4125			178/400 = 0.4450			195/400 = 0.4875		
	Obs		Exp	Obs		Exp	Obs		Exp
Mean^o	0.4125		0.3697	0.4450		0.4030	0.4875		0.4747
Var^o	0.2423		0.2330	0.2470		0.2406	0.2498		0.2494
Mean^t	0.4125		0.2448	0.4450		0.2798	0.4875		0.3876
Var^t	0.2423		0.1849	0.2470		0.2015	0.2498		0.2374
Var^u	0.2423		0.0931	0.2470		0.0966	0.2498		0.0920

χ^2 Co = contribution to χ^2, 6 degrees of freedom; ^{o} = expected values in odd-even explanation; ^{t} = expected values in tetrad explanation; ^{u} = uncorrected from Griffiths et al. (1993)'s formula; Obs = observed; Exp = expected

χ^2 Co = contribución al χ^2, 6 grados de libertad; ^{o} = valores esperados en explicaciones impares-par; ^{t} = valores esperados en explicaciones en tétradas; ^{u} = no corregido formula de Griffiths et al. (1993); Obs = observado; Exp = esperado

in SCEs of the longest chromosome (chromosome 1) of Chinese Hamster Ovary (CHO) cells, in culture, treated with BrdU in the second metaphase and stained with Giemsa. This was accomplished by counting in the left hand chromatid of chromosome 1 the color (dark or light) agreement (C = concordant) or disagreement (D = discordant) between both telomere ends (SCEs within the chromosome) and between the telomere and the respective pericentromeric zone (SCEs within a chromosome arm). Now, let p and q denote the short and the long chromatid arm, respectively. Table 1 shows this analysis. We assume that the expected number of breaks follows a Poisson distribution$[(1 - e^{-2m})/2]$. The inclusion of the expected RF and variance according to the tetrad explanation for crossovers $[(1 - e^{-m})/2]$ is made only as a hypothetical comparison. This distribution was applied to SCEs, in studies with factors that increase their frequency (Gutierrez & Calvo 1981).

Breaks distributed according to the expected Poisson values. The χ^2 test with 6 degrees of freedom reaches the 0.05 significant level at a value equal to 12.59. Thus, neither arms nor the complete chromatid showed significant deviations. However, p and q arms, as well as the chromatid, showed systematically higher observed than expected proportions for one break. In case of the q arm the difference from the expected value was significant (χ^2, 1 d.f. = 6.0, $P < 0.025$). In SCEs two simultaneous "crossovers" at the same site are impossible. It is remarkable the agreement between observed and expected proportions and variances in case the odd-even explanation, and the disagreement with expected values from the tetrad model. With m as small as 0.6725 (p arm) a RF equals to 0.4125 (expected 0.3697) was obtained.

DISCUSSION

We have been teaching, through decades, the tetrad model to explain the maximal value of 50 % of genetic recombination between two linked loci,

without a critical analysis. Perhaps someone may think that a correction of this explanation is unnecessary, because, numerically, the result, that is, the maximal 50 % of recombination and the formula for RF are the same for both explanations. Our view point is different. We believe that any conceptual improvement is worthy. It may enlighten or enrich with a new view concerning knowledge of biotic processes. Or, it could imply a precision needed for further development of genetics. The only necessary and sufficient chromatid outcome, which determines RF, is the proportion of chromatids with an odd number of crossovers between two gene loci or chromosome sites. This is so, no matter the number of chromatids involved in exchanges, because it is due to the double chromatid structure of meiotic chromosomes that generates a binomial distribution of exchanges with its algebraic properties. Evidently, if the expected number of exchanges is small, the number of chromatids could influence the recombination fraction. Also, a truncated distribution due to interference could greatly alter the expected fraction of recombination. For example, if the expected number of SCEs is two and there is interference once a SCE has been produced, the observed recombination value could be higher than expected, because the class of one break should be increased. This could be an alternative for RF over 50 %. It seems that some interference of this kind may occur in our experiment with SCEs, because the class with one break is over represented.

Some ideas of this article were presented in the Haldane Centenary Celebration held at Calcutta (India), December 1992.

Invited Editors: R. Godoy-Herrera and G. Gajardo
Received January 15, 2000; accepted September 18, 2000

ACKNOWLEDGEMENTS

Prof. Danko Brncic was very critical on the application of mathematics to biotic systems. He taught us "math" is just an auxiliary tool for biology. This is mostly correct, but not for the present study.

LITERATURE CITED

ALBERTS B, D BRAY, J LEWIS, M RAFF, K ROBERTS & J WATSON (1994) Molecular biology of the cell. Third edition. Garland Publishing, Inc., New York, New York. xx + 1294 pp.

FISHER RA, MF LYON & ARG OWEN (1947) The sex chromosome in the house mouse. Heredity 1: 355-365.

GRIFFITHS AJF, JH MILLER, DT SUZUKI, RC LEWONTIN & WM GELBART (1993) An Introduction to genetic analysis. Fifth edition. W.H. Freeman and Company, New York, New York. vi + 840 pp.

GUTIÉRREZ C & A CALVO (1981) Approximation of baseline and BrdU-induced SCE frequencies. Chromosoma (Berlin) 83: 685-695.

HALDANE JBS (1919) The combination of linkage values, and the calculation of distances between the loci of linked factors. Journal of Genetics 8: 299- 309.

OWEN ARG (1950) The theory of genetical recombination. Advances in Genetics 3: 117-157.

RUSSELL PJ (1996) Genetics. Fourth edition. Harper Collins College Publishers, New York, New York. v + 784 pp.