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Genetic Expectations of Polar Body Twinning

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The expected correlation between polar body twins depends upon the frequency and distribution of chiasmata occurring during oogenesis. We have estimated the expected values of these correlations using assumptions believed to be biologically valid. The expected value of the overall correlation between first polar body twins is estimated to be 0.38 and that between second polar body twins is estimated to be 0.51. There is little difference between the correlation of DZ twins and that expected for second polar body twins.

The correlation for a specific locus depends upon its distance from the centromere for both types of polar body twins. This effect is especially marked for second polar body twins. For second polar body twins, loci at or near the telomere will have a correlation close to that expected for first polar body twins. It is concluded that only those marker genes that lie at or close to the centromere are appropriate for the detection of polar body twinning.

Key words: Polar body twinning, Genetic correlation, Chiasmata, Oogenesis

INTRODUCTION

Polar body twinning is the result of fertilization of the ovum and its first or second polar body. This is a phenomenon that is believed to occur, if at all, with a low frequency. This paper examines the genetics of polar body twinning in an effort to determine if such twins are easily differentiable from dizygous twins.

For the purpose of clarity, the twin types are defined below.

Monoluteal Dispermic I (MD I)—the result of fertilization of the ovum and a second division derivative of the first polar body.

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Monoluteal Dispermic II (MD II)—the result of fertilization of the ovum and the second polar body.

In the following discussion, the term MIBD will mean maternally derived genes identical by descent. It is assumed that the paternal contribution to all types of polar body twins is random but from a single male and consequently the probability of IBD for any paternally derived gene is 1/2.

EFFECT OF CROSSING OVER

Centromeric Loci

It is assumed that first meiotic division or reduction division results in the separation of homologous but necessarily genetically nonidentical centromeres. Let C and c represent two alleles at a centromere locus. At the time of the reduction division, any centromeric gene can be represented as *C-C* ad *c-c* to illustrate the centromeric genes in the four-strand state. The *C-C* bivalent goes to one pole and *c-c* to the other. Crossing over is not a factor and a C-c bivalent cannot occur, since it is assumed that crossing over occurs from the centromere outwards. The first polar body and the ovum are necessarily genetically distinct, one C and the other c. The second polar body and the egg are genetically identical, C and C or c and c. Consequently, for genes at and around the centromere, MDI twins will be nonidentical and MDII twins will be identical for maternal genes.

Telomeric Loci

Consider a locus at the telomere with alleles T and t. With no crossing over, the bivalents go to each pole intact and the result is identical to that expected for a locus at the centromere. If a single chiasma occurs, however, the bivalents at the two poles will carry the genotypes *T-t* and *T-t*. The MDII twins will be necessarily nonidentical (P[MIBD] = 0) and MDI twins will have a probability of MIBD of 0.5 at this locus, assuming random selection of chromatids for the ovum and the first and second polar bodies.

Multiple chromatids may be involved when two or more chiasmata are formed and it is assumed that no sister chromatid interference is operating. Thus, for the case of two chiasmata, the ratio of two-strand to three-strand to four-strand doubles is 1:2:1, and the genotypes at the two poles after the first division would be (*T-T* and *t-t*) or (*T-t* and *T-t*) occurring in a 1:1 ratio. Consequently, the ratio of identity to nonidentity for MDII twins is 1:1 and for MDI twins it is 1:3.

The conditional probabilities of MIBD, P_i(MIBD), at a telomeric locus given 0,1,2,3, and 4 chiasmata (Table 1) have been calculated for MDI and MDII twins. Each possible number of chiasmata on a given chromosome arm occurs in the population with a certain frequency, f_i, and the overall P(MIBD) for that arm is the sum of P_i(MIBD) f_i for i = 0,1,2,3,4, . . . chiasmata. The results show that as the number of chiasmata increases, the difference in terms of genetic identity between MDI and MDII twins becomes quite small. It should be mentioned that the values in Table 1 are derived from an oscillating function that describes the proportion of recombinant gametes given i chiasmata, and that the limiting value of one-third for both types of twins arises because the limit of this function as i approaches infinity is equal to two-thirds.

Frequency of Chiasmata

Hulten [4] has studied the frequency and distribution of chiasmata in human males. Similar meiotic data on females is understandably difficult to obtain and that which is

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*TABLE 1. Telomeric Genotype of Gametic Pair**

Number of chiasmata	MD I			MD II		
	T and T or t and t	T and t or t and T	P(MIBD)	T and T or t and t	T and t or t and T	P(MIBD)
0	0	1	0.0	1	0	1.0
1	1/2	1/2	0.5	0	1	0.0
2	1/4	3/4	0.25	1/2	1/2	0.5
3	3/8	5/8	0.375	1/4	3/4	0.25
4	5/16	11/16	0.3125	3/8	5/8	0.375
Limit	1/3	2/3	0.333	1/3	2/3	0.333

*Conditional probabilities of MIBD for a telomeric locus (T and t) for polar body twins. The four-strand model was used and no interference was assumed. Conditional probabilities are given for 0,1,2,3,4, and an infinite number (limit) of chiasmata. T and t refer to both gametes being alike, each with a haploid genotype of T.

available suggests that the female map may be shorter than that of males [5]. However, females have a higher rate of recombination as observed in classical linkage studies [1,3]. Renwick [6] estimated that the female map length is approximately 50% greater than that of males. There are not enough data to reconcile these opposing views.

The most significant observation by Hulten was the existence of an obligatory chiasma on all chromosome arms except the short arms of the acrocentrics. The distribution of chiasmata is truncated with little to no chance of zero chiasmata occurring. Also, no more than three chiasmata were ever observed on any one given arm.

Distribution of Chiasmata Along the Chromosome Arm

Hulten's observations suggest that chiasmata do not occur randomly (in males) along the chromosome arm and are clustered towards the telomere. This type of nonrandom distribution of chiasmata could be due to terminilization; however, Hulten's observations do not support this argument. Nothing is known about the physical distribution of chiasmata in females.

It should be noted that with regard to the expected overall correlation between polar body twins, the important factor is the distribution of chiasmata along the arm relative to the distribution of genes. If, for example, both genes and chiasmata are distributed with a higher density at the ends of the arms, then the random model would be more appropriate for the derivation of the expected correlation and its variance.

GENETIC MODELS

Because of the considerable gaps in our knowledge about the mechanics of meiosis, especially with regard to the frequency and distribution of chiasmata and the distribution of genes relative to the chiasmata, we have used, for our estimation of correlation, two different models of frequency distribution and three different models of physical distribution of chiasmata.

For the distribution of chiasma frequencies the two models are A) female frequencies equal to male frequencies of 0,1,2, and 3 chiasmata are as observed by Hulten. The total average number of chiasmata is 54; B) female frequencies of 0,1,2, and 3 chiasmata are as extrapolated by Suarez [7]. The total average number of chiasmata is estimated to be 81.

For the physical distribution of chiasmata, the three models are 1) the chiasmata have a higher density at the telomere as observed by Hulten. The algorithm used is that provided by Suarez [7]; 2) the chiasmata are distributed randomly along the chromosome arm; 3) the chiasmata have a higher density at the centromere. Suarez's algorithm was used but with the centromere substituted for telomere.

Six different situations can be evaluated using these models. These can be referred to unambiguously as A1, A2, A3 and B1, B2, and B3.

Critical assumptions are a) Each chiasma results in physical crossing over and crossing over cannot occur without the cytological observation of a chiasma; b) neither chiasma nor sister chromatid interference is present; c) crossing over proceeds from the centromere outwards; d) each of the four genetic products of female meiosis is equally likely to be found in the ovum; and e) genes are randomly distributed along the chromosome arm.

MD II TWINS

We will assume that each chromosome has a unit length with 0 representing the centromere and 1 representing the telomere. We wish to derive R_m, the average probability of MIBD for the whole chromosome and P(MIBD at L), the probability that a particular locus is maternally identical by descent given that it is a distance L from the centromere. These will be derived for 0,1,2, and 3 chiasmata and then weighted to derive the function for the whole arm.

a) No chiasmata: the solution is trivial:

$$R_m = 1 \text{ and } P\{\text{MIBD at L}\} = 1 \text{ for all loci L.}$$

b) One chiasma occurs at position X_1: MD II twin pairs will be identical at all loci located between the centromere (zero) and X_1, and nonidentical at loci located between X_1 and the telomere:

$$R_m = X_1 \text{ and } P\{\text{MIBD at L}\} = P\{L < X_1\}.$$

c) Two chiasmata occur at X_1 and X_2; $0 < X_1 < X_2 < 1$: whenever two or more chiasmata occur, the correlation depends upon the number of strands involved as well as the positions of the chiasmata. For two- and four-strand double crossovers

$$R_m = X_1 + 1 - X_2; \quad P\{\text{MIBD at L}\} = P\{L < X_1\} + P\{L > X_2\}.$$

For three-strand doubles

$$R_m = X_1 \quad P\{\text{MIBD at L}\} = P\{L < X_1\}.$$

Since we have assumed that there is no sister chromatid interference, two- and four-strand doubles occur with a probability of 0.25 each, and three-strand doubles occur with probability 0.5. Thus for two chiasmata,

$$R_m = (¼ + ¼)\cdot(X_1 + 1 - X_2) + ½\cdot X_1 = X_1 + ½(1 - X_2)$$

and

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$$P\{\text{MIBD at L}\} = P\{L < X_1\} + \tfrac{1}{2}P\{L > X_2\}.$$

d) Three chiasmata at X_1, X_2, X_3; $0 < X_1 < X_2 < X_3 < 1$. In this case, three distinct correlations can arise depending on the number of strands involved and the pattern of strand involvement. The three correlations that can be distinguished and their relative frequencies are

$$\begin{aligned} R_m &= X_1 + X_3 - X_2 \text{ with probability } 0.5, \\ R_m &= X_1 + 1 - X_3 \text{ with probability } 0.25, \\ R_m &= X_1 \text{ with probability } 0.25, \end{aligned}$$

and, consequently,

$$R_m = \tfrac{1}{2}(X_1 + X_3 - X_2) + \tfrac{1}{4}(X_1 + X_1 + 1 - X_3) = \tfrac{1}{4}(4X_1 - 2X_2 + X_3 + 1)$$

and

$$P\{\text{MIBD at L}\} = P\{L < X_1\} + \tfrac{1}{2}P\{X_2 < L < X_3\} + \tfrac{1}{4}P\{X_3 < L < 1\}.$$

For a given number of chiasmata, and a specific model of the chiasmata positions, the probability of maternal identity at a locus L can be obtained by integrating the probability density function of the chiasmata locations over the appropriate regions. For example, consider the situation where two chiasmata occur and their locations are uniformly distributed along the chromosome arm:

$$P\{\text{MIBD at L}\} = P\{L < X_1\} + \tfrac{1}{2}\,P\{L > X_2\},$$

$$P\{\text{MIBD at L}\} = f(L) = \int_L^1 \int_L^{x_2} f(X_1,X_2)\,dX_1\,dX_2 + \tfrac{1}{2}\int_0^L \int_0^{x_2} f(X_1,X_2)\,dX_1 dX_2$$

$$= \int_L^1 \int_L^{x_2} 2\,dX_1\,dX_2 + \tfrac{1}{2}\int_0^L \int_0^{x_2} 2dX_1\,dX_2 = (1-L)^2 + \tfrac{1}{2}L^2.$$

The expected value of R_m for a given number of crossovers can be obtained by integrating f(L) from zero to one; it is the probability of maternal identity at locus L, averaged over all possible values of L. In the above example,

$$E(R_m) = \int_0^1 (1-L)^2 + \tfrac{1}{2}L^2\,dL = L - L^2 + \tfrac{1}{2}L^3\Big|_0^1 = \tfrac{1}{2}.$$

For a particular chromosome arm, let p_i be the probability that i chiasmata occur on that arm and $E(R_m/i)$ and P(MIBD) at L_i be the expected maternal correlations and probabilities of maternal identity as derived above. Then, for that chromosome arm

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$$E(R_m) = \sum_{i=0}^{3} E(R_m \mid i)\, p_i,$$

$$P\{\text{MIBD at L}\} = \sum_{i=0}^{3} P\{\text{MIBD at L} \mid i\}\, p_i.$$

The results for the probability of MIBD for locus L as a function of proportional distance from the centromere is given in Figure 1 for chromosome arms 2q, 10q, and 22q, for models A1, A2, A3, B1, B2, and B3 described above. It is obvious that there is little difference in the form of the distribution for the different chromosome arms. This implies that the major effect on P(MIBD at L) comes from the requirement of a first obligatory chiasma upon each of the models. Also, it should be noted that the distributions of P(MIBD) for two models (Random and Telomeric) are quite similar.

Correlations on a per chromosome basis for chromosome arms 2q, 10q, and 22q and for the total genome are given in Table 2. The overall correlation for the Random (A2 and B2) and Telomeric (A1 and B1) models are quite close to 0.5 except for Model A1 (telomeric clustering of chiasmata and map length of 2,700 cm), where the correlation is 0.665. It is also evident that if the chiasmata are clustered near the centromere, relative to the distribution of genes (models A3 and B3), correlations are considerably less than expected. Thus, the MDII type of twin would mimic MDI twins (see Table 3) if the chiasmata were clustered nearer to the centromere.

If females have no fewer chiasmata than males and if the distribution of chiasmata is approximately random, then it is reasonable to conclude that MDII twins are, in terms of overall genetic correlation, indistinguishable from DZ twins.

MDI TWINS

The calculations for MDI twins are simplified by the relationship

$$P(\text{MIBD/MDI}) = 1 - 2\, P(\text{MIBD/MDII}).$$

This relationship was used to determine both P(MIBD at L) and $E(R_m)$ for MDI twins.

These results are presented in Figure 2. Again, there is little effect of chromosome length on the general distribution of P(MIBD) as a function of L, the relative position of any locus on the chromosome arm. The greatest change in the distribution is seen in the shortest arm, 22q, and under the condition of fewer (w = 2,700 cm) crossovers. The simplicity of the distribution of P(MIBD) for 22q for MDI and II twins reflects the condition that always one and only one chiasma occurs for the chromosome arm when the total number of chiasmata is restricted to 54.

The correlations for chromosome arms 2q, 10q, and 22q and for the whole genome are given in Table 3. The lowest R_m occurs when the chiasmata are distributed towards the telomere (0.17 and 0.24 for models A1 and B1, respectively). When the chiasmata are clustered towards the centromere, R_m is 0.39 (model A3) and 0.36 (model B3). A random distribution of chiasmata yields an overall R_m of 0.25.

DISCUSSION

We shall assume for the following discussion that the physical distribution of chiasmata in females is either 1) similar to that in males but more frequent (Model B1), or 2) random

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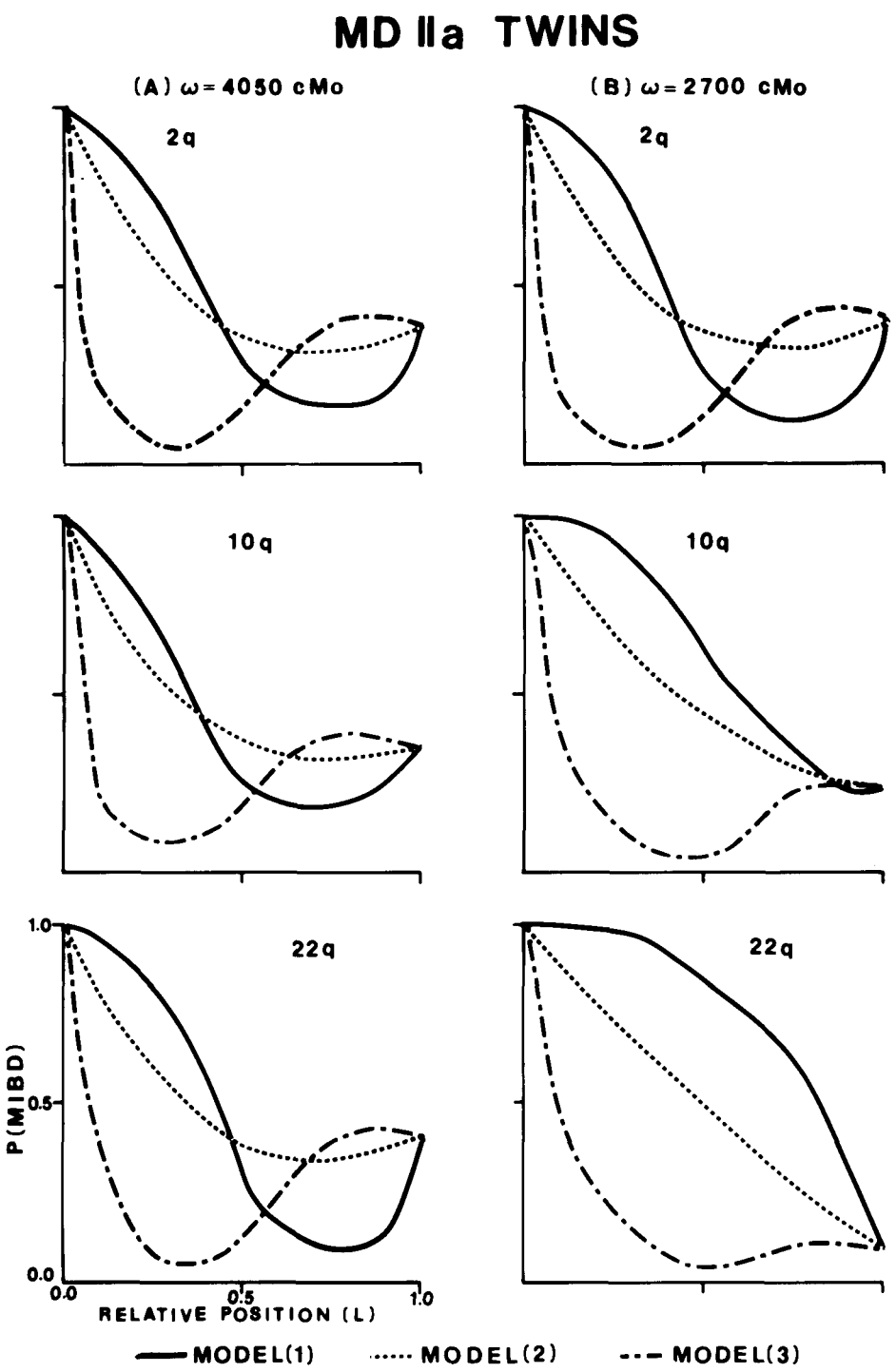

Fig. 1. Probability of maternal identity P(MIBD) at a locus as a function of its relative distance L from the centromere for MD II twins.

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*TABLE 2. R_m or Average P(MIBD) for MD II Twins Given the Models Discussed in the Text**

Chiasmata		Chromosome arm			
Distribution	Number	2q	10q	22q	Total genome
A1 telomeric	54	0.448	0.628	0.478	0.665
B1	81	0.457	0.451	0.463	0.520
A2 random	54	0.490	0.500	0.494	0.510
B2	81	0.485	0.475	0.494	0.506
A3 centromeric	54	0.257	0.217	0.188	0.226
B3	81	0.258	0.266	0.251	0.287

*Results are presented for chromosome arms 2q, 10q, and 22q and for the total genome.

*TABLE 3. R_m or Average P(MIBD) for MD I Twins Given the Models Discussed in the Text**

Chiasmata		Chromosome arm			
Distribution	Number	2q	10q	22q	Total genome
A1 telomeric	54	0.276	0.187	0.126	0.168
B1	81	0.272	0.275	0.269	0.241
A2 random	54	0.255	0.250	0.250	0.245
B2	81	0.258	0.263	0.253	0.247
A3 centromeric	54	0.372	0.394	0.406	0.387
B3	81	0.371	0.367	0.375	0.357

*Results are calculated for chromosome arm 2q, 10q, and 22q and for the total genome.

with a frequency equal to or greater than that in males (Model A2 or B2). These seem to be reasonable assumptions about the behavior of chiasmata during female meiosis; however, it should be pointed out that the formation of a fertilizable polar body wuld be a defect of meiosis and may be accompanied by some derangement of chiasma formation which could invalidate any model even if it were based upon empirically derived parameters of normal female meiosis.

On the basis of the results presented above, the following conclusions have been reached.

1) The successful use of a genetic marker to distinguish the two types of polar body twins from each other and from DZ twins depends critically upon its distance from the centromere.

2) For some loci, depending upon distance from the centromere, both types of polar body twins and DZ twins will show the same frequency of "concordance" for a maternally derived allele.

3) For loci near the telomere, MDII twins could show a maternal "concordance" rate lower than 0.5 and more compatible with what would be expected from MDI twins.

4) For polygenic traits, the correlation between MDII twins is not expected to be detectably different from that between DZ pairs. For MDI twins, however, the expected correlation is substantially lower than that of DZ twins.

Elston and Boklage [2] stated that MDII twins might be detected using marker data and presented a method whereby this could be done. The results presented here indicate that only centromere markers could differentiate MDI and MDII from each other and from DZ twins correctly and with any chance of success. It should be pointed out that

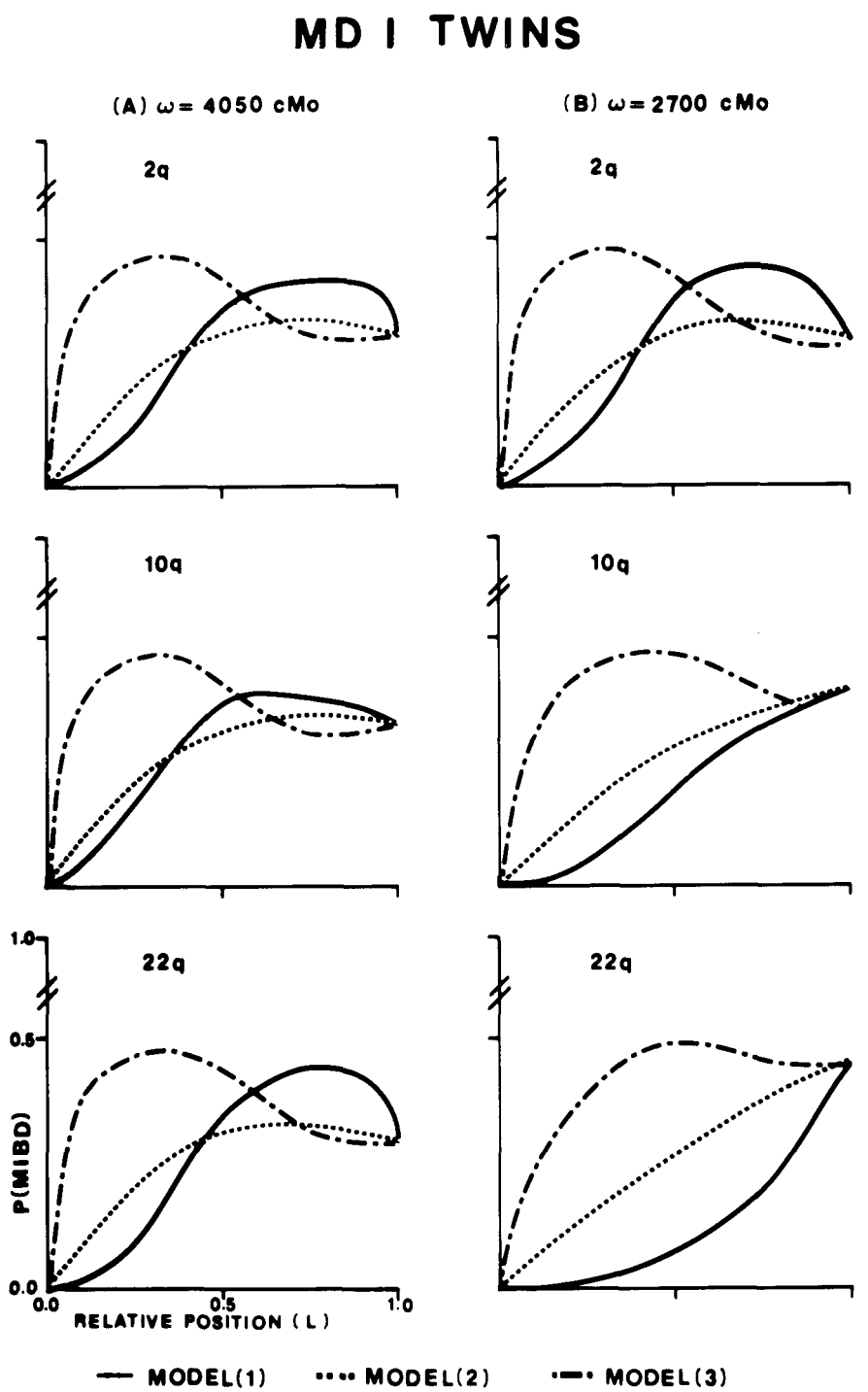

Fig. 2. Probability of maternal identity P(MIBD) at a locus as a function of its relative distance L from the centromere for MD I twins.

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the correlations of all three types are close enough to one another that it would be unreasonable to have expected their detection, consequently we must conclude that there is no evidence which rules out the possibility that polar body twins exist. Indeed, the hypothesis that the majority of nonidentical twins have arisen from polar body fertilization cannot be excluded. The assumption that dizygosity is always the result of two separate ovulations is and will remain but an assumption until evidence to the contrary is accumulated.

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