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G-Band Position Effects on Meiotic Synapsis and Crossing Over

Terry Ashley

Department of Zoology, University of Tennessee, Knoxville, Tennessee 37996

Manuscript received February 24, 1987
Revised copy accepted October 27, 1987

ABSTRACT

An examination of synaptic data from a series of *X*-autosome translocations and crossover data from an extensive series of autosome-autosome translocations and autosomal inversions in mice has lead to the development of a hypothesis which predicts synaptic and recombinational behavior of chromosomal aberrations during meiosis. This hypothesis predicts that in heterozygotes for chromosomal rearrangements that meiotically align G-light chromatin with G-light chromatin lack of homology will be recognized. If homologous synapsis cannot proceed, synaptonemal complex formation will cease and there will be no physical suppression of crossing over in such rearrangements. However, if a chromosomal rearrangement aligns G-light chromatin with G-dark chromatin at the time of synapsis, lack of homology will not be recognized and synaptonemal complex formation will proceed nonhomologously through the G-dark chromatin. Crossing over will be physically suppressed in this region and this suppression of crossing over will be confined to the chromosome in which the G-light chromatin is nonhomologously synapsed with G-dark chromatin. When G-light chromatin is once again aligned with G-light chromatin, lack of homology again will be recognized and either homologous synapsis will be reinitiated (as in an inversion loop), or will cease altogether (as in some translocations). Unlike the previously described "synaptic adjustment," this nonhomologous synapsis of G-light with G-dark chromatin appears to compete with homologous synapsis during early pachynema.

ALTHOUGH neither the structural relationship nor the specificity of association of particular DNA sequences is known, there is extensive evidence that the synaptonemal complex in normal autosomal bivalents aligns homologous regions of chromosomes and facilitates the process of crossing over (*cf.* Moses, Poorman and Dresser 1985). However, it has also become increasingly apparent that not all synapsis, as evidenced by alignment of lateral elements of the synaptonemal complex in meiotic prophase, is homologous. Chromosome aberrations have proved especially valuable in defining parameters of homologous versus nonhomologous synapsis. For instance, a type of meiotic behavior termed "synaptic adjustment" (Moses 1977; Moses and Poorman 1981) has been described in certain aberrations in which synapsis appears to be confined to homology during early pachynema, but not later.

This paper describes a previously uncharacterized relationship between type of synapsis (nonhomologous/homologous), crossing over (suppression/nonsuppression), and type of chromatin (G-dark/G-light) at the position of breakpoints. The nonhomologous synapsis described here differs further from that previously reported in that it competes with homologous synapsis during zygonema-early pachynema (Ashley and Russell 1986).

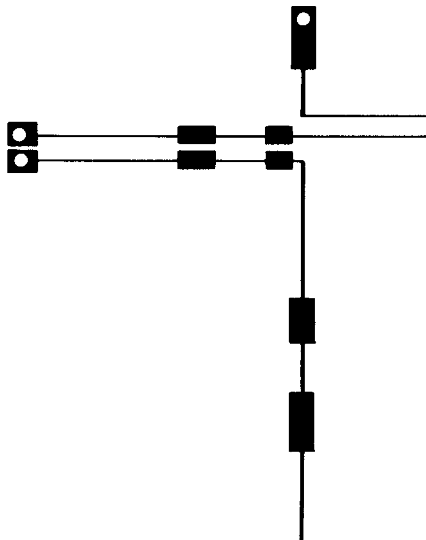
This paper is dedicated to the memory of Dr. Margaret Y. Menzel as a tribute to her ability to instill in her students both the joys and the rigors of formulating and developing ideas.

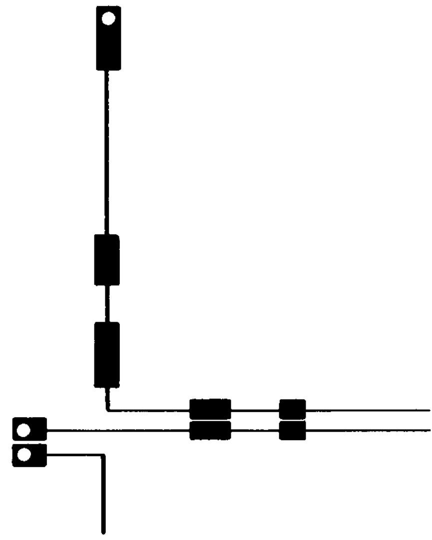
RESULTS AND DISCUSSION

Synaptic effects

In the course of an electron microscopic study of synaptonemal complex configurations in pachytene spermatocytes of mice heterozygous for seven different *X*-autosome (*X-A*) translocations, it became apparent that different translocations exhibited distinctive patterns of synaptic behavior. For example, in two translocations, *T(X;7)3Rl* (*R3*) and *T(X;7)5Rl* (*R5*), measurements in a population of quadrivalents in heterozygotes suggested that synapsis was restricted to homology (Ashley, Russell and Cacherio 1982). However, in other *X-A* translocations there was nonhomologous synapsis (Ashley, Russell and Cacherio 1983). Translocations demonstrating this type of synaptic behavior included *T(X;7)6Rl* (*R6*) with 14% of the autosome involved nonhomologously synapsed (Ashley, Russell and Cacherio 1983); *T(X;4)1Rl* (*R1*) with 16% (Ashley and Russell 1986); *T(X;7)2Rl* (*R2*) with 2% (Ashley, Russell and Cacherio, 1983); *T(X;7)18Rl* with 4% and *T(X;16)16H* with 38% (T. Ashley, personal observations).

In search of an explanation for the difference in synaptic behavior of these translocations, positions





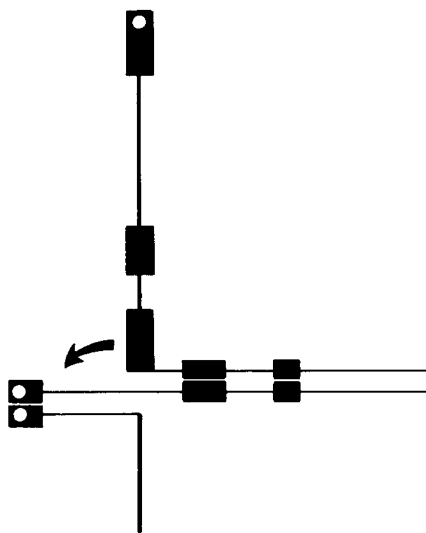


FIGURE 1.—Synaptic configuration of translocation chromosomes for *R3*, *R5*, and *R6* translocations. The *Y* chromosome has been omitted for simplicity. The breakpoint positions for synaptic configurations are taken from the various papers previously referenced. The positioning of the G-dark bands (*black boxes*) are based on the relative lengths and sizes computed from the G-band diagrams of breakpoint positions presented by SEARLE and BEECHEY (1981). In *R3* (A) and *R5* (B) synapsis is restricted to homology and G-dark bands are not near breakpoints. In *R6* (C) there is nonhomologous synapsis which proceeds as indicated by the *arrow*. As is shown, the *X* chromosome break in *R6* is in, or very near, a G-dark band.

of the breakpoints relative to G-bands were examined and a possible correlation was observed. For the purpose of this discussion, all solid black bands as portrayed in the diagrams of NESBITT and FRANKE (1973) are referred to as G-dark, and all other bands, both white and hatched or stippled, are referred to as G-light (Figures 2–4).

In *R3* and *R5*, each with both breaks in G-light bands on both the *X* and chromosome 7 (Figure 1, A and B), synapsis of one translocation chromosome, the *7X*, could be demonstrated to proceed along the autosome involved to within 1% of the maximum extent of synapsis of the *X7* with the *7*, but not beyond (Figure 1, A and B). In other words, synapsis was restricted to homology. Within the population of quadrivalents measured in the remaining 5 translocations each with one break in, or very near, a G-dark band, there were varying degrees of overlap of extent of synapsis of the *XA* (*A* = autosome) with extent of synapsis of the *AX* with the autosome involved. This overlap was interpreted as nonhomologous synapsis. The position of the G-bands with respect to one of these (*R6*) relative to the homologous synaptic configuration is illustrated in Figure 1C. The other translocations could be similarly diagramed and in each case, a G-dark band lay at or, in the junction of one of the break points.

If homologous *vs.* nonhomologous synapsis is unrelated to G-dark versus G-light bands and if it is equally likely to occur the synaptic behavior of these translocations should form a random pattern with respect to breakpoint position. Instead, in each of the seven translocations there was a correlation between breakpoint position relative to G-bands and synaptic behavior. Based on the assumptions mentioned above, the probability of synapsis being re-

stricted to homology in all translocations with breaks clearly in G-light bands, but not being so restricted in all translocations with breaks in, or very near, G-dark bands for this set of seven translocations is 1 of 128. In fact, one has been lead to expect exclusively homologous synapsis, at least during early pachytene (MOSES and POORMAN 1981). This expectation makes these results even more significant. The data strongly suggest that position of the breakpoints in these *X*-autosome translocations influences their synaptic behavior. These observations form the cornerstone of the current hypothesis.

Genetic effects of crossing over

It has long been realized that some, but not all, translocations in mice exhibit suppression of crossing over in the vicinity of the breakpoint of one of the chromosomes. The mechanism of this suppression has not been explained. To test the possibility of a correlation between breakpoint position relative to G-bands and crossover behavior (suppression versus nonsuppression of crossing over) similar to the correlation found between breakpoint position and synapsis, previously published data summarized by SEARLE and BEECHEY (1981) and SEARLE (1981) has been reexamined. In many translocations breakpoints have not been mapped to specific bands; in other translocations there is insufficient information on crossover frequency to be informative. However, there are data on both breakpoint position and recombination frequency for 18 reciprocal autosome-autosome (*A-A*), seven reciprocal *X*-autosome (*X-A*) and two insertional translocations (one *A-A* and one *X-A*).

Autosome-autosome translocations

Rational for categories: In the synaptic analysis of the *X*-autosome translocations, three (*R1*, *R5* and *R6*) had a breakpoint in band XF1, a G-light band adjacent to the G-dark band XE. In this series of translocations both the extensive genetic analysis (RUSSELL 1983) and the synaptic data (ASHLEY, RUSSELL and CACHERIO 1982, 1983; ASHLEY and RUSSELL 1986) made it obvious that the *X* breakpoints for *R1* and *R6* are much more proximal and, by inference, much nearer the G-dark band XE, than for *R5*. This difference in breakpoint position offers a reasonable explanation for the difference in synaptic behavior of these three translocations. Similarly, crossover behavior of translocations with a break in a G-light band adjacent to a G-dark band might be expected to depend on how close the break is to a G-dark band. On the basis of the above information, one might predict that those with a break very *near* a G-dark band would behave like those *in* a G-dark band, while those more removed from the G-dark-G-light boundary would behave like those with breaks clearly in G-light. However, for most *A-A* translocations such subband resolution of breakpoints is impossible.

Since I have temporarily classified "G-light bands" as those that are either white, hatched or stippled in the diagrams of NESBITT and FRANKE (1973), the translocations can be grouped into three categories: (1) those with one break in a G-dark band, (2) those with both breaks in a G-light band not adjacent to a G-dark band, and (3) those with at least one break in a G-light band adjacent to a G-dark band. The twenty *A-A* translocations (19 reciprocal plus one insertional) were classified according to position of breakpoints with respect to bands as described above and suppression versus nonsuppression of crossing over was noted. This information is summarized in Figures 2–4.

Analysis: There are six translocations with one break in a G-dark band (Figure 2). Five of these exhibit suppression of crossing over. The exception, which involves chromosome *17*, is most likely attributable to a different mechanism and will be discussed below. In addition there are three translocations with both breaks in G-light bands not adjacent to G-dark bands (Figure 3). None of these exhibit suppression of crossing over, although one falls into the chromosome *17* exceptional category mentioned above.

Enhancement of crossing over has been reported in each of the three translocations involving chromosome *17* for which linkage data is available: *T(1;17)190Ca* (LYON and BECHTOL 1977); *T(16;17)43H* [BEECHEY and SEARLE (1978) (in SEARLE 1981)]; and *T(9:17)138Ca* (KLEIN and KLEIN 1972; LYON and PHILLIPS 1959). Studies on one of these translocations: *T(9;17)138Ca* (LYON and GLENISTER 1977) suggest that this phenomenon, in *T138Ca* at least, may be the result of inviability of zygotes that receive only a paternal homologue of a certain region of chromosome *17* (JOHNSON 1974, 1975). It is likely that the "enhancement" of crossing over noted for *T43H* with a break in a G-dark band (suppression otherwise expected) and *T190Ca* with both breaks in G-light bands (normal crossover frequency expected) can also be attributed to a differential recovery of gametes in translocations involving chromosome *17*. When these two translocations involving chromosome *17* are removed from the sample on this basis, *all* of the remaining seven translocations behave as though a break in a G-dark band result in suppression of crossing over, while breaks in G-light bands do not. Assuming suppression versus nonsuppression of crossing over is unrelated to G-dark *vs*. G-light bands and has an equal probability of occurrence, the probability of such a correlation between crossover behavior and breakpoint position occurring by chance alone is 1 in 128. It therefore seems likely that recombinational behavior of translocations, like syn-

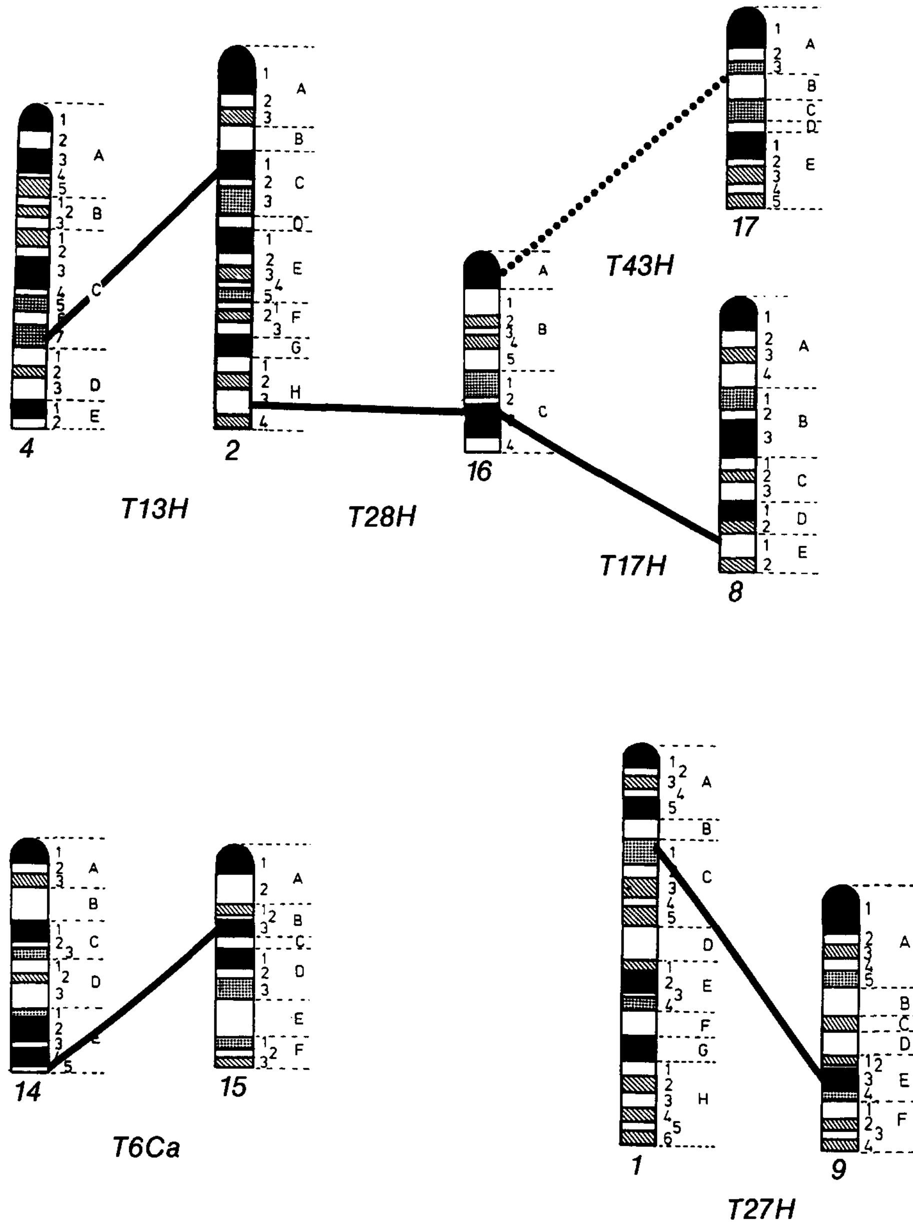


FIGURE 2.—Autosome-autosome translocations with one break in a G-dark band. *Solid lines* indicate breakpoint positions of translocations exhibiting suppression of crossing over; *dotted lines* indicate the breakpoint position of the translocation exhibiting enhancement of crossing over.

aptic behavior, is affected by the position of breakpoints relative to G-bands.

Of the remaining 12 autosome-autosome translocations for which there is genetic data, all have at least one break in a G-light band adjacent to a G-dark band (Figure 4). Based on the uncertainty of subband resolution of breaks in G-light bands adjacent to G-dark bands discussed above, these translocations can be expected to exhibit a mixed behavioral pattern with respect to suppression versus nonsuppression of crossing over. These translocations indeed form a mixed population with suppression of crossing over reported in five and no apparent suppression of crossing over reported in the remaining seven, including the insertional (SEARLE 1981). It would seem likely that a more detailed genetic or cytological analysis of those translocations with breakpoints in G-light bands adjacent to G-dark bands will reveal breakpoints close to the junction with G-dark bands for those translocations exhibiting suppression and breakpoint positions further remover from the G-light-G-dark boundary for those in which there appears to be no suppression. It can also be predicted that in those translocations in which there is suppression of crossing over there will also be nonhomologous synapsis, while in those in which there is no suppression of crossing over, synapsis will be confined to homology. Unfortunately to date there is no in-

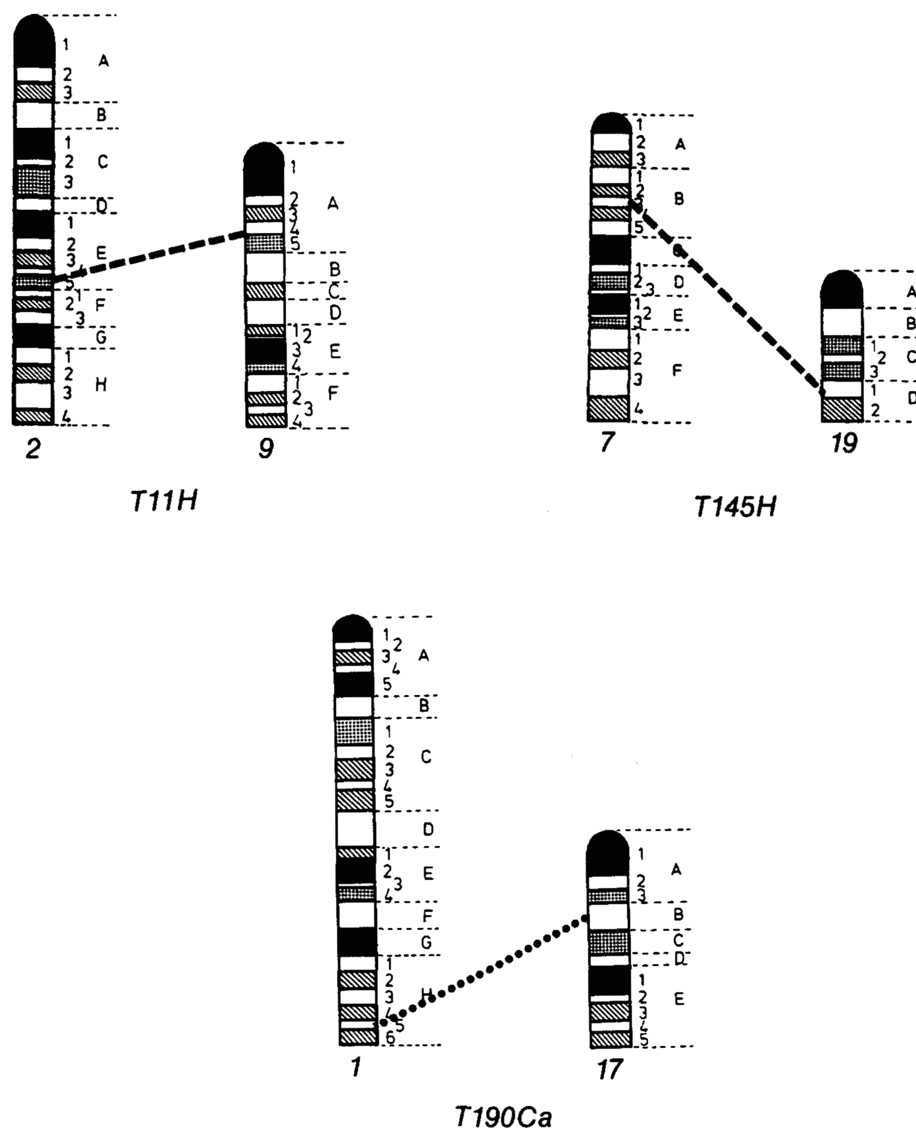


FIGURE 3.—Autosome-autosome translocations with both breaks in G-light bands not adjacent to G-dark bands. *Dashed lines* indicate breakpoint positions of those translocations exhibiting no suppression of crossing over; *dotted lines* indicate the breakpoint position of the translocation exhibiting enhancement of crossing over.

formation available on synaptic behavior of any of the *A-A* translocations discussed above.

***Trans*-action:** While nonhomologous synapsis obviously involves both chromosomes, crossover suppression has consistently been reported in only one of these. The chromosome exhibiting suppression is generally *not* in the chromosome with the break in the G-dark band, but in the chromosome with the break in the G-light band (data extracted from Searle, 1981). The single apparent autosome-autosome exception is *T(1;9)27H*. Apparently nonhomologous synapsis of the G-light chromatin with G-dark chromatin reduces the frequency of crossing over that normally occurs in the G-light region (see discussion below), *i.e.*, the suppression effect is *trans*. This meiotic position effect appears comparable to mitotic position effects in which transcription is inhibited by movement of heterochromatin into the vicinity of normally expressed euchromatin, in that the type of chromatin at the position of the breakpoint is altering the normal behavior of chromatin with which it must now interact.

X-autosome translocations

Comparison of synaptic behavior and crossover suppression relative to G-band position is theoretically possible for *X-A* translocations. However, a direct comparison is currently not available, since synaptic data are entirely from examination of spermatocytes of heterozygous males and all known *X-A* translocation males are sterile (RUSSELL 1983), while the genetic data, of necessity, are from females. While oocyte spreads of synaptonemal complexes have been done (SPEED 1982; MOSES and POORMAN 1984), the necessity of removing oocytes prenatally has severely limited such studies. Therefore, comparisons can

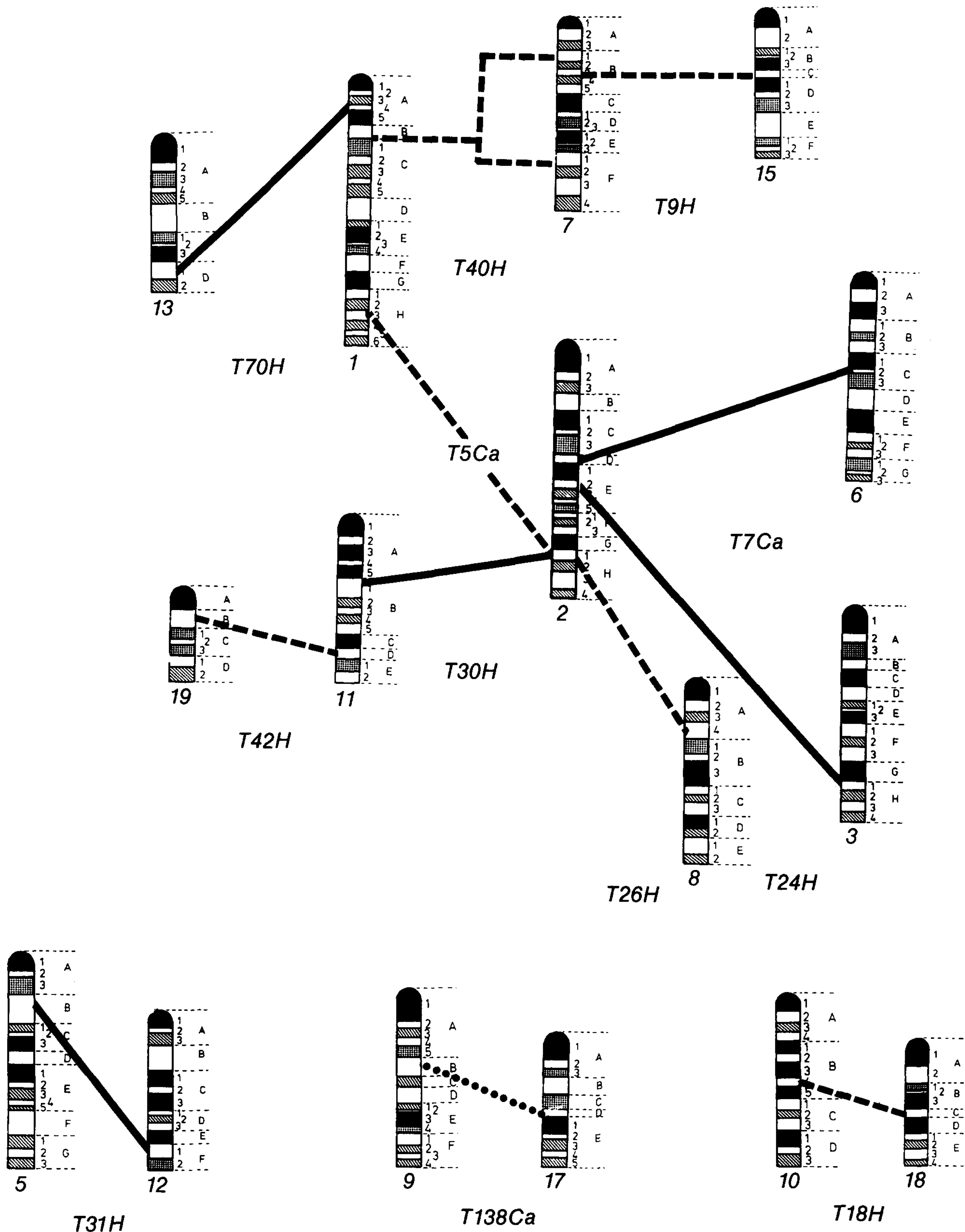


FIGURE 4.—Autosome-autosome translocations with one break in a G-light band adjacent to a G-dark band. *Solid lines* indicate breakpoint positions of those translocations exhibiting suppression of crossing over; *dashed lines* indicate the breakpoint positions of those translocations exhibiting no suppression of crossing over, and *dotted lines* indicate the breakpoint positions of the translocation exhibiting enhancement of crossing over.

TABLE 1

Correlation between G-band position, homologous *vs.* nonhomologous synapsis, and suppression of crossover in *X*-autosome translocations

Translocation	Breakpoint	Location	Crossing over suppressed (chromosome)	Nonhomologous synapsis	Comments
Translocations with a break in or very near a G-dark band. The hypothesis predicts nonhomologous synapsis and suppression of crossing over					
T(7;X)1Ct	7C	D	Yes (*X*)	Unknown	Synaptic behavior undescribed
	7E3	L			
	XE1 or XF1	D			
T(X;7)2R1	XA2 or XA3	L/A	Yes (*X*)	Yes	Concordance with hypothesis
	7D3 or 7E1	D			
T(X;16)16H	XD	L/A	Yes (*X*)	Yes	Concordance with hypothesis
	16B5	L			
T(X;7)6R1	XE or XF1	D	No (*X*)	Yes	Suppression in 7 not studied
	7B3	L/A	? (7)		
		L			
T(X;4)1R1	XF2[a]	L/A	?	Yes	Crossover information unavailable
	4A5	L			
Translocations with both breaks in G-light bands. The hypothesis predicts homologous synapsis only and no suppression of crossing over					
T(X;7)5R1	XF1	L/A[b]	No	No	Concordance with hypothesis
	7A3	L			
T(X;7)3R1	XA2	L/A	No	No	Concordance with hypothesis
	7F1	L			
T(X;4)7R1	XA2	L	No	Unknown	Synaptic behavior undescribed
	4D1	L			

The breakpoints of each translocation are given (column 2) and the type of band indicated in column 3 (D = G-dark, L = G-light, L/A = G-light adjacent to G-dark). Suppression of crossing-over is indicated by a "yes" with the chromosome exhibiting suppression indicated in parenthesis; no suppression in either chromosome is indicated by a "No"; and uncertainty by a "?" in column 4. Occurrence or nonoccurrence of nonhomologous synapsis is summarized in column 5. Additional comments are given in column 6.

[a] Genetic (RUSSELL 1983) and synaptonemal complex data (ASHLEY, RUSSELL and CACHERIO 1983) clearly indicate this is a misassignment of the breakpoint and that the actual break is very similar to R6.

[b] Genetic (RUSSELL 1983) and synaptonemal complex data (ASHLEY, RUSSELL and CACHERIO 1982, 1983) suggest that the *X* break of R6 is proximal to that of R5 and very near the G-dark band XE.

currently be made only between synaptic behavior of spermatocytes and recombination data from females.

Of the 14 *X-A* translocations summarized by SEARLE (1981), data on crossover suppression *vs.* nonsuppression are available for only eight (Table 1). In several of these no, or insufficient, data are available for either synaptic or crossover behavior. In each case for which both synaptic and crossover data are available, those translocations with a break in a G-dark band (*R2* and *T16H*) show both nonhomologous synapsis and suppression of crossing over, while those with breaks in G-light bands (*R3* and *R5*) show homologous synapsis only and no suppression of crossing over. For these translocations the genetic data and synaptic data are as predicted by the hypothesis. When the genetic data from these four *X*-autosome translocations are added to the data from the seven autosome-autosome translocations with clearly defined breakpoints, the probability of correlation between breakpoint position (G-dark/G-light) and suppression *vs.* nonsuppression of crossing over occurring by chance alone rises to $1:2^{11}$ or 1 in 2048.

Several translocations warrant additional comment. The synaptic behavior of Cattanach's translocation has not been fully described, therefore no correlation between synaptic and crossover information is possible. However, suppression of crossover of *jp* (jimpy), a neurological mutant located distally on the *X*, has been noted and follows the pattern of suppression reported above for the autosomes. That is, suppression is observed on the *X* where G-dark chromatin (band 7C) from the 7 has been moved into the proximity of G-light chromatin on the *X*. It is important to note that while 7C is the proximal break on the 7 in this insertional translocation, the segment was inserted in inverted sequence into the *X*. On this basis, the hypothesis predicts suppression *distal* to the insertion and, as noted above, this is indeed where suppression has been reported.

The *X* chromosome break in *R6* is probably in, or

immediately adjacent to, a G-dark band (Table 1), and nonhomologous synapsis has been reported (ASHLEY, RUSSELL and CACHERIO 1983). On the basis of the current hypothesis, crossover suppression on 7 is predicted. This information is not available, however information is available for the *X* (*cf*. SEARLE 1981). No suppression is predicted for this chromosome and none has been reported.

The *X* breakpoint for *T16H*, also referred to as Searle's translocation is located distally in a G-light band very near the boundary of XE, a G-dark band (Table 1). If this band synapses nonhomologously, crossover suppression would be predicted for genes on chromosome *16*. Although insufficient data are available for crossover on 16, unexpectedly, there is crossover suppression reported for genes on the *X*. With this single exception, the available information supports the hypothesis that breaks in G-dark bands result in nonhomologous synapsis and suppression of crossing over, while breaks in G-light chromatin lead to homologous synapsis only and do not result in crossover suppression.

Inversions

Since the autosomes of laboratory mice are normally all acrocentric, inversions in this species should be primarily paracentric. A single crossover within a paracentric inversion loop will produce an anaphase I bridge. Assuming synapsis in mice is initiated from both ends, the hypothesis predicts that inversions with both breaks in G-light bands will recognize lack of homology at the breakpoints and cease synapsing until homologous G-light sequences are realigned (loop formation is initiated). Synapsis of such inversions should be strickly homologous and the hypothesis predicts no physical suppression of crossing over (*i.e.*, no reduction in anaphase I bridge frequency). Genetic "suppression" due to loss of gametes or embryos from chromosomal imbalance should still occur however. Alternately, if one break is in a G-dark band or on the border of a G-dark band, with the G-dark band lying *inside* the inverted segment, the hypothesis predicts nonhomologous synapsis will occur. In addition, the hypothesis predicts that crossing over, which would normally lead to anaphase I bridges, will be reduced or absent, *i.e.*, suppressed (depending on the extent of alignment of G-dark chromatin confluent with the inversion breakpoints) and the genetic consequences of crossover within the loop should be less than expected.

A large number of inversions have been identified in a series of mutagenesis experiments at the Jackson Laboratory, Bar Harbor, Maine (RODERICK 1971, 1983). These inversions were identified by screening for chromosome bridges at anaphase I (*i.e.*, crossover within the inverted segment). Since this test selects for crossover within loops, the hypothesis predicts a bias toward recovery of inversions in which there is extensive homologous synapsis of the inverted segment (*i.e.*, loop formation). According to the hypothesis, this type of inversion will tend to have both breaks in G-light bands. Of the 28 inversions that have been examined at the Jackson Lab, all but one [*IN(15)21Rk*] have *both* breaks in G-light bands (RODERICK and HAWES 1974; RODERICK 1983; M. T. DAVISSON and T. H. RODERICK, personal communications). Synaptonemal complex analysis of heterozygotes from each of nine of these inversions that have been examined to date has shown that loops are routinely formed during early pachynema (POORMAN *et al.* 1981b; MOSES, DRESSER and POORMAN 1984).

This extraordinary high correlation between high frequency of anaphase I bridges and breaks in G-light bands probably represent an oversimplification of the actual situation. A break at a G-light-G-dark boundary (read as a G-light break) could result in nonhomologous synapsis, if the G-dark band involved lay just inside the inverted sequence. Nonhomologous synapsis of this band (from both directions), followed by realignment of G-light bands and initiation of homologous loop formation can be expected to result in a reduced loop size at pachynema. (Loops are the result of homologous synapsis.) This in turn should lead to a decreased crossover frequency within the inverted segment observed as a reduced anaphase I bridge frequency. The frequency of anaphase I bridges is less than expected based on the size of the inverted sequence in six of the Jackson inversions (T. H. RODERICK, personal communication). In three of these [*In(5)2Rk*, *In(5)30Rk*, and *In(15)35Rk*] a G-dark band (black in the diagrams of NESBITT and FRANKE 1973) lies just inside the breakpoint, as might be predicted. In two others [*In(4)32Rk* and *In(8)14Rk*] a "stippled" band on the diagrams of NESBITT and FRANCKE, heretofore arbitrarily classified as "G-light," lies just inside one of the breakpoints. (See discussion below on bands.) In the sixth inversion [*In(1)12Rk*], both bands just inside are "hatched" bands in the diagrams, and these have also been classified as "G-light." Therefore, the cytogenetic behavior (reduced bridge frequency) of three of these inversions can be credited to G-dark bands, and three can not based on current definitions and existing information. However, it can be predicted that an examination of extent of synapsis is mice heterozygous for these inversions will reveal a loop smaller than that predicted from the size of the inverted segment.

It must be mentioned that while the presence of "G-dark bands" just inside the inverted segment provide a logical explanation for the reduced anaphase I bridge frequency of several of these inversions, other inversions with no reduction in bridge

frequency also have G-dark bands near the breakpoints and inside the inverted region. If the hypothesis is correct, one must assume that in these inversions more G-light chromatin in the band designated as the location of the break is available to initiate homologous loop formation.

One large inversion has been reported in which crossover appears to be almost totally suppressed: *In(2)2H* [EVANS and PHILLIPS (1978) in SEARLE 1981]. The Anaphase I bridge frequency was only 2%, which is less than that usually found in mice not carrying inversions. The breaks were reported to lie in 2D or 2E1 (a G-dark band) and 2H1. This inverted sequence results in the extensive alignment of G-dark chromatin with G-light chromatin. This alignment of G-dark bands offers an explanation for the reduced anaphase I bridge frequency. The hypothesis predicts that there will be extensive nonhomologous synapsis in this inversion.

All together, information is available for 29 paracentric inversions in mice. In all except three (one if stippled bands can be classified as "G-dark"), the anaphase I bridge frequencies can be explained on the basis of the hypothesis.

C-band polymorphism

A polymorphism for chromosome *1* has been reported in the mouse (TRAUT, WINKING and ADOLPH 1984) for a block of heterochromatin (late replicating, C-band positive, and a G-band which can be classified as "stippled") of unknown origin that can amount to up to 24% of that chromosome. H. WINKING and A. WEITH (personal communication) have never observed a buckle in heterozygous animals. Instead they find only nonhomologous synapsis of this chromatin with a normal chromosome *1* even during early pachynema.

Type of G-bands

Four types of bands are portrayed in the G-band diagrams of NESBITT and FRANCKE (1973). These bands in increasing order of intensity of Giemsa staining are: white, hatched, stippled, and black (Figures 2–4). So far in this discussion the black bands have been referred to as G-dark and the remaining three categories as G-light. The evidence presented above clearly suggests that black bands fail to recognize homology and synapse nonhomologously, while the white bands in chromosomally abnormal situations recognize lack of homology and either cease synapsis or reinitiate homologous synapsis following realignment of homologous sequences. Behavior of hatched bands can be inferred from the *R5* translocation. In *R5* the autosomal break is in 7A3, a hatched band. Since synapsis in this translocation is restricted to homology, it appears that hatched bands recognize homology or lack of homology and can be classified as "G-light" bands. The synaptic behavior of an informative aberration with a break in a stippled band has not yet been examined. However, the reduced anaphase I bridge frequency of the two inversions that result in positioning a "stippled" band just inside the inversion and the polymorphism on chromosome *1* suggests that the meiotic behavior of stippled bands may be similar to that of black bands and therefore be classified as "G-dark." However, final classification of stippled bands must await synaptic analysis of such an aberration.

Characteristics of chromatin types

When SOLARI (1980) compared the relative chromosome lengths and arm ratios of synaptonemal complexes of pachytene spermatocytes to the mitotic karyotype in humans, he found that the synaptonemal complexes of bivalents with more than the average amount of G-light chromatin were longer than those with more G-dark chromatin. This information suggests a possible differential packaging of G-light and G-dark chromatin in normal bivalents, or unequal participation in the synaptic process.

STACK (1984) has shown that the amount of heterochromatin associated with the synaptonemal complex at pachynema is far less than the relative length it occupies in mitotic chromosomes. This information likewise suggests a differential packaging of types of chromatin. Stack has suggested that this under-representation of heterochromatin in meiotic synapsis may be caused by greater compaction of heterochromatin compared to euchromatin, which may, in turn, provide physical constraints on the crossover process. If differential packaging is the case, it may provide an explanation for the long recognized phenomenon of suppression of crossing over in heterochromatic regions (*cf.* JOHN 1976). The data presented above suggest that G-dark bands share some meiotic properties with heterochromatin.

It is generally assumed that matching of homologous DNA sequences may be a final prerequisite for crossover. Since crossovers are generally reduced in heterochromatin (despite homology), it appears likely that chromatin conformation of heterochromatin and of G-dark bands may provide additional constraints and restrictions on the crossover process. In nuclei heterozygous for chromosome aberrations that result in nonhomologous synapsis between G-light and G-dark chromatin this difference in chromatin conformation may provide an additional safeguard that prevents genetic exchange between nonhomologous sequences.

There is evidence that G-light bands (also called R bands) replicate in early S phase of the mitotic cycle, while G-dark bands replicate later in S phase (GANNER and EVANS 1971). CHANDLEY (1986) has recently proposed that during meiotic prophase the G-light

bands are (1) sites of homologous synaptic initiation and (2) the location of predetermined or potential crossover sites. The current observations suggest that when chromatin in a G-light band is brought into alignment with nonhomologous G-light chromatin, it recognizes lack of homology and does not synapse as might be predicted from the CHANDLEY model. However, when G-light chromatin encounters chromatin from a G-dark band, it fails to recognize lack of homology and synapses nonhomologously. Such behavior had never before been suspected.

The fact that nonhomologous synapsis of G-light with G-dark chromatin results in suppression of crossing over of genes located in G-light chromatin (but not the reciprocal situation) suggests that crossing over may normally preferentially occur in G-light (R) bands as suggested by CHANDLEY (1986).

The possible relationship between (1) the relatively higher G-C content of G-light compared with G-dark bands (HOLMQUIST *et al.* 1982), (2) the higher G-C content relative to the rest of the genome of "zygotene DNA" though to be intimately associated with the synaptic process (HOTTA and STERN 1975) and (3) the apparently greater participation of G-light bands in homologous synapsis is unknown, but deserves further exploration.

G-synapsis and synaptic adjustment

MOSES (1977) has previously described a type of nonhomologous synapsis. In *Dp(7)1Rl* duplication heterozygotes (MOSES 1977; POORMAN *et al.* 1981a) and certain inversion heterozygotes [*In(1)1Rk* and *In(2)5Rk*] (MOSES 1977; POORMAN *et al.* 1981b), heteromorphic bivalents with buckles and loops expected from homologous synapsis of these chromosome aberrations were observed during early pachynema. However, in late pachynema, the bivalent heterozygous for the aberration could not be identified, although transitional stages were observed (MOSES and POORMAN 1981; MOSES *et al.* 1982). From these studies they concluded that the synaptic process could be divided into two stages. The first stage, which occurs during early pachynema, appeared in these studies to be confined to homology, while the second stage, which occurs later, and which they termed "synaptic adjustment," does not.

If G-synapsis is equivalent to synaptic adjustment, there should be no nonhomologous synapsis of G-dark chromatin during early pachynema. Spermatocyte death associated with *X-A* translocations occurs during pachynema (*cf.* RUSSELL 1983), therefore nonhomologous synapsis of the "synaptic adjustment" type should occur in a relatively restricted subpopulation of pachytene nuclei of *X-A* translocation heterozygotes. However, if "G-synapsis" is a separate phenomenon that competes with homologous synapsis, nonhomologous synapsis of G-dark chromatin should not be restricted to the later substages of pachynema. This supposition has been tested (ASHLEY and RUSSELL 1986) by comparing the behavior of three *X-A* translocations: *R5, R1* and *R6*. In *R5* synapsis in quadrivalents of heterozygotes was restricted to homology, and nonhomologous synapsis occurred in only 37% of the population of heteromorphic bivalents. This limited amount of nonhomologous synapsis suggests that the *R5* heteromorphic bivalents are undergoing synaptic adjustment. However, in *R6* and *R1* heterozygotes, both with a break in a G-dark band, there was extensive nonhomologous synapsis in the quadrivalents and 76% and 96% nonhomologous synapsis respectively in the heteromorphic bivalents. This higher frequency of nonhomologous synapsis in *R1* and *R6* heteromorphic bivalents suggests that nonhomologous synapsis in the later two translocations is competing with homologous synapsis and that it persists throughout pachynema. This comparison of synaptic behavior, suggests that the nonhomologous synapsis associated with G-dark bands should be considered a different phenomenon from "synaptic adjustment." I suggest the term "G-synapsis."

Implications

Although the evidence for G-synapsis is, at present, primarily from mouse, it can be predicted that the phenomenon will prove to be far more widespread. In summary, the hypothesis predicts that chromosome aberrations leading to meiotic alignment of G-light chromatin with G-light chromatin result in recognition of homology or lack thereof. There is no suppression of crossing over associated with this type of aberration. However, whenever a chromosome aberration or polymorphism meiotically aligns a G-dark band, or a late replicating region of heterochromatin such as the chromosome *1* polymorphism discussed above, on one chromosome with a G-light region on another, there will be nonhomologous synapsis and suppression of crossing over.

This research was supported by National Institute of Health RO1-HD184470 and by the Office of Health and Environmental Research, U.S. Department of Energy, under contract DE-ACO5-84OR21400 with the Martin Marietta Energy Systems, Inc. I would like to thank STEVE BURMAN for technical assistance, WYNNE BROWN of Brownline Graphics for diagrams and C. A. HAZENKAMP, S. L. DELLAPORTA, I. M. GREENBLATT, M. A. HANDEL, M. Y. MENZEL, and L. B. RUSSELL for their comments on the manuscript. I am especially grateful to M. T. DAVISSON and T. H. RODERICK for making available their unpublished data on the inversions and to H. WINKING and A. WEITH who likewise shared their unpublished observations on the chromosome *1* polymorphism. The observations of H. WINKING and A. WEITH, which they have generously shared, were instrumental in the early evolution of the current hypothesis. I would also like to thank one of the reviewers of the manuscript for pointing out several technical errors.

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Communicating editor: D. BENNETT