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Marjorie P. Maguire

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# Homologous chromosome pairing

By Marjorie P. Maguire
Department of Zoology, University of Texas at Austin, U.S.A.

[Plate 1]

Commonly accepted precepts are challenged: (1) that homologous chromosome pairing is normally mediated by nuclear envelope attachment sites; (2) that crossover site establishment awaits synaptic completion; and (3) that it is the function of the synaptonemal complex to hold homologues in register so that equal crossing over can occur, and perhaps to provide machinery for the crossover process. Although these views may eventually be shown to be true, it is felt that currently available evidence does not warrant their full acceptance, and that alternatives should be considered. As examples of alternatives the following ideas, with some supporting evidence, are suggested: (1) homologous chromsome pairing (in non-haplont organisms) may be accomplished by chance meeting of homologue segments (followed by establishment of invisible, elastic connectors) at congression for a mitotic metaphase (in many cases perhaps the premeiotic mitosis); (2) crossover sites may be established before, during, or immediately following initiation of synapsis; and (3) the synaptonemal complex may somehow function in the crossover process at the inception of its formation, but its complete deployment throughout each normal bivalent may serve some other role, such as mediation of the binding of sister chromatids apparently required for chiasma maintenance until anaphase I.

## Introduction

The nature of events which lead to synapsis and crossing over is still conjectural. There is a highly respected line of reasoning which suggests that homologous chromosomes may be predisposed to pairing by virtue of attachment by their telomeres and/or centromeres to specialized sites on the nuclear envelope, arranged in an appropriately ordered fashion. Intimate pairing of homologues is then thought to proceed from the vicinity of these initially paired points, as the synaptonemal complex is formed, until synapsis is complete. It is recognized that synapsis can accommodate pairing of the degree assumed to be required for crossing-over, that is at the DNA base pairing level, for only small portions of the total chromosome extent (Westergaard & von Wettstein 1972), and that these potentially base paired regions would probably be scattered along most of the bivalent length. The synaptonemal complex is then envisaged as a structure which holds the chromosomes in register while this base pairing for crossing over occurs at a few places around its periphery, or alternatively, it is thought that the synaptonemal complex may somehow accommodate the meeting of short, matching segments of the two homologues across its central region in a few places. The latter alternative may be favoured by the evidence reported by Westergaard & von Wettstein (1970) that cross strands of chiasmata may actually traverse remnants of the synaptonemal complex at diplotene in *Neotiella*.

Fundamental precepts just listed deserve scrutiny. Among these are: (1) that specific attachment sites on the nuclear envelope provide the basis for initiation of homologous chromosome pairing, (2) that synapsis must be completed before positions of crossover sites are established, and (3) that it is the function of the completed synaptonemal complex to hold homologues in

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register so that crossing over can occur and perhaps to provide machinery for the crossover process (except in special cases where the complex persists until metaphase and appears to serve the disjunctional role (Gassner 1969)). After examination of these precepts, an alternative model for homologous chromosome pairing will be suggested.

## The nuclear envelope homologue attachment site model

A role for nuclear envelope attachment sites in homologous chromosome pairing imposes stringent requirements. First, these attachment sites must be characterized by numerous different specificities arranged in adjacent pairs, the minimum number in the simplest case being equal to the number of chromosomes. Then, a mechanism is needed to provide for the transport of each chromosome to its specific site. At induction of polysomy an additional, appropriately specific site must be provided for each additional chromosome. It is conceivable that each homologue at some stage in the cell cycle contributes to the development of such a site in the nuclear envelope. It is admittedly difficult, however, to imagine how these sites can come to be adjacently positioned for homologues, in the absence of prior association of these homologues. Moens (1973) has concluded, from studies at the electron microscope level of reconstructions of zygotene nuclei, that chromosome attachment sites in the nuclear envelope may move with the chromosomes during synapsis. If this is generally true, then the nuclear envelope may play a dynamic rather than a static role in chromosome pairing, or alternatively, it may be a passive element in the process.

An apparently more unwieldy obstacle to acceptance of the nuclear envelope attachment site model for initiation of homologue pairing is the familiar fact that rearranged segments of chromosomes, such as those involved in inversions and translocations (even insertional translocations), frequently synapse homologously with their matching parts in normal sequence chromosomes. In some cases evidence suggests that homologous synapsis in heterozygotes for these rearranged regions is sufficiently frequent to allow the frequency of crossing over which occurs within them to approximate the standard frequency expected for the same region in its normal location (Maguire 1965). To account for initiation of synapsis of such regions by the mediation of specific nuclear envelope attachment sites seems to require the existence of an extremely detailed array of such attachment sites, i.e. sites for virtually all intercalary chromosome regions capable of autonomous homologous synapsis from rearrangement locations.

## The temporal sequence of completion of synapsis and crossover site establishment

The concept that synapsis must be completed before crossover sites are established is backed by long tradition. It has been suggested from studies of the latest stage during meiotic prophase at which crossover frequency can be experimentally altered, that this stage is indeed pachytene (Lawrence 1961 *a*, *b*; Henderson 1966; Westerman 1971, 1972; Lu 1969; Peacock 1970; Raju & Lu 1973). Investigations of the biochemistry of meiosis in conjunction with cytological observations have led other workers to a similar conclusion (Parchman & Stern 1969; Stern & Hotta 1969, 1974; Roth & Parchman 1971; Shepard, Boothoyd & Stern 1974). In these reports it is often suggested, however, that the latest stage of crossover commitment is early pachytene or the zygotene–pachytene interface. Others have reported evidence that generally the latest

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stage for commitment to crossing over in their material seems to be zygotene (Church & Wimber 1969; Maguire 1968, 1974*a*). It is generally recognized, however, that the accuracy of observational distinction between pachytene and zygotene is subject to question. Such distinction is ordinarily cytologically difficult at best at both light and electron microscope levels. It is also well known that meiotic cells are rarely perfectly synchronized and may in addition progress at varying rates. In view of these difficulties of technique and interpretation, results from other approaches to the problem should also be considered. Some of these are described below. At this point it should be emphasized that the question of concern is whether the establishment of crossover sites must normally await synaptic completion; it is acknowledged that completion of the crossover process, perhaps involving DNA repair synthesis, might follow site establishment by a substantial period of time. At the outset it should be noted that crossing over occurs regularly within synaptic configurations in which complete synapsis is precluded (such as trivalents), as well as within homologously synapsed regions in meiocytes with incomplete synapsis conditioned by synaptic mutants, experimental treatment or interspecific hybridization.

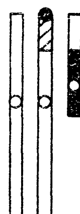

Figure 1. Diagrammatic representation of probable initial exchange between the short arm of maize chromosome 2 and a *Tripsacum* chromosome. Maize chromosome 2 is represented by open areas, the *Tripsacum* segment transferred to chromosome 2 by a crosshatched area (with a solid terminal knob), and the remainder of the *Tripsacum* chromosome by a solid area. Approximate centromere locations are marked by open circles.

*Comparisons of frequencies of pachytene synapsis and crossing over in material heterozygous for rearranged chromosome segments*

A reciprocal exchange between a maize chromosome and an apparently homoeologous *Tripsacum* chromosome from which the reciprocal products were recovered together, provided the basis for the development of an array of different recombinant or secondary exchange 21 chromosome plants in which trivalent frequency could be readily studied at both pachytene and metaphase I (Maguire 1965). The initial reciprocal exchange products are illustrated in figure 1. There is genetic evidence that the short arm of maize chromosome 2 and the long arm of the *Tripsacum* chromosome share homology for at least four loci. These include most of the known markers readily available for testing in the short arm of maize chromosome 2. (Similar testing of the remaining arms has revealed no shared homology for known markers.) There is strong preferential synapsis (with crossing over) between corresponding segments of two maize or two *Tripsacum* chromosomes, in those cases where the choice is available, when both *Tripsacum* and maize regions which share marker homology are present in the same meiotic nucleus. On the other hand in diploid plants which contain only one *Tripsacum* and one maize segment for the region, crossover frequency within it has been found to be about 1 % of that in normal diploid maize in the same region. Synapsis at pachytene, however, approximates normal in these diploids which are heterozygous for maize and *Tripsacum* chromosome segments.

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The array of 21 chromosome constitutions studied is illustrated in figure 2. The data on trivalent frequency which emerged from systematic scanning of pachytene and metaphase I microsporocyte slides of all these constitutions are listed in table I and illustrated graphically in figure 3. The striking feature of these data is the consistent similarity of pachytene trivalent frequency to metaphase I trivalent frequency in the same plant in each case. This surprising 1:1 relation seemed to exist even in those cases where genetic map extent of common homology between the extra chromosome and either or both of the other two was estimated (by comparisons of genetical and cytological maps) to be substantially less than 50 units. This extent of common homology was probably much less than 50 units in at least 4 of the 11 constitutions diagrammed in figure 2 (i.e. constitutions *d*, *e*, *f* and *k*).

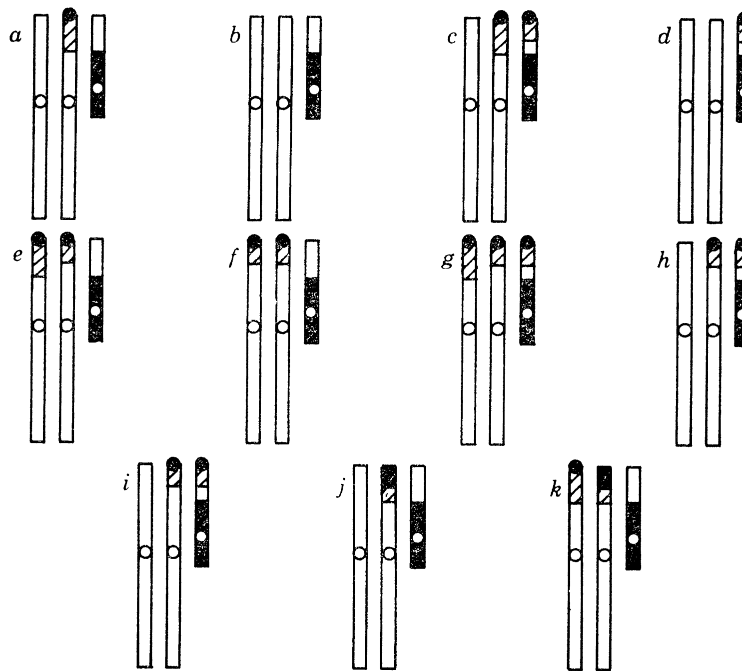


FIGURE 2. Diagrammatic representation of the array of recombinant or secondary exchange 21 chromosome constitutions derived from the initial exchange illustrated in figure 1. As in figure 1 maize chromosome 2 is represented by open areas, the *Tripsacum* segment originally transferred to chromosome 2 by crosshatched areas (with a solid terminal knob), and the remainder of the *Tripsacum* chromosome by solid areas. Approximate centromere locations are marked by open circles.

Conventional expectation calls for one crossover on the average, for every 50 genetic map units synapsed at pachytene. Thus as the extent of genetic map available for homologous synapsis is reduced below 50 units, a corresponding decrease in frequency of crossing over is expected. For example, if trivalent formation at metaphase depends on crossing over for a region of shared homology of 29 map units (as estimated for constitution *e*), and this region synapses homologously at pachytene in 50 % of the meiocytes, trivalent frequency at metaphase I would be expected to approximate 30 % as a maximum instead of the near 50 % found. In fact, the actual extent of pachytene synapsis observed in the appropriate regions was frequently much less than the probable shared homology available, so that a still smaller frequency of metaphase I trivalent frequency would be expected on the basis of conventional considerations. Assuming absence of artefacts in the system (discussed in detail in Maguire 1972*a*), the

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conclusion to be drawn from these early observations seemed to be that two plausible explanations for the 1:1 relation existed: either (1) synapsis usually accompanies or closely follows establishment of a crossover site in these cases where alternative courses of synapsis are available, or (2) in a completed synaptic configuration with change of pairing partner (e.g. a trivalent configuration), it is somehow determined that a crossover site will usually be established somewhere in the regions on *each* side of the point of change of pairing partner, even if one of these regions is genetically short. In the first explanation it is envisaged that most crossover sites are

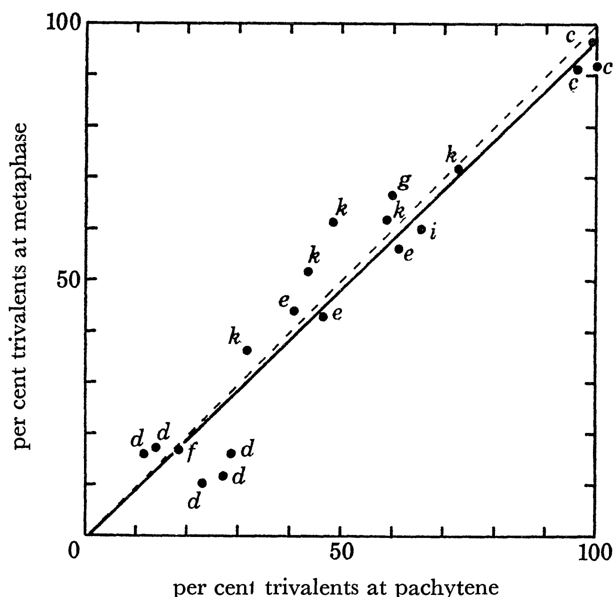


FIGURE 3. Metaphase I trivalent frequency as a function of pachytene trivalent frequency. Points are plotted for each plant where both measurements of frequency are based on at least 25 cells. The constitution of each plant is indicated by a letter which corresponds to a diagram in figure 2. The linear regression for the data is illustrated by a solid line; the dotted line has slope 1, $Y$ intercept 0.

established before, during or shortly after events of synaptic initiation and therefore are determined during zygotene as the course of synapsis itself is established. The machinery of the synaptonemal complex or its precursors might play a role in such crossover site establishment. In fact, at the early stages of formation of the complex, it may be easier than after its completion to imagine pairing between homologues at the DNA base level (in order to account for probable traversal of the complex by cross strands at chiasmata). Observations of short or abortive synaptonemal complex-like elements in heterozygotes for a meiotic mutant (Smith & King 1968) and in the male of *Drosophila ananassae* (Moriwaki & Tsujita 1974) seem to be consistent with such a view. These represent cases where substantial (although less than normal map) crossover frequency has been reported. It seems probable, however, that crossover site establishment is not essential for initiation of formation of the synaptonemal complex, because regions which are not homologous (or do not cross over for some other reason) have been reported nevertheless to be bound together by synaptonemal complex at pachytene (Menzel & Price 1966; Gassner 1969; Gillies 1973, 1974; Jones 1973; Ting 1973), sometimes in ways which require that synaptic initiation occurred within these regions. It is conjectured here, however, that crossover site establishment (or, conceivably, abortive attempts at crossover site establishment) may determine the course of synapsis where alternatives exist. Thus this explanation for



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a 1:1 relation between crossover frequency and synapsis (in genetically short regions heterozygous for rearrangement) sets the time of crossover site establishment at close to the time of synaptic initiation for a given chromosome region and also suggests some functional causality between the two events (although their order is unclear).

TABLE 1. SUMMARY OF PACHYTENE AND METAPHASE I TRIVALENT FREQUENCIES FOR ALL CONSTITUTIONS

| constitution | average pachytene trivalent frequency % | average metaphase trivalent frequency % |
|---|---|---|
| a | 98 | 90 |
| b | 65 | 70 |
| c | 99 | 93 |
| d | 17 | 15 |
| e | 50 | 48 |
| f | 18 | 17 |
| g | 60 | 67 |
| h | 64 | 71 |
| i | 66 | 72 |
| j | 100 | 95 |
| k | 54 | 58 |

In the second explanation it is envisioned that in completed synaptic configurations the existence of change of pairing partner somehow conditions increase in crossover frequency at pachytene. It is conjectured, for example, that such change of pairing partner results in stress at the point of exchange, which in turn yields nicks in DNA, and the presence of these nicks tends to increase crossover frequency. Such a model would probably be more appropriate to the hypothetical situation in which a *simple increase* in crossover frequency is observed in the vicinity of pairing partner change in a trivalent configuration; it is more difficult to reconcile this model with the apparently close to unfailing induction of crossover site establishment with change of pairing partner (which has been observed throughout the array of differing rearrangement constitutions). Another model compatible with the second explanation relies upon the commonly observed suppression of synapsis in the region of heterozygous exchange breakpoints and the supposition that crossovers are suppressed within the unsynapsed portions. Crossover suppression in one region often appears to be accompanied by approximately compensating enhancement of crossover frequency in adjoining regions (Rhoades 1968), and if such compensating enhancement were of necessary magnitude in each cell, and at the same time somehow shunted into the region where crossing over is needed to yield a trivalent at metaphase I, the observed 1:1 relation of pachytene to metaphase trivalent frequency might be accounted for.

Additional experiments were conducted to test whether a 1:1 relation of crossing over to homologous synapsis prevails in other kinds of aberrant chromosome configurations where fresh initiations of synapsis (change of pairing partner) must accompany homologous synapsis of the regions in question. A search was also conducted for a quantitatively meaningful relationship of extent of synaptic failure around breakpoint regions to conjectured enhancement of crossover frequency in adjacent regions.

Specifically, in maize material heterozygous for a short paracentric inversion (estimated to contain 19 map units), frequency of homologous synapsis within the inversion at pachytene

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was compared to crossover frequency within the inversion, as assayed by estimation of bridge and fragment frequency at anaphase I (Maguire 1966, 1972*a*). Results are summarized in table 2. It seems apparent that a consistent 1:1 relation existed between the occurrence of any observable homologous synapsis within the region of inversion heterozygosity and the occurrence of crossing over within this region. In conventional terms, then, the frequency of occurrence of a crossover within the homologously paired portion of the region heterozygous for the inversion approximated the expectation for a genetic extent of 50 map units instead of the 19 map units presumed to exist within the inversion.

Table 2. Frequencies of homologous synapsis and bridge and fragment formation

| plant | frequency of homologous synapsis at pachytene | | combined anaphase I bridge and fragment, and fragment only frequency | |
|---|---|---|---|---|
| | number | % | number | % |
| 1 | 182/505 | 36.0 | 466/1303 | 35.8 |
| 2 | 149/495 | 30.1 | 303/1023 | 29.6 |
| 3 | 190/544 | 34.9 | 426/1244 | 34.2 |
| 4 | 223/701 | 31.8 | 242/665 | 36.4 |

Summaries of quantitative measurements of extent of synapsis within the inversion and extent of synaptic failure in adjacent regions are presented in table 3; summaries of quantitative measurements of extent of synaptic failure in cells with no synapsis in the inverted region are presented in table 4. These data, importantly, show large standard deviations. The frequency of cells with some homologous synapsis within the inversion was 31.8 %, of cells with no synapsis within the inversion was 37.2 %, and of cells with complete nonhomologous synapsis within the inversion was 31.7 %. Probable genetic map extents of the means of these regions were estimated with the reasonable assumption that genetic map per unit cytological length was average for chromosome 1 (Maguire 1974*a*) which has a known total map of 161 units. The data then suggested that the mean extent of the sum of homologous synapsis in the inversion plus adjacent pairing failure approximated a total of 34 crossover units, a quantity far short of the needed 50 units. Similarly the estimates of the mean genetic extents of the region not synapsed in cells with no synapsis in the inverted region, and of the region nonhomologously synapsed in cells with complete non-homologous synapsis in the inverted region suggested that additional genetic map extent within these two potential sources was about 15.5 map units. Total mean map extent estimates of the sum of extent homologously synapsed within the inversion, plus the extent of synaptic failure in the same cells, plus the extent of homologous synaptic failure in cells with no homologous synapsis within the inversion, therefore approximated 50 map units (with large variability among cells). It was concluded from these computations that results could be considered consistent with a compensatory crossover inhibition–enhancement hypothesis, but only if the following strictures were attached: (1) all the compensatory crossover frequency enhancement, from inhibition of crossing over in regions both not synapsed and non-homologously synapsed, is somehow shunted into the homologously paired segment of the inverted region; and (2) that the balancing of crossover frequency (inhibition *v.* enhancement) pertains to a population of cells and not just to the chromosomes within a cell, so that an

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information or substance-sharing mechanism among cells is called for. For example, to achieve compensation it appears that a substantial part of the impetus to crossover frequency enhancement in cells with homologous synapsis within the inverted region must come from other cells in which there is either no synapsis or complete non-homologous synapsis in the inverted region. It is conceivable that intercellular adjustors of crossover frequency among cells operate at pachytene; it may also be possible that a mechanism exists which localizes crossover frequency enhancement from various sources, to the region heterozygous for the inversion. Such adjustments obviously require complex assumptions.

Table 3. Summary of pachytene measurements in cells with any homologous synapsis in inversion (52 cells)

| statistic | total length | extent synaptic failure (A) | extent homologous synapsis in inversion (B) | Sum of A and B |
|---|---|---|---|---|
| $\bar{x}$ | 175.5 | 11.3 | 10.0 | 21.3 |
| $s$ | 24.1 | 6.3 | 6.2 | 7.1 |
| $V$ | 13.1 | 55.7 | 61.8 | 33.3 |

$\bar{x}$, Mean; $s$, standard deviation; $V$, coefficient of variation $= (100s)/x$.
Total length of chromosome 1 is expressed in arbitrary units (mm × 1900).
Synaptic failure and homologous synapsis in inversion extents are given as percent of total length.

Table 4. Summary of pachytene measurements in cells lacking synapsis in inversion (28 cells)

| statistic | total length | extent synaptic failure |
|---|---|---|
| $\bar{x}$ | 172.2 | 17.5 |
| $s$ | 20.4 | 9.9 |
| $V$ | 11.8 | 56.7 |

$\bar{x}$, Mean; $s$, standard deviation; $V$, coefficient of variation $= (100s)x/$.
Total length of chromosome 1 is expressed in arbitrary units (mm × 1900). Extent synaptic failure is given as percent of total length.

Economy of hypothesis on the basis of comparisons of synaptic and crossover frequencies in chromosome rearrangement material thus may favour the view that crossover site establishment is usually associated with the initiation of synapsis. Other reports of simultaneous quantitative study of frequency of pachytene synapsis and crossover frequency within the regions involved (when alternate courses of synapsis are available) are scarce. Nur (1968) reported results similar to those described above for a region heterozygous for an inversion in a grasshopper. Rhoades (1968) noted nearly normal crossover frequency in the vicinity of a heterozygous deficiency where pachytene synapsis was usually nearly complete, and conversely found crossover frequency depressed in the vicinity of the corresponding heterozygous insertion into another chromosome where pachytene synapsis was incomplete and irregular. Unfortunately a direct comparison of frequency of events of synaptic initiation and crossing over cannot be made in this case. It is not known here to what extent synaptic failure was a result of irregularity of its spreading as opposed to irregularity of its initiation. From a study of pachytene configuration

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frequencies of various types in crosses of reciprocal translocations involving opposite arms of the same two chromosomes in maize it has been reported that the probability of homologous synapsis of interchanged regions was substantially higher than the probability of homologous synapsis of the differential segments which contained the centromeres (Burnham *et al.* 1972). The conclusion seems justified that homologous synapsis does not depend on homologous centromere associations. Also the probability of homologous synapsis of these differential segments seemed to be directly proportional to their cytological lengths (with an approximate slope of 1.0). These findings appear in part, at least, roughly consistent with expectation from synaptic initiation frequency dependence on genetic map extent present for homologous synapsis, although estimations of genetic map extents are not available, and additional complications seem to be superimposed. Roberts (1970, 1972) studied crossover suppression in *Drosophila melanogaster* heterozygous for reciprocal translocations with variously located breakpoints. Translocations with both breakpoints near telomeres or near centromeres were not recovered as crossover suppressors; it thus seems unlikely that telomere or centromere pairing plays an important direct role in synaptic initiation. On the other hand, results seemed to indicate that the chromosome regions located one-third to one-half the physical distance from the telomeres are most important for pairing for crossing over. It is probably also approximately these regions in which the crossover map is most concentrated relative to the physical map.

On the other hand, special adaptations of some species seem to impose idiosyncracies of behaviour. For example, it has been reported that possible somatic associations of homologues in wheat are conditioned by homologous centromeres since isochromosomes for opposite arms (with only centromeres homologous) seemed to show a mutual affinity as strong as that of full homologues (Feldman, Mello-Sampayo & Sears 1966). More recent work of Avivi & Feldman (1973) has suggested that the three genomes of wheat may normally occupy different regions of the nucleus such that homoeologues rarely mix. This situation is said to prevail in the presence of the gene on chromosome 5B which is associated with normal bivalent pairing in wheat, but not in its absence (where multivalent pairing is expected at meiosis). It has also been reported that this gene on chromosome 5B alters spindle tubulin (Avivi, Feldman & Bushuk 1970). Such findings seem consistent with the interpretation that each of the three wheat genomes may have a specific centromere relationship to a special spindle or spindle region of its own and that a normal chromosome 5B gene is needed for the maintenance of the relationship.

It is a question of great interest whether a tendency for crossing over to accompany synaptic initiation is reconcilable with observations in normal bivalents. It was inferred above from observations (that rearranged segments synapse and cross over normally with their counterparts in normal sequence chromosomes) that potential points for synaptic initiation are probably numerous and widely distributed throughout the genome (if not ubiquitous). Grell (1967) suggested, on the basis of studies of recombination between normal homologues in the presence of extra fragments containing varying extents of shared homology to these, that a minimum size for full recognition for competitive pairing was of the order of 1.5 crossover units. Direct observations of zygotene are difficult and scarce. In cytological studies of zygotene in organisms which exhibit well-developed bouquet or Rabl orientations at early meiotic prophase the impression is often gained that synapsis begins at telomeres and proceeds to completion from these points (Kezer & MacGregor 1971). It is difficult to rule out the possibility that synapsis does not also begin in these cases at other points as well which are more scattered and

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therefore less spectacularly demonstrable. Of course, homologous synapsis of rearrangements would probably require that this be true. It has been observed that the central component of the synaptonemal complex seems to be first formed at zygotene at a number of points of independent initiation between previously formed segments of the lateral components of paired homologous regions (Moens 1968, 1969; M. Y. Menzel, personal communication).

From reconstruction of serial sections of electron micrographs of a few zygotene nuclei in maize Gillies (paper presented at the 13th International Congress of Genetics) has suggested that synapsis is initiated in many intercalary regions and that the average number of points of initiation per bivalent may approximate 4. If a crossover usually accompanied each synaptic initiation, an average of 4 crossovers per bivalent would imply a total genetic map for the maize genome of 2000 units. Darlington (1934) estimated the average chiasma frequency per microsporocyte in maize to be about 27, implying a total genetic map of about 1350 units, and the known genetic map of maize comprises about 1100 units. Thus, the estimated number of synaptic initiation points is substantially higher than correspondence with average chiasma formation frequency and known genetic map extent would predict. The three quantities are, however, of the same order of magnitude and admittedly subject to substantial error. The estimation of average number of synaptic initiation points per bivalent is, of course, especially tentative. Another question which deserves consideration in this context is concerned with the relation of gene conversion events to synapsis. Chovnick (1973) reported the frequency of conversion events (without flanking marker exchange) at the rosy locus in *Drosophila melanogaster* to be of the same order of magnitude in a paracentric inversion containing the rosy locus as in flies homozygous for normal sequence homologues. On the other hand, as expected, recovery of classical crossovers within the inversion was strongly suppressed. It is inferred from such results that the frequency of homologous chromosome pairing of the sort presumed to be required for gene conversion is approximately normal in the inversion heterozygote. It might reasonably be expected that conversion events also occur regularly in maize and that a substantial proportion of these are unaccompanied by crossing over for flanking markers. If so, it seems improbable that occurrence of such conversion events is related to occurrence of events of lasting homologous synaptic initiation (at least in regions where change of pairing partner is required) since a corresponding increment in frequency of homologous synapsis at pachytene would be expected (instead of the 1:1 relation of pachytene synapsis to crossing over which was found). It can be asked whether electron micrograph observation of additional sites of apparent synaptic initiation (beyond the proposed expectation of one per crossover site) in normal bivalents actually might represent sites of gene conversion without accompanying crossing over; if this is indeed the case, the additional assumption that these represent abortive synaptic initiations is required to preserve a 1:1 relationship of synapsis to crossing over. Since synapsis is known to be initiated between non-homologous regions without crossing over and may be initiated between normal homologues without crossing over, the possibility should be considered that it is only synaptic initiation *priority* which is established for those regions with crossover commitment, and that this is responsible for the 1:1 relation observed in heterozygous rearrangements. If this is true, the 1:1 relation is none the less instructive, and the validity of other conclusions suggested above would be unaffected by such a finding.

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## Function of the synaptonemal complex

It has been suggested above that the simplest model reconcilable with a variety of experimental and observational data could be that commitment to crossing over occurs before, during or just after initiation of synapsis, perhaps usually with each event of synaptic initiation. However, the main function of the synaptonemal complex is generally thought to consist of providing a rigid binding of point by point homologous pairing throughout the length of the bivalent containing it, so that crossover sites can then somehow be established along it at random with respect to the genetic map. (Although a challenge to this conventional role is suggested here, the idea that newly formed, or forming, short regions of the complex may somehow serve to mediate the crossover process remains unquestioned.) It is commonly acknowledged, however, that homologues must be at least segmentally closely associated before synaptonemal complex formation can be initiated, and evidence has been mentioned above that the number of points of synaptic initiation in a bivalent may be of the same order of magnitude as the number of crossover sites to be established, and also that points of synaptic initiation (where tests are available with chromosome rearrangements) seem to be randomly distributed with respect to the genetic map. If these conditions indeed prevail, regardless of other considerations, a need for synaptic completion to provide machinery for random (map) distribution of crossover sites is obviated. In any case it seems likely that a structure as impressive as the synaptonemal complex, deployed along the entire length of a normal bivalent, must serve a function along its entire length. The following speculations, descriptions of observations and suggestions for lines of inquiry are submitted in this context.

It has been known for many years that sister chromatids of bivalents are somehow bound together throughout their length from early meiotic prophase until anaphase I, except where they have been separated, apparently forcibly, by the terminalization of chiasmata. In fact, chiasmata exist apparently only because of this tendency of sister chromatids to stick together. It may be worth inquiring whether it could be a role of the synaptonemal complex to mediate this cohesion (Maguire 1974*b*). It is a common observation that in trivalent configurations at pachytene sister chromatids become separated throughout univalent regions so that they are easily discernible as separate entities with light microscope resolution although the same sister chromatids generally appear fused into an apparently single structure with both light and electron microscope resolution in synapsed portions of the same configuration. Sister chromatids are thought to become bound together by the elaboration of the lateral component or core between them in preparation for synapsis (Westergaard & von Wettstein 1972). It seems unlikely that it is preordained at this prezygotene stage which segments will finally be left univalent when synapsis has been completed in a trivalent configuration. Thus it can be asked whether cohesion of sister chromatids in this case is somehow conditioned by the elaboration of the full synaptonemal complex (with central element) between homologues. Another suggestive common observation along these lines is that univalents often separate equationally at metaphase I, and that when they do so, there is usually no apparent cohesion between the sister chromatids, i.e. they offer no apparent resistance to this separation, as do sister chromatids in bivalent configurations. It has been reported that in yeast commitment to meiotic disjunction follows commitment to meiotic recombination (Esposito & Esposito 1974). It might well be considered whether commitment to meiotic disjunction in this case depends upon the establishment of sister chromatid cohesion. Claret-nondisjunctional is known as a mutant in *Drosophila*

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*melanogaster*, which, it is suspected, is defective in maintenance of chiasmata after apparently normal crossing over. Desynaptic mutants are known in tomato (Moens 1969) in which a defect may be present in the process of chiasma maintenance. Electron microscope observation of meiotic prophase of claret-nondisjunctional flies and of desynaptic mutant material might be instructive. Although a functional role is unclear, as described below, sister chromatid cohesive resistance to anaphase separation has been observed at the premeiotic mitosis in maize, where homologous association seems to exist without crossing over (figure 4*c–f*, plate 1). Reports of observation of premeiotic mitosis with electron microscope resolution in maize are lacking, but it is of some interest that synaptonemal complexes have been reported to occur (although rarely) in the ascogenous hyphae of Ascophanus (Zickler 1973).

## Alternative to nuclear envelope mediated homologous chromosome pairing

A substantial body of evidence has been accumulated which supports the view that homologues are actually paired to some extent in advance of early meiotic prophase, in preparation for synapsis (reviews: Comings 1968; Grell 1969; Comings & Okada 1972; more recent work: Buss & Henderson 1971; Maguire 1972*b*, 1974*c*; Dover & Riley 1973). If a nuclear membrane attachment site model for homologue pairing is unwieldy, it is a question whether a more appealing model can be proposed. A novel alternative has been suggested by direct observations of the premeiotic mitosis in maize. In this material homologues are not obviously associated at the premeiotic prophase but seem to pair during congression to the metaphase plate for this division (figure 4*a*, *b*). It is conjectured that more or less random stirring of chromosomes during congression may result inevitably in eventual juxtaposition of homologous segments, and that at this time actual physical (elastic) connections are established between them at a number of corresponding points, some of which later function in synaptic initiation as the elastic connectors contract (Maguire 1974*c*). Such connectors could be analogous to the fibrillar proteins hypothesized by Holliday (1968) to be involved in homologous chromosome pairing and to the fibrillar material connections between chromatin masses reported by Bennett, Stern & Woodward (1974). Homologous segments so attached might nevertheless become positioned relatively far apart in the stages intervening between premeiotic metaphase and zygotene. At early anaphase of the last premeiotic mitosis in maize very similar configurations of separating sister chromatids were seen to lie adjacent to each other in pairs (figure 4*d–f*). At later stages of the premeiotic anaphase some homologues appeared to remain paired in squash preparations while others were not obviously paired (figure 4*g*, *h*). It should also be noted that sister chromatids at early premeiotic anaphase seemed to resist separation distally and to form configurations which superficially resembled a bivalent at metaphase I to early anaphase I of meiosis (figure

### Description of plate 1

Figure 4. Photomicrographs of the premeiotic mitosis in maize: *a*, *b*, Metaphase or prometaphase showing apparent pairing of homologues; *c*, early anaphase showing terminal cohesion or resistance to separation of sister chromatids; *d–f*, early anaphase showing terminal cohesion of sister chromatids and adjacent, very similar configurations which are thought to represent pairing of homologues; *g*, *h*, different focal levels of the same cell at late anaphase showing probable pairing of several homologues. Arrows indicate examples of probable homologue pairing in the anaphase cells. (Magn. × 1600.)

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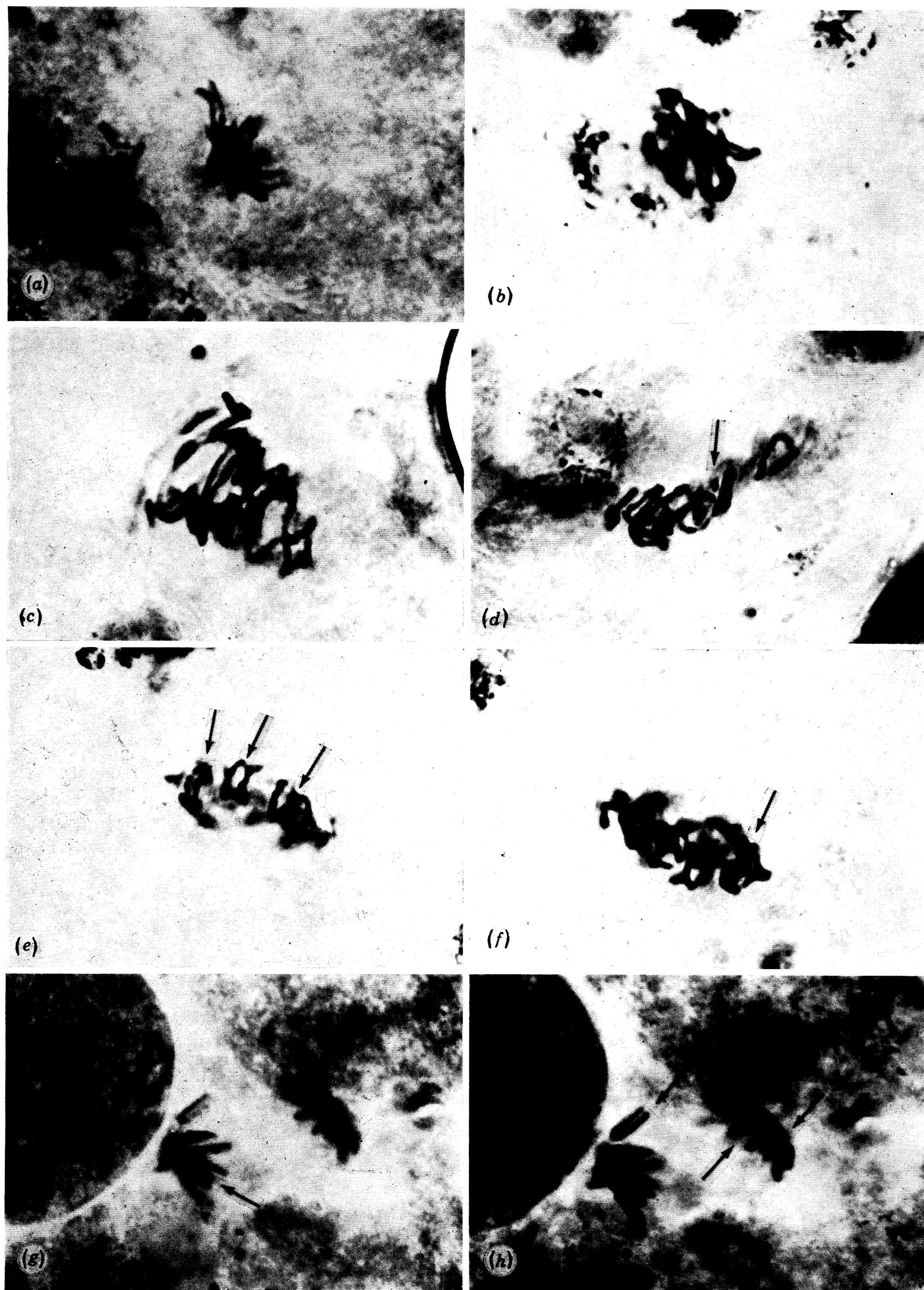


FIGURE 4. For description see opposite.

(*Facing p.* 256)

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4*c–f*). Such association is not understood at this time, and it is speculated that cells at premeiotic mitosis may develop some of the attributes of meiosis prematurely, in this case some kind of generalized tendency for cohesiveness of sister chromatids.

The model proposed above includes the supposition that heterozygously rearranged homologous chromosome segments become associated by elastic connectors, often about as readily as homozygous normal sequence segments. Appropriately contorted configurations might then be observable at premeiotic metaphase and anaphase, and a search for these is planned.

With such a model, organisms with a zygotic meiosis would seem to require a stirring mechanism other than the congression at premeiotic mitosis to provide for homologous chromosome pairing. On the other hand organisms with clear somatic homologue pairing might have homologous connectors established at early embryogeny which persist through multiple cell generations. Colombera (1973) has recently reported that in Ascidians homologues appear to pair during congression at somatic mitoses and are still obviously paired at anaphase.

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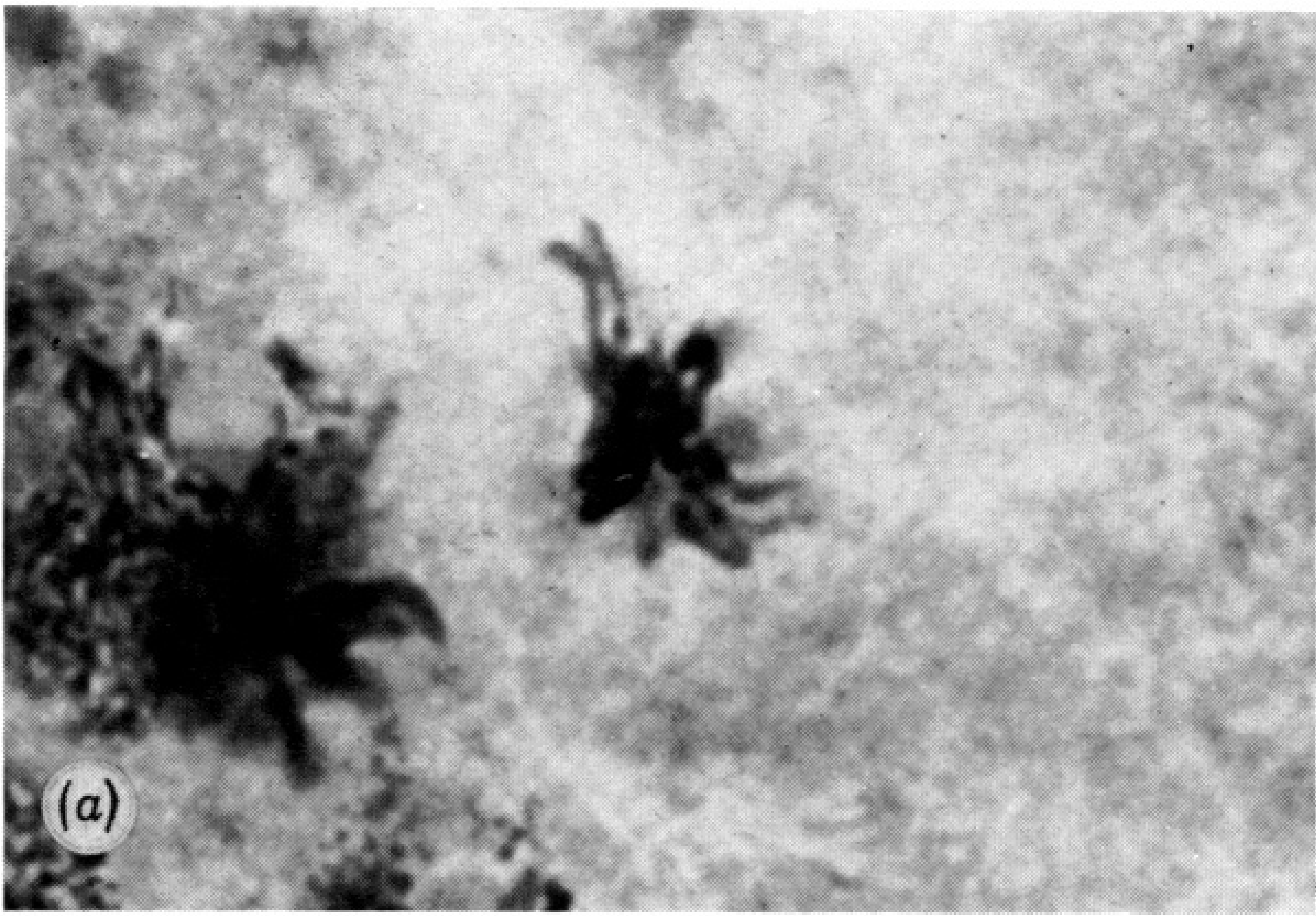


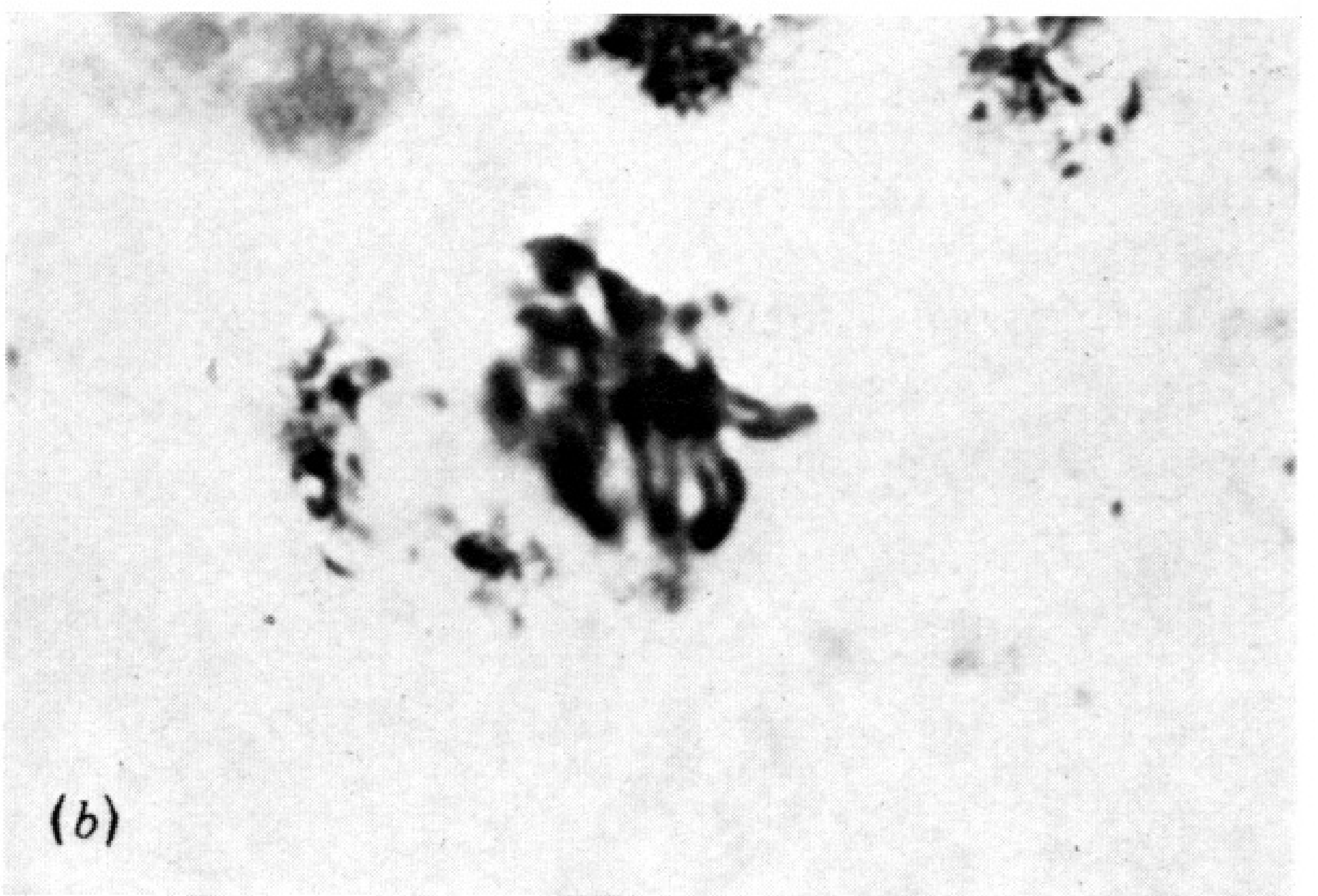


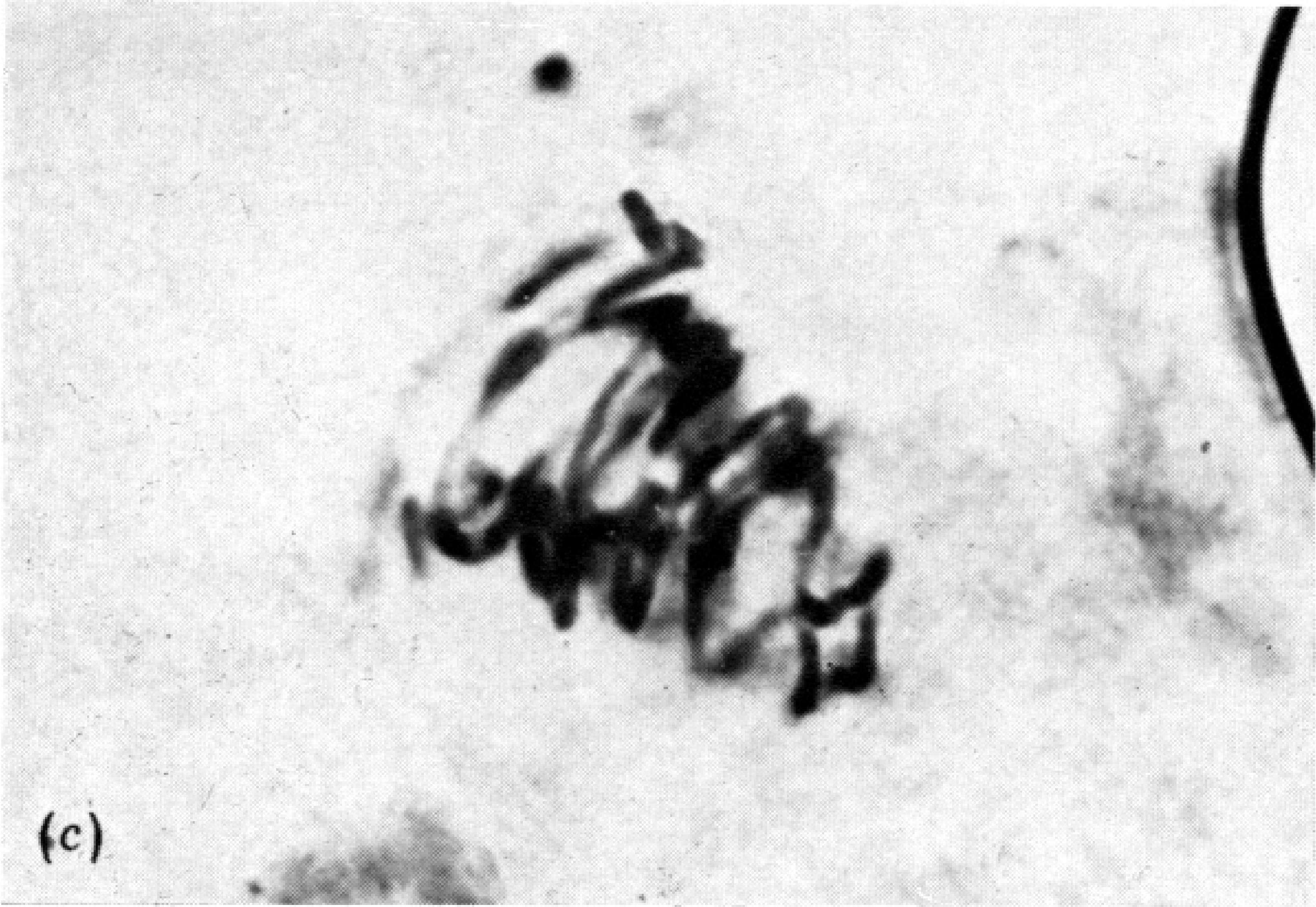


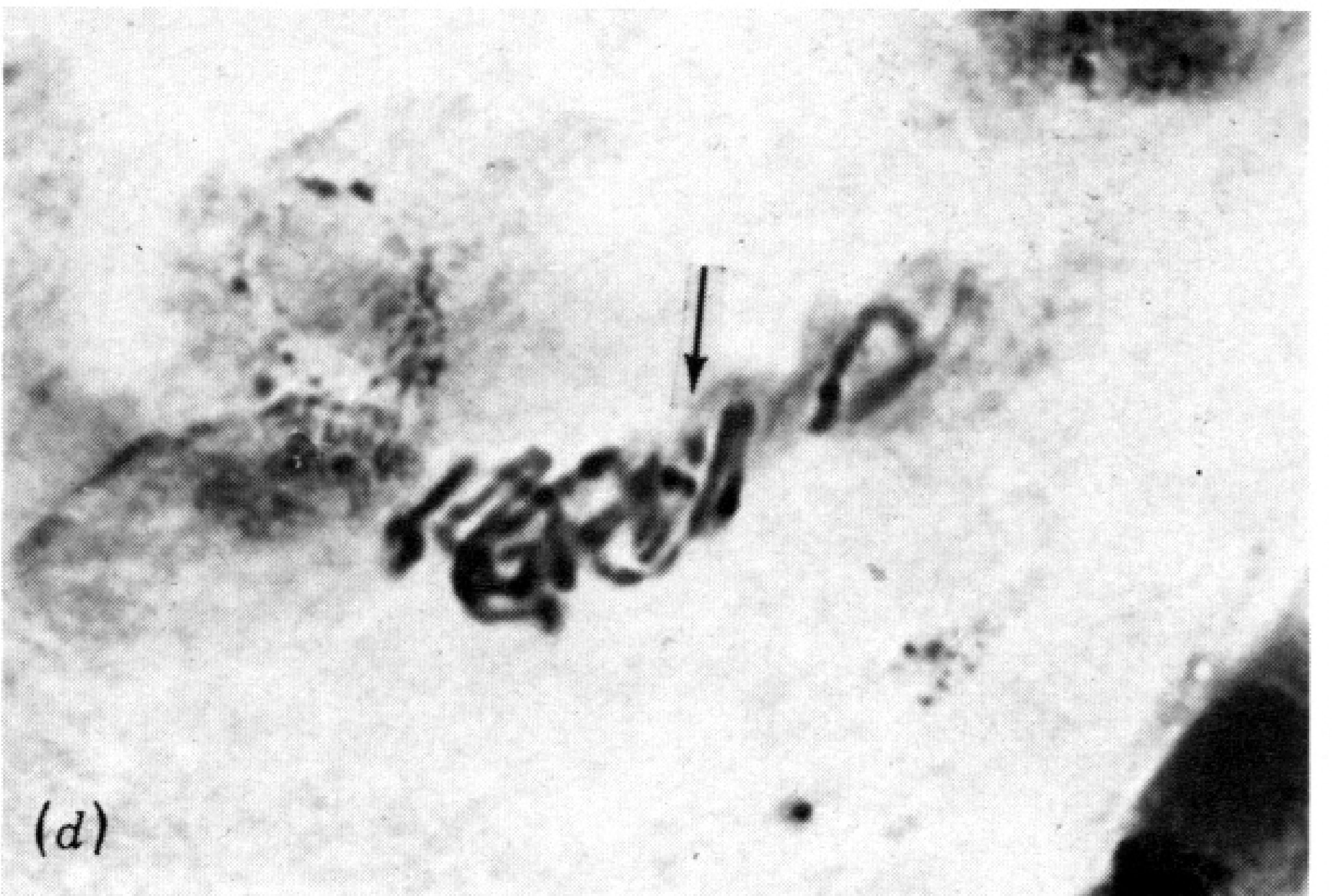

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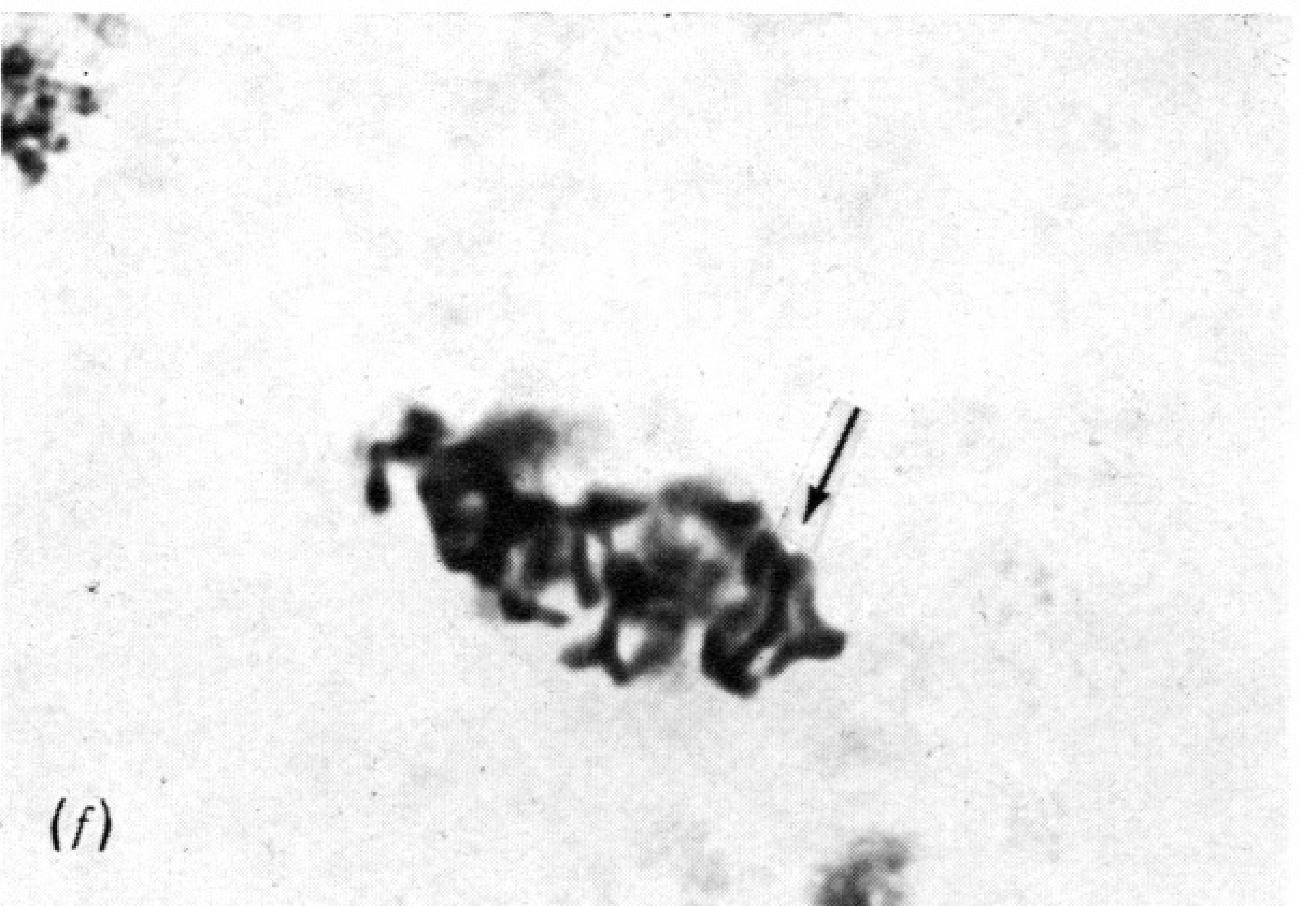


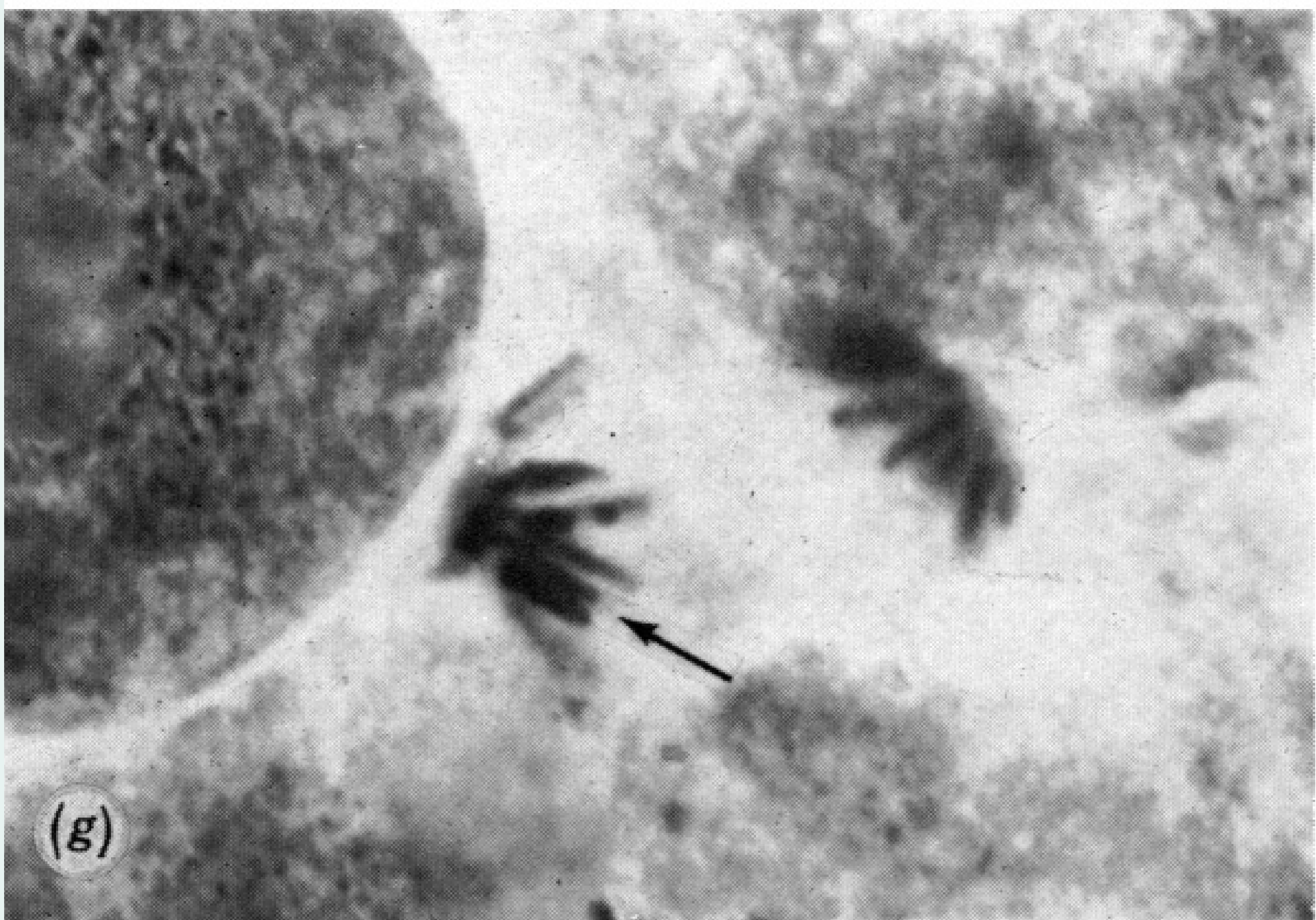


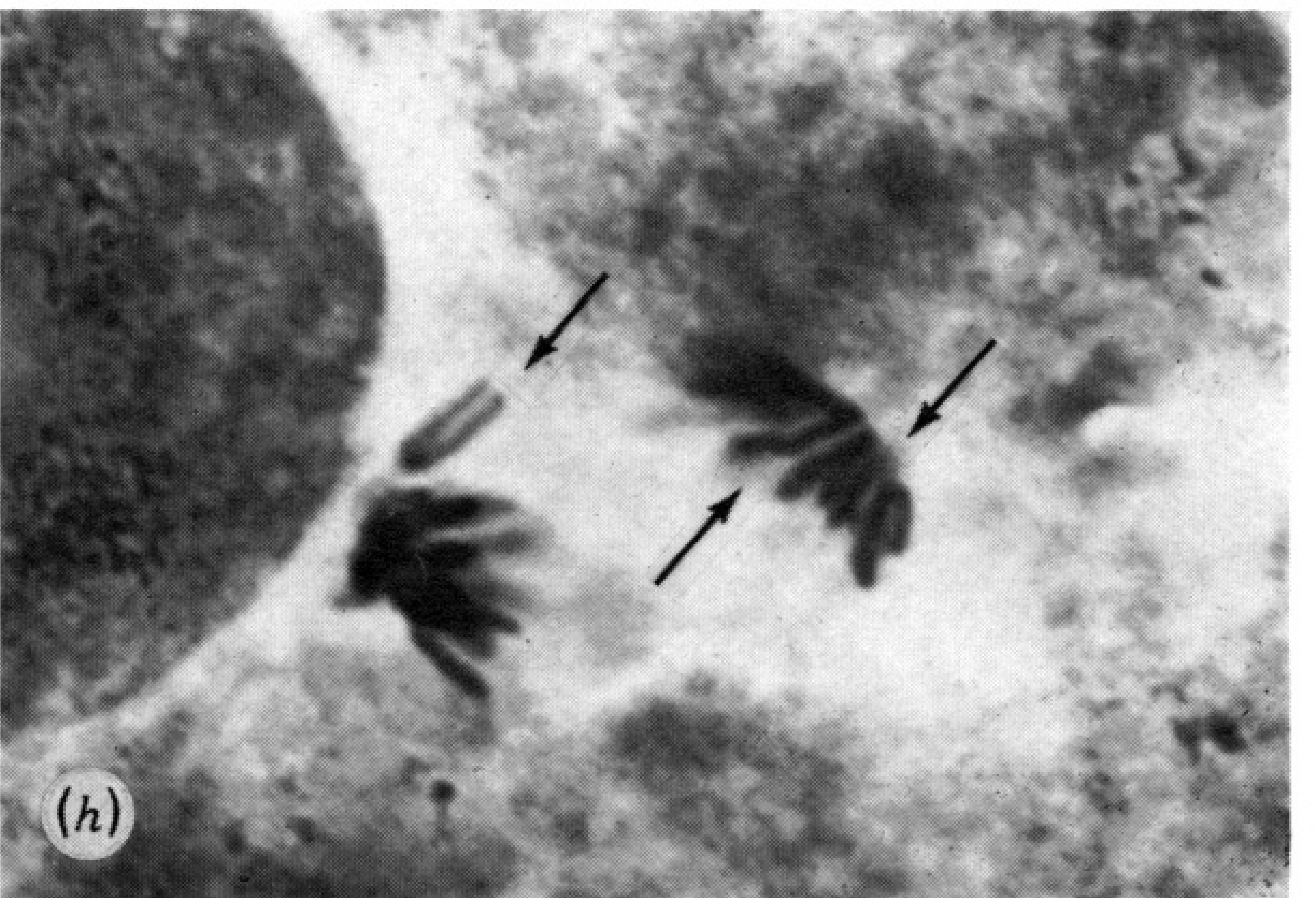


FIGURE 4. For description see opposite.

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