ARTICLES

CHROMOSOMAL CHANGES IN MAMMALIAN SPECIATION: A LITERATURE REVIEW

L. James Gibson
Geoscience Research Institute

WHAT THIS ARTICLE IS ABOUT

Species are defined as groups of individuals which do not interbreed with other groups under natural conditions. In order for a new species to appear, it is necessary that some change occur which prevents natural interbreeding between two groups which formerly could interbreed. Several mechanisms by which this could be accomplished have been proposed. One proposal which has been widely discussed is based on structural changes in chromosomes. Various kinds of structural changes in chromosomes and how they affect fertility are discussed in this article.

Fusion of two chromosomes and reversal (inversion) of a portion of a chromosome are the most commonly observed structural changes in mammalian chromosomes. Some populations which differ by such chromosomal rearrangements can interbreed, while other populations with similar chromosomal differences cannot. This suggests that the reasons for sterility are somewhat complex and may often be caused by factors other than differences in chromosomal structure. The fact that most species show chromosomal differences may be due to changes which have occurred after the species became reproductively isolated.

INTRODUCTION

The way in which new species arise has long been a subject of speculation and debate. From Darwin (1869) up to recent times (e.g., Mayr 1970, Fitch 1982) it has been believed that species change gradually over long periods of time. In recent years this concept has been challenged by both paleontologists (e.g., Eldredge & Gould 1972, Gould & Eldredge 1977, Stanley 1975) and geneticists (e.g., Carson 1975, Dover 1982, White 1978a, Wilson, Maxson & Sarich 1974, Wright 1982). One mechanism which has been proposed as important in rapid speciation is changes in chromosomal structure (e.g., White 1978a). This idea has stimulated a great deal of research and discussion.

Comparisons based on the number of chromosomes, or the number of chromosome arms, have not generally been helpful in determining relationships between species (e.g., see Greenbaum & Baker 1978). The development of modern techniques of studying chromosomes (see Hsu 1979) has made it possible for scientists to make much more accurate and detailed comparisons of chromosomes in various species of animals. The development of banding techniques, beginning about 1970 (Caspersson, Zech & Johansson 1970, Pardue & Gall 1970, Seabright 1971) made it possible to identify each pair of chromosomes with certainty, at least for most species of mammals, and to compare chromosome structure in different species to an extent not possible previously. This method

has received a great amount of attention in recent years (e.g., Fredga 1977, Patton & Sherwood 1983, White 1978a).

Results from these kinds of studies have led to the discovery that some species of mammals were actually composed of two or more chromosomal races which could not interbreed. Since interbreeding is the basic criterion for defining a species, each of these chromosomal races can now be considered a separate species (e.g., see Wahrman, Goitein & Nevo 1969). In addition, the results have been important in proposing relationships between species (e.g., Baker, Koop & Haiduk 1983, Rumpler et al. 1983), and even to infer modes of evolutionary change (Bickham & Baker 1979, Key 1968, White 1978b). This paper will review several kinds of chromosome variability and their effects on reproductive success. A future paper will discuss examples of comparative studies of G-banding patterns in chromosomes of mammals, especially those which have been used to propose or to clarify relationships.

VARIATION IN CHROMOSOMES

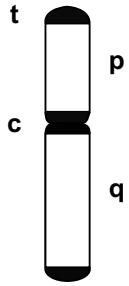

FIGURE 1. Parts of a chromosome: t = telomere; c = centromere; p = short arm; q = long arm.

Chromosomes can be classified on the basis of the position of the centromere (see Figure 1). Chromosomes with two nearly equal arms are called *metacentric*. Chromosomes with the centromere at or near one end of the chromosome are called *acrocentric* (White 1973; see also Levan, Fredga & Sandberg 1964). The chromosomal complement of an organism is called its *karyotype*.

In comparing chromosomes, it is necessary to take into account the possibility of structural changes which may have occurred. These changes in the chromosomal structure can be detected by using a special staining technique called *G-banding* (Seabright 1971). Chromosomal rearrangements may alter the number of chromosomes, the number of chromosome arms, or both, with no apparent effect on the animal's appearance. Some kinds of rearrangements produce obvious chromosomal changes, while other kinds may be less obvious. Genes may be duplicated or deleted, or their sequence on the chromosome may be changed. Change in the position of a gene may affect its action (see Lewis 1950, Wahl, de Saint Vincent & DeRose 1984). A brief discussion of the various mechanisms producing chromosomal rearrangements will help in understanding their significance in comparative studies.

Changes in Chromosome Number

Robertsonian rearrangements. A Robertsonian rearrangement (see Figure 2) is the result either of the fusion of two centromeres into one, or the fission of one centromere into two. Occasionally, a metacentric chromosome is

found in one population which matches in banding pattern two acrocentric chromosomes of a different population. Matching patterns of G-banding indicate that the chromosomes are *homologous* (members of a pair) (see John & Freeman 1975).

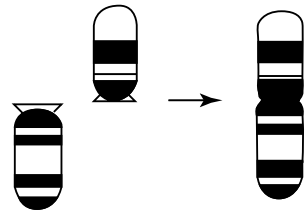

FIGURE 2. Robertsonian fusion in *Mus musculus poschiavinus* between two acrocentric chromosomes (12 and 14), producing a metacentric chromosome. (Capanna at al. 1975).

The situation in which a species shows a large variation of chromosome numbers due to Robertsonian rearrangements is called a *Robertsonian fan*. The house mouse, *Mus musculus*, provides a good example. The "normal" complement of chromosomes (karyotype) consists of 40 acrocentrics. This karyotype is seen in laboratory strains of the mouse, and in wild populations from North America and many other parts of the world (see White 1978a, p 206).

A population of house mice from the Italian Alps, which had previously been discovered to possess slight morphological differences, was discovered to have 22 chromosomes. This difference was used to confirm its specific status under the name *Mus poschiavanus* (Gropp, Tettenborn & Von Lehmann 1970). Many other populations have been discovered, with chromosome numbers ranging from 22 to 40 (Gropp & Winking 1981). In each case, the total number of arms is the same. Banding studies have shown that each metacentric chromosome is homologous with two acrocentric chromosomes from the "normal" karyotype (Capanna et al. 1975). It is clear that either "fusion" or "fission" is involved.

To determine whether fission or fusion is responsible for changes in chromosome number in the house mouse, it is helpful to examine the metacentric chromosomes and see which acrocentrics are involved in each. If any specific acrocentric is found only in combination with one specific partner in metacentrics from many populations, one would interpret this as evidence for the mechanism of fission. On the other hand, if any particular acrocentric may have different partners in metacentrics from many populations, one would interpret this as evidence for the mechanism of fusion. The results show that fusion has been the mechanism responsible for Robertsonian rearrangements in the house mouse, since a specific acrocentric may be found fused to a number of different partners in different populations.

Odd numbers of chromosomes are found in some individuals (Gropp & Winking 1972). This represents cases where one member of each of two pairs of acrocentrics have fused to form a metacentric, but their respective homologs have remained separate. If one of the sex chromosomes is involved, the result will be that males and females of a species will have different numbers of

chromosomes. Several examples are known of species in which the number of chromosomes is different for each sex (Vorontsov 1973).

Although Robertsonian fusion is one of the more common types of chromosomal rearrangement (Fredga 1977), *Robertsonian fission* appears to be relatively rare in mammals. It has been seen in cultured cells (Kato, Sagai & Yosida 1973), in a family of zebras (Whitehouse et al. 1984), and has been suggested to have occurred in the black rat of Mauritius (Yosida 1980, p 61-73). In addition, Todd (1970, 1975) has proposed that fissioning of the entire complement of chromosomes (*karyotypic fissioning*) has happened during the evolution of canids and artiodactyls, but this theory has not gained general acceptance.

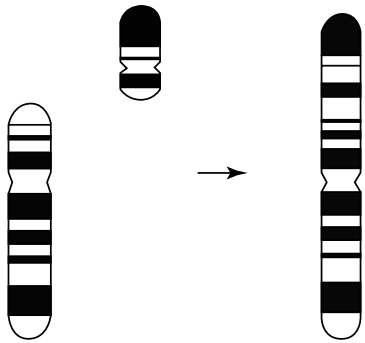

FIGURE 3. Tandem fusion between chromosomes 4 and 9 of the water buffalo. (After Bongso & Hilmi 1982).

Tandem fusion. A tandem fusion is a fusion of two chromosomes in which the end of one chromosome is fused either to the end or to the centromere of another chromosome. An example of a tandem fusion distinguishing Malaysian swamp water buffaloes from Asian river buffaloes is illustrated in Figure 3.

Probably the most interesting example of this kind of variation is the case of the muntjacs, a small group of Asian deer. One species, *Muntiacus muntjac*, has only 6 chromosomes in the female, and seven in the male. This is the smallest chromosome number known in mammals (Wurster & Benirschke 1970). Another species, *M. reevesi*, has 46 chromosomes in both male and female (Liming, Yingying & Xingsheng 1980). Comparison of banding patterns suggests that essentially the same genetic material is present in both species, since there is a one-to-one correspondence of bands, and indeed they appear very similar. However, in order for the chromosome number to be so drastically different, it appears that either the large chromosomes of an ancestral species have fragmented to produce the many small chromosomes seen in *M. reevesi*, or tandem fusion has occurred in an ancestral species to produce the large chromosomes present in *M. muntjac*.

A third species, *M. feae*, has 13 chromosomes in the female (Soma et al. 1983). The male has not been studied. Comparison of banding patterns has not been done with original data, but a comparison of the photographs in the papers seems to indicate that the larger chromosomes of *M. muntjac* and *M. feae* are derived from different tandem fusions of the smaller chromosomes of an ancestor having chromosomes like *M. reevesi*, since the banding patterns of the larger chromosomes in *M. muntjac* and *M. feae* do not appear to match.

Supernumerary chromosomes. Still another type of variation in chromosome number is seen occasionally in mammals, and more frequently in birds and reptiles. This is the presence of extra, often very small chromosomes, called *B chromosomes* or *supernumerary chromosomes*. These have been found in several species of mammals (Volobujev 1980). The number of supernumerary chromosomes may vary between individuals in the same population. No difference in appearance is generally seen between individuals differing in the number of B chromosomes, and it has been proposed that they are not genetically active (Shellhammer 1969). However, Ellenton & Basrur (1981) found a positive correlation between the number of B chromosomes and weight in male red foxes. In addition, they may increase the potential for genetic variability of a species (Volobujev 1980). They may interact with the genetically active chromosomes and become incorporated into the ordinary karyotype (Henriques-Gil, Arana & Santos 1983). They are usually, but not always, in a tightly condensed state known as *heterochromatin*. Their origin in unknown, but they may be remnants of chromosomal rearrangements (White 1973, p 314).

Changes in Arm Number

Pericentric inversions. The number of arms of which a chromosome is made is determined by the position of the centromere. If the centromere is terminal or nearly so, there is one arm. If the centromere is near the middle, two arms are present. If the position of the centromere is changed, as in a *pericentric inversion* (an inversion in which the centromere is included, see Figure 4), the number of arms may be changed. An acrocentric chromosome may be converted to a metacentric chromosome, or the reverse may happen.

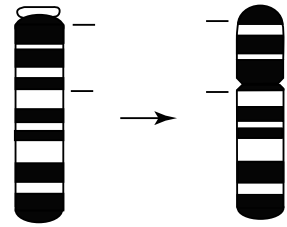

FIGURE 4. Pericentric inversion in chromosome 4 of *Peromyscus maniculatus*. The portion between the lines has been inverted. (After Dixon, Nelson & Priest 1980).

Examples of genera with species which differ by pericentric inversions include *Neotoma* (Mascarello & Hsu 1976) and *Peromyscus* (Robbins & Baker 1981). However, some differences in arm number which were originally interpreted as pericentric inversions before the advent of chromosomal banding techniques have been reinterpreted as due to additions or deletions of heterochromatin (Ohno et al. 1966, Pathak, Hsu & Arrighi 1973). Pericentric inversions have also been proposed to have occurred in speciation of bats (Baker & Bickham 1980).

Heterochromatin. Heterochromatin can be identified by a technique called *C-banding* (Pardue & Gall 1970). The development of this technique led to the discovery that some species differ in arm number because of the presence or

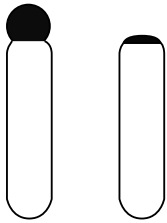

FIGURE 5. Arm difference in chromosome 18 between *Peromyscus maniculatis* (left) and *P. melanotis* (right). The short arm of *P. maniculatus* stains darkly with the C-band staining technique, showing it to be heterochromatic. (After Greenbaum, Baker & Bowers 1978).

absence of chromosome arms made of heterochromatin. This was first discovered in *Peromyscus* (Duffy 1972, and see Figure 5), and has since been found in other genera as well (e.g., Hatch et al. 1976, Patton & Sherwood 1982). The extra heterochromatic arms appear to be inactive genetically, and their origin is unknown. It is generally believed that the original chromosomes lacked the heterochromatic arms, and that they have been added at some time in the past. Blocks of heterochromatin may be found *interstitially* (within a chromosome arm) (e.g., see Mascarello & Mazrimas 1977; and see Figure 6) and may also represent additions to the original chromosomes.

In summary, tandem fusion and karyotypic fissioning change both chromosome number and arm number; Robertsonian rearrangements change chromosome number but not arm number; and pericentric inversions and the gain or loss of heterochromatin arms change the arm number but not the chromosome number. The presence of supernumerary chromosomes would change both chromosome number and the arm number, but they are generally counted separately.

Other Changes in Chromosomes

FIGURE 6. Interstitial heterochromatin of chromosome 3 of *Ammospermophilus insularis*, stained by C-banding. (After Mascarello & Bolles 1980).

Translocations. Chromosomes may change in other ways, with no change in either the chromosome number or the arm number. A *translocation* occurs when a piece of one chromosome breaks off and attaches to another chromosome. Ordinary translocations between unlike chromosomes result in a change in shape of the chromosomes involved, but not in the number of chromosomes or chromosome arms. An example of a translocation found in a human is illustrated in Figure 7.

Deletions and duplications. A portion of a chromosome may be deleted or duplicated as a result of an inversion or translocation. If the deleted or duplicated segment carries essential genetic material, the individual is likely to be unable to survive. Deletions and duplications of heterochromatin seem to be viable, and many examples are known in which variations in heterochromatin occur. A possible example of a partial deletion of an X chromosome in a female ground squirrel is described by Nadler & Hughes (1966).

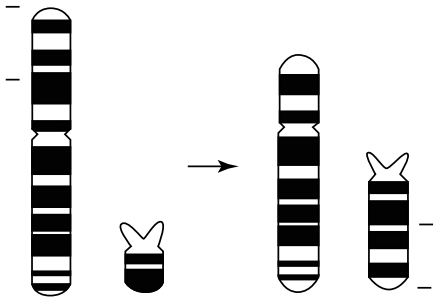

FIGURE 7. Translocation in a human of a segment of chromosome 5 onto chromosome 18. The portion between the lines has been translocated from the large chromosome to the small chromosome. (After Schultz-Schaeffer 1980).

Paracentric inversions. A *paracentric inversion* (an inversion of a part of one arm; see Figure 8) will change the order of genes on a chromosome without changing the size or shape of the chromosome. Differences between species due to a paracentric inversion appear to be uncommon in mammals, but such inversions have been proposed as a factor in speciation of bats (Baker & Bickham 1980), hares (Schroeder, Antoni & van der Loo 1978), and apes (Yunis & Prakesh 1982). A paracentric inversion found in the laboratory mouse (Davisson & Roderick 1973) is illustrated in Figure 8.

Radical reorganization. In addition to these relatively simple kinds of chromosomal changes, a more complex situation may sometimes occur. In a comparison of G-bands of the bats *Tonatia minuta* and *T. bidens* (Baker & Bickham 1980), the authors were unable to determine homologies or to trace the changes which had occurred. The same situation applied to another pair of bat species in the same study, *Micronycteris megalotis* and *M. minuta*. Apparently the *genome* (genetic material) has been completely rearranged. The mechanism for this is unknown.

It would be of interest to know whether such extensive chromosomal rearrangements occur all at once or whether they accumulate over time. White (1978b) has suggested that chromosomal rearrangements may accumulate in a series of independent events. A possible example of a geographic sequence of chromosomal rearrangements is found in the mole rats, genus *Spalax*, of Israel (Wahrman, Goitein & Nevo 1969). King (1982) has argued for the opposite view, that many rearrangements may occur simultaneously. Bickham & Baker (1979) have suggested that many new rearrangements are produced in a short time "when a new adaptive zone is invaded" (see below under Canalization model).

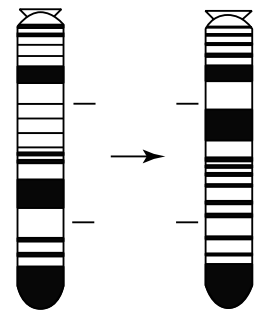

FIGURE 8. Paracentric inversion in chromosome 1 of *Mus musculus*. The region between the lines has been inverted. (After Davisson & Roderick 1973).

Transposable elements, or movable elements, are segments of DNA which can move from one chromosomal location to

another, sometimes resulting in the movement of genes. The discovery that transposable elements are widespread in natural populations has prompted some to suggest that multiple chromosomal breaks and rearrangement might occur simultaneously by this mechanism (e.g., Patton & Sherwood 1983). Breakage sites might be determined by specific DNA sequences which would depend on the particular transposable element involved (Inouye, Yuki & Saigo 1984, Nevers & Saedler 1977).

Effects on Heterozygote Fertility

Meiosis. An individual which possesses two different forms of a gene or chromosomal arrangement is said to be *heterozygous*. Individuals heterozygous for a chromosomal rearrangement may not be able to reproduce normally. During *meiosis* (the production of reproductive cells), homologous chromosomes line up side by side along their entire length in a process called *synapsis*. The pair of chromosomes, called a *bivalent*, is held together at certain points by attraction of their corresponding parts, and some of the corresponding parts are exchanged by the two chromosomes. When the chromosomes later separate, it is important that each chromosome be complete and be free to move away from its partner, and that each chromosome move to the proper location in one of the *daughter cells*.

If the chromosomes are different due to a rearrangement, they may not line up correctly. This may result in the exchange of parts which are not equivalent, so that one chromosome has extra material and one chromosome is missing some material. Such chromosomes are almost always inviable. Individuals with such abnormalities would not be able to reproduce very well, and their line would soon die out. This creates a problem in understanding how such chromosomal rearrangements could be important in speciation.

Since chromosomal structure and the processes of meiosis seem to be controlled by some of the same genes (see Baker et al. 1976), chromosomal rearrangements could sometimes be associated with meiotic irregularities in heterozygotes without either being the cause of the other (see Patton & Sherwood 1983). Mutations in such genes could cause both the rearrangement and the failure of meiosis to proceed normally.

In any case, if the two chromosomes are different due to a rearrangement, it is likely that something will go wrong during meiosis, and that such a heterozygous individual will be partially sterile. Different kinds of rearrangements differ in their effects on meiosis in the heterozygote. The most important of these are discussed below.

Robertsonian rearrangements. A *Robertsonian heterozygote* is a cell which contains one metacentric chromosome which is homologous to two acrocentric chromosomes. If only one such Robertsonian fusion has occurred in a cell line, three chromosomes line up together during meiosis, rather than a bivalent. If the chromosomes separate properly during cell division, such hetero-

zygotes may be fertile. If the chromosomes do not separate properly, the individual will be at least partially sterile. In a heterozygote for multiple Robertsonian rearrangements, a group of as many as fifteen chromosomes may line up together during meiosis (Capanna et al. 1976). In this situation the chromosomes will not separate properly, and the individual will probably be sterile (Gropp & Winking 1981).

In populations which differ only by a single Robertsonian rearrangement, hybrid fertility may not be significantly impaired, but hybrids between two chromosomal races which differ by multiple Robertsonian rearrangements are usually at least partially sterile (Gropp & Winking 1981, Searle 1984). Extensive study of karyotypes of European house mice, *Mus musculus*, has shown that *reproductive isolation* (inability to interbreed) exists between at least some of the chromosomal races (Capanna & Corti 1982). This species appears to be in the process of speciating (Capanna et al. 1976). Congruence has been found between chromosomal and *morphological* (anatomical) differences among at least some chromosomal races (Thorpe, Corti & Capanna 1982).

***Tandem fusions*.** An individual heterozygous for a tandem fusion will likely suffer a reduction in fertility of 50% if the chromosomes exchange parts in the area between the centromere and the point of fusion (White 1973, p 225). This is due to the formation of deletions and duplications in the chromosomes.

A tandem fusion has been identified in one race of the Asian water buffalo, which has not interfered with cross-breeding in attempts to improve the breed (Bongso & Hilmi 1982), although its potential for survival without the aid of man is uncertain. Similar species differing by one or more tandem fusions are known in cotton rats, *Sigmodon* (Elder 1980) and in muntjacs, *Muntiacus* (Liming, Yingying & Xingsheng 1980), but the fertility of hybrids is not known.

***Inversions*.** The effects of inversions on fertility in heterozygotes depend on the relationship of the positions of the inversion, the centromeres, and the parts of the chromosomes which are exchanged. If an exchange takes place within the inverted segment, the individual will be partially sterile. Otherwise, the individual may be fertile (White 1973, p 216).

Inversions probably contribute to loss of fertility in heterozygotes in many cases, but their importance in speciation has been minimized by Zouros (1982). Two populations of *Peromyscus leucopus* which differ by three pericentric inversions are known to be interfertile (Baker et al. 1983b).

***Translocations*.** Translocations between non-homologous chromosomes can severely reduce the fertility of a heterozygote because of mechanical difficulties during meiosis. Two pairs of chromosomes will be involved, which will form a group of four at synapsis. The effects on fertility depend upon the number of chromosomal exchanges and their location, as well as the way in which the chromosomes separate. In general, translocation heterozygotes suffer a loss of fertility due to improper separation of the chromosomes during meiosis. However, in some plants and insects (see Schultz-Schaeffer 1980, p 227), there

seems to be a special mechanism (termed *meiotic drive*) which causes the chromosomes to separate properly as much as 95% of the time.

Different translocations have been discovered to distinguish the karyotyes of the goat and the ox, and those of the goat and the oryx (Buckland & Evans 1978). In eleven species of the genus *Oryzomys* (Baker, Koop & Haiduk 1983), 21 translocations were identified among 55 rearrangements. On the other hand, an extensive study of bats (Robbins & Baker 1981) failed to discover any translocations.

Heterochromatin. The effect of heterochromatin on heterozygote fertility varies with the specific situation. Some populations of the pocket gopher, *Thomomys bottae*, differ from other populations in having extra arms on some of their chromosomes (Patton & Sherwood 1982). C-banding studies reveal these extra arms to be heterochromatic. The populations are interfertile. A similar situation is reported in the woodrat *Neotoma lepida* (Mascarello & Hsu 1976) and in the vole *Microtus pinetorum* (Wilson 1984). In general, it appears that differences in arm number due strictly to heterochromatin additions or deletions may not affect fertility.

When heterochromatin blocks are found interstitially, reproductive success may be affected. In the study of *Thomomys* mentioned above, populations which differed in the arrangement of interstitial heterochromatin were not interfertile. However, the authors suggested the reason for this might not be due to the heterochromatin itself, but that the interstitial heterochromatin may be a result of a pericentric inversion, and the inversion is the actual isolating mechanism. That interstitial blocks of heterochromatin may be remnants of chromosomal rearrangements is supported by a study of the Australian rodent *Uromys* (see Baverstock, Gelder & Jahnke 1982) but not by a study of the American rodent genus *Sigmodon* (Elder 1980).

A study of an Australian rat, *Uromys caudimaculatus*, revealed two chromosomal races which differ significantly in the amounts of both terminal and interstitial heterochromatin (Baverstock, Gelder & Jahnke 1982). In spite of the differences, hybrids show no abnormalities at meiosis, and are fertile.

Supernumerary chromosomes. The presence of B chromosomes does not seem to have any major effect, but if the number of such extra chromosomes becomes too large, fertility may be affected (John 1973, Gillies 1975, Volobujev 1980). This is presumably because they may interfere with normal separation of the ordinary chromosomes. The presence of B chromosomes also may increase the frequency of chromosomal exchanges in the regular chromosomes (Patton 1977).

In summary, some types of rearrangements are more effective than others in reducing heterozygote fertility. The fact that some populations are interfertile in spite of differences in chromosomal structure shows that one cannot always determine in advance whether a particular chromosomal rearrangement is important in reproductive isolation. However, there often seems to be an associ-

ation between chromosomal rearrangements and species differences (Bengtsson 1980). The kinds of changes most frequently involved in reducing heterozygote fertility appear to be Robertsonian rearrangements (but see Ponsa et al. 1981) and inversions (but see Zouros 1982). This may be because these are the most common types of rearrangements seen in mammals.

CHROMOSOMAL REARRANGEMENTS AND SPECIATION

In order for speciation to occur, a *reproductive barrier* (a biological factor which prevents successful interbreeding under natural conditions) must be formed between members of a species. Chromosomal rearrangements themselves would not prevent mating between different chromosomal forms but could act as post-mating reproductive barriers (Mayr 1970) by lowering hybrid fertility. Abnormal separation of chromosomes during meiosis will reduce the percentage of viable gametes produced by such a hybrid animal, thus reducing the reproductive ability of the individual. In the presence of significant competition, such individuals will be at a reproductive disadvantage, and their family line will soon be crowded out.

The Heterozygote Bottleneck Problem

Chromosomal rearrangements are estimated by White (1978a, p 171) to occur in about one of every 500 individuals. A very important question in chromosomal speciation is how a chromosomal change, once it arises in an individual, is established in a population. Because individuals *heterozygous* for a chromosomal aberration generally have lowered fertility, it is to be expected that they will be eliminated from the population by competition. Those rearrangements which are most easily established would be those having the least effect on heterozygote fertility, but which would therefore be the least effective in speciation. This problem has been much discussed and is frequently referred to as the *heterozygote bottleneck*.

Despite our difficulties in explaining it, or in determining cause and effect, the results of many studies in natural populations clearly show that chromosomal changes have occurred and are often associated with species differences.

If the rearrangements most likely to survive in a population are those which have the least effect on heterozygote fertility, and if they occur with any reasonable frequency, one would expect to find examples of populations with chromosomal *polymorphisms* (more than one form in the same population). Examples of polymorphisms are discussed in the next section, and further problems in the establishment of rearrangements are discussed in succeeding sections.

Polymorphisms

Most populations exhibit a uniform karyotype, but chromosomal polymorphisms are occasionally found in natural populations. The most common

chromosomal polymorphisms seen are those involving Robertsonian rearrangements (e.g., Koop, Baker & Genoways 1983), supernumerary chromosomes (e.g., Shellhammer 1969), and in the amount and distribution of heterochromatin (e.g., Patton & Sherwood 1982, Rao et al. 1983).

Polymorphisms for pericentric inversions have also been reported in *Rattus rattus* (Yosida 1980, pp. 13-42) and in *Mus dunni* (Sen & Sharma 1983). In another study, a female Belding ground squirrel and her presumed offspring were found to differ from the main population by a partial deletion in an X chromosome (Nadler & Hughes 1966).

Are Chromosomal Rearrangements Adaptive?

If chromosomal rearrangements are not *adaptive* (contributing to the ability of an organism to survive and reproduce in a particular environment), then chromosomal speciation is a totally random process. The establishment of newly arisen rearrangements by chance would be very difficult. It may be possible that a new population could be established by an individual carrying a rearrangement (*founder effect*), which could then become established in the new population through inbreeding. The probability of such an event seems too low to account for the many examples of chromosomal differences between species.

Because founder events seem so rare, some have argued that a chromosomal rearrangement may confer some kind of advantage, thus making it easier for a new rearrangement to become established (White 1978b). If so, then one would expect to find some relationship between chromosomal rearrangements and genetic or environmental factors.

In a study of *Peromyscus* (Dixon, Nelson & Priest 1980) a relationship between the number of acrocentric chromosomes and altitude was discovered. However, in one study of *Thomomys* pocket gophers (Patton 1970), more acrocentrics were found at high elevation, while in another study (Berry & Baker 1971), more acrocentrics were found in warmer, drier habitats. There does not seem to be a consistent relationship between the environment and the number of acrocentrics, at least in this case.

The notable lack of congruence between karyotypic variation and morphological differences (see below) also casts doubt on the idea that the karyotype is subject to *natural selection* (interaction of individuals with the environment which favors the survival and reproduction of one individual over another, due to genetic differences). Nevertheless, Baker et al. (1983a) present evidence which they believe shows that a selective advantage of a heterozygous karyotype exists in a population of *Geomys* pocket gophers from Texas. They argue that such chromosomal heterosis supports the idea that the karyotype may be *adaptive*. Differential survivorship among chromosomal races of mole rats has also been reported (Nevo, Heth & Beiles 1982). Robbins, Moulton & Baker (1983) reported that species of *Peromyscus* with larger geographic ranges have

higher numbers of chromosomal rearrangements, suggesting some possible advantage to species with more rearrangements.

Chromosomal Variation and Geographic Barriers

The relationship between geographic barriers and chromosomal speciation has been vigorously debated. The controversy centers over whether geographic separation is required for chromosomal speciation, or whether such speciation may occur within a population. Some examples from the real world may help to shed some light on the problem.

Coincidence with geographical barriers. Differences in karyology can be found within a species, across a geographical barrier. The desert woodrat, *Neotoma lepida*, is found on both sides of the Colorado River. Woodrats from east of the river have at least 10 large biarmed chromosomes, while on the west side, eight or fewer biarmed chromosomes are found (Mascarello & Hsu 1976). The difference between the two populations is due to heterochromatic arms.

Two species of antelope squirrels provide another example (Mascarello & Bolles 1980). *Ammospermophilus insularis*, found only on Espiritu Santo Island (in the Gulf of California), has a karyotype most similar to that of *A. harrisii* on the mainland. Differences in the banding patterns are apparently due to a translocation and an inversion. The situation is made more interesting by the fact that a third species, *A. leucurus*, occupies a range between the two more similar species.

Geographical barriers lacking. Chromosomal differences can also be found within a nominal species without the presence of an obvious geographical barrier. In this case, it appears the forms are reproductively isolated by a chromosomal rearrangement. An example of this is found in the ground squirrel *Spermophilus richardsonii* (Nadler, Hoffmann & Greer 1971). One form, *S. r. richardsonii*, has 36 chromosomes. Another form, which has been considered as a subspecies, *S. r. aureus*, has only 34 chromosomes. A study of the boundary between the two forms indicated almost no hybridization. Because of this, these two forms are now considered to be different species, with *S. r. aureus* taking the name *S. elegans aureus* (Honacki, Kinman & Koeppl 1982). Partial reproductive isolation between species as a result of chromosomal differences is also known in the *Peromyscus maniculatus* species complex (Caire & Zimmerman 1975).

Lack of chromosomal differences in isolated populations. On the other hand, geographic isolation may exist between populations without chromosomal differences. Some interesting examples are found in the ground squirrel genus, *Spermophilus*. An Asian species, *S. undulatus*, and an American species, *S. columbianus*, have identical chromosome numbers and identical G-banding patterns (Nadler et al. 1975). The two species are separated by *S. parryi*, which lives on both sides of the Bering Strait and has a different chromosome number. Two other forms in the same genus, *S. elegans nevadensis* and *S. e. elegans*,

have ranges separated by over 100 miles, yet apparently have identical karyotypes (Nadler, Hoffmann & Greer 1971).

Based on these examples, it appears that geographic isolation and chromosomal variation are not necessarily related. However, they are often associated, and it seems likely that some rearrangements would be more easily conserved in small isolated populations. The problem is complicated because one cannot conclude, on the basis of present distributional patterns, that a population has never been isolated in the past.

Genetic Aspects of Chromosomal Variation

Genetic changes can be divided into two groups (Carson 1975), those which result in changes in proteins, such as enzymes, and those which affect *regulatory genes* (genes which regulate the activity of other genes are known as regulatory genes). Changes in the genes which produce proteins are known to be very common (e.g., see Avise & Aquadro 1982), and there is increasing evidence that regulatory genes are also subject to change (MacIntyre 1982).

There often is a relationship between chromosomal differences and differences in proteins within species (Patton & Yang 1977, Cothran & Smith 1983). Such differences need not be causally related (Patton & Sherwood 1983), and sometimes the differences are not congruent (Baker, Bleier & Atchley 1975). Species which differ by chromosomal rearrangements sometimes appear to be more similar genetically than other species pairs with nearly identical karyotypes (e.g., see Baker and Bickham 1980).

If a chromosomal rearrangement removes a gene from the influence of its regulators, the organism could be affected in a very significant way. If the affected gene was important in controlling the development of the embryo, such a genetic change might result in a sudden morphological change (Wilson, Maxson & Sarich 1974). However, chromosomal changes are not required in order for malfunction of a regulatory gene. In addition, chromosomal rearrangements do not necessarily cause morphologically significant genetic changes. This is demonstrated by the existence of *sibling species* (species which are morphologically very similar, but are reproductively isolated) which were not detected as different until chromosomal studies were applied (e.g., Olert & Schmid 1978). Further evidence of this is the existence of species in the same genus which have karyotypes so different that the changes cannot be traced (see above on Radical reorganization).

Karyotypic Orthoselection

One result of the numerous comparative studies has been the discovery that different types of rearrangements are often typical of different taxonomic groups. The tendency for similar types of changes to accumulate in a lineage has been termed *karyotypic orthoselection* (see White 1978a, p 49). The use of the term "selection" could be misleading, as there is no evidence that selection

is involved. The reason for the trend is not known, but it can be illustrated with a few examples.

In a study of 18 species of *Peromyscus* (Robbins & Baker 1981), a minimum of 60 chromosomal changes were proposed as having occurred in divergence from a common ancestor. Thirty-four of these involved heterochromatin additions, and the remaining 26 were pericentric inversions. No fusions or translocations were detected. In a comparison of four families of bats, involving 78 species (Baker & Bickham 1980), Robertsonian fusions and pericentric inversions were dominant, with tandem fusions uncommon, and heterochromatin arms very rare. In the much-studied *Mus musculus* complex, Robertsonian fusions are by far the most common rearrangement (Gropp & Winking 1981).

Models of Chromosomal Speciation

The most widely accepted model of speciation is the *allopatric model* (based on geographic isolation), according to which speciation occurs when genetic changes accumulate in geographically separated populations (see Mayr 1970, Futuyma & Mayer 1980). Speciation is achieved when the extent of genetic change is enough to act as a *reproductive barrier* (a factor contributing to reproductive isolation) between the two populations. Among the more important challenges to this allopatric model of speciation has been the so-called *stasipatric model* (see below) proposed by White (1968, 1973, 1978a), in which chromosomal rearrangements play an important role.

Stasipatric speciation. According to the stasipatric model of speciation (White 1978a, chapter 6), a new chromosomal rearrangement may spread from its point of origin throughout a population, in spite of the reproductive disadvantage of the heterozygote. Because the fertility of the heterozygote will be reduced, a partial reproductive barrier will exist between individuals carrying the original chromosomal arrangement and those carrying the new rearrangement. In order for the new rearrangement to persist, some means of overcoming the reproductive disadvantage must be obtained by the heterozygotes. White (1968, 1978a) proposed that several factors, alone or in combination, would be sufficient to permit establishment of the rearrangement. These factors are *meiotic drive* (preferential movement of chromosomes during meiosis, see above on translocations), random *genetic drift* (random changes in gene frequencies) in small populations, *selective advantage* (superiority) of individuals carrying the new rearrangement, and *inbreeding*.

The four factors advocated by White as helping in the establishment of a rearrangement were analyzed by Hedrick (1981). He concluded there were four situations which could theoretically be important in this respect. They are meiotic drive alone, meiotic drive plus genetic drift, inbreeding plus selective advantage of the new rearrangement, and inbreeding plus genetic drift. White's model has stimulated a great deal of discussion, and several attempts have been made to modify or refute it (e.g., Walsh 1982).

Negative heterosis. In order for speciation to occur, a reproductive barrier must be established between members of the parent species. The importance of *negative heterosis* (disadvantage suffered by individuals due to being heterozygous) in chromosomal speciation is discussed by Templeton (1981). He concluded that chromosomal speciation probably does occur, but that negative heterosis is not likely to be effective in providing the necessary reproductive barrier. He admits that a rearrangement could become fixed in a local *deme* (interbreeding population) under conditions of extremely small population size and intense inbreeding, but he argues that such fixation in a local deme is not speciation. However, if fixation of a chromosomal rearrangement in a local deme results in the reproductive isolation of that deme from the main population, this would seem to be speciation, by definition. The effectiveness of negative heterosis in speciation is also challenged by Spirito, Rossi & Rizzoni (1983).

Importance of geographic isolation. Perhaps the most controversial aspect of White's model has been the issue of whether geographic isolation is necessary for establishment of a new chromosomal variant. Key (1968) suggested that geographic isolation was necessary for initial establishment of a chromosomal rearrangement, which could then slowly spread through the range of the original species if the new rearrangement carried a selective advantage over the previous one. This seems very much like the allopatric model of speciation, followed by secondary contact of the populations.

Lande (1979) argued that random genetic drift in a small geographically isolated deme is the only way a rearrangement could be fixed initially. He compared the rate of fixation of a chromosomal rearrangement in a species composed of many nearly isolated demes to the rate of fixation of a genic mutation in a local population. He concludes that many species must have arisen from small demes with populations in the range of 50 to 200.

Social behavior and small demes. The importance of social behavior in maintaining small semi-isolated demes with resulting inbreeding has been stressed by some authors (e.g., Bush et al. 1977, Wilson et al. 1975). Bush (1975) gives as an example the difference in chromosome variability between dogs and foxes. All members of the dog genus, *Canis*, have 78 chromosomes, while in foxes the number varies at least from 38 to 78. The uniformity of chromosome number in *Canis* could be due to the fact that dogs range widely and interbreed freely. Foxes live in smaller family groups and do not range over such a wide territory. This means that a new chromosomal rearrangement would be more likely to persist among foxes, due to inbreeding.

The relationship between population structure and rate of chromosomal speciation has been challenged in a study of two genera of lemmings (Gileva 1983). The genera *Lemmus* and *Dicrostonyx* have similar population structures, but there is little chromosome variability in *Lemmus* and much variability in *Dicrostonyx*.

Area effects. In another paper White (1978b) has proposed that groups of genes which are advantageous in a particular environment can be protected against mixing with other genes from a neighboring population by chromosomal rearrangements. As these chromosomal changes accumulate, they act to prevent the chromosomes of a heterozygous individual from lining up properly during meiosis, thus producing a reproductive barrier between the two populations. This is the so-called *area effects* phenomenon. This paper has been vigorously criticized by Bickham & Baker (1980), who attack the concept of *group selection* (natural selection acting on groups rather than on individuals) espoused in White's paper.

Canalization model. Bickham & Baker (1979) have presented their own model of chromosomal evolution, termed the *canalization model*. They argue that the karyotype is adaptive, and that there is an optimum karyotype for each *adaptive zone* (way of life). When a new adaptive zone becomes available , the karyotype will be destabilized by selection until the optimum or near-optimum karyotype is evolved. During this process of optimization, rapid changes in chromosomes will occur. After stabilization, evolutionary change will be primarily by other mechanisms, such as changes in proteins. This model did not provide a satisfactory explanation of chromosomal speciation in cricetid rodents (Baker, Koop & Haiduk 1983) or in bats (Baker & Bickham 1980) in studies by those who proposed it.

Genomic disease. Transposable elements (see above under Radical reorganization) appear to be important in gene regulation in bacteria (Cohen 1976), and it is reasonable that a similar mechanism might be present in animals (Bresler 1983, Whitney & Lamoreux 1982). Changes in the DNA of a transposable element might result in a change in the genetic program of embryological development or gene regulation, which could have significant morphological effects. Transposable elements are also able to carry genes with them, which may be established in the reproductive cells of an infected individual (Rubin & Spradling 1982).

It is known that chromosomal rearrangements can be caused by the action of transposable elements (Campbell 1980, Wahl, de Saint Vincent & DeRose 1984). A theory of speciation, called genomic disease by Rose & Doolittle (1983) proposes that transposable elements may sometimes act to produce reproductive barriers by disrupting development, increasing the mutation rate, and causing chromosomal rearrangement. However, one should not assume such a mechanism without definite evidence (Doolittle & Sapienza 1980).

SUMMARY

In summary, there is little doubt that species differences are often associated with chromosomal rearrangements, but this does not show a cause and effect relationship (Patton & Sherwood 1983). Reproductive isolation may be achieved by several genetic mechanisms, among which is chromosomal rearrangement.

Many karyotypic differences between species may be the result of different events occurring in populations already reproductively or geographically isolated. Reproductive isolation and chromosomal rearrangements may both be the result of mutations in genes controlling chromosome structure and behavior. Transposable elements may play a part in such mutations, or in other genetic incompatibilities between species. In any case, we do not yet understand the events which connect speciation with chromosomal changes (Fredga 1977).

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