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CHAPTER 2

ROLE OF CHROMOSOMAL BANDING PATTERNS IN UNDERSTANDING MAMMALIAN EVOLUTION

ROBERT J. BAKER, MAZIN B. QUMSIYEH,
and CRAIG S. HOOD

1. INTRODUCTION

Understanding and elucidating the forces affecting chromosomal evolution is not a simple task and is by no means nearing completion. A major obstacle is documenting the exact time of fixation of a new chromosomal rearrangement in a natural population. Currently, it is not possible to determine at what point in its past a chromosomal rearrangement became established in the karyotype of a species. Therefore, we can only speculate on the circumstances surrounding fixation of a rearrangement in a single population that subsequently becomes characteristic of the entire species. An even more basic example is the lack of documentation that individuals with a new chromosomal rearrangement are more fit than individuals with the primitive condition. A list of the features of chromosomal evolution that have not been observed is long enough to suggest a huge gap between theoretical and empirical studies.

ROBERT J. BAKER, MAZIN B. QUMSIYEH, and CRAIG S. HOOD • Department of Biological Sciences and The Museum, Texas Tech University, Lubbock, Texas 79409.

Examples of theories proposing different primary forces regulating chromosomal evolution include what we call the deme size model and the adaptive karyotype model and are similar in principle to the neutralist–selectionist arguments associated with molecular variation. Although these models are not mutually exclusive, they clearly emphasize alternative primary forces in chromosomal evolution.

The deme size model has its roots in Wright's (1941) observation that for some types of chromosomal rearrangements, the chromosomal heterozygote for a new arrangement will be less fit than either the homozygotes for the original chromosomal condition or those for the rearrangement. This lower fitness results from impairment of the reduction division in meiosis, which causes the production of unbalanced gametes. Wright reasoned that if there is a large effective population size, a new chromosomal rearrangement has essentially no chance of increasing in frequency (and eventually becoming fixed), because of lowered fitness in heterozygous individuals. However, if the effective population size (deme) is small enough, then on some occasions a new rearrangement could become fixed through sampling error (genetic drift). Basically a new mutation has a finite probability of becoming fixed through genetic drift (Wright, 1941) in a natural population only when the size of the breeding population is small. This is especially true if the new mutation is a chromosomal rearrangement that causes its possessor to be less fertile than other individuals in the population that are homozygous for the old chromosomal condition (Lande, 1979; Chesser and Baker, 1986).

An extension of Wright's observations is that chromosomal evolution is restricted primarily to species with highly inbred demes or small founder populations. Lande (1979) defined several aspects of this model and presented formulas that would permit calculation of effective population size over the long term if certain assumptions are made concerning negative heterosis, mutation rate of chromosomal rearrangements, and the number of rearrangements that have become fixed in the history of a lineage.

An alternative theory is a more direct extension of neo-Darwinian evolution and natural selection (Darwin, 1859; Bickham and Baker, 1979). The adaptive karyotype theory is based on the hypothesis that the karyotype is adaptive and that under some circumstances natural selection will favor the incorporation of a new chromosomal rearrangement. This model will work only when (1) a new chromosomal rearrangement provides its possessor with a positive phenotypic or genetic benefit, (2) the benefit is present in the heterozygous as well as the homozygous condition, and (3) the magnitude of the benefit is greater

than any reduced fitness resulting from meiotic malassortment in the heterozygote. In the adaptive karyotype model the effective population size is unimportant because the heterozygote for the new chromosomal rearrangement is more fit than the homozygote for the primitive state. The homozygote with the derived chromosomal condition would be more fit than the heterozygote because it would have the benefit of the new rearrangement, but no meiotic problems.

Given two populations of the same species with different chromosomal rearrangements, how can we determine which, if either, of the proposed models best explains the origin of the chromosomal differences? The truth is that there are so many variables associated with the factors potentially affecting chromosomal evolution that investigators do not agree on what kinds of data would result in the rejection of alternative theoretical explanations. Nonetheless, unless a theory is presented in a manner that permits falsification, it has limited value to science.

2. G-BANDS AS A MEASURE OF GENETIC HOMOLOGY AND TYPES OF CHROMOSOMAL CHANGE

The ability to determine accurately the type and number of rearrangements being studied is as critical to understanding chromosomal evolution as are theoretical considerations. Nondifferentially stained karyotypes can provide data on the number and size of chromosomes (diploid number) as well as general observations on centromere position. However, nondifferentially stained karyotypes provide little estimate of genetic homology of chromosomes. Some differential staining methods provide unique banding patterns over the entire karyotype and these patterns can be used to hypothesize homologous segments among individuals, populations, and even species. The most commonly used banding technique is G-banding. However, R-banding also has been used in a number of published reports (for example, Dutrillaux et al., 1981; Viegas-Piquignot et al., 1985). R-Bands produce the reverse patterns of those seen in G-banding. See Pathak (1976) for an explanation of the various types of banding techniques.

A critical question concerning any similarity measure of banding patterns used to indicate homology among individuals or species is, "does the similarity document genetic homology, that is, common evolutionary origin?"

Correspondence between G-band pattern and genetic homology of chromosomal segments has been demonstrated by numerous studies

(Francke and Taggart, 1980; Stubblefield, 1980; Creau-Goldberg et al., 1981; Ma et al., 1982; Stallings et al., 1985). Certain linkage groups have been conserved in mammals as evolutionarily divergent as *Mus musculus* and man (Lalley et al., 1978). Using gene mapping techniques, Francke and Taggart (1980) demonstrated that although the same loci were present, the order of the loci on the X chromosome of *Mus* and man are different, and that this difference corresponds to an inversion that was predicted by G-band analysis. Sawyer and Hotier (1986) also documented that high resolution of G-bands in *Mus* and humans predicted the specific location of homologous genes in the autosomes. Therefore, there are data documenting that similarity in G-band pattern can be valuable in identifying genetically homologous segments. Some chromosomes are so small as to have few bands, and in such cases there are no comparable patterns. Also, there is a certain amount of technical skill required to prepare comparable karyotypes. Finally, even for some species that are thought to be closely related, techniques presently available can detect little G-band similarity between karyotypes (Baker and Bickham, 1980, 1984).

Because there are many studies on the patterns, rates, and modes of chromosomal evolution based entirely on variation revealed by nondifferentially stained karyotypes (Wilson et al., 1974, 1975; Bush et al., 1977; Bengtsson, 1980; Imai and Crozier, 1980; Cothran and Smith, 1983; Imai, 1983; Imai et al., 1983; Bianchi and Merani, 1984; Larson et al., 1984), it is important to understand just how accurate such estimates are. This problem was addressed specifically in Haiduk et al. (1981) in a study of megachiropteran bats. Based on nondifferentially stained karyotypes, a minimum of seven rearrangements could explain the observed differences in their sample. However, a minimum of 34 rearrangements were required to explain the variation observed in G-band pattern. Additionally, in a study of phyllostomid bats (Baker and Bickham, 1980), over five times as many rearrangements were observed in G-band analysis as were required to explain the variation in nondifferentially stained karyotypes. Other studies document that chromosomal variation has not been estimated correctly by nondifferentially stained karyotypes (felids, Wurster-Hill and Gray, 1973, 1975; equids, Ryder et al., 1978; primates, Dresser and Hamilton, 1979; and vespertilionid bats, Bickham and Baker, 1977, Bickham, 1979a).

On the other hand, there are examples where nondifferentially stained karyotypes were accurate in estimating the magnitude of chromosomal evolution (carnivores, Wurster-Hill and Gray, 1975; primates, Dutrillaux, 1979; phyllostomid bats, Baker and Bass, 1979; vespertilionid bats, Bickham, 1979b). If the magnitude of underestimation was

relatively constant, one could simply correct by an appropriate factor, but, this does not appear to be the case.

Another significant problem in using nondifferentially stained karyotypes is that such data cannot be used to determine unequal amounts of chromosomal evolution when two taxa are being compared. Therefore, when taxa in such groups as bats or rodents are being compared, they are usually labeled as conservative or rapidly evolving. However, when the magnitude of chromosomal change is partitioned by a cladistic analysis of G-banded karyotypes, a different perspective is obtained. There are several examples where one species in a genus has retained the primitive karyotype for the genus (such as *Reithrodontomys fulvescens*), whereas other species in the genus have undergone 15 or 20 euchromatic rearrangements (such as *Reithrodontomys megalotis* and *R. montanus*; Hood et al., 1984). The data clearly show that within groups such as bats, horses, and rodents, some species have undergone extensive chromosomal evolution, whereas others have experienced little change (Baker and Bickham, 1980; Ryder et al., 1978; Hood et al., 1984). Therefore, to classify bats as having a slow rate of chromosomal evolution and rodents as having a rapid rate (for example, Bush et al., 1977; Bengtsson, 1980; Patton and Sherwood, 1983) is inaccurate. Clearly, some species of bats have experienced relatively rapid chromosomal evolution and some species of rodents have undergone a relatively conservative rate of chromosomal change. Any study designed to elucidate patterns of chromosomal evolution should be based on a more detailed examination of chromosomal evolution than is revealed by nondifferentially stained karyotypes.

3. NEGATIVE HETEROSIS AND ITS ROLE IN CHROMOSOMAL EVOLUTION

The idea that heterozygotes are less fit for certain rearrangements, known as negative heterosis in chromosomal evolution, has been well explored from a theoretical standpoint (Wright, 1941; Lande, 1979; Chesser and Baker, 1986). This aspect of heterozygosity for a chromosomal rearrangement potentially makes chromosomal evolution unique from neutral or adaptive genic evolution. If negative heterosis is significant, and the new rearrangement causes no selective advantage, then any individual heterozygous for a chromosomal rearrangement (assuming that new chromosomal mutations first appear in a population in a single individual in the heterozygous state) will be less fit than the homozygotes for the primitive chromosomal condition. The extent to

which the heterozygous individual is less fit will equal the magnitude of meiotic malassortment resulting in the production of unbalanced gametes.

From the literature, it is obvious that some chromosomal rearrangements do cause meiotic problems in the heterozygous condition (White, 1978). However, there is a growing body of evidence that some species have found means of reducing meiotic problems for some types of rearrangements. Individuals of Peter's tent-making bat, *Uroderma bilobatum*, heterozygous for three rearrangements (a centric fusion, a translocation of an acrocentric to the telomere of a small biarmed element, and a tandem fusion) were fertile and played a significant role in the production of the next generation (Baker, 1979, 1981; Baker and Bickham, 1980).

In a sample of ten specimens of rice rats (genus *Oryzomys*) collected from a natural population on an isolated mountain top in Suriname, Koop et al. (1983) found nine different centric fusion/fission polymorphisms (Fig. 1) and only two of the ten individuals were homozygous for all chromosomal fusions. Three of the remaining eight individuals were heterozygous for a single fusion, two were heterozygous for two fusions, one was heterozygous for four fusions, and two were heterozygous for five fusions. It is difficult to explain how an isolated population could maintain such extensive polymorphism if each fusion heterozygote experienced significantly reduced fitness. The most viable explanation to us is that heterozygosity for centric fusions in this species of *Oryzomys* causes little or no negative heterosis.

The extent and nature of this polymorphic system could not have been determined if only nondifferentially stained karyotypes had been available. Eleven specimens of *Oryzomys* were collected and karyotypic preparations were made under field conditions (tents and no electricity) in Suriname, with G- and C-band preparation done subsequently at Texas Tech as described by Baker et al. (1982). Of the 11 animals obtained, analyzable G- and C-banded karyotypes were prepared from ten individuals. The lack of data for one individual was the result of a cryotube exploding upon being removed from liquid nitrogen. Figure 1 documents that analyzable G-bands can be prepared under typical field conditions.

Another example where a group of organisms appear to be experiencing reduced negative heterosis is in the peromyscine rodents. In *Peromyscus* two types of rearrangements (pericentric inversions and heterochromatic additions or deletions) have become fixed in the 30 species that have thus far been examined (Stangl and Baker, 1984). Within mammals, it is generally accepted that there is little or no neg-

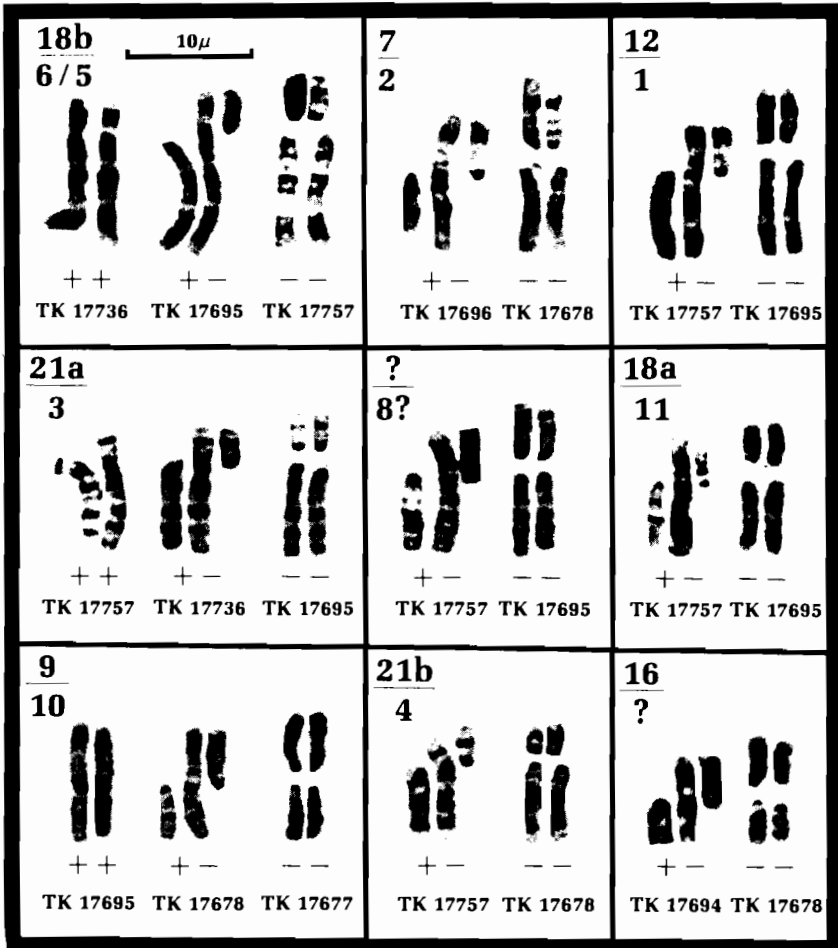


FIGURE 1. G-Banded chromosomes showing the nine polymorphic centric fusions/fissions observed in a population of *Oryzomys* (Koop et al., 1983). The numbering of the chromosomes refers to the proposed homology to those of *Peromyscus*; TK numbers are field numbers used to reference tissues and voucher specimens. (+) Fusion morph; (-) fission morph.

ative heterosis associated with the heterozygous condition for the presence or absence of heterochromatic short arms. However, for pericentric inversions the consensus is that most organisms incur an appreciable heterozygous disadvantage (White, 1978). Data from several sources suggest that pericentric inversions cause little or no heterozygous disadvantage in *Peromyscus*.

One such data set involves a G- and C-band study of a chromosomal hybrid zone in *P. leucopus* where three pericentric inversions distinguish the two parental races (Baker et al., 1983c; Stangl, 1986). An indirect evaluation of the magnitude of selection gradients, b , can be obtained from static cline models (Slatkin, 1973; May et al., 1975; Ender, 1977) as $b = l^2(1.66/w)^3$, where l is the gene flow parameter or estimate of average dispersal distance per year. The formula assumes homogeneous gene flow, large population size, and no dominance (Hafner, 1982). Dispersal distance l in *Peromyscus leucopus* averages 0.33 km/yr (Krohne et al., 1984). Results of a karyotypic study across this hybrid zone yielded an average zone width w of 30.6 km (Stangl, 1986). Thus, the intensity of selection b necessary to maintain the zone would be 1.7×10^{-5} km. Hence, little selection is necessary to maintain the zone, implying that there is essentially no negative heterosis associated with the three pericentric inversions. An extension of this observation is that the chromosomes are not functioning in a manner to facilitate speciation, or the zone would be much more narrow.

Another suggestion that meiotic problems associated with the presumed pericentric inversions in *Peromyscus* are minimal comes from the work on the synaptonemal complex by Ira Greenbaum and his students. Studies on individuals of *Peromyscus maniculatus* and *P. sitkensis* heterozygous for one or more pericentric inversions showed the pairing of the inverted region to be nonhomologous, and inversion loops were not formed (Greenbaum and Reed, 1984; Greenbaum et al., 1986). An analysis of diakinesis in these same species indicated that crossing over does not occur in the inverted regions (D. Hale, personal communication). This observation is important because if crossing over does not occur in the inverted chromosomal segments, then no unbalanced gametes are produced.

Frequencies of three pericentric inversion polymorphisms in populations of *Peromyscus boylii* from Mexico suggest little or no negative heterosis associated with these rearrangements. Davis et al. (1986) studied chromosomal morphs at a number of geographic localities and found that the frequencies did not vary significantly from those predicted by Hardy-Weinberg equilibrium. This finding is compatible with the hypothesis that pericentric inversions in *Peromyscus* cause little or no negative heterosis, because, if there was strong selection against the heterozygotes, one would predict that the frequencies would not be in Hardy-Weinberg equilibrium. At this point we might add a word of caution concerning the types of rearrangements found in *Peromyscus*. We are not convinced that it has been proven that the euchromatic rearrangements in peromyscine rodents are indeed pericentric inver-

sions and not centric transpositions. Regardless of which type of eu-chromatic rearrangements prove to be characteristic of these rodents, the following statements on karyotypic orthoselection are still applicable.

These studies indicate that several species of *Peromyscus* have undergone karyotypic orthoselection (repeated occurrence of a single specific type of rearrangement in a species; White, 1978) for pericentric inversions which cause little or no negative heterosis in *Peromyscus*. A hypothesis to explain these data is that other types of rearrangements that have not become fixed in 30 species of *Peromyscus* cause severe negative heterosis, but pericentric inversions have become fixed in *Peromyscus* because they cause little or no negative heterosis. An extension of this hypothesis is that groups that have experienced karyotypic orthoselection for a given chromosomal rearrangement have evolved mechanisms by which negative heterosis for that type of rearrangement has been reduced or eliminated. A critical test of this hypothesis would involve examining mammalian taxa that exhibit karyotypic orthoselection for other types of rearrangements, to see if these rearrangements are likewise tolerated in the heterozygous condition with minimal meiotic problems. In *Aethomys* (Baker et al., 1986) and *Muntiacus* (Brinkley et al., 1984), it is possible that negative heterosis for tandem fusions has been reduced.

Finally, in computer simulations of fixation of newly formed chromosomal mutants, rearrangements that were assigned 0 and 10% reduction in fertility were essentially equal in frequency of fixation, whereas those mutants causing a greater loss of fertility (25 and 50%) rarely became fixed for the new rearrangement (Chesser and Baker, 1986). These data suggest that at higher levels of negative heterosis (25–50% loss of fitness), there is considerable stabilizing selection to maintain the original karyotypic condition, but at lower levels of loss of fitness (10% or less) considerable chromosomal evolution may occur.

4. THE PROBLEM OF CONVERGENT CHROMOSOMAL EVOLUTION

A neutral hypothesis of random chromosomal breakage leading to a new rearrangement would predict that the probability of encountering convergent (independently derived) chromosomal rearrangements would be exceedingly low. If the fixation of chromosomal rearrangements within natural populations of mammals is governed by bottlenecks in small

populations, then the probability of fixing exactly the same rearrangement in independent lineages would be even further reduced.

Cladistic analyses of G-band data for a variety of mammalian taxa have documented that convergence of chromosomal rearrangement events is a significant feature in the evolution of some groups of mammals. Within many species of peromyscine rodents, chromosome 6 has undergone pericentric inversion repeatedly (Robbins and Baker, 1981; Rogers, 1983; Rogers et al., 1984; Stangl and Baker, 1984; Hood et al., 1984). In the 30 species of *Peromyscus* examined to date, chromosome 6 has been inverted at least seven times (Fig. 2) (Stangl and Baker, 1984). Pericentric inversions of this chromosome are also found in the related genera *Reithrodontomys* and *Neotoma*, and in several cases the rearrangement breakpoints were located in the exact same G-band of the chromosome (Hood et al., 1984; Koop et al., 1984).

One explanation for these observations is that there are specific sites on some chromosomes that are susceptible to breakage at a higher frequency than would be expected due to chance alone. Examples of nonrandom breakage are well-documented in the human cytogenetic literature. An extreme example involves a reciprocal translocation between segments at specific G-band locations of chromosomes 11 and 22 in the human karyotype found in unrelated families (Fraccaro et al., 1980).

The significance of repeated chromosomal mutations resulting in karyotypic convergence has the following cytogenetic and evolutionary implications. First, the accumulation of chromosomal rearrangements in these cases is not random, and may involve factors that affect the rate of specific chromosomal mutations (King, 1982; Shaw et al., 1983). Second, if intrinsic rates of chromosomal mutation have not been affected, then it seems unlikely that population bottlenecks represent the sole driving force for fixation of new chromosomal rearrangements in independent lineages. Finally, the extent to which convergence and reversal (homoplasy) of chromosomal conditions occur reduces the resolving power of G-band chromosomal data for systematic studies (Baker et al., 1983b).

5. CANALIZATION AND DEME SIZE MODELS AS EXPLANATIONS OF VARIATION IN RATES AND TYPES OF CHROMOSOMAL EVOLUTION

The canalization model of chromosomal evolution (Bickham and Baker, 1979, p. 78) makes the assumption that the karyotype "contrib-

utes significantly to the fitness of the individual." This model was based on comparative studies of G-banded chromosomes of assemblages of turtles and bats. The patterns of chromosomal variation in these taxa indicate that chromosomal evolution occurs more rapidly "immediately after a lineage breaks into a new adaptive zone." In bats, most karyotypic divergence occurred simultaneously with the morphological evolution that distinguishes the modern families. This was followed by a slower rate of chromosomal evolution when the morphological characteristics of recent genera and species evolved.

The predictions from this model are that chromosomal evolution is more rapid as a lineage breaks into an adaptive zone and that once an optimum karyotype has developed for a lineage the rate of chromosomal evolution slows down. Additionally, the model predicts that when a group initially breaks into an adaptive zone the chromosomal rearrangements incorporated into the various lineages within the group will be more severe (from a standpoint of breaking up linkage groups; Bickham, 1981) than after the group has occupied the adaptive zone for a considerable time. The model received considerable comment and debate (Futuyma and Mayer, 1980; Bickham, 1981; Capanna, 1982; Shields, 1982; Sites, 1983; Tegelstrom et al., 1983; King, 1985). The model is based on the hypothesis that the karyotype can be adaptive, yet this is a difficult point to prove. The only example from the literature on mammals that demonstrates a statistically significance between a chromosomal rearrangement and a positive selective advantage involves a balanced polymorphism in pocket gophers of the genus *Geomys* (Baker et al., 1983a).

The model does not describe all data from chromosomal studies (Baker and Bickham, 1980; Baker et al., 1983b). The predictions of the canalization model do not seem to apply in cases of karyotypic megaloevolution (Baker and Bickham, 1980; see Section 6) and in the chromosomal patterns observed in some muroid rodents (Baker et al., 1983b; Koop et al., 1984). Patterns of chromosomal evolution in rodents are sufficiently interesting to warrant further discussion here. In Fig. 3, we present the number of chromosomal rearrangements (in the 14 largest pairs of autosomes) that have accompanied the evolution of the morphological features on which 24 genera of muroid rodents are identified. The G-band data published for these genera were compared in an attempt to identify homologous sequences in the largest 14 autosomal pairs of the *Peromyscus* karyotype (Committee for Standardization of Chromosomes of *Peromyscus*, 1977). G-Bands of these genera were obtained from the following sources: *Peromyscus* (Stangl and Baker, 1984), *Onychomys* (Baker et al., 1979), *Baiomys* (Yates et al., 1979), *Reith-*

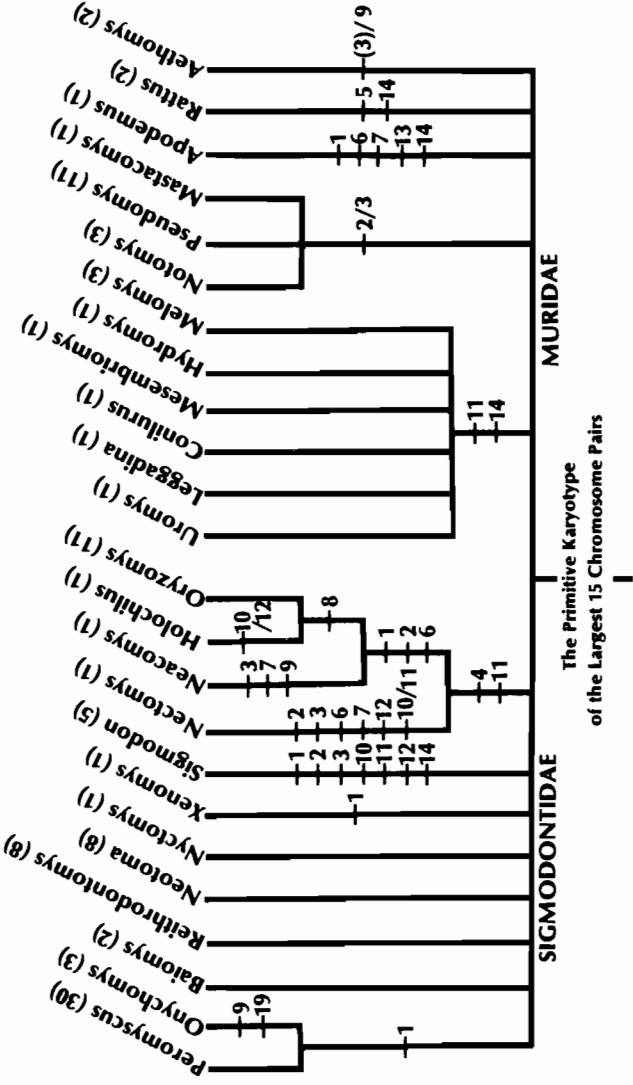


FIGURE 3. Cladistic relationships of the proposed primitive karyotypes for 24 genera of murid and sigmodontid rodents based on G-band analysis of the 14 largest autosomal pairs and the X chromosome. Numbers on branches refer to chromosomes that showed a derived character state (have undergone rearrangement) in the lineage indicated. Numbers after generic names indicate number of species examined in that genus.

rodontomys (Hood et al., 1984), *Neotoma* (Koop et al., 1985), *Nyctomys* and *Xenomys* (Haiduk et al., 1986), *Sigmodon* (Elder, 1980), *Holochilus*, *Neacomys*, *Nectomys*, and *Oryzomys* (Baker et al., 1983b), *Uromys*, *Leggadina*, *Conilurus*, *Mesembriomys*, *Hydromys*, *Notomys*, *Pseudomys*, *Mastacomys*, and *Melomys* (Baverstock et al., 1980, 1983), *Apodemus* (Koop et al., 1984), *Aethomys* (Baker et al., 1986), *Rattus* (Baverstock et al., 1982; and unpublished data from our laboratory).

Figure 3 shows the rearrangements in the largest 14 pairs of autosomes postulated to have occurred since genera diverged from the proposed primitive condition for the common ancestor of these genera and up to the establishment of the primitive karyotype of each genus. As can be seen from this figure, the proposed primitive condition for the 14 largest autosomes for the genus *Peromyscus* (Stangl and Baker, 1984) is divergent from that proposed as primitive for the *Sigmodontidae* by only one rearrangement, a biarmed chromosome 1, which is also shared with *Onychomys*. On the other hand, since the establishment of the primitive condition for *Peromyscus*, 43 pericentric inversions are postulated to have occurred in the 30 species thus far examined (Fig. 2) (Stangl and Baker, 1984). A similar pattern is observed in *Reithrodontomys*, *Neotoma*, and *Oryzomys*, where the primitive conditions for the 14 largest pairs were the same for a genus as they were for the family, yet considerable chromosomal variation was documented between species within a genus (for example, *Reithrodontomys*, Hood et al., 1984, and *Oryzomys*, Baker et al., 1983b). These patterns contradict the canalization model, which predicts that a greater amount of chromosomal rearrangement should have accompanied the establishment of muroid families and a lesser amount should have accompanied speciation within the various genera.

Several possible explanations for the muroid data are suggested. If muroids had large deme sizes earlier in their evolution, whereas modern species have smaller deme sizes (Lande, 1979), then these data are compatible with Wright's (1941) deme size model. This would imply that bats had small demes earlier in their evolution, whereas modern species are characterized by large demes. Alternatively, it could be that chromosomal evolution was slow or nonexistent earlier in muroid evolution and that subsequently chromosomal change accelerated, perhaps by an increased mutation rate. A third possibility is that there was an equal amount of chromosomal evolution through time, but the ancestors of modern genera were derived only from the chromosomally conservative species. The third explanation would suggest that the primitive karyotype may be valuable to a species in surviving a period of ex-

inction compared to other species that possessed more derived karyotypes.

It must be emphasized that these ideas are based on the examination of the 14 largest pairs of autosomes. Additional variation likely exists in smaller chromosomes or small rearrangements not detectable from the quality of G-bands available for study of muroid rodents. Recent investigations of the muroid family Gerbillidae (Qumsiyeh, 1986a, 1986b), in which all the euchromatic segments can be identified across genera, indicate numerous rearrangements characterizing the family, genera, and species and that the rate of chromosomal evolution was relatively constant through time.

Test of the canalization model primarily include correlating age with chromosomal diversity, and comparing chromosomal banding patterns among higher categories to determine inter- versus intra-higher category variation. If there is no correlation between age and chromosomal diversity within many groups, this would represent a falsification of the model and would mean that the canalization model is not of general applicability (Bickham and Baker, 1979, p. 82). Data sets for bats and turtles (Bickham, 1981) are best explained by this model, but the data from muroid rodents do not fit the predictions of the canalization model.

An alternative explanation of why there is variation in rates of chromosomal evolution among mammalian taxa is that chromosomal evolution occurs in small inbred demes (Wilson et al., 1975; Bush et al., 1977; Larson et al., 1984). Therefore, these models conclude that the magnitude of chromosomal evolution is a reflection of long-term effective deme size that has been characteristic of a species (Lande, 1979). For a number of reasons we conclude that for mammals this explanation is not compatible with the available data. In computer simulations of factors affecting the fixation of chromosomal rearrangements, Chesser and Baker (1986) using data from *Myotis lucifugus*, concluded that if the effective population size was in excess of 20, there was little probability of a new chromosomal rearrangement becoming fixed through genetic drift. Additionally, if the deme size becomes lower than 20, there is a high probability that the population will become extinct. Therefore, demes of such small sizes have a lower probability of becoming the progenitors of a species than do demes composed of larger numbers of individuals.

Data from mammals suggest that long-term effective population sizes are considerably larger than the values shown to be critical in these calculations (Chesser and Baker, 1986). Wilson et al. (1985, p.

390) calculated that long-term effective populational sizes for ten mammalian species ranged from 6,000 to 2,900,000. Although we are of the opinion that their values are too high, clearly their values are several orders of magnitude above the populational sizes needed to produce an accelerated rate of chromosomal evolution. This is especially critical in the case of *Peromyscus maniculatus*, for which they calculate a long-term effective population size of 2,900,000 yet, chromosomally, *P. maniculatus* may well be the most actively evolving species in the genus *Peromyscus* (Stangl and Baker, 1984; Rogers et al., 1984).

In addition to an initial small deme size, genetic drift can be generated by inbreeding. However, Ralls et al., (1986) indicate that studies on natural populations of mammals fail to document the kind of inbreeding that would be required to fix chromosomal rearrangements, and Chesser and Ryman (1986) show that from a theoretical standpoint substantial dispersal among demes is required to avoid inbreeding depression. Even minimal dispersal among demes would negate the likelihood of fixation of chromosomal rearrangements.

If deme size is the most critical factor regulating the rate of fixation of chromosomal rearrangements (this would mean that mutation rate and magnitude of negative heterosis for a given type of chromosomal rearrangement is relatively constant), then rearrangements that cause the most severe negative heterosis would be expected to occur less frequently than rearrangements that cause little or no negative heterosis. Additionally, rearrangements that cause severe negative heterosis would be expected to occur as isolated events or if they occurred as clusters on branches of cladograms then the rearrangements that cause severe negative heterosis would be expected on the same branches of the cladogram to be outnumbered by rearrangements that cause little or no negative heterosis. However, the pattern that we observe in different groups of mammals is often an extension of White's (1978) karyotypic orthoselection. For example, *Mus* has undergone many centric fusions whereas peromyscine rodents have undergone many pericentric inversions (or centric transpositions) and no centric fusions. Another point to consider is the distribution of tandem fusions which are thought to cause severe negative heterosis. Tandem fusions rarely become fixed in mammalian populations, yet in several species of mammals, tandem fusions have become fixed almost to the exclusion of other types of rearrangements, for example in *Sigmodon* (Elder, 1980), *Muntiacus* (Shi et al., 1980), and *Aethomys* (Baker et al., 1986). It is difficult to explain such variations by simple manipulation of deme size to produce genetic drift. Clearly in these examples the most significant factors regulating the types of chromosomal rearrangements being incorporated must in-

volve either variations in the rates of mutation for a given type of chromosomal rearrangement and/or variation in the magnitude of negative heterosis associated with a given type of chromosomal rearrangement.

We hypothesize that, species that have the fastest rate of chromosomal evolution are those that have: (1) evolved means of reducing negative heterosis (this would include but not be restricted to genetic or phenotypic benefits associated with a rearrangement that partially compensated for or even outweighed the negative heterosis associated with the rearrangement, Baker et al., 1983), for rearrangements that become fixed, and/or (2) experienced a greater mutation rate.

We think that this explanation is more compatible with the variations we see in rates (especially as related to different types of chromosomal rearrangement) of incorporation observed from recent studies based on cladistical analysis of G-banded chromosomes of various mammalian taxa as well as with data from studies on deme size and inbreeding in natural populations (Ralls et al., 1986).

6. KARYOTYPIC MEGAEVOLUTION

The phenomenon of karyotypic megaevolution was described by Baker and Bickham (1980) based on phylogenetic analysis of G-band patterns for 78 species of bats. Viewed in a cladistic framework, magnitude, type, and pattern of chromosomal change can be apportioned within and among taxa. For many lineages, G-band linkage groups are conserved among closely related taxa and chromosomal variation is limited to a few well-defined rearrangement events. However, Baker and Bickham (1980) documented examples of chromosomal change within lineages of closely related taxa (phyllostomid bats and a wide variety of other vertebrates) that present a fundamentally different pattern. There are cases where, within a lineage of closely related taxa, one taxon has undergone little or no chromosomal evolution, while a sister taxon has a G-band karyotype that has been radically reorganized. These taxa are considered karyotypically megaevolved.

In all examples of karyotypic megaevolution described to date (see also Baverstock et al., 1983), the following observations hold: (1) karyotypically megaevolved taxa have undergone extensive euchromatic rearrangement such that the G-band patterns of many, if not all, euchromatic arms have been altered (Baker and Bickham, 1984, referred to those arms as euchromatic linkage groups, but they should be referred to as G-band-defined arms); (2) little morphological and/or, in some

cases, little genic divergence (as measured by starch gel electrophoresis; Nelson et al., 1984) has accompanied the extensive chromosomal divergence; (3) many different types of rearrangements are involved; and (4) these rearrangements include many that would be predicted to cause severe negative heterosis in the heterozygote (White, 1978) and therefore should rarely become fixed in natural populations.

The disparity in the amounts of morphological and genic change on the one hand and extensive chromosomal change on the other imply relatively rapid karyotypic divergence. Compared with the small amount of chromosomal variation that typically characterizes closely related mammalian taxa, this observation is striking.

Karyotypic megaevolution is not simply a fast rate of chromosomal evolution (Marks, 1983; Baker and Bickham, 1984). In a wide variety of mammalian examples, including *Mus* (Capanna et al., 1977; Capanna, 1982; Bickham and Baker, 1980), *Onychomys* (Baker et al., 1979; Baker and Barnett, 1981), *Sigmodon* (Elder, 1980), primates (Rumpler et al., 1983), and horses (Ryder et al., 1978), there is a rapid rate of chromosomal evolution. In many of these cases extensive chromosomal change occurred predominately through accumulation of a single type of rearrangement (for example, heterochromatic short-arm additions in *Onychomys* and centric fusions in *Mus*) that does not alter the internal structure of the euchromatic segments. Furthermore, in these examples of rapid chromosomal evolution, the types of rearrangements involved could occur in the heterozygous condition without causing severe negative heterosis. These patterns of chromosomal variation represent examples of karyotypic orthoselection (White, 1975).

We recently discovered an interesting example of an accelerated rate of chromosomal evolution in two species of the murid genus *Aethomys*. One species, *Aethomys chrysophilus* ($2n = 44$), has retained a karyotype that is very similar to that proposed as primitive for the family Muridae, whereas the other, *A. namaquensis* ($2n = 24$), has undergone eight tandem and five centric fusions. *Aethomys namaquensis* apparently has undergone karyotypic orthoselection for both tandem and centric fusions. This example possesses some characteristics of karyotypic megaevolution, such as a large number of rearrangements (tandem fusions) that would be predicted to encounter problems of negative heterosis have accumulated in one taxon, associated with little morphological evolution that distinguishes it from its congener. Nonetheless, *A. namaquensis* has not undergone as many chromosomal rearrangements as is generally characteristic of karyotypic megaevolution. Further study of examples such as that presented

by *A. namaquensis* could contribute significantly to understanding the nature of accelerated rates of chromosomal evolution.

The pattern of karyotypic megaevolution has involved some cytogenetic mechanism that has allowed rapid and extensive repatterning of the euchromatic genome. Baker and Bickham (1980, 1984) suggested that karyotypically megaevolved species may have encountered one or more of the following: (1) periods of transposition activity (McClintock, 1978), (2) reduced meiotic constraints, and/or (3) radical changes in nuclear or cellular factors that normally stabilize chromosomal evolution (Bennett, 1982). Karyotypic megaevolution remains a phenomenon that is not easily explained by current theories of chromosomal evolution.

7. SYSTEMATIC VALUE OF G-BAND STUDIES

Identifying chromosomes by G-banding was first developed for studies of human chromosomes in the early 1970s. Since then, the use of G-banding has mushroomed for studies of higher vertebrates. G-Band sequences can be compared between species and even between higher taxonomic categories (Fig. 4) (Mascarello et al., 1974; Qumsiyeh and Baker, 1985; Sawyer and Hozier, 1986), and chromosomal rearrangement differences between taxa can be more accurately identified by these methods than by simple nondifferential-staining techniques.

Data from G-bands lend themselves to phylogenetic analysis by cladistic methods (Baker, 1979; Baker et al., 1983b). Variation in G-band patterns in different taxa can be treated as character states and the identification of primitive character states allows determination of kinds and number of rearrangements incorporated during the course of evolution. Character states that are derived (apomorphies) can be used to identify subsets of taxa as monophyletic. The resulting cladogram represents a hypothesis of phylogenetic relationship that tests previous hypotheses based on other data sets (for example, morphology, protein electrophoresis, immunology, or DNA analysis). Data from G-bands represent an independent data set for testing systematic relationships of taxa that have been traditionally grouped together on the basis of highly specialized morphological adaptations. Examples include studies of the nectar-feeding bats (Haiduk and Baker, 1982, 1984; Haiduk, 1983). Recently, data from G-bands have proved useful in identifying cryptic species of mammals (Capanna, 1982; Baker, 1984; Baker et al., 1985; Baker and Bickham, 1986).

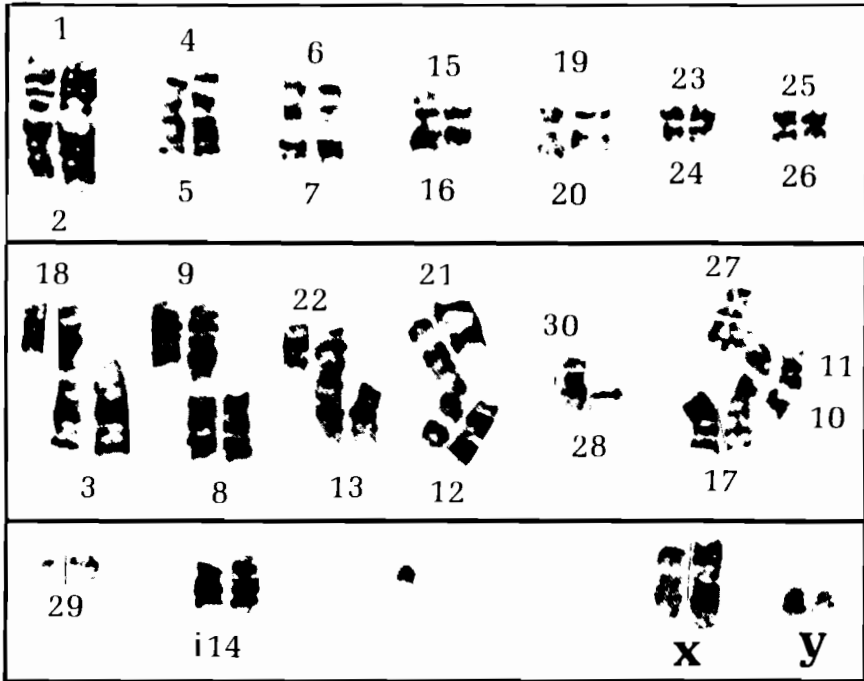


FIGURE 4. Comparison of G-banded haploid complements of the phyllostomid bats *Macrotus waterhousii* (Phyllostominae) and *Rhinophylla fisheae* (Carollinae). Chromosomes in the top panel are completely homologous; those in the middle have undergone Robertsonian changes; and the bottom panel illustrates the sex chromosomes and autosomal elements. In all comparisons, the chromosome on the right (or center) is from *Macrotus*; those to the left (or left and right) are from *Rhinophylla*. Numbering system is that based on *Macrotus* (Patton and Baker, 1978).

Two problems that are not unique to G-bands arise in using these data for systematic studies. Chromosomal rearrangement characters are subject to reversals and convergence (see Section 4), and thus we are forced to choose the most parsimonious (least homoplastic) explanation of character change in the absence of additional data. A second problem is the fact that in many taxa, conservatism is the rule, and thus, shared primitive chromosomal conditions (symplesiomorphies) provide little resolution of relationships. An example of this conservatism was discussed for the muroid rodent genera. Other examples include some genera of vespertilionid bats (Bickham, 1979a).

In mammals, a multitude of G-band studies have been conducted to understand relationships of subspecies, species, genera, and even

families. We will not attempt here to review all the literature in this area, but provide some examples of the utilization of G-banding for systematic studies in groups of mammals.

Order Marsupialia (Rofe and Hayman, 1985).

Order Insectivora (Searle, 1984).

Order Chiroptera. Family Pteropodidae (Haiduk et al., 1981; Haiduk, 1983), Rhinopomatidae (Qumsiyeh and Baker, 1985), Emballonuridae (Hood and Baker, 1986), Noctilionidae (Patton and Baker, 1978; Baker and Bickham, 1980), Phyllostomidae (Patton and Baker, 1978; Baker, 1979; Baker and Bass, 1979; Baker et al., 1982), Mormoopidae (Patton and Baker, 1978; Sites, et al., 1981), Vespertilionidae (Bickham, 1979a, 1979b; Baker et al., 1985).

Order Primates (Rumpler et al., 1983; Dutrillaux et al., 1981; Yunis and Prakash, 1982; Viegas-Pequignot et al., 1985).

Order Lagomorpha (Robinson et al., 1983, 1984).

Order Rodentia. Sigmodontidae (Mascarello et al., 1974; Mascarello and Hsu, 1976; Greenbaum and Baker, 1978; Bianchi et al., 1976; Rogers, 1983; Rogers et al., 1984; Stangl and Baker, 1984; Modi and Lee, 1985), Muridae (Baverstock et al., 1980, 1983), Gerbillidae (Qumsiyeh, 1986a, 1986b), Arvicolidae (Modi, 1986).

Order Carnivora (Wurster-Hill and Centerwall, 1982; Wurster-Hill and Bush, 1980).

Order Cetacea (Arnason, 1974).

8. C-BANDS AND GENETIC HOMOLOGY

Another banding technique produces bands referred to as C-bands, which indicate the presence of constitutive heterochromatin. This technique is distinctly different from those that produce a banding pattern throughout the entire karyotype. C-Bands are thought to appear where the sequence of nucleotides in the DNA is highly repetitive (often referred to as heterochromatin or satellite DNA, although the two terms are not exactly synonyms). Basically, the technique involves treatment of the chromosomes to preferentially extract non-C-band chromatin (Pathak, 1976). It is not well understood why the C-band positive regions remain unaltered while the euchromatic regions are extensively changed. It is clear that the C-band positive areas represent clusters of highly repetitive DNA sequences. Even though highly repetitive DNA would reassociate more rapidly than areas of single copy DNA, this simplistic mechanism has not been supported by other studies. This treatment is valuable to the study of chromosomal evolution because

it distinguishes the highly repetitive regions of the chromosome from the region of the chromosome containing single-copy genes. Further, regions of highly repetitive DNA are thought to occur in the heterozygous condition with little or no negative heterosis.

Highly repetitive DNA varies quantitatively in mammalian genomes from approximately 50% to as little as 5% (Hsu and Arrighi, 1971; Miklos et al., 1980; Patton and Sherwood, 1982; Sherwood and Patton, 1982). The presence of blocks of heterochromatin does not necessarily indicate genetic homology, because several different highly repetitive DNA sequences may exist within uniformly C-banded chromosomal segments (John and Miklos, 1979). It is likely that all mammalian chromosomes have some C-band material associated with the centromere. C-Band material and/or highly repetitive DNA sequences have been suggested as important in a wide array of biological features, such as successful pairing of homologues, mutation rates, recombination rates, cell metabolism, and gene expression and speciation (John and Miklos, 1979; Brutlag, 1980; Singer, 1982).

9. SUMMARY AND CONCLUSIONS

1. There is a huge gap between theoretical considerations of chromosomal evolution and the available empirical data to test such theories.

2. G-Band variation provides a measure of genetic homology and allows for an assessment of type and magnitude of chromosomal variation in mammalian groups.

3. From a technical standpoint, it is now possible to prepare specimens for G- and C-banding as well as for a variety of other techniques under field conditions with adequate sample sizes to conduct evolutionary studies (Baker et al., 1982, 1983b,c). High-resolution G-bands (Yunis, 1980, 1981; Yunis and Prakash, 1982) and localization of DNA sequences within individual bands (in situ hybridization; Harper et al., 1981; Harper and Sanders, 1981) have been developed for humans and a few other mammalian taxa. These techniques promise to provide a precise measure of homology, and consequently of chromosomal change.

4. Nondifferentially stained karyotypes are undependable indicators of the magnitude of chromosomal evolution. To elucidate patterns of chromosomal evolution, studies should be designed to include more detailed examination than is revealed by nondifferentially stained karyotypes and should account for in-group variation in rates of evolution.

5. Data from several studies on mammalian chromosomes support the conclusion that "the negative heterosis assumption is an overstatement and leads one to question how important negative heterosis is in rearrangements which are successfully incorporated during chromosomal evolution" (Baker, 1981, p. 303). A possible explanation for some karyotypic orthoselection (White, 1978) is that negative heterosis for that particular type of rearrangement has been avoided.

6. Convergent evolution of chromosomal rearrangements appears to be a problem, at least with the level of G-bands available to workers doing comparative studies.

7. The canalization model is a testable hypothesis of chromosomal evolution that needs further empirical tests. The model explains patterns of chromosomal evolution in some groups, such as bats and turtles, but data from other groups, such as muroid rodents, do not fit the predictions of the model.

8. Models concerned with rate of fixation of chromosomal rearrangements that are based on variation in long-term effective population size have not been tested by empirical studies on natural populations. Such models do not appear to predict the observed patterns resulting from cladistical analyses of G-banded chromosomes.

9. Some species of mammals have undergone extensive reorganization of their euchromatic genome compared to closely related species. This phenomenon of karyotypic megaevolution, which may occur more widely among mammals than is currently documented, remains unexplained by current theories of chromosomal evolution.

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