Social structuring of mammalian populations and rate of chromosomal evolution
(fossil record/inbreeding/speciation/vertebrates/molluscs)

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ABSTRACT To test the hypothesis that the evolution of organisms is dependent to a large degree on gene rearrangement, we devised a way of estimating rates of evolutionary change in karyotype. This non-biochemical method is based on consideration of chromosomal variability within taxonomic groups having a fossil record. The results show that chromosomal evolution has been faster in placental mammals than in other vertebrates or molluscs. This finding is consistent with published evidence that placentals have also been evolving unusually fast in anatomy and way of life. However, the structural genes of placentals seem not to have experienced accelerated evolution. Possibly, therefore, anatomical evolution may be facilitated by gene rearrangement.

To explain how placentals achieved this high rate of chromosomal evolution, we consider the process by which a new gene arrangement becomes fixed and spreads. The structure and dynamics of placental populations may be especially favorable for this process. The key factor involved seems to be the type of social behavior which was essential for producing small effective population sizes and inbreeding. As Bush points out elsewhere, such social structuring of populations may promote rapid fixation of gene rearrangements and rapid speciation.

To elucidate the genetic basis of evolutionary change at the organismal level, it is valuable to measure evolutionary rates. Any type of genetic change whose evolutionary rate correlates with rate of organismal evolution could be at the basis of organismal evolution. The vertebrates provide an opportunity to search for such correlations because some vertebrate lineages have experienced faster rates of evolutionary change in anatomy and way of life than others. The classic studies of comparative anatomists and paleontologists established that the lineage leading to mammals passed successively through the following organismal stages:

Fish → Amphibian → Reptile → Mammal.

It is also well known that the tempo of anatomical evolution has been greater in the lineages leading to placental mammals than in those lineages leading from ancestral fishes to modern fishes, ancestral amphibians to modern amphibians, or ancestral reptiles to modern reptiles (1–3). Hence any type of genetic change that occurs rapidly in placentals but slowly in other vertebrates could be at the basis of organismal evolution.

Gene rearrangement could be such a process. This possibility arises from studies of rates of evolutionary change in the number of chromosomes and in the number of chromosomal arms per genome. Changes in chromosome number usually result from fission or fusion events, whereas changes in arm number are attributable to inversions (Fig. 1) or to gain or loss of heterochromatin. Such karyotypic changes may be regarded as crude manifestations of the phenomenon of gene rearrangement.

A previous study showed that frogs, an anatomically conservative group, appeared to have been undergoing slower karyotypic evolution than mammals (4). However, this inference was based on the use of albumin as a device for estimating the time of divergence of the species pairs whose chromosomes were compared. Because the utility of proteins as evolutionary dating devices (5) is not yet widely accepted, we have devised another way of estimating rates of evolutionary change in karyotype. With this non-biochemical method we have estimated the average rates of karyotypic evolution not only for placentals and frogs but also for several other major groups of vertebrates and molluscs. A more detailed presentation is intended for publication elsewhere.

METHODS AND RESULTS

Anatomical Resemblance and Karyotypic Resemblance. The first step in our analysis was to test the hypothesis that morphological change is correlated with karyotypic change. As the measure of morphological difference between organisms, we used their degree of taxonomic difference. The taxonomic categories of species, genus, family, order, and class are based mainly on studies of anatomical resemblance. Thus organisms classified in different families, for instance, are usually more different in anatomy than those in the same family, genus, or species. So, we asked whether the probability that two organisms will differ in karyotype is related to their degree of taxonomic difference.

The karyotype data used in this calculation came only from vertebrate species for which both chromosome number and arm number have been reported. Most of the data we used are given in recent karyotypic reviews (6, 7). A further restriction was that these species should belong to genera known to occur as fossils, according to Romer (2). The sample included 1230 species, belonging to 201 genera, 45 families, 19 orders, and 4 classes.

For each taxonomic category, we estimated the proportion of included taxa that were heterogeneous with respect to either chromosome number or arm number. As shown in Fig. 2, most individuals examined within a species, defined morphologically, have the same chromosome number and arm number. But species within a genus often differ from

* We use the term placental mammals or placentals as a synonym for eutherians, i.e., living mammals other than marsupials and monotremes.

1 A difficulty arises with the species category because biologists today strive to define species in terms of gene flow rather than morphology. Although we are firm believers in the utility of biological species concept, it was essential for this analysis of the relationship between gene rearrangement and anatomical change to use the old morphological definition of species.
Fig. 1. Schematic diagram illustrating how dissociation and fusion events can change the number of chromosomes (left) and how inversions can change the number of arms in a chromosome (right). As shown on the left, two chromosomes, each with one arm, may fuse to produce a single chromosome with two arms (this process probably occurs by "whole arm transfer"). The reverse process, dissociation, may also occur. Fusion and dissociation affect the number of chromosomes but not the number of arms. As shown on the right, inversion may convert a two-armed chromosome into a one-armed chromosome and vice versa. Such changes in arm number do not change the number of chromosomes. The addition or loss of heterochromatin can also cause changes in arm number.

one another karyotypically. Furthermore, species belonging to different families or orders almost always differ in karyotype. Thus, karyotypic evolution seems to be correlated with morphological evolution.

Independence of Karyotypic Evolution and Time. However, there is little or no dependence of karyotypic evolution on elapsed time. This was shown by considering karyotypic variability among species within a genus, thereby restricting attention to species that have diverged only to a small extent in morphology. By analyzing intragenic variation we could estimate the number of changes in arm number or chromosome number that have occurred along a typical lineage leading to a species within that genus. This quantity, $m$, is given by Eq. 1.

$$m = (k - 1)/n$$

where $n$ is the number of species examined per genus and $k$ is the number of different karyotypes per genus. This equation is based on the assumption that the number of evolutionary changes in karyotype since the origin of the genus is $k - 1$. This is a reasonable assumption only when $k$ is much less than $n$; as $k$ approaches $n$, $m$ will seriously underestimate the number of karyotypic changes per lineage.

We next considered $t$, the time of first recorded occurrence of each genus in the fossil record. For each major group of vertebrates (placental, marsupial, reptile, amphibian, and fish), we plotted $m$ for each genus against $t$ for that genus. In no case was a significant correlation coefficient observed. The average correlation coefficient was $-0.06$ while the average slope was $-0.001$. In other words, an old genus is no more variable karyotypically than a young one. The implication here is that in those old lineages which have undergone little morphological change, karyotypic evolution has also been slow.

The result contrasts with the result of studies on structural gene evolution, which is strongly dependent on elapsed time (5), and has not been convincingly related to morphological evolution (8–12). The strong time-dependence accounts for the observation that species belonging to an ancient genus of frogs, for instance, can differ greatly at the structural gene level although they are extremely alike in anatomy and way of life (11, 13, 14) as well as in karyotype (4).

Rates of Chromosomal Evolution. The next step was to estimate the average rate of karyotypic evolution for various groups of vertebrates. This rate ($r$) represents the number of karyotypic changes per lineage per 100 million years:

$$r = (100) \left( \frac{\sum_{i=1}^{N} (k_i - 1)/n_i}{\sum_{i=1}^{N} t_i} \right)$$

In effect, we computed the average number of karyotypic changes per lineage for each group (containing N genera) and divided it by the average age of the genera in the group. The results are shown in Table 1.

Karyotypic evolution has proceeded more rapidly in placental than in other vertebrates by a factor of at least 5. This is evident from both the chromosome number and arm number estimates in Table 1. The average rate of change in arm number (calculated as changes per lineage per 100 million years) has been 5 for placental and about 1 for other vertebrates. Likewise, for chromosome number, the value is 4 for placental and 0.6 for other vertebrates. Each of these differences is statistically significant at the 0.01 level; the $r$ values for eight groups of placental were compared by the "sum of squares-simultaneous procedure" (15) to the $r$ values for the seven groups of other vertebrates.

A similar calculation was done for the chromosome numbers of molluscs (16) as indicated in Table 1. In accordance with their very low rates of organismal evolution (1, 19),

Another method of calculating $r$ is to divide the $(k - 1)/n$ value for each genus by $t$ for that genus and then to average the $(k - 1)/n$ values. However, $t$ values always underestimate the true age of a genus. Furthermore, small $t$ values are likely to underestimate grossly the true age of a genus, whereas large $t$ values probably have small errors. The alternate method weights genera with low $t$ values more heavily than genera with high $t$ values in calculating $r$, whereas Eq. 2 gives more weight to genera with large $t$ values. For this reason, we prefer Eq. 2 for estimating $r$. In practice, the alternate method gives $r$ values that are about 6-fold higher than those given in Table 1. Nevertheless the results of the two methods are highly correlated; in particular both show that placental mammals have experienced faster karyotypic evolution than other vertebrates.
molluscs exhibit very low rates of evolutionary change in chromosome number.

**Comparison of Biochemical and Fossil Methods.** Although the fossil-based method used above is subject to large errors, it gives estimates of evolutionary rates that agree approximately with estimates made by the molecular evolutionary clock approach. According to both methods, as shown in Table 2, the rates of karyotypic evolution for placentals are much higher than those for frogs.

**Rate Variation Within Placental Mammals.** The rate of karyotypic evolution is not uniformly high among placentals. As shown in Table 1, primates and rodents have experienced faster karyotypic evolution than bats or whales. This is a clue that mobility (or vagility) is an important factor in karyotypic evolution. Since mobility is correlated with body size in nonflying mammals (20), we analyzed the data statistically to see if karyotypic variability was size dependent. We divided nonflying placentals into large, medium, and small genera on the basis of published lengths (from snout to vent) and into slow, medium, and rapidly evolving genera, on the basis of karyotypic variability. The G test showed a very significant relationship ($P < 0.005$): the bigger the animal, the slower its karyotypic evolution.

**DISCUSSION**

To explain the extraordinarily high rate of chromosomal evolution in placentals we consider two possibilities. One is that the rate of chromosomal mutation is unusually high in these animals. This possibility seems unlikely, since chromosome structure and composition are similar in all vertebrates examined (6, 21, 22). The second possibility involves population structure. Placental populations may be structured in such a way that chromosomal mutations have a better chance of surviving, becoming fixed, and spreading than is the case for other vertebrates.

**The Problem of Fixing New Gene Arrangements.** A newly arisen chromosomal mutation is initially present in the heterozygous state in a diploid individual. During meiosis in this individual, problems of chromosome pairing often occur (21). For this reason, the heterozygote frequently has reduced fecundity. The conditions under which such a chromosomal mutation can become fixed are severely limited. It is extremely unlikely that such a mutation will become fixed in a large outbreeding population. The gene rearrangement must occur, but not necessarily arise, in a small population of 10 or less breeding individuals who remain isolated reproductively from other members of the species long enough for the rearrangement to become fixed in the homzygous condition through inbreeding (23). A minimum of two generations would be required. Furthermore, the rearrangement must be of a type that does not reduce viability of the heterozygote and, if it is to spread, must confer some advantage to the homzygote.

**Social Structuring of Mammalian Populations.** Following Bush’s suggestion (24), we propose that placentals have achieved the requisite inbreeding and small population size by the social structure of their populations. Social behavior and other factors divide a typical species into many populations, referred to here as social units. The number of breeding individuals in a social unit is often 10 or less (25–27).

The social patterns of mammals originated evolutionarily from the social bonds existing between mother and offspring during lactation (27). These bonds are especially strong and persistent in most placentals. Even species which are classified as solitary possess strong social bonds between mother and offspring as well as among siblings, which tend to disperse within the close vicinity of the mother. These bonds greatly enhance the probability of inbreeding. Other features of placentals which would also enhance inbreeding and small effective population size are the prevalence of polygamy and the existence of dominance hierarchies among males. As a result, few of the males contribute genetically to the next generation (28).

Polygamy is rare in other vertebrates, which are usually solitary without maternal care or, as is usually the case in birds, monogamous (27). In general, vertebrates other than placentals do not organize their populations into small, persistent, social cohesive units.

**Mobility and Body Size.** High mobility limits the ability of a species to establish small isolated populations (24). This fact is reflected in our finding that the rate of chromosomal evolution is much slower in larger mammals which have much larger home ranges than small ones. Bats have also experienced unusually slow karyotypic evolution relative to placental mammals of similar body size. This is consistent with their high mobility.

Home range and body size are also highly correlated in reptiles (29), yet reptiles of a given body size have experienced far slower rates of evolutionary change than have placentals of comparable body size. The difference lies in the

| Table 1. Rate of karyotypic evolution in polytypic genera of vertebrates and molluscs |
|---------------------------------|-----------------|-----------------|
| Group                          | No. of genera examined | Average age of genera* | Karyotypic changes per lineage per 10⁴ years |
| Placental mammals               | Arm no. | Chromosome no. |
| Rodents                        | 42      | 4.6             | 9.6 | 8.2 |
| Primates                       | 12      | 4.4             | 7.1 | 7.1 |
| Rabbits                        | 3       | 9.0             | 7.6 | 5.2 |
| Ungulates                      | 14      | 4.3             | 4.3 | 7.2 |
| Insectivores and edentates      | 8       | 11.0            | 4.4 | 2.1 |
| Carnivores                     | 11      | 11.6            | 3.1 | 1.4 |
| Bats                           | 17      | 10.7            | 2.1 | 1.2 |
| Whales                         | 3       | 6.3             | 1.7 | 0   |
| Average                        |         | 7.7             | 5.0 | 4.1 |
| Other vertebrates              |         |                 |     |     |
| Marsupials                     | 8       | 1.9             | 1.3 | 0   |
| Snakes                         | 12      | 12.4            | 2.1 | 0.3 |
| Lizards                        | 15      | 23.0            | 1.3 | 1.1 |
| Turtles and crocodiles         | 13      | 51.0            | 0.15| 0.06|
| Frogs                          | 12      | 16.7            | 0.8 | 1.0 |
| Salamanders                    | 9       | 21.5            | 0.3 | 0.3 |
| Teleost fishes                 | 23      | 18.8            | 1.5 | 1.1 |
| Average                        |         | 20.6            | 1.1 | 0.6 |
| Molluscs                       |         |                 |     |     |
| Prosobranch snails             | 16      | 64.7            | —   | 0.3 |
| Other snails                   | 15      | 49.0            | —   | 0.4 |
| Bivalves                       | 3       | 77.0            | —   | 0.1 |
| Average                        |         | 64.0            | —   | 0.3 |

* Average time of first recorded appearance (from refs. 2, 17, and 18) in millions of years.
Table 2. Comparison of biochemical and fossil methods of estimating rate of karyotypic evolution

<table>
<thead>
<tr>
<th>Method and taxonomic group</th>
<th>No. of species examined</th>
<th>Chromosome no.</th>
<th>Arm no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placental s*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biochemical</td>
<td>93</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Fossil</td>
<td>606</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Frogs†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biochemical</td>
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<td>0.4</td>
</tr>
<tr>
<td>Fossil</td>
<td>194</td>
<td>1.0</td>
<td>0.8</td>
</tr>
</tbody>
</table>

*Biochemical estimates (4) of rates of karyotypic evolution in placentals are higher than estimates based on the fossil record. This is expected because $(k - 1)/n$ is a minimum estimate of the number of karyotypic changes in genera with high rates of karyotypic evolution; so, $r$ values based on Eq. 2 underestimate the rates of karyotypic evolution in most groups of placental species, especially rodents.

†The paleontological estimates of the rate of karyotypic evolution in frogs, however, are higher than the biochemical ones (4). This is probably because the frog fossil record is poorly known. Only 10% of the living genera of frogs are known as fossils, whereas for living genera of placentals the corresponding figure is 48%. When the frog fossil record is better known, the $r$ values for frog genera will increase and, consequently, the estimates of $r$ made by use of Eq. 2 will fall. The discrepancies between the biochemical and paleontological method of measuring $r$ are therefore understandable.

degree of socialization and how the social behavior affects the potential for inbreeding and the effective population size.

If it were not for their social behavior, large mobile mammals would be expected to exhibit very low rates of karyotypic evolution, far slower than those of reptiles. Horses (Equus) exemplify how social behavior can override mobility effects and lead to extensive karyotypic evolution. Their chromosome numbers range in a step-wise cline from 2n = 32 in E. zebra of southwestern Africa to 2n = 66 in the Eurasian E. przewalskii (6, 21, 30). Most species are subdivided into coherent family groups with a large home range (3–200 km²). Each group consists of a stallion, several mares (which remain with the group their entire lives), and their young (31). The young leave the family at 2–4 years of age to join a bachelor group or in the case of females to join or form a new family group. When an adult family member dies it is replaced by a younger individual from either the same or a neighboring group.

Inbreeding sufficient to fix new chromosome rearrangements can occur rapidly in two ways in these animals. In situations where a family group becomes isolated temporarily (2–3 generations) from the main population (e.g., in a valley or at the periphery of the range) replacement would be from close relatives and inbreeding would occur. Even in open field situations tight family groups may move together in clans of related individuals. Such groupings have been noted throughout the placental mammals (27).

Speciation. The fixation of a new gene arrangement in a social unit may produce a population which is reproductively isolated from the parental species. Any hybrids formed between the parental species and the mutant social unit will be heterozygous for the rearrangement and will frequently exhibit reduced reproductive capacity. In effect, the mutant

![FIG. 3. Modes of speciation, based on Bush (24). Type Ia is the classic model of geographic speciation. Type Ib is the founder effect. Types Ia and Ib are probably of major importance in speciation of nonmammalian vertebrates. Type II is the stasispatric model (21) and has probably been the major mode of speciation in placental mammals.](image)

social unit is a new species. Provided the rearrangement produced an advantageous pattern of gene expression, the new species may be able to displace the parental species over part or all of its range or expand into a new adaptive zone. Thus the fixation of a new gene arrangement is frequently a speciation event.

We propose that there are two major types (I and II) of speciation in vertebrates (see Fig. 3). For vertebrates other than placentals speciation usually occurs by geographic isolation (type I). Two types of geographic isolation (Ia and Ib) are shown in Fig. 3 and in both speciation is very slow. Speciation of type Ia is the inevitable outcome of small divergent adaptive genetic changes that accumulate slowly in large populations isolated by some geographic barrier. Gene rearrangements with reduced fitness in the heterozygote have essentially no chance of spreading in such populations.

In this case we suppose that mutations in regulatory genes account for the slow adaptive changes in anatomy and way of life. Speciation by the founder principle (type Ib) involves the geographic isolation of a small population on the fringe of the species range (Fig. 3). Fixation of an advantageous gene rearrangement is possible in such a population if present among the founders. When the geographic barrier disappears, perhaps after a very long time, the mutant population can spread and displace the parental species over part or all of its range. We expect chromosomal evolution in animals of this type (Ib) to be slower than in animals with socially structured populations.

For placental mammals we propose that speciation occurs in social units which generally persist for only a few generations. This type of speciation (type II, Fig. 3) is necessarily more rapid than type Ib speciation because the number of small social units in a placental species is greater than the number of founder populations in a nonplacental species.

Intraspecific Variation. Although this discussion has focused on the problem of how karyotypic and organismal differences among species arise, one should also consider individual variation within a species. Is it possible that karyotypic differences are responsible for many of the phenotypic differences among individuals? In addition to the major gene rearrangements discussed above, adaptations in anatomy and way of life may result from localized changes in
regulatory genes. These changes may be either point mutations or rearrangements too small to cause meiotic problems in the heterozygote; neither would lead to reproductive isolation from the parental type. Social structuring would increase the chance that these mutations will reach the homozygous state and thus increase the probability of their survival. Since structural gene mutations are usually codominant, this factor might only be important for the survival of regulatory mutations, which are often recessive. Thus, the social structure of mammalian populations might also accelerate slightly the rate of regulatory evolution due to mutations other than major rearrangements. The rate of structural gene evolution would probably not be affected. Unfortunately, little is known about either the level of polymorphism in regulatory genes or the size and frequency of very small gene rearrangements in populations. Until such knowledge is available, a critical examination of this problem is not possible.

CONCLUSIONS AND PROSPECTS

Two main conclusions emerge tentatively from the above findings and discussion. First, placental mammals have experienced unusually rapid evolution at both the chromosomal level and the organisinal level, though not at the structural gene level. Hence, gene rearrangement may have a major role in organisinal evolution, as Goldschmidt (32) suggested 35 years ago. Although the mechanism involved is not known, one possibility is that gene rearrangement provides new phenotypes by altering the patterns of gene expression during embryonic development.

Second, the factor that enables placentals to evolve so rapidly at the chromosomal level may be the social structuring of their populations. Further study will be required to ascertain whether such social structuring is dependent on some feature of the brain that is especially well developed in placental mammals.

To test the above conclusions and suggestions, additional studies are needed at many levels of biological organization. For example, thorough comparative studies are needed of chromosome banding patterns, effective population size, and degree of inbreeding, as well as of social structuring and the brain. Valuable also, would be comparisons of the rates of chromosomal mutation in diverse vertebrates. Finally, it is important to examine quantitatively the relationship between chromosomal evolution and organisinal evolution; this will require the application of numerical methods for measuring organisinal resemblance.


18. Moore, R. C., ed. (1960–1969) in Treatise on Invertebrate Paleontology (Geol. America and Univ. Kansas Press, Lawrence, Kansas), parts I and N.