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Mosaic evolution: an integrating principle for the modern synthesis

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Modern synthetic theories of evolution, regardless of the degree to which they emphasize other factors, are all agreed that change through time is chiefly a product of interaction between genotypes and their environment which, construed in the broadest sense, includes the genotypic background of each gene that contributes to the change. Theories that postulate an inner urge, able to produce continual change in a particular direction regardless of environmental influence or selection pressure, are chiefly of historical interest. The recent hypothesis of 'molecular drive', proposed by G. Dover[1] needs much more factual confirmation before it can be generally accepted. Consequently, the different characteristics of an organism can be expected to evolve at different rates and times depending upon selection or mutation pressures – unless particular characteristics are bound together by the fact that they all contribute to the same adaptive syndrome, or because of developmental constraints, pleiotropic action of genes, or genetic linkage.

For this quasi-independent evolution of different characteristics, DeBeer[2] coined the term 'mosaic evolution'. He showed that this kind of evolution exists for each of the anatomical characteristics responsible for major transitions between classes of vertebrates. Transitional forms are not intermediate with respect to all of the characteristics that distinguish typical or modal representatives of each class. They are, rather, composed of a mosaic of characteristics, some of which are typical of the ancestral class, while others show the condition of the descendant class in a fully developed state. His prime example is *Archaeopteryx*. With respect to 8 of its characteristics (brain, long tail, simple articulation of vertebrae, short sacrum, free metacarpals, free metatarsals, simple ribs, gastralia) it retains the reptilian condition to such an extent that specimens of this genus in which feathers are not preserved have often been identified as small dinosaurs. Nevertheless, it is completely birdlike in possessing feathers that agree with those of birds with respect to details of structure and arrangement, as well as its fused clavicles, pubes directed backward, and opposable hallux. With respect to other well known intermediate fossils, *Ichthyostega* is a mosaic that possesses 8 fish characters, 5 amphibian characters, and 2 specialized characters peculiar to this genus. *Seymouria* combines 12 reptilian characters with 18 amphibian characters, and 2 characters characterized as 'preamphibian'. The reptilian-mammalian transition is represented by the fossil Ictidosauria and the modern *Ornithorhynchus*, both of which are mosaics that include 1 set of characteristics similar to reptiles, and others that have evolved to the mammalian condition.

Although DeBeer[2] confined his attention to anatomical and gross morphological characteristics found in vertebrates, modern knowledge allows us to extend the principle of mosaic evolution to all kinds of animals and plants, and to show that characteristics of behavior, evolution of chromosomal fine structure, and of individual proteins follow the same principle. Particularly instructive are mosaics that are revealed when changes with respect to anatomy, behavior, chromosomes, gene structure and protein molecules are compared with each other. The value of these comparisons lies chiefly in their contribution toward a better understanding of adaptive syndromes, and the ways in which they can change in response to challenges posed by changing environments. An axiom that motivates these comparisons is that organisms can rarely, if ever, achieve perfect adaptations to newly encountered environments. Successful response to an environmental challenge depends upon putting together a combination that works better than any other combination that competing organisms have achieved. Often, an opportunistic, jerry-built collection of similar genotypes can succeed because the individuals carrying them are the first that have become established in a new habitat. Later, the evolutionary line and lines branching from the initial population can tighten their hold upon a series of similar environmental niches by means of slower adjustments of various characteristics. On the other hand, many species populations have gene pools of such a nature that they cannot be modified to respond to drastic environmental challenges, and so join the ranks of the great majority of species and genera that have appeared from time to time, only to become extinct rather than evolve in new directions. I hope that the following review and discussion will help to provide a better understanding of those properties of gene pools that favor evolution rather than extinction.

The adaptive significance of morphological-anatomical mosaics

Although DeBeer paid little attention to the functional or adaptive significance of transitional mosaics, this aspect has been treated in detail by more recent paleontologists, particularly Schaeffer[3] and Thomson[4] for the fish-amphibian transition, Carroll[5] for the transition between amphibians and reptiles, Ostrom[6] for the reptile-bird transition, and Crompton and his associates[7,8] for mosaics that combined reptilian and mammalian characteristics. I shall confine my attention to the fish-amphibian transition, because of its fundamental significance for the conquest of the land. I shall first discuss the question: 'Why was only one group of fishes preadapted to make the transition, since no other group of aquatic chordates gave rise to terrestrial descendants'. Four characteristics were of primary importance as preadaptations: 1. adaptation to fresh rather than salt water, 2. lungs or air sacs as auxiliary organs for obtaining oxygen from the air, 3. thick, firm lateral fins having well developed internal skeletons, 4. dentition adapted to seizing active prey.

Fresh water fishes would have been much more likely to colonize the land because many bodies of fresh water are temporary in terms of geological time, and many of the fishes inhabiting them would be forced to adapt to terrestrial life or become extinct. On the other hand, salt water fishes inhabiting the littoral belt could retain previous adaptations by migrating into new marine habitats as levels of the ocean rose and sank. Following the principle that organs having new functions are most easily acquired via an intermediate stage during which 2 different organs serve the same function[9], fishes that could take in oxygen either from water via gills or from air via lungs would be favored candidates for the transiton from aquatic to terrestrial life. Szarski[10] points out that lungs originated in the remote past, and most probably were present, at least as air sacs, in all of the ancestors of modern bony fishes (teleosts) as well as amphibia. The common ancestor of fishes (excluding Cyclostomes and Elasmobranchs) and amphibia was already a mosaic that possessed at least rudimentary air sacs as lungs. In the descendant bony fishes the air sac was converted to the swim bladder, a hydrostatic organ. This conclusion carries with it the corollary that bony fishes as well as amphibia are descended from ancestors that occupied a specialized habitat: fresh water that at least seasonally become depleted in oxygen.

Paleontologists are generally agreed that amphibia are descended from fishes that belonged to the subclass Sarcopterygii[3,10-13]. Unfortunately, members of this subclass first appear in the fossil record contemporaneously with the earliest ancestors of bony fishes (Paleoniscoidea), in the early Devonian, so that the common ancestor of the subclasses Sarcopterygii and Teleostomi is unknown. Two conspicuous differences separate paleoniscids from Sarcopterygii: small vs large size and thin fins devoid of internal skeleton vs thick fins that possessed an internal skeleton. A reasonable speculation about the relationships and ancestry of these 2 groups is that they evolved during the late Silurian, a period that is devoid of strata laid down in fresh water. They must have been 2 extreme branches of an adaptive radiation within the habitat of fresh water that became seasonally low in oxygen. The smaller paleoniscids could use their fins for swimming no matter how shallow the water became, but among larger forms only those could survive who could tolerate shallow water by acquiring thick, fleshy fins capable of propelling them along the bottom of the lake or river, or which could serve as fulcra for sudden lunges at active prey by individuals partly buried in mud[3]. While the first amphibian characteristic acquired by fishes was probably an adaptation to a particular aquatic habitat - fresh water seasonally depleted in oxygen, the second characteristic - lateral appendages equipped with an internal skeleton, may have been acquired in association with a particular way of exploiting this habitat.

The fourth preadaptive characteristic possessed by the fishes that gave rise to amphibia, dentition adapted to seizing active prey, was held in common by bony fishes and early amphibians. It deserves attention, however, since a shift in dentition evolved by one group of Sarcopterygii, the dipnoans, was responsible for their totally different way of becoming adapted to terrestrial conditions. The dipnoan strategy led to evolutionary stagnation, while the rhipidistian strategy gave rise to the dominant vertebrate fauna of land and air. When they first appear in the fossil record of the early Devonian, Sarcopterygii were already divided into 2 distinctive orders, Crossopterygii and Dipnoi. The former retained the sharp pointed teeth characteristic of most fishes; the latter had evolved teeth that coalesced to form large plates capable of crushing hard animals, such as shelled molluscs. Associated with such teeth were thin, almost tendril-like lateral fins. Most probably, these early dipnoans resembled their contemporary descendants in occupying shallow fresh water, and leading a sluggish life that was based upon a diet of shelled molluscs, which they crushed with their broad hard teeth. Consequently, when toward the end of the Devonian period, shallow lakes and pools became seasonally dry, dipnoans met this challenge by surviving the temporary drought in a state of dormancy, encased in mud. Rhipidistians and their descendants used their strong, skeletal and muscular fins for waddling from one pool to another, and their sharp teeth for impaling not only smaller fishes, but also arthropods, such as isopod and amphipod crustaceans, both aquatic and terrestrial, as well as scorpions and ancestors of insects.

The final restriction of amphibian ancestry to a particular suborder of crossopterygians, the rhipidistians, may well have been their mode of locomotion. Schaeffer[3] points out that rhipidistians differ from their sister group, the coelacanths, in possessing strong fins concentrated near the hind ends of their bodies. Coelacanths, having fins distributed equally over their bodies, resembled their modern relictual survivor, *Latimeria*, in swimming actively through open water while chasing their prey. According to Schaeffer, however, a rhipidistian can be imagined as 'stalking prey by moving slowly along the bottom with its lobed fins, and then making a sudden powerful upward lunge to capture its victim'. An alternative behavior, equally plausible would be making the lunge from a stationary position, hiding in mud and vegetation. As water became low in oxygen, it would have become poor in available prey. Coelacanths would have responded to these conditions by hunting prey as far out in open water as possible, and by following rivers down to the seas, the habitat that they later exploited. Rhipidistians, on the other hand, would have succeeded best by searching out and capturing terrestrial invertebrates on the surrounding shores of the lakes or pools. Rhipidistians, therefore, became preadapted to their evolution into amphibia first by their radiation into a specialized fresh water habitat, and later by specialized ways of exploiting that habitat. In them, mosaic-like transitions, possessing a few amphibian characteristics or conditions that could be converted into amphibian adaptations with relative ease, were evolving in fishes for millions of years before the actual fish-amphibian transition took place.

Moreover, some paleontologists[3,14], suggest that the most distinctive feature of amphibia and other land vertebrates, limbs provided with feet and digits rather than fins, may well have evolved in an animal that was primarily aquatic. They point out that *Ichthyostega*, usually regarded as the earliest amphibian, in the adult state possessed fin-like margins of its tail, as well as well developed sensory neurons along a lateral line. Both of these structures are universal adaptations to aquatic life in fishes, and would be useless or even harmful in a terrestrial environment. Eaton, moreover, points out that if the animal became adapted to spending its entire life in shallow water near the margins of pools, thus isolated from more fish-like and larger predators, the shift from fins to feet would enable it to move around and stalk prey more easily in this habitat. If the animal used sudden lunges to capture its prey, feet would be more efficient fulcra for this function than would be fins. This suggests that even the major transition from fishes to amphibia was a continuation of a mosaic type sequence of specializations to successively more specialized and restricted aquatic habitats that began with the differentiation of the earliest teleosts. The final characteristics that led to typical amphibians – loss of fin-like tail margin, great reduction of the lateral line and its sensory neurons, and reduction or elimination of fish-like scales over most of the body – must have been achieved as the last of a long series of mosaic transitions, finally making possible continuous existence on land.

Another transition among vertebrates, from apes to humans, is likewise of a mosaic character. *Australopithecus afarensis* ('Lucy') resembles humans with respect to posture and the shape of its pelvic bones, and its dentition but is more ape-like with respect to overall size and cranial capacity[15]. The same is true of other species of *Australopithecus*[16]. Although the position of *Rampithecus* is now dubious, and may not be ancestral to *Australopithecus*, nevertheless the resemblance of its dentition to that of hominids is great enough so that one can reasonably infer that the earliest hominids had similar dentition, indicating a diet different from that of contemporary African apes. Hence the major anatomical changes that led from ape-like ancestors to humans appear to have evolved separately, mosaic fashion, over a time span that lasted at least 5 million years and possibly longer. The first of these, a change in diet from fruit and vegetable parts like bamboo shoots to seeds, nuts and tubers and small animals, may have been completed 4–5 million years ago. The second, from quadrupedal or knuckle walking to erect posture, began before 3.5 million years ago and was virtually complete by the *Homo habilis* stage, 1.5 million years ago[16]. I agree with Lovejoy[17] as well as Leakey and Lewin[18] in suggesting that the strongest selective pressure for this shift, was the adaptive value of using forelimbs and hands for carrying food to a home base. The increase in cranial capacity, that required in more than 3 million years but was most rapid from about 1 million to 100,000 years ago, was promoted by a variety of selective pressures, among the most important of which were probably the use of tools and collective hunting that required increased proficiency in language. Like amphibian evolution, hominid evolution was of a mosaic nature because its entire course required millions of years, during which different selective pressures successively were dominant.

Mosaic evolution in higher plants

Unfortunately, the fossil record of flowering plants does not record the relative rates of evolution of different organs through time, as does the record of vertebrates. Nevertheless, comparisons between modern representatives of this class support the hypothesis that major transformations of their basic organization took place mosaic fashion, under the influence of different selective pressures. Within a single family, the grass family (Gramineae), examples exist not only wherein comparative stability of vegetative characters are accompanied by strikingly divergent evolution of the reproductive characters, but also where vegetative diversity is combined with reproductive constancy. Species belonging to the tribe Stipeae are nearly all perennial bunch grasses that are much alike in gross appearance, anatomy and histology. With respect to spikelets and fruits, however, they have evolved a great variety of sizes, shapes, length of awns and other structures associated with dispersal by wind or animals. Their aimilarity in vegetative characteristics is associated with life in similar open, semiarid evironments which they exploit in a similar fashion. The diversity of their spikelets and fruits is due chiefly to coevolution with animal vectors. On the other hand, species of the large genus *Panicum* are all very much alike in spikelet and fruit structure, but are highly diverse with respect to growth habit and inflorescences. This latter diversity is associated with adaptation to a great variety of climates from margins of tropical rain forests to savannas and even deserts, as well as to cool temperate climate in the northeastern United States.

In other examples, mosaic evolution can be detected among related genera belonging to the same family. In the Ranunculaceae, for instance, the genera *Delphinium* and *Aconitum* have diverged from generalized types similar to *Caltha* and *Trollius* very greatly in terms of the structure and color of their flowers, but relatively little with respect to their leaves and seed capsules. Their vegetative constancy is due to their restriction to mesic, temperate habitats, or to seasonal dormancy on the part of species that have invaded seasonally dry habitats. Since the habitats that they occupy have remained relatively constant over long periods of time, selective pressures for extensive seed dispersal have been minimal. Floral specialization and diversity have been promoted by coevolution with specialized pollen vectors, chiefly bumblebees *(Bombus)* but also, in California, hummingbirds (Trochilidae).

On the other hand, the genus *Ranunculus* has retained flowers and pollen vectors very similar to those of *Caltha* and *Trollius* but has evolved a great variety of leaf structures and specialized seed-bearing achenes. This is associated with adaptive radiation of the genus into a great variety of habitats, from warm temperate to alpine and arctic, and from semi-xeric to mesic, hydric and even aquatic. This diversity of habitats is associated with the evolution of achenes that are readily dispersed by wind or animals, and so increase greatly the probability that seedlings will arise in habitats different from those of the maternal plants.

In the related genera *Anemone* and *Clematis,* evolution of easily dispersed achenes is likewise associated with adaptation to a great variety of different habitats.

Mosaic evolution for behavioral characteristics

Mosaic evolution is by no means confined to morphological and anatomical characteristics. With respect to behavior it can be expected whenever 2 kinds of behavior patterns are serving very different functions. It is particularly conspicuous among insects that feed and grow chiefly during the larval stage, and in which the adult is concerned primarily with reproduction. A prime example is the large genus *Drosophila.* The diversity of courtship patterns among its species are well known and have been studied intensively[20]. Particularly instructive examples are sibling species such as *Drosophila melanogaster* and *D. simulans.* Both species are adapted to feeding on yeast from fermenting fruit, and to relatively high temperatures. Nevertheless, their courtship patterns differ strikingly, and interspecific matings are rare[21]. Mosaic evolution in this example is associated with similar selection pressures for survival of larvae associated with particular selective pressures against fruitless interspecific matings. Among advanced vertebrates, such as primates and rodents, diverse selective pressures associated with activities such as nursing and care of young, hunting of food by adults, and the establishment of societies bring about complex mosaic evolution with respect to their patterns of behavior.

Mosaic evolution with respect to chromosomes

During the past 15 years, knowledge about chromosome fine structure in eukaryotes has increased explosively. This new knowledge has forced upon us revolutionary changes in our theories about gene mutations and chromosomal changes. Formerly, cytogeneticists could be content with a sharp dichotomy. Gene mutations were believed to consist chiefly of single nucleotide substitutions, while chromosomal aberrations, particularly in flies having giant salivary chromosomes, such as *Drosophila,* were believed to be large enough to be detected through the light microscope. Now, the distinction between these categories is completely blurred. Genes are recognized as highly complex structures, in many of which transcribed, coding segments of DNA are interspersed with noncoding introns. Many of the classical mutations consist of rearrangements involving hundreds or thousands of base pairs, but are still changes within the domain of a single gene, and are far below microscopic resolution. Even more rearrangements of base pairs take place in spacer DNA, that separates genes from each other, and lacks a coding function. Many of these changes, also, are too small to be detected by conventional methods. The hypothesis proposed by this author in 1946[22,23] that many species are differentiated from each other by numerous chromosomal differences too small to be detected by the methods then available, has now been amply verified by analyses of nucleotide sequences[24-26].

At the level of nucleotide sequences, mosaic evolution becomes most evident when coding, genic DNA is compared with noncoding DNA, that consists either of highly repetitive 'satellite' DNA or of middle repetitive spacer[27]. Satellite DNA varies greatly among populations of the same species, as maize[28] and rye[29]. It evolves much more rapidly than the DNA that codes for structural genes. Evolutionary rates of middle repetitive spacer DNA are by themselves of a mosaic nature. This was demonstrated for the amphibian genus *Plethodon*[29,30], that lacks easily recognizable satellite knobs or centromeric heterochromatin. When the species *P. cinereus* and *P. unnii* were compared by the usual DNA-DNA hybridization procedures, most of the middle-repetitive DNA was recognized as more different than was single copy DNA. Still, relatively short, highly similar sequences could be detected. In middle repetitive DNA of primates[31,32], families of similar nucleotide sequences about 300-500 base pairs in length are scattered throughout the genome. On the other hand, much of the middle repetitive spacer DNA in *Drosophila* exhibits intraspecific variation with respect to both total amount and nucleotide sequences[33,34].

This mosaic nature of chromosomal DNA is probably due to 3 totally different functions that have been attributed to it. In addition to its primary function, coding for the amino acid sequences of proteins, chromosomal DNA may have a second kind of function, promoting or inhibiting transcription, as well as providing signals for termination of the transcription process. Indirect evidence for this kind of function has been deduced by Davidson et al.[35], Grosschiedl and Bernstein[36], Biezunski[37] and others. A third kind of function for particular nucleotide sequences, facilitation of efficient coiling contraction and 'packaging' of the chromosomal helix into rod-like chromosomes such as prevail during mitosis, must be postulated because of the discovery that the DNA contained in any eukaryotic chromosome is one continuous double helix that is enormously long compared to its width[38]. The magnitude of the mechanical problem involved can be realized by imagining such a double helix magnified 10^7 times, thus bringing it into visible proportions. If this is done, a chromosomal double helix of *Drosophila* (width 20 Å, length 1 cm) becomes 20 mm in width and 100 km in length! Magnified to the same degree, a mitotic chromosome of *Drosophila* becomes 4 m in diameter and 20 m long. Hence the feat accomplished by the chromosomal helix of *Drosophila* during the prophase of each of its mitotic divisions is equivalent to packaging 100 km of videotape into a cylinder 4 m in diameter and 20 m long. By no stretch of the imagination could one conceive that this feat would be possible without some kind of mechanical aid. The most probable 'mechanical aid' would be a stereo-chemical attraction of certain regions of DNA to a stable protein skeleton[39,40].

A fourth suggestion, that non-coding DNA acts to regulate genetic recombination via its effects on chiasma and crossover frequency[41], is less well supported by data.

Mosaic evolution of polypeptides and proteins

Perhaps the most striking examples of mosaic evolution are different rates of evolution among genes coding for different proteins. Wilson[42] has shown that fibrinopeptides, snake venom toxins and immunoglobulins of vertebrates have evolved several hundred times more rapidly than have certain histones (H_3 and H_4). Other histones (H2A, 2B), fibrous proteins such as collagen and crystallin, several cellular enzymes and cytochromes have also evolved at fairly slow rates, while rates of evolution among oxygen-binding proteins such as hemoglobins, as well as secreted enzymes, such as trypsinogen, have been intermediate. Great differences in evolutionary rate exist among hormones. Insulin C peptide has evolved more than 20 times faster than glucagon.

The prevailing explanation for these differences is the functional constraint hypothesis[43-45]. This postulates that proteins differ among each other greatly with respect to the number of sites at which several different residues can be substituted without loss of serious impairment of function. If few such sites exist, evolution is necessarily slow. If there are many of them, chance substitutions can often occur, can be tolerated by the molecule, and so can become established. Wilson[42] calls attention to the lack of direct evidence for this hypothesis. I find it hard to imagine that polypeptide chains of immunoglobulins differ so greatly from those of histones that the latter have 400 times as many functional constraints as the former. An alternative hypothesis has been suggested[46]. This is that slow evolution is based upon stabilizing selection exerted on a protein that has the same or very similar functions in a wide variety of organisms, while other proteins that perform functions characteristic of a restricted group of organisms and characteristic of their particular physiology and/or ecological relationships, are more subject to diversifying selection in association with their specific adaptive properties. Histones and cytochrome c, for example, are associated with generalized features of cellular metabolism that are very similar among most eukaryotes. Hemoglobins, myoglobin and secreted enzymes, having intermediate rates of evolution, are associated with functions necessary for animal metabolism, but their maximum efficiency differs greatly according to the size, the basic habitat (e.g. aquatic vs terrestrial) and degree of temperature regulation (poikilothermy vs homoiothermy) of the animal concerned. The rapidly evolving fibrionopeptides control wound healing, a process that is strongly subjected to the external environment, and can be expected to vary considerably among related animals having different ways of life.

Mosaics involving different kinds of characteristics

Morphology-anatomy vs behavior. Mosaic evolution involving rapid divergence in behavior accompanied by greater constancy with respect to morphology and anatomy is most evident among species of *Drosophila.* The divergence in courtship patterns between the sibling species *D. melanogaster* and *D. simulans* has already been mentioned. Among the Hawaiian species of the genus, morphological differences are more pronounced. But nevertheless those characteristics that are closely associated with courtship patterns, such as wing ornamentation and tarsal structure, are by far the most diverse[47]. For adult characteristics associated with escape from predators and overall fecundity, similarity of ecological relationships has favored stabilizing selection, while characteristics associated with courtship, that reduce the probability of unfavorable interspecific matings, have been subjected to pressures of diversifying selection. A similar situation exists among other insects, such as Orthoptera[48] as well as among tree frogs[49,50].

Morphology vs chromosomes. Plants are the best organisms for comparing the relative rates of evolutionary diversification with respect to morphology as compared to chromosome structure. This is because studies of meiosis in numerous interspecific hybrids have made possible comparisons between the parental chromosomes by studying their pairing in the hybrids. Such comparisons show that in some groups morphological differences evolve much more rapidly compared to chromosomes, while in others the reverse is true. This subject has been reviewed by Stebbins[23] and Grant[51]. In some groups, such as the Compositae subtribe Madiinae, comparisons can be made between related genera and species. Suitable data are presented by Clausen[52]. Particularly instructive is a comparison between the complex of *Madia elegans* and the genus *Holocarpha.* The former species, as recognized by Keck and Clausen includes 3 well marked subspecies, one of which, ssp. *Wheeleri,* was placed by earlier botanists (A. Gray and W. L. Jepson) in a different genus *(Hemizonia Wheeleri).* Hybrids between these subspecies are fully fertile and have normal chromosomal pairing at meiosis, indicating that they are very similar with respect to chromosomal structure. On the other hand, most of the populations placed by Keck and Clausen in the genus *Holocarpha* look so much alike that Gray and Jepson placed them in a single species *(Hemizonia virgata).* Nevertheless, crosses between many different populations, particularly those found in the Coast Ranges and southern California, either failed to produce hybrids or gave rise to sterile hybrids having abnormal meiotic behavior. In the *M. elegans* complex, differentiation with respect to morphology has proceeded much more rapidly than chromosome structure, while in *Holocarpha,* extensive changes in chromosome structure have been accompanied by little morphological differentiation. An intermediate situation exists in the genus *Layia,* but even within this genus a pattern can be recognized that is similar to that formed by *Madia elegans* and the genus *Holocarpha. Layia platyglossa* like *Madia elegans,* exhibits considerable morphological and ecological differentiation, but chromosome behavior in hybrids between its extreme variants is fully normal. A trio of species, *L. jonesii, L. munzii* and *L. leucopappa* are localized variants that are somewhat differentiated from each other chromosomally. Another species, *L. septentrionalis,* is a sibling species that resembles *L. platyglossa* and occupies a marginal position in the northwestern corner of the range of the genus. It has a different chromosome number ($n=8$ vs, $n=7$) and does not produce hybrids with *L. platyglossa.* Finally, *Layia carnosa,* a specialized and highly localized inhabitant of coastal sand dunes, is strongly isolated from all other species of the genus both ecologically, morphologically and genetically.

This pattern of morphological, ecological and cytogenetical differences, which is matched by several other genera of annual flowering plants, is best explained in the following manner. The widespread species that are differentiated into well-marked subspecies but are chromosomally homogneous, *Madia elegans* and *Layia platyglossa,* are both adapted to generalized habitats that for many years have been - and still are - widespread in California. Most probably, neither of them has been subjected to severe environmental pressures that have forced them through 'bottlenecks' of small size. On the other hand, the Coast Range populations of *Holocarpha,* which are the most strongly differentiated from each other cytogenetically, are now localized in small interior valleys, and probably have had a history involving repeated passage through 'bottlenecks' of small size. The same history is probably true for *Layia carnosa* and *L. septentrionalis,* and to a lesser extent for *L. jonesii, L. munzii* and *L. leucopappa.*

The relationship between passage through localized bottlenecks and speciation is a general feature of the California flora. I reached this conclusion by comparing the treatment of various genera in the manual written in 1920-1925 by W. L. Jepson[53] before cytogenetic data existed, and that by Munz and Keck[54] that uses cytogenetic data, where available, as a partial basis for classification. Jepson had a broader concept of species than Munz and Keck, so that some of the extra splitting in the latter volume may reflect different concepts of delimiting species.

For the flora as a whole (table), the genera in which cytogenetic data suggested that species should be split more finely was balanced by an early equal number of genera in which broader limits of species are indicated. On the other hand, the situation is strikingly different when woody groups, perennial herbs and annual herbs are compared. Cytogenetic data indicate consistently that if biological criteria based upon reproductive isolation are applied, species limits among woody plants become broader than they appear to be on the basis only of morphological differences. The reverse is true for annual herbs: most of them become more split when cytogenetic data and reproductive isolation are considered. Among perennial herbs, the overall situation is similar in the two kinds of treatments, but a noteworthy fact is that the genera that have become more split, or would be finely split if reproductive isolation were made the principal criterion of species delimitation, consist of plants that are regularly or frequently self pollinated, and would therefore be likely to survive bottlenecks consisting of a single individual. Those that would be more lumped are predominantly those that have large, conspicuous flowers, are regularly visited by pollen vectors, or that have either unisexual or self incompatible flowers. Because of their rapid turnover of generations, as well as their frequent self pollination, annual plants are much more likely to pass through bottlenecks than are woody species.

The best explanation for the kind of mosaic evolution that is revealed when related species of annual angiosperms are compared with respect both to morphological-ecological differentiation and to chromosomal differentiation is the following. Differentiation with respect to morphological characteristics that adapt populations to new habitats adjacent to the old ones and relatively extensive in area is accomplished without chromosomal differentiation, and is usually unaccompanied by barriers of reproductive isolation. Polytypic species, containing several subspecies or clines are formed in this way. On the other hand, if

Changes in number of species per genus brought about by adding cytogenetic to morphological information 1925-1958, in 66 genera of the Californian flora

	More species	No change	Fewer species
Woody	None	None	11 genera
Perennial	6	11	14 genera
Annual	12	11	1 genus
Total	18	22	26 genera

the populations of a species are subjected repeatedly to drastic fluctuations in size, or 'bottlenecks', either because of repeated oscillations of environmental factors during time, or because of repeated migrations of a few individuals into new habitats, drastic reorganizations of chromosomal structure will be favored and strong barriers of reproductive isolation will be set up, which may be accompanied by relatively little visible differentiation of the newly formed populations. This will give rise to clusters of sibling species. If bottlenecks and migrations occur within a relatively restricted area, the resulting pattern will resemble that which White[55] has attributed to stasipatric speciation. If bottlenecks and habitat fluctuations are such that adaptation to entirely new conditions takes place, the result may be the rapid origin of a species such as *Layia carnosa*, that is both highly distinctive morphologically and strongly isolated cytogenetically. Furthermore, if such a species is exposed to an environment that is expanding and becoming diversified, it may give rise to a cluster of descendant species that can form a new genus.

Morphology vs proteins. The striking differences that many groups exhibit with respect to morphological-anatomical differentiation as compared to molecular alteration of intracellular proteins has been fully discussed by A.C. Wilson[43,56]. He emphasized 2 examples: frogs vs mammals and anthropoid primates. Since placental mammals first evolved, about 90–100 million years ago, they have become differentiated into many strikingly different orders, which are highly diversified with respect to both outward appearance and chromosome structure. Nevertheless, they are much less strongly differentiated with respect to their proteins such as serum albumins, hemoglobin and various enzymes. On the other hand, during this same period frogs (order Anura) have differentiated no new families, and even most of their genera probably existed already 90 million years ago (mid-Cretaceous). Nevertheless, with respect to the above mentioned proteins, families and genera of frogs are as strongly differentiated from each other as are orders of mammals. Among anthropoid primates, morphological and anatomical differences between chimpanzees and humans are great and obvious, but with respect to proteins they are no more different from each other than are different species of some mammalian genera. The opposite situation has been found by Lessios[57] to be true of sea urchins separated by the isthmus of Panama. All populations belonging to the same genus (in *Diadema, Eucidara* and *Echinometra*) differ only slightly from each other in morphology, but in *Eucidara* and *Echinometra* populations that inhabit opposite sides of the isthmus differ greatly from each other with respect to molecular structure of proteins.

Wilson attributes the differences between mammals and frogs to unspecified distinctive characteristics of each evolutionary lineage. I believe that a different interpretation is possible. The order Anura is much older than the subclass Eutheria or placental mammals. Their differentiation from other orders of amphibia probably took place between the beginning of the Triassic and the middle of the Jurassic period, from 220 to 150 million years ago[11]. Although their fossil record during this interval is so scanty as to be almost non-existent, they must have been undergoing considerable anatomical changes. Perhaps, therefore, at the beginning of the Cretaceous period, 136 million years ago, the relative amount of molecular as compared to anatomical differentiation in Anura was similar to that which prevails among mammals today. Since then, Anura have remained well adapted to their particular kind of ecological niche, so that selective pressures for anatomical modifications have been weak. Molecular evolution of intracellular proteins, being less connected with adaptation to a particular niche, and in some instances nearly or quite neutral with respect to adaptation, has continued at an appreciable rate during the past 135 million years. This interpretation suggests to me a principle that I call the 'hare and tortoise' principle (fig.). Morphological and anatomical characteristics are the 'hares'.

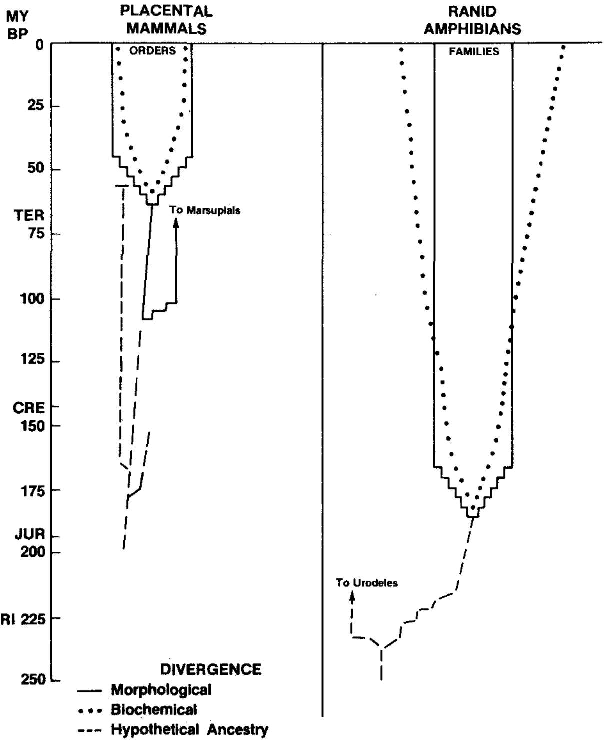

Diagram showing how mosaic evolution, according to the 'hare and tortoise' principle (see text), can cause biochemical differences to be less than morphological-anatomical differences in a relatively young group, and to exceed them in an old group. Further explanation in the text. (MY BP = million years before present).

When an evolutionary lineage is becoming adapted to a radically new habitat, selective pressure is strong for establishing mutations responsible for drastic modifications in morphology and anatomy. It is more indirect and weak for mutations of genes coding for proteins that do not contribute directly to morphology and anatomy. Hence during the initial stages of adaptation, modifications of morphology and anatomy (the 'hares') will race far ahead of molecular alterations of intracellular proteins (the 'tortoises'). After a few thousand or at most a few million years, morphological and anatomical adaptation to the new niches will have reached the maximum fitness of which the gene pool is capable, and will slow down or cease altogether. Intracellular proteins, on the other hand, will continue to evolve, either because they produce refinements of adaptations to minor variants of the original niches, or due to stochastic establishment of neutral differences. In recently evolving groups, morphological and anatomical differences will be greater than molecular differences between most proteins; in older groups the reverse will be true. In terms of modern concepts of macroevolution, morphological and anatomical characteristics, that are visible to the paleontologist and are the basis of taxonomic classification, will follow the pattern of punctuated equilibria[58-60], while intracellular proteins will evolve according to the gradualistic or 'evolutionary clock' model[42]. The number of genes that are responsible for morphological and anatomical differentiation is probably a few hundred at most, and therefore less than 10% of the total genotype. When mean rates are estimated for the genotype as a whole, this subset of rapidly evolving genes is offset by an equally large number of genes such as those coding for histones that do not evolve at all during a 10-million-year period. Hence, the mean rate of evolution for the nuclear DNA as a whole will reflect the rates of the majority of genes, those that code for intracellular proteins, and so will approximate an evolutionary clock.

This hypothesis is well supported by a comparison between anthropoid primates and echinoderms. The most recent evidence suggests that the separation between chimpanzees and humans began not more than 5-10 million years ago[42,61]; therefore, their anatomical differences should greatly exceed molecular differences. This, in fact, is the case[62-63]. Modern genera of echinoderms, on the other hand, acquired their structural organization more than 50 million years ago. Hence the relatively great protein differences between populations of genera that have been isolated from each other for long periods of time, in combination with slight morphological differences[51] is in accord with the hypothesis.

Behavioral vs molecular differences. Patterns of behavior are likely to evolve even more rapidly than morphological and anatomical structure. This is because they are exposed to two different kinds of selection pressure, as well as to phenotypic modification. Behavioral evolution can be particularly rapid in highly complex vertebrates, such as birds and social mammals. These animals alter their social structure and territoriality in response both to climatic and ecological differences as well as to interactions between individuals of the same and related species[64]. Moreover, such patterns as the structure of many bird songs are acquired by imprinting and imitation, and so can become different without accompanying genetic changes[65]. Consequently, the 'hare and tortoise' pattern should be particularly evident in passerine birds and this has actually been demonstrated by Avise and his associates[66,67].

Chromosomes and genes. Wilson[56,68] has shown that rates of evolution with respect to chromosome structure parallel those with respect to morphology and anatomy. Chromosomes, therefore, are also 'hares'. Direct evidence for this pattern can be obtained from some genera of woody plants, such as *Ceanothus*[69,70]. Evidence from interspecific hybridization shows that the species belonging to either one of its 2 subgenera, *Euceanothus* and *Cerastes,* are identical with respect to those characteristics of chromosome structure that affect meiotic pairing; i.e. meiotic behavior in all hybrids between species belonging to the same subgenus is completely normal. On the other hand, intersubgeneric hybrids have highly abnormal meiosis, indicating that the parental species differ from each other by at least 10-20 different rearrangements of chromosome structure. Paleobotanical evidence indicates that each of the 2 subgenera is about 25 million years old (Oligo-Miocene). If we try to account for the age of the genus by assuming a constant rate of chromosomal changes, we would have to conclude that the genus *Ceanothus* is at least 75 million years old, a conclusion which is in direct conflict with fossil evidence from pollen that indicates an age of only 65-70 million years for the entire order Rhamnales[71]. Most probably, chromosome differentiation in the genus *Ceanothus* was proceeding more rapidly during the Eocene or Oligocene epochs than during later epochs.

Three kinds of factors could promote a 'hare' type of pattern for chromosomal changes. First, adaptive gene clusters or 'supergenes' play important roles in morphological and ecological adaptations. When such adaptations become drastically altered, chromosomal changes that assemble new gene clusters will be strongly selected for and so will become rapidly established. Later during the history of an evolutionary line, when new adaptations are chiefly modifications of a well established adaptive syndrome, alterations of genetically linked gene clusters or 'supergenes' will have lower adaptive values, and new chromosomal changes are less likely to become established. In addition, when new genera are in early stages of their evolution, their species may still be restricted to a relatively small number of localized habitats, and as climatic changes oscillate through time, populations are likely to pass through bottlenecks in which the 'Founder Principle' acts to establish new chromosomal changes in chance association with adaptive characters[72]. Third, as Wilson[42] has suggested, many chromosomal changes are accompanied by position effects, that may establish a direct connection between morphological changes and chromosomal alterations. The relative importance of these 3 factors cannot be estimated until more information is available on a variety of organisms.

Given this similarity between the dynamics of change with respect to morphology and chromosome structure, the low degree of correlation between chromosomal changes and molecular alteration of cellular proteins is to be expected. The 'hare and tortoise' pattern, illustrated in the figure, holds also for the present comparison.

General considerations

The most important generalization that emerges from these comparisons is the following. Mosaic evolution is an expected consequence of the complexity of evolutionary processes, and of the opportunistic nature of evolutionary change. In each of the 4 kinds of differences that have been reviewed, the basis of mosaicism is somewhat different. With respect to morphological and anatomical characteristics, those that contribute to an adaptive syndrome that is being subjected to strong, novel selection pressures as a result of environmental change will evolve rapidly while other features of morphology, that are just as adaptive in a new environment as in an old one will change little or not at all. This kind of mosaicism is particularly evident when biotic factors, such as new predators or sources of food, are changing in an environment that is not undergoing climatic or edaphic change.

Behavioral characteristics are similar to morphological differences with respect to their response to environmental changes, except that interactions of a social nature between individuals of the same species, such as male rivalry for possession of females and dominance hierarchies introduce additional stimuli for change. Mosaic evolution is particularly evident with respect to social factors as compared to behavioral patterns associated with food getting.

The basis for mosaic evolution with respect to chromosomal differences is of an entirely different nature. Alterations of chromosomal fine structure are now known to be far more common than gene mutations that are based upon nucleotide substitutions. The probability of their fixation in populations is correspondingly great. Since this fixation is greatly increased when populations pass through bottlenecks of small size, mosaic evolution involving chromosomal changes depends more on the dynamics of population structure and fluctuations in population size than upon specific environmental factors that affect the adaptiveness of individual phenotypes. Moreover, certain nucleotide sequences of non-coding DNA are kept constant because they apparently regulate activation or deactivation of genes, while other non-coding sequences can and do become altered very rapidly. Chromosomal mosaicism, therefore, depends both upon population size and structure as well as internal relationships within the genome.

Mosaicism of coding genes depends largely upon relationships with other genes and their functions. Genes that code for basic functions of cellular metabolism evolve relatively slowly; those responsible for more superficial or specific functions evolve more rapidly. Genes that code for intracellular proteins are subject to selective pressures of an internal nature, and their mosaicism is based upon shifting balances with respect to the genotype and phenotype as a whole. Moreover, they are probably more subject to stochastic influences than are the genes that contribute primarily to adaptive interactions between populations and their environment.

In view of the pronounced differences between factors that affect each of these 4 different kinds of characteristics, an expected result is the diversity of mosaic evolutionary patterns that emerges when different categories of characters are compared with each other. The progress of evolutionary lines through time does not resemble the direct flights of birds or airplanes from one point to another. It is more like the irregular course that a vehicle must follow when passing through a succession of country lanes or of ancient cities devoid of boulevards or freeways. When one studies evolution, one must begin by becoming thoroughly familiar with these complex byways in the particular group under study. Valid generalizations must be built up from below, on the basis of detailed factual information. They cannot be deduced from broad theories or generalized models, however sophisticated these may be. Mathematics and other generalized techniques are tools for handling data, not instruments that by themselves can generate theories or generalizations.

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Molecular selforganization and genesis of life

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The origin of life has presented challenging problems for modern biologists, because it is difficult to account for the development of even the simplest of living organisms. Beginning with Oparin[1], many modern authors[2–5] have attacked this problem. Present-day mechanisms of replication and translation of genetic information must have developed through many stages, through mutation and culling out by natural selection. A fundamental difficulty is that living systems operate by means of enzymes, the manufacture of which requires many enzymes in the first place.

It is our contention that a fruitful approach to this problem is to consider a model consisting of many small but physically and chemically plausible steps. It is easy enough to claim (erroneously) that the origin of life could never be explained on the basis of physical laws simply by considering some large step and showing that its probability is ridiculously small. However, it turns out that the probabilities for the steps we consider are of an appropriate order of magnitude to assure near certainty for their occurrence under model conditions[6–10].

Model requirements

Living organisms consist of macromolecules that act together like the components of a machine. Some of these molecules are capable of replication and moreover contain the blueprints of the machine, permitting its reproduction. The emergence of such systems in their most primitive form requires the presence of a) a structurally diversified environment as that which existed, for example, on prebiotic earth in form of porous rock formations; b) a suspension of energy-rich nucleotide-like compounds presumed to have existed on prebiotic earth; and c) a regime of periodic temperature changes as caused, for example, by the rhythm of light and shadow generated by the daily motion of the sun and by local shadow-casting objects. Inside suitable pores, such conditions favor the creation and later drive the replication of short polymer strands, with (+) strands acting as templates for (−) strands and vice versa. Pores above a certain size cannot be colonized by such strands, even though sufficient monomers are present, because strands that are too short diffuse too quickly from the minute region in which the required regime of critical temperature changes exists. In the model, short strands are lengthened by repeated doubling, thereby coloninzing larger pores, but there is a limit to the number of monomers a replicable strand may contain because of the unavoidability of copying errors. That is, the probability that replicate strands be error free must be large enough to assure their survival.

An error filter

In the model, the resulting impasse is broken by a mechanism in which the strands convolute into the conformation of a hairpin (fig. 1) with legs twisted into a double helix. Such hairpin strands would be capable of interlocking into picket-fence like aggregates (fig. 2), stabilized perhaps by bivalent cations, such as Mg^{+2} or Ca^{2+} ions, that form links between negatively charged phosphatidyl groups on the outside of neighboring hairpin strands. Not only is diffusion of such aggregates slowed by their size, but it is of the greatest importance that practically all erroneous copies are rejected during aggregation because of the precision required for interlocking. Aggregation therefore serves the function of an error filter.