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Human Races: A Genetic and Evolutionary Perspective

Race is generally used as a synonym for *subspecies*, which traditionally is a geographically circumscribed, genetically differentiated population. Sometimes traits show independent patterns of geographical variation such that some combination will distinguish most populations from all others. To avoid making "race" the equivalent of a local population, minimal thresholds of differentiation are imposed. Human "races" are below the thresholds used in other species, so valid traditional subspecies do not exist in humans. A "subspecies" can also be defined as a distinct evolutionary lineage within a species. Genetic surveys and the analyses of DNA haplotype trees show that human "races" are not distinct lineages, and that this is not due to recent admixture; human "races" are not and never were "pure." Instead, human evolution has been and is characterized by many locally differentiated populations coexisting at any given time, but with sufficient genetic contact to make all of humanity a single lineage sharing a common evolutionary fate. [*race, subspecies, lineage, haplotype tree, genetic differentiation*]

The word *race* is rarely used in the modern, nonhuman evolutionary literature because its meaning is so ambiguous. When it is used, it is generally used as a synonym for *subspecies* (Futuyma 1986:107–109), but this concept also has no precise definition. The traditional meaning of a subspecies is that of a geographically circumscribed, genetically differentiated population (Smith et al. 1997). The problem with this definition from an evolutionary genetic perspective is that many traits and their underlying polymorphic genes show independent patterns of geographical variation (Futuyma 1986:108–109). As a result, some combination of characters will distinguish virtually every population from all others. There is no clear limit to the number of races that can be recognized under this concept, and indeed this notion of subspecies quickly becomes indistinguishable from that of a local population. One way around this difficulty is to place minimal quantitative thresholds on the amount of genetic differentiation that is required to recognize subspecies (Smith et al. 1997). A second solution is to allow races or subspecies to be defined only by the geographical patterns found for particular "racial" traits or characters. A similar problem is faced in defining species. For example, the biological species concept focuses attention on characters related to reproductive incompatibility as those important in defining a species. These reproductive traits have priority in defining a species when in conflict with other traits, such as morphology (Mayr 1970). Unfortunately, there is no such guidance at the subspecies level, although in practice easily observed morphological traits (the very ones deemed not important under the biological species concept) are used. There is no evolutionary justification for this dominance of easily observed morphological traits; indeed, it merely arises from the sensory constraints of our own species. Therefore, most evolutionary biologists reject the notion that there are special "racial" traits.

Because of these difficulties, the modern evolutionary perspective of a "subspecies" is that of a distinct evolutionary lineage within a species (Shaffer and McKnight 1996) (although one should note that many current evolutionary biologists completely deny the existence of any meaningful definition of subspecies, as argued originally by Wilson and Brown [1953]—see discussions in Futuyma [1986:108–109] and Smith et al. [1997:13]. The Endangered Species Act requires preservation of vertebrate subspecies (Pennock and Dimmick 1997), and the distinct evolutionary lineage definition has become the de facto definition of a subspecies in much of conservation biology (Amato and Gatesy 1994; Brownlow 1996; Legge et al. 1996; Miththapala et al. 1996; Pennock and Dimmick 1997; Vogler 1994). This definition requires that a subspecies be genetically differentiated due to barriers to genetic exchange that have persisted for long periods of time; that is, the subspecies must have historical continuity in addition to current genetic differentiation. It cannot be emphasized enough that *genetic differentiation alone is insufficient to define a subspecies.* The additional requirement of historical continuity is particularly important because many traits should reflect the common evolutionary history of the subspecies, and therefore in theory there

is no need to prioritize the informative traits in defining subspecies. Indeed, the best traits for identifying subspecies are now simply those with the best phylogenetic resolution. In this regard, advances in molecular genetics have greatly augmented our ability to resolve genetic variation and provide the best current resolution of recent evolutionary histories (Avise 1994), thereby allowing the identification of evolutionary lineages in an objective, explicit fashion (Templeton 1994b, 1998a, 1998b; Templeton et al. 1995).

The purpose of this paper is to examine the existence of races in humans using an evolutionary genetic perspective. The fundamental question is: Are human populations genetically differentiated from one another in such a fashion as to constitute either sharply genetically differentiated populations or distinct evolutionary sublineages of humanity? These questions will be answered with molecular genetic data and through the application of the same, explicit criteria used for the analyses of nonhuman organisms. This last point is critical if the use of the word *race* in humanity is to have any general biological validity. This paper will not address the cultural, social, political, and economic aspects of human "races."

Are Human "Races" Geographically Circumscribed, Sharply Differentiated Populations?

The validity of the traditional subspecies definition of human races can be addressed by examining the patterns and amount of genetic diversity found within and among human populations. One common method of quantifying the amount of within to among genetic diversity is through the F_{st} statistic of Wright (1969) and some of its more modern variants that have been designed specifically for molecular data such as K_{st} (Hudson et al. 1992) or N_{st} (Lynch and Crease 1990). F_{st} and related statistics range from 0 (all the genetic diversity within a species is shared equally by all populations with no genetic differences among populations) to 1 (all the genetic diversity within a species is found as fixed differences among populations with no genetic diversity within populations). The F_{st} value of humans (based on 16 populations from Africa, Europe, Asia, the Americas, and the Australo-Pacific region) is 0.156 (Barbujani et al. 1997), thereby indicating that most human genetic diversity exists as differences among individuals within populations, and only 15.6% can be used to genetically differentiate the major human "races." To put the human F_{st} value into perspective, humans need to be compared to other species. F_{st}'s for many plants, invertebrates, and small-bodied vertebrates are typically far larger than the human value, but most of these organisms have poor dispersal abilities, so this is to be expected. A more valid comparison would be the F_{st} values of other large-bodied mammals with excellent dispersal abilities. Figure 1 shows the values of F_{st}'s and related statistics for several large-bodied mammals. As can be seen, the human F_{st} value is one of the lowest, even though the human geographical distribution is the greatest. A standard criterion for a subspecies or race in the nonhuman literature under the traditional definition of a subspecies as a geographically circumscribed, sharply differentiated population is to have F_{st} values of at least 0.25 to 0.30 (Smith et al. 1997). Hence, as judged by the criterion in the nonhuman literature, the human F_{st} value is too small to have taxonomic significance under the traditional subspecies definition.

This does not mean that the low human F_{st} value is without any evolutionary significance. Suppose for the moment that the F_{st} values in humans truly reflect a balance between gene flow versus local drift/selection and are not due to isolated human lineages. One convenient method for quantifying this balance is Nm, the product of local effective population size (N) with m, the migration rate between demes. Under the idealized population structure known as the island model, the relationship between F_{st} and Nm is (Wright 1969):

$$F_{st} = \frac{1}{4Nm + 1} \qquad (1)$$

Most real populations do not fit an island model (which assumes that gene flow is independent of geographical distance). Nm is therefore not the actual number of individuals exchanged per generation, but rather is an effective number of migrating individuals per generation relative to this simple, idealized model of population structure. This allows comparisons across different species in effective amounts of gene flow with respect to a common standard. For the human F_{st} value of 0.156, Nm = 1.35. This result is consistent with the work of Santos et al. (1997) who examined several human data sets with a variety of statistical procedures and always obtained $Nm > 1$. With Nm on the order of 1, massive movements of large numbers of individuals are not needed to explain the level of genetic differentiation observed in humans. Moreover, Nm = 1.35 does not mean that precisely 1.35 effective individuals migrate among the "races" every generation; rather, this is the long-term average. Assuming a generation time of 20 years, the levels of racial differentiation in humanity could be explained by interchanging 1.35 effective individuals every 20 years, or 13.5 every 200 years, or 135 every 2,000 years. Since humans often move as populations, gene flow could be very sporadic on a time scale measured in thousands to tens of thousands of years and still yield an effective number of migrants of 1.35.

An Nm value of 1.35 would insure that the population evolves as a single evolutionary lineage over long periods of time (Crow and Kimura 1970). Nevertheless, population genetic theory also indicates that fluctuations around

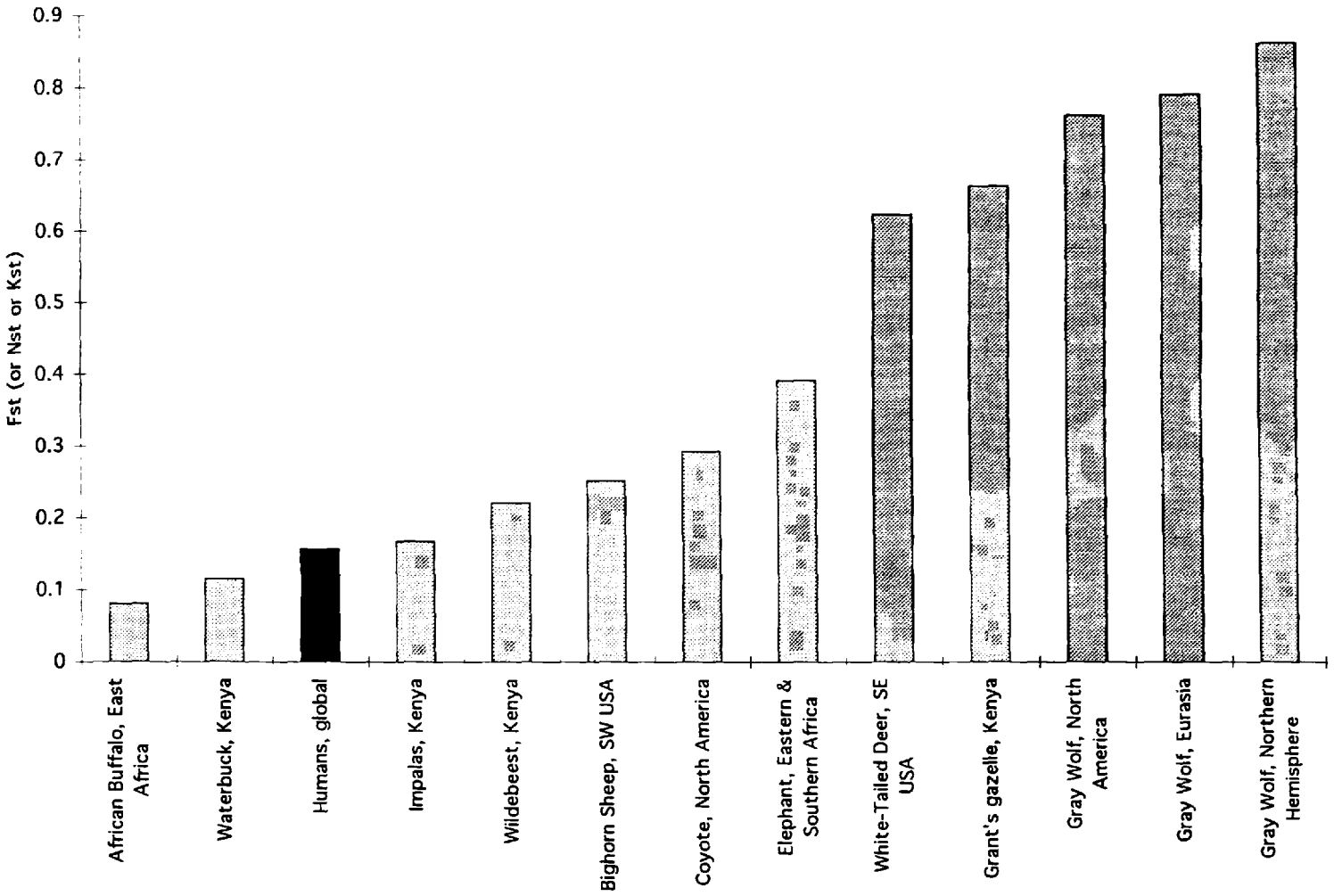

Figure 1. F_{st} (or K_{st} or N_{st}) values for various species of large-bodied mammals with excellent dispersal abilities. The figure shows F_{st} (or its multiallelic analogue, G_{st}) values for African buffalo (Templeton and Georgiadis 1996), humans (Barbujani et al. 1997), bighorn sheep (Boyce et al. 1997), elephants (Georgiadis et al. 1994), and white-tailed deer (Ellsworth et al. 1994); K_{st} values for waterbuck, impalas, wildebeest, and Grant's gazelle (Arctander et al. 1996); and N_{st} values for coyotes (Lehman and Wayne 1991) and wolves (Wayne et al. 1992). The geographical scale of the study is indicated by the species name. Values are given in order of size, with the human value indicated in black and nonhuman values in gray.

an average *Nm* of order one is conducive both to the rapid spread of selectively favored genes throughout the species and to local population differentiation and adaptation (Barton and Rouhani 1993). If anatomically modern traits did indeed first evolve in Africa, the human *Nm* value implies that such traits could rapidly spread throughout all of humanity through gene flow if selectively favored even though local populations could still display genetic differentiation for other loci. Studies on nonhuman organisms indicate that *Nm* values can be larger than those in humans and yet the species can still display much local differentiation and adaptation, as predicted by this theory. For example, populations of *Drosophila mercatorum* on the slopes versus the saddle of the Kohala mountains on the island of Hawaii (a distance of 3 km) have an estimated *Nm* of between 4 and 8 (DeSalle et al. 1987). Nevertheless, these populations show extreme differentiation and local adaptation for the abnormal abdomen syndrome, a complex polygenic suite of phenotypes that affects morphology, developmental time, female fecundity, male sexual maturation, and longevity in adaptively significant ways (Hollocher and Templeton 1994; Hollocher et al. 1992; Templeton et al. 1993; Templeton et al. 1989). Similarly, garter snake populations in Lake Erie have an *Nm* value between 2.7 and 37.6 among sites with populations that differ greatly in the amount of melanism (King and Lawson 1995, 1997; Lawson and King 1996). These examples (and many more could have been given) clearly show that *Nm* values higher than the estimated *Nm* value for humans are still compatible with much local differentiation across space even though the gene flow is sufficiently high to ensure that the species as a whole evolves as a single lineage over time.

The above discussion was predicated upon the *assumption* that the human F_{st} value arose from the balance of gene flow versus local drift and selection. Unfortunately,

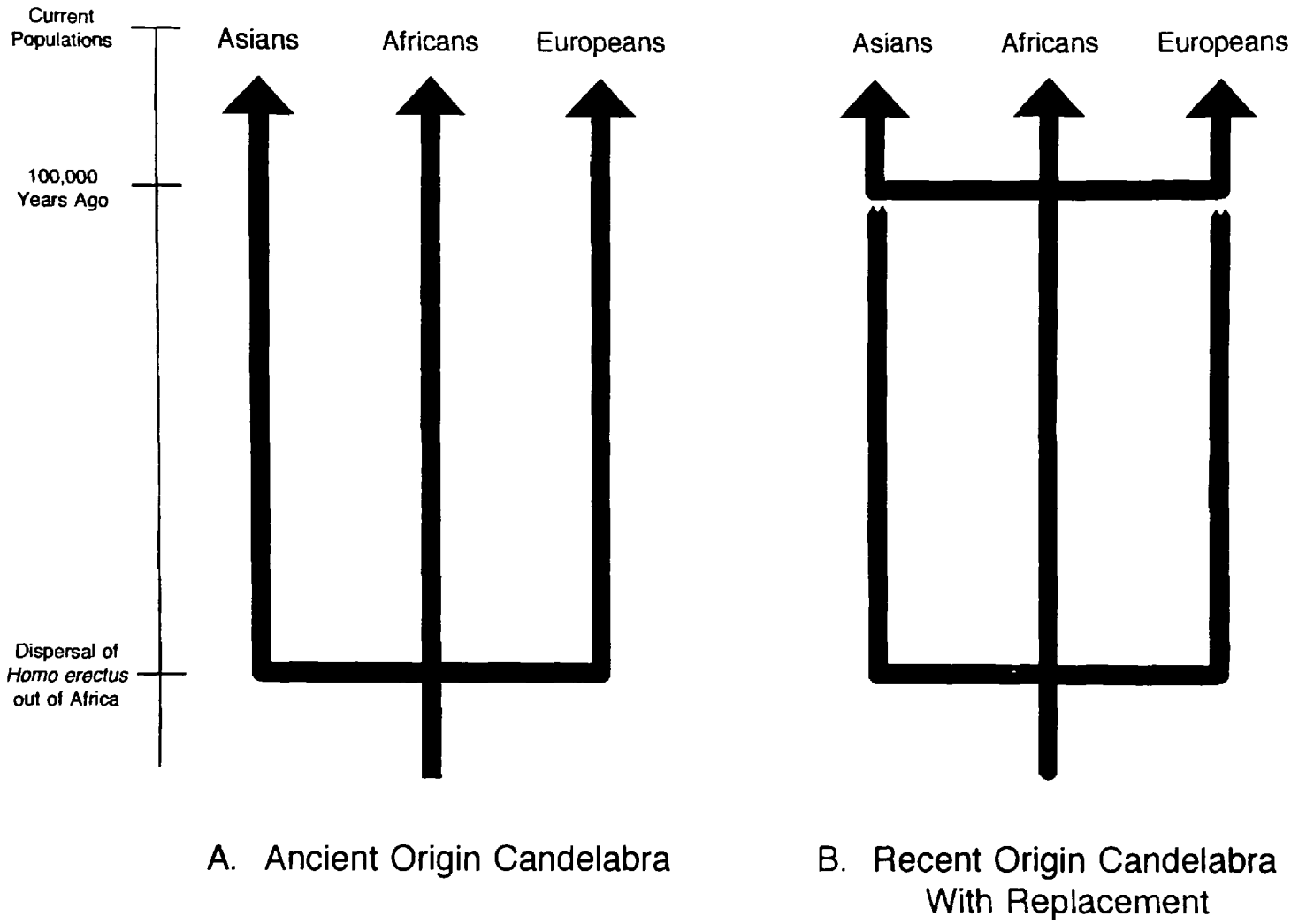

Figure 2. Candelabra models of recent human evolution. Part A illustrates the ancient origin version of the candelabra model. Under this hypothesis, the major human "races" split from one another at the time of dispersal of *Homo erectus* out of Africa. After that initial split, the various "races" behaved as separate evolutionary lineages and independently evolved into their modern forms. Part B illustrates the recent origin version of the candelabra model with replacement. Under this hypothesis, an initial candelabra existed as illustrated in part A. However, anatomically modern humans then arose in Africa and dispersed out of Africa around 100,000 years ago. This second dispersal event was marked by the complete genetic extinction of the earlier *Homo erectus* populations (indicated by the broken lineages in B) and by a split of these anatomically modern humans into separate evolutionary lineages that then independently acquired their modern "racial" variation.

the F_{st} statistic per se cannot discriminate among potential causes of genetic differentiation (Templeton 1998a). Although human "races" do not satisfy the standard quantitative criterion for being traditional subspecies (Smith et al. 1997), this does not necessarily mean that races do not exist in the evolutionary lineage sense. Under the lineage concept of subspecies, all that is needed is sufficient genetic differentiation to define the separate lineages. If the lineages split only recently, the overall level of divergence could be quite small. Therefore, the quantitative levels of genetic diversity among human populations do not rule out the possibility that human "races" are valid under the evolutionary lineage definition of subspecies. The remainder of this paper will focus upon this more modern definition of subspecies.

Are Human "Races" Distinct Evolutionary Lineages?

Models of Human Evolution and Human Races

When a biological race is defined as a distinct evolutionary lineage within a species, the question of race can only be answered in the context of the recent evolutionary history of the species. The two dominant models of recent human evolution during the last half of this century are the

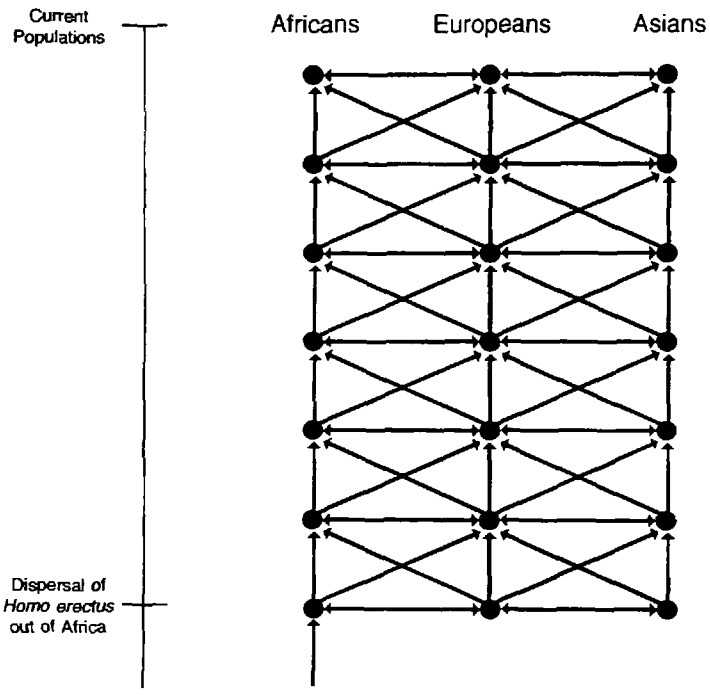

Figure 3. The trellis model of recent human evolution. Under this hypothesis, *Homo erectus* dispersed out of Africa and established populations in Africa and southern Eurasia, as indicated by the large dots. These populations were interconnected by gene flow so that there were no evolutionary sublineages of humanity or independent evolution of the various "races." Arrows with heads on both ends indicate gene flow among contemporaneous populations, and arrows with single heads indicate lines of genetic descent.

candelabra (Figure 2) and trellis (Figure 3) models. Both models accept the evolutionary origin of the genus *Homo* in Africa and the spread of *Homo erectus* out of Africa a million years ago or more. Candelabra models posit that the major Old World geographical groups (Europeans, sub-Saharan Africans, and Asians) split from one another and since have had nearly independent evolutionary histories (but perhaps with some subsequent admixture). Therefore, the evolutionary relationships among Africans, Europeans, and Asians can be portrayed as an evolutionary tree—in this case with the topology of a candelabra (Figure 2). The major human geographical populations are portrayed as the branches on this candelabra and are therefore valid "races" under the evolutionary lineage definition. The ancient origin candelabra model regarded the split between the major "races" as occurring with the spread of *Homo erectus* (Figure 2A) followed by independent evolution of each "race" into its modern form. This version has been thoroughly discredited and has no serious advocates today. However, a recent origin candelabra model known as the out-of-Africa replacement hypothesis (Figure 2B) has become widely accepted. Under this model, anatomically modern humans evolved first in Africa. Next, a small group of these anatomically modern humans split off from the African population and colonized Eurasia about 100,000 years ago, driving the *Homo erectus* populations to complete genetic extinction everywhere (the "replacement" part of the hypothesis). The ancient (Figure 2A) and recent (Figure 2B) candelabra models differ only in their temporal placement of the ancestral node but share the same tree topology that portrays Africans, Europeans, and Asians as distinct branches on an evolutionary tree. It is this branching *topology* that defines "races" under the evolutionary lineage definition, and not the *time* since the common ancestral population. Hence, human "races" are valid evolutionary lineages under either candelabra model.

The trellis model (Figure 3) posits that *Homo erectus* populations not only had the ability to move out of Africa but also back in, resulting in recurrent genetic interchange among Old World human populations (Lasker and Crews 1996; Wolpoff and Caspari 1997). It is also important to note that, under the trellis model, the taxonomic designations of *Homo erectus* and *H. sapiens* only have morphological significance and do not imply reproductive isolation as under the biological-species concept (Mayr 1970). Therefore, anatomically modern traits could evolve anywhere in the range of *Homo erectus* (which includes Africa) and subsequently spread throughout all of humanity by selection and gene flow. Hence, an African origin for anatomically modern humans is compatible with both the trellis and candelabra models. The two models do differ in their interpretation of interpopulational genetic differences. Populational genetic differences reflect the time of divergence from a common ancestral population under the candelabra models. With the trellis model, the genetic distances reflect the amount of genetic interchange and not time of divergence from an ancestor. However, the most important distinction between the candelabra and trellis models for the discussion at hand is that under the trellis model there was no separation of humanity into evolutionary lineages, and hence human "races" are not valid subspecies. In summary, human "races" as evolutionary lineages do exist under the candelabra models but do not exist under the trellis model.

Although these two models are frequently presented as mutually exclusive alternatives (Wolpoff and Caspari 1997), there is no biological reason why some human populations may be genetically differentiated because they are historical lineages, whereas other populations are differentiated because of recurrent but restricted gene flow. Moreover, the genetic differences between any two human populations may represent a mixture of both gene flow and historical events. Much genetic evidence is equally compatible with both models and hence is noninformative. The emphasis in this paper will therefore be upon data sets that discriminate between gene flow and historical splits as non-mutually exclusive causes of differentiation among human populations.

Genetic Diversity Levels within and among Human Populations

Do the levels of genetic diversity found within and among human "races" discriminate between evolutionary lineage and genetic interchange models of recent human evolution? As pointed out earlier, F statistics and related measures of within to among diversity levels do not discriminate per se. However, one conclusion reached in that section has great relevance to the debate over the validity of human races as evolutionary lineages; namely, that the estimated gene flow levels in humans are compatible with local differentiation across geographical space even though the species as a whole could evolve as a single lineage over time. Much skepticism about the trellis model stems from the belief that a delicate balance is required between gene flow (to insure all humans are a common evolutionary lineage over time) and local genetic drift/selection (to maintain humans as a polytypic species at any given moment in time) (Aiello 1997; Nei and Takezaki 1996). Indeed, even proponents of the trellis model have argued that only rarely can a species be polytypic under a trellis model. For example, Wolpoff and Caspari (1997:282) state that "the human pattern . . . of a widespread polytypic species with many different ecological niches . . . is a very rare one." However, polytypic species are not rare (Futuyma 1986; Mayr 1970). Moreover, as illustrated by the examples given earlier, polytypic species occur over a broad range of values for Nm and are a robust evolutionary outcome. There is no difficulty either in population genetic theory or observation for the conclusion that humans can be both a polytypic species and a single evolutionary lineage.

Although F statistics are compatible with either model of human evolution, the claim is made in much of the recent literature that within "race" diversity levels support the recent candelabra model. Africans have higher amounts of genetic diversity than non-Africans for many nuclear loci (Armour et al. 1996; Jorde et al. 1997; Perez-Lezaun et al. 1997), mitochondrial DNA (mtDNA) (Comas et al. 1997; Francalacci et al. 1996), and some regions of Y-DNA (Hammer et al. 1997). These results are often interpreted as supporting the recent candelabra model by assuming that only a small number of individuals left Africa to colonize Eurasia with little or no subsequent gene flow. As a result, a bottleneck effect reduced the levels of genetic variation in non-Africans. This interpretation of genetic diversity also implies that at least Africans and non-Africans are distinct evolutionary lineages and hence are valid races. However, alternative explanations of diversity levels exist. Under the neutral theory, the expected heterozygosity for a DNA region (a standard measure of genetic diversity) is given by:

$$\text{Heterozygosity} = \frac{1}{1 + 4N_e\mu} \qquad (2)$$

where N_e is an effective size of the population and μ is the mutation rate of the DNA region of interest. Equation (2) reveals that differences in effective size can explain differences in the level of genetic diversity. Africans are expected to have higher genetic diversity simply because their population sizes were larger during much of the last million years (Harpending et al. 1996; Relethford and Harpending 1994, 1995). Indeed, the patterns of genetic diversity found in humans are more consistent with differences in population sizes and growth rates than with differences in population ages from presumed bottlenecks (Harding et al. 1997; Perez-Lezaun et al. 1997). The danger of using diversity levels as an indicator of population age from a bottleneck is illustrated by the observation that mitochondrial DNA diversity *within Africa* is higher in food-producing populations than in hunter-gatherers (Watson et al. 1996). By equating diversity to age, this result would imply that agricultural peoples in Africa represent the ancestral populations, whereas the hunter-gatherers are the recent descendant populations. Such a conclusion is not credible, and the diversity levels within Africa are interpreted as reflecting effective size differences (Watson et al. 1996).

Note that equation (2) has no time component. The reason is that equation (2) describes the diversity levels at equilibrium. When the equilibrium is disturbed by bottlenecks or rapid population growth, time enters as a factor (Templeton 1997a). Fortunately, different causes of departure from equilibrium can be discriminated. For example, a bottleneck and split should affect all genetic systems. However, nuclear DNA and mitochondrial DNA show discordant patterns in humans, a result inconsistent with the presumed population bottleneck and the sharing by all genetic systems of a common demographic history (Hey 1997; Jorde et al. 1995). One can also discriminate by the patterns of diversity across genetic systems that differ in mutation rate (Templeton 1997a). A bottleneck reduces genetic variation, and temporal dependence enters because mutation takes time to restore genetic diversity. Hence, the longest lasting discrepancies in relative genetic diversity levels are for low mutation rate systems. Therefore, under the bottleneck hypothesis, Africans should show the greatest excess in relative genetic diversity for low mutation rate systems. However, the excess genetic diversity in Africans is found with the high mutation rate systems (Armour et al. 1996; Comas et al. 1997; Francalacci et al. 1996; Jorde et al. 1997; Perez-Lezaun et al. 1997), whereas the classic, low mutation rate systems show comparable levels of genetic diversity (Bowcock et al. 1994; Jorde et al. 1995), and a low polymorphic section of Y-DNA shows greater levels of diversity in Europeans than in Africans (Mitchell 1996). An alternative non-equilibrium pattern can be generated by rapid population

growth which causes an increase—not a decrease—in levels of genetic diversity. The high mutation rate systems show the earliest and strongest response to increased population size, which is consistent with the observed pattern. Hence, the observed diversity patterns reflect human population growth rather than population bottlenecks.

The within "race" genetic diversity levels do not support the idea that Eurasians split off from Africans via a small founder population, but they do not necessarily falsify the notion that a Eurasian/African split occurred without a bottleneck. Therefore, the within population genetic diversity data are inconclusive on the status of Eurasians and Africans as separate evolutionary lineages and thereby valid races.

Genetic Distances and Evolutionary "Trees"

An alternative method to F_{st} of measuring the extent of genetic differentiation among populations is to convert the genetic differences into a genetic distance. There are several genetic distance measures available, and sometimes the biological conclusions are strongly dependent upon the precise measure chosen (Perez-Lezaun et al. 1997). However, this problem will be ignored in this paper because the relative distances among the major human "races" appear robust to differing genetic distance measures (Cavalli-Sforza 1997). Genetic distances in turn can be converted into an evolutionary tree of populations by various computer algorithms. Figure 4A shows such a population tree (Cavalli-Sforza et al. 1996). This and most other human genetic distance trees have the deepest divergence between Africans and non-Africans, and this split is commonly estimated to have occurred around 100,000 years ago (Cavalli-Sforza et al. 1996; Cavalli-Sforza 1997; Nei and Takezaki 1996). All this seems consistent with the recent candelabra model, but non-zero genetic distances can also arise and persist between interbreeding populations with recurrent gene flow (Wright 1931, 1943, 1969). As shown by Slatkin (1991), recurrent gene flow results in an average divergence time of gene lineages between populations even when no population-level split occurred and the divergence levels are at equilibrium and thereby time invariant. Therefore, an apparent genetic time of divergence does not necessarily imply a time of population splitting—or any population split at all. Under a trellis model, genetic distances reflect the patterns and amounts of gene flow and *not* the age since some "separation" or "split."

Fortunately, these two interpretations of genetic distance can be distinguished. If human populations can truly be represented as branches on an evolutionary tree, then the resulting genetic distances should satisfy several constraints. For example, under the candelabra model, all non-African human populations "split" from the Africans at the same time, and therefore all genetic distances between African and non-African populations have the same expected value (Figure 4A). When genetic distances instead reflect the amount of gene flow, "treeness" constraints are no longer applicable. Because gene flow is commonly restricted by geographical distance (Wright 1943), gene flow models are expected to yield a strong positive relationship between geographical distance and genetic distance. Figure 4B places the populations on a two-dimensional plot in a manner that attempts to reflect their genetic distances from one another, particularly nearest-neighbor distances, while otherwise attempting to minimize the total sum of branch lengths (formally, a neighbor-joining dendrogram). Figure 4B uses the same genetic distance data used to generate the tree in Figure 4A, but without imposing all the constraints of treeness (Cavalli-Sforza et al. 1996). Note that Europeans fall between Africans and Asians as predicted by their geographical location—in contrast to the candelabra model prediction of equal genetic distances of Europeans and Asians to Africans. The computer programs used to generate "trees" from genetic distance data will do so regardless

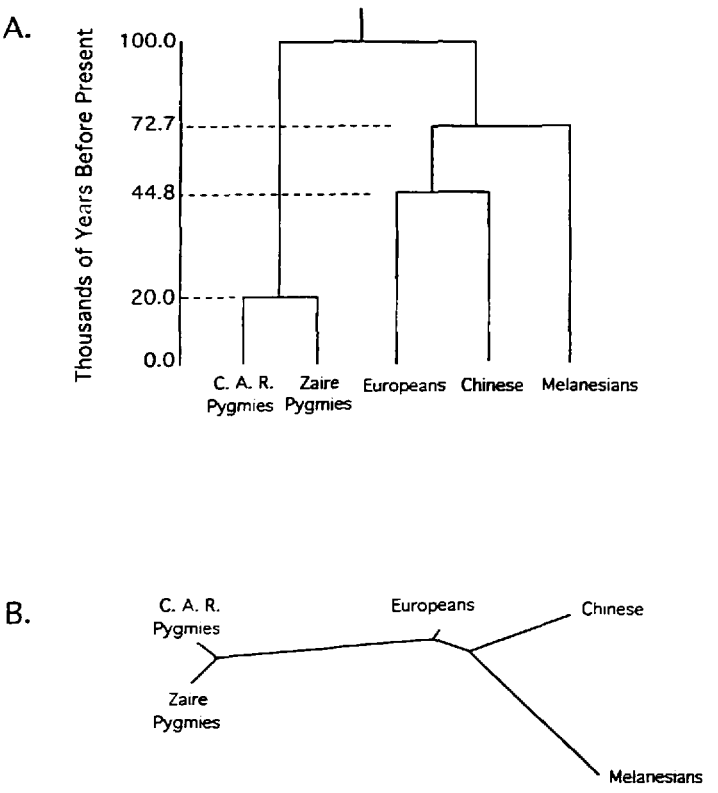

Figure 4. Genetic distances and recent human evolution. Part A shows an evolutionary tree of human populations as estimated from the genetic distance data given in Bowcock et al. (1991). Human population evolution is depicted as a series of splits, and the numbers on the left indicate the estimated times of divergence in thousands of years. This figure is redrawn from Figure 2.4.4, Cavalli-Sforza et al. (1996:91). Part B shows the same genetic distance data drawn with the neighbor-joining method but without all the constraints of a tree. This figure is redrawn from Figure 2.4.5, Cavalli-Sforza et al. (1996:91).

of what evolutionary factors generated the distances. It is therefore the obligation of the users of such programs to ensure that the genetic distance data have the properties of treeness before representing their data as a tree. To present trees that do not have the properties of treeness is analytically indefensible, and worse, it is biologically misleading.

The failure of human genetic distances to fit treeness is ubiquitous whenever tested (Bowcock et al. 1991; Cavalli-Sforza et al. 1996; Nei and Roychoudhury 1974, 1982). Nevertheless, these same authors persist in presenting the relationships of the major human "races" as an evolutionary tree. Worse, many recent papers do not even test for treeness. For example, Nei and Takezaki (1996) give several trees for both old and new genetic data sets, but not a single test of treeness is given or even mentioned. However, the older data sets given in Nei and Takezaki (1996) have long been known not to fit treeness (Nei and Roychoudhury 1974, 1982). The newer data sets in Nei and Takezaki (1996) were not tested for treeness in the original papers, so a test will be given here using a standard measure of treeness—the cophenetic correlation (Rohlf 1993). Because the trees are themselves estimated from the genetic distance data, a large, positive cophenetic correlation is always expected and any correlation less than 0.8 is regarded as a "poor" fit (Rohlf 1993). The cophenetic correlations for the new data sets given in Nei and Takezaki (1996) are 0.75 for the microsatellite data of Bowcock et al. (1994), 0.69 for the microsatellite data of Deka et al. (1995), 0.79 for the restriction fragment length data of Mountain and Cavalli-Sforza (1994), and 0.45 for the *Alu* insertion polymorphism data of Batzer et al. (1994). Not one of the data sets fits treeness.

In marked contrast, the genetic distance data fit well to a restricted gene flow model. In their analyses of the older data sets, Nei and Roychoudhury (1974, 1982) not only rejected treeness, but showed that the deviations were those expected from genetic interchange among the "races." Similarly, Bowcock et al. (1991) not only rejected treeness for their data, but also showed that their data fit well to a model of "continuous admixture, in time, in space, or in both: a chain of populations somewhat similar to a stepping-stone model in which the ancestors of Europeans are geographically intermediate between the two extremes, Africans and Asians" (p. 841). The phrase "continuous admixture" is an oxymoron, as will be evident later, but in this case it is used as a synonym for recurrent gene flow (Cavalli-Sforza, personal communication). The "stepping-stone model" is a classic isolation by distance model, so Bowcock et al. (1991) show an excellent fit of their data to the recurrent gene flow model of isolation by distance. Santos et al. (1997) analyzed several human data sets with a variety of statistical procedures and found that the pattern is one of isolation by distance with high gene flow between geographically close populations. Finally, Cavalli-Sforza et al. assembled a comprehensive human data set and concluded that "the isolation-by-distance models hold for long distances as well as for short distances, and for large regions as well as for small and relatively isolated populations" (1996:124). Figure 5 is a redrawing of one of the figures from Cavalli-Sforza et al. (1996) that illustrates how well an isolation by distance model fits the human data.

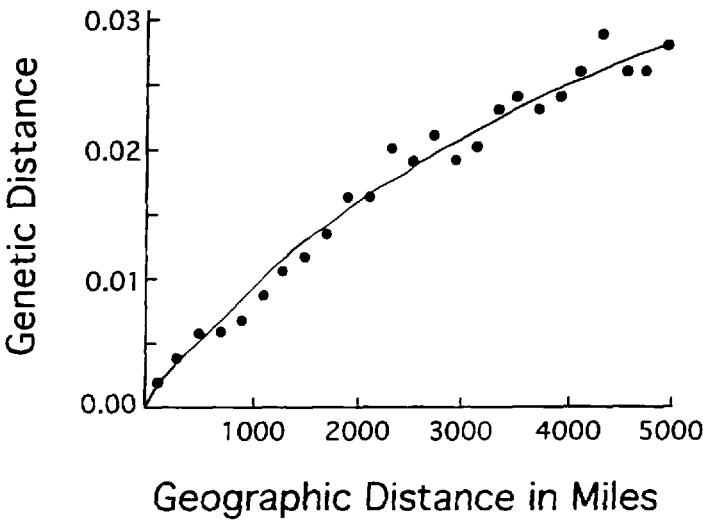

Figure 5. Genetic distances and isolation by geographical distance. The global human genetic distances (the ordinate) are plotted against geographical distance in miles (the abscissa). The circles indicate the observed values, and the curved line is the theoretical expectation under an isolation-by-distance model. This figure is redrawn from Figure 2.9.2, Cavalli-Sforza et al. (1996:123).

Given that there is no tested human genetic distance data set consistent with treeness and that isolation by distance fits the human data well, proponents of the recent candelabra model have attempted to salvage the candelabra model by postulating a complex set of "admixtures between branches that had separated a long time before" (Cavalli-Sforza et al. 1996:19). The key phrase in this proposal is *between branches that had separated a long time before* (Terrell and Stewart 1996). Admixture occurs when genetic interchange is reestablished between populations that had separated in the past and undergone genetic divergence (i.e., the gene flow patterns have been discontinuous). Proponents of the recent candelabra model then attempt to reconcile the genetic distance data with an admixture model that mimics some of the effects (and the good fit) of recurrent gene flow. By invoking admixture events as needed, human "races" can still be treated as separate evolutionary lineages, but now with the qualification that the "races" were purer in the past—the paradigm of the "primitive isolate" (Terrell and Stewart 1996). However, even advocates of the recent candelabra model acknowledge that these postulated admixture events are "extremely specific" and "unrealistic" (Bowcock et al. 1991:841).

For example, consider Melanesians and Africans. As shown in Figure 4B, these two human populations have nearly maximal genetic divergence within humanity as a whole with respect to molecular markers. Moreover, note that Europeans are closer to both Africans and to Melanesians than are Africans to Melanesians (Figure 4B). However, Melanesians and Africans share dark skin, hair texture, and cranial-facial morphology (Cavalli-Sforza et al. 1996; Nei and Roychoudhury 1993)—the traits typically used to classify people into races. One obvious conclusion from this gross disparity between racially defining traits and the molecular genetic data is that classifications based on these "racial" traits have no evolutionary validity. However, in order to salvage the racial types emerging from the candelabra model, Nei and Roychoudhury (1993) propose two dispersal events out of Africa. The first group of people moved through the Middle East to Northeast Asia and then moved southward to occupy Southeast Asia. Later, a second group of humans migrated out of Africa to the Indian subcontinent and then to Southeast Asia, where admixture occurred with the earlier Asian group. Nei and Roychoudhury then propose that the resultant admixed population in Southeast Asia absorbed most of its gene pool from the older Asian group, but "retained the genes for dark skin, frizzled hair, etc. from Africans, because of natural selection in tropical conditions" (1993:937). This admixed group then moved out to the islands of the Pacific and Australia. The part of this admixed population that remained in Southeast Asia and India then experienced additional admixture events involving the older Asians and Europeans. This second round of admixture wiped out most of the "African traits" in India and Southeast Asia except for a few isolated subpopulations (Nei and Roychoudhury 1993).

Nei and Roychoudhury argue that this complicated, ad hoc scheme is more plausible than the hypothesis of "independent evolution of African traits in this area" (1993: 938). However, no mention is even given to the trellis model interpretation in which these traits are not "African" traits at all, but rather tropical adaptive traits that are favored in human populations living in the appropriate environment—populations that are *not* evolutionarily independent because they were and are in genetic contact. Moreover, even this complicated scheme of multiple admixture and massive population movements still does not explain the genetic distance data. Admixed populations are expected to be intermediate in genetic distance between the original parental populations, but Melanesians are not intermediate between mainland Asian populations and Africans (Figure 4B). This example shows that although complex, multiple ad hoc admixture events are invoked to reconcile the recent candelabra model with the genetic distance data, they still fail to do so. In contrast, isolation by distance fits the human data well and all that it requires is that humans tend to mate primarily with others born nearby but often outside one's own natal group (Lasker and Crews 1996; Santos et al. 1997).

The hypothesis of admixture can be tested directly. When admixture occurs between branches that have differentiated under past isolation, genetic clines are set up simultaneously for all differentiated loci. This results in a strong geographical concordance in the clines for all genetic systems, both neutral and selected. In contrast, isolation by distance may result in geographical concordance for systems under similar selective regimes (Endler 1977; King and Lawson 1997), but otherwise no concordance is expected. Hence, the lack of concordance of "African traits" with molecular genetic distances is not surprising under an isolation by distance model. The lack of concordance in the geographical distribution of different elements has been thoroughly and extensively documented by others and has been one of the primary traditional arguments against the biological validity of human races (Cavalli-Sforza et al. 1996; Futuyma 1986). This lack of concordance across genetic systems falsifies the hypothesis of admixture of previously isolated branches and the idea that "races" were "pure" in the past.

The genetic distance data are therefore informative about the status of human "races" as evolutionary lineages. Genetic distance analyses strongly and uniformly indicate that human "races" cannot be represented as branches on an evolutionary tree as under the candelabra models, even by invoking ad hoc admixture events. Genetic distances, when properly analyzed, undermine the biological validity of human races as evolutionary lineages.

Haplotype Trees

The final type of genetic evidence to be considered is that arising from phylogenetic reconstructions of the genetic variation found in homologous regions of DNA that show little or no recombination. All the homologous copies of DNA in such a DNA region that are identical at every nucleotide (or in practice, identical at all scored nucleotide sites) constitute a single haplotype class. A mutation at any site in this DNA region will usually create a new haplotype that differs initially from its ancestral haplotype by that single mutational change. As time proceeds, some haplotypes can acquire multiple mutational changes from their ancestral type. All the different copies of a haplotype for each of the haplotypes in a species are subject to mutation, resulting in a diversity of haplotypes in the gene pool that vary in their mutational closeness to one another. If there is little or no recombination in the DNA region (as is the case for human mitochondrial DNA or for small segments of nuclear DNA), the divergence of haplotypes from one another reflects the order in which mutations occurred in evolutionary history. When mutational accumulation reflects evolutionary history, it is

possible to estimate a network that shows how mutational changes transform one haplotype into another or from some common ancestral haplotype. Such a network represents an unrooted evolutionary tree of the haplotype variation in that DNA region and is called a haplotype tree. In some circumstances, the ancestral haplotype is known or can be inferred, thereby providing a rooted haplotype tree. In practice, haplotype trees are sometimes difficult to infer from the mutational differences among a set of observed haplotypes because the same mutation may have occurred more than once, thereby destroying the relationship between mutational state and evolutionary history, and/or recombination may have scrambled up the DNA region so thoroughly that accumulated mutational differences reflect both evolutionary history and recombination in a confounded fashion. When they can be estimated, haplotype trees directly reflect only the evolutionary history of the genetic diversity being monitored in the DNA region under study. Haplotype trees are *not necessarily* evolutionary trees of species nor of subpopulations within species. For example, suppose a species is and always has been completely randomly mating as a single population and therefore has no subpopulation evolutionary history at all; yet that same randomly mating species will have haplotype trees for all homologous DNA regions that show little or no recombination.

The publication of mitochondrial haplotype trees (Cann et al. 1987; Vigilant et al. 1991) motivated much of the current debate over recent human evolution. These and subsequent papers (Stoneking 1997) on mitochondrial haplotype trees make a threefold argument in favor of the recent candelabra model: (1) all mtDNA types in current human populations can be traced back to a single common ancestor (mitochondrial "Eve"), (2) the root of the mitochondrial tree is in Africa, and (3) the tree coalesces to its common ancestral type about 200,000 years ago. Although the original haplotype trees were estimated incorrectly because of an improper use of a computer program (Maddison 1991; Templeton 1992), this error is trivial in light of the fact that these three arguments are noninformative about the status of human populations as evolutionary lineages and therefore do not discriminate between the candelabra and trellis models (Templeton 1994a). Point (1) is a universal for all models of human (and indeed, nonhuman) evolution because all homologous segments of DNA are expected to coalesce to a common ancestral molecule under any model of evolution in a finite population (Tavaré et al. 1997). Indeed, haplotype trees would not exist at all if this were not true. With respect to point (2), the trellis model is compatible with any root location occupied by humans at the time of coalescence, which includes Africa. Because the bulk of humanity lived in Africa hundreds of thousands of years ago (as previously noted), an African root is the most likely result under the trellis model. Argument (3) is based on the premise that mitochondrial DNA can spread only when populations expand geographically, so mitochondrial DNA either spread with *Homo erectus* (a million years ago or more) or with the presumed spread of anatomically modern humans about 100,000 years ago (Cann et al. 1987; Stoneking 1997; Vigilant et al. 1991). This premise equates the mitochondrial haplotype tree to a population tree. Haplotype trees may or may not reflect population history (indeed, as pointed out above, there may be no population history at all), and this proposition needs to be tested rather than assumed. In particular, when dealing with populations that are exchanging genes (the premise of the trellis model), a haplotype can spread geographically at any time via gene flow. Hence, a coalescence time of 200,000 years ago is compatible with either model of human evolution (Templeton 1994a).

A fourth argument, not present in the original "Eve" papers but related to mtDNA coalescence time, is that the human population size at the time of coalescence was too small to be compatible with the trellis model (Rogers 1997). Under neutrality, the expected coalescence time of mtDNA is $2N_e$ generations, where N_e is the inbreeding effective size of females. Assuming a coalescence time of 200,000 years ago and a generation length of 20 years yields $N_e = 5{,}000$. More complicated coalescent models yield different estimates, but all are on the order of thousands for N_e (Rogers 1997). N_e is not the census size of females. In general, effective sizes are much smaller than census size. For example, in conservation biology it is standard to assume that the effective size is only one-fifth the census size for large-bodied mammals. This fivefold correction factor from conservation biology assumes a stable or declining census size, but when population sizes are increasing, as seems to be the case for humans over the past hundred thousand years or so, inbreeding effective size can be orders of magnitude smaller than census size or other effective sizes, such as the variance effective size (Templeton 1980). Hence, a fivefold correction for inbreeding effective size to census size is undoubtedly conservative for recent human evolution. Moreover, the census size should be doubled to include males. Thus, the estimate of $N_e = 5{,}000$ implies a census size of 50,000 humans or more. Also, coalescence time is not known to be exactly 200,000 years but rather has a broad confidence interval due to a lack of precise knowledge about the neutral mutation rate and evolutionary stochasticity (Tavaré et al. 1997; Templeton 1993). Using the full range of ambiguity given in Templeton (1993), population sizes up to 200,000 cannot be excluded. Moreover, since 1993, the ambiguity on the mtDNA mutation rate has actually increased (Arnason et al. 1996; Howell et al. 1996; Parsons et al. 1997), taking the upper limits of the confidence range close to a population size of 500,000. All of these calculations depend upon the assumption of neutrality. Deleterious mutations will cause this procedure to underestimate

effective size, and such mutations are known to exist (Hey 1997; Nachman et al. 1996; Templeton 1996). Therefore, all of the above calculations are *lower* bounds given this demonstrated violation of assumptions. More importantly, even a *single* advantageous mutation occurring *anywhere* within the mtDNA genome at *any time* during the past few hundreds of thousands of years of human evolution will make the effective size estimator quantitatively meaningless (Rogers 1997). Given the broad confidence ranges associated with this estimation procedure and its extraordinary sensitivity to deviations from neutrality, it is patent that the population size argument does not discriminate among the alternatives.

Fortunately, there is much information in haplotype trees that can be used to test the hypothesis that human "races" are evolutionary sublineages whose past purity has been somewhat diminished by admixture. For example, in order to reconcile the candelabra model with the genetic distance data, it is necessary to regard Europeans as a heavily admixed population (Bowcock et al. 1991; Cavalli-Sforza et al. 1996). When admixture occurs, haplotypes that differ by multiple mutational events with no existing intermediate haplotypes should coexist in the admixed population's gene pool (Manderscheid and Rogers 1996; Templeton et al. 1995). The detection of such highly divergent haplotypes requires large sample sizes of the presumed admixed population in order to have statistical power. When large sample surveys have been performed upon the presumed admixed European populations, no highly divergent haplotypes or evidence for admixture are observed for either mtDNA (Manderscheid and Rogers 1996) or Y-DNA (Cooper et al. 1996). In contrast, isolation by distance (the trellis model) produces gene pools without strongly divergent haplotypes (i.e., most haplotypes differ by one or at most just a few mutational steps from some other haplotype found in the same population), as is observed.

The candelabra and trellis hypotheses are models of how genes spread across geographical space and through time, and hence a geographical analysis of haplotype trees provides a direct test of these two models. Statistical techniques exist that separate the influences of historical events (such as population range expansions) from recurrent events (such as gene flow with isolation by distance) when there is adequate sampling both in terms of numbers of individuals and of numbers and distribution of sampling sites (Templeton et al. 1995). This statistical approach first converts the haplotype tree into a nested statistical design. The lowest level of analysis is the haplotypes themselves, and the first level of nesting is created by starting at the tips of the haplotype network and moving one mutational step in, forming a union of any haplotypes that are reached by such a single mutational step or that converge upon a common node. This first set of "1-step clades" (Templeton et al. 1987) on the tips of the haplotype network is then pruned off and the process repeated until all haplotypes are included in 1-step clades. Now one has a tree of 1-step clades, and this tree can be nested into "2-step clades" using exactly the same nesting rules, but using 1-step clades instead of haplotypes as the base unit. These nesting rules are used at successively higher levels until the next level of nesting would place the entire original haplotype tree into a single clade (for more details, see Templeton and Sing 1993).

The age of a higher order nesting clade has to be as old or older than the clades nested within it. Thus, even in the absence of a root for the haplotype tree, the nested design provides relative age information. By studying how a series of nested clades is distributed in space, it is therefore possible to make inferences about how haplotype lineages spread geographically through time. Moreover, the geographical range of a clade relative to that of the other clades it is nested with at the next higher level indicates how far spatially a haplotype lineage can spread during the time it takes to accumulate a single mutation. Hence, the nested design based on the haplotype tree automatically adds a temporal dimension to the spatial data gathered with the sample of current haplotypes. It is therefore possible to reconstruct the historical dynamics of the geographical spread of haplotype lineages, with the dynamical resolution being limited by the average amount of time it takes a lineage to accumulate a single mutation. Moreover, by making the analysis nested, no assumption of homogeneity is being made about how lineages spread geographically over time. That is, at one time or place, haplotype lineages may have spread through gene flow restricted by geographical distance; at another time or place, there may have been a rapid range expansion; and at yet another time or place, all genetic interchange between two geographical regions may have been severed. The nested analysis does not exclude any of these possibilities a priori, but rather regards all of them (or any mixture) as legitimate factors influencing the movement of haplotype lineages through time and space (Templeton et al. 1995). This statistical approach therefore treats historical and recurrent events as joint possibilities rather than as mutually exclusive alternatives.

These different factors, however, leave different signatures in the nested analyses. If gene flow restricted by isolation by distance dominated during the place and time when a certain subset of mutations occurred, then the older clades defined by these mutations should be more widespread and the younger but evolutionarily close clades should be in the same general area as the older clades. This expectation follows from the simple fact that under isolation by distance, genes spread only a little every generation, and the longer a gene lineage exists, the more generations it has to spread geographically and to accumulate additional mutations. If two geographical regions split from one another (i.e., severed genetic interchange), then

the clades that mark those geographical regions and that time of isolation would accumulate many mutational differences but without movement into each other's space. Finally, if a subset of the original population (containing only a subset of the haplotype variation that existed at that time) suddenly expanded into and colonized a new geographical region, then the subset of haplotypes they carried and the lineages derived from them would have widespread geographical distributions for their frequency relative to the population as a whole. Thus, gene flow and different historical events leave distinct genetic-spatial signatures in a nested analysis and are thereby distinguishable. Moreover, the areas affected by these forces and events can be inferred, as can their time relative to the nested design of the haplotype tree.

The ability to discriminate the genetic signatures of range expansions from recurrent but restricted gene flow is critical to discriminating the candelabra from the trellis models and thereby inferring the evolutionary validity of race. The criteria used to identify range expansions in this nested approach have been empirically validated by analyzing data sets with strong prior evidence of range expansion and were found to be accurate and not prone to false positives (Templeton 1998a). Application of this statistical approach to human mtDNA haplotype trees yields the significant results summarized in Figure 6 (Templeton 1993, 1997b, 1998a).

As shown in Figure 6, human mtDNA yields a pattern of isolation by distance between Africans and Eurasians throughout the *entire* time period marked by mtDNA coalescence (Templeton 1993, 1997b), thereby significantly rejecting both the candelabra hypothesis of no gene flow between Africans and non-Africans and the admixture models used to reconcile the candelabra models with the genetic distance data. Recurrent gene flow in this analysis is relative to the time scale defined by the coalescence and mutation rates of mtDNA, so gene flow among Old World human populations could have been sporadic on a time scale of several tens of thousands of years.

Figure 6 also reveals that range expansions played a significant role in recent human evolution. Among the statistically significant range expansions is a relatively recent range expansion across Europe (Templeton 1993, 1997b), an inference supported by other mtDNA data sets (Calafell et al. 1996; Comas et al. 1997; Francalacci et al. 1996). A recent study on mtDNA isolated from a Neandertal (Krings et al. 1997) is suggestive (but not conclusive as the sample size is one) that Neandertals were replaced in Europe. This inference is compatible with the statistically significant European expansion shown in Figure 6, but further data are obviously needed to determine if

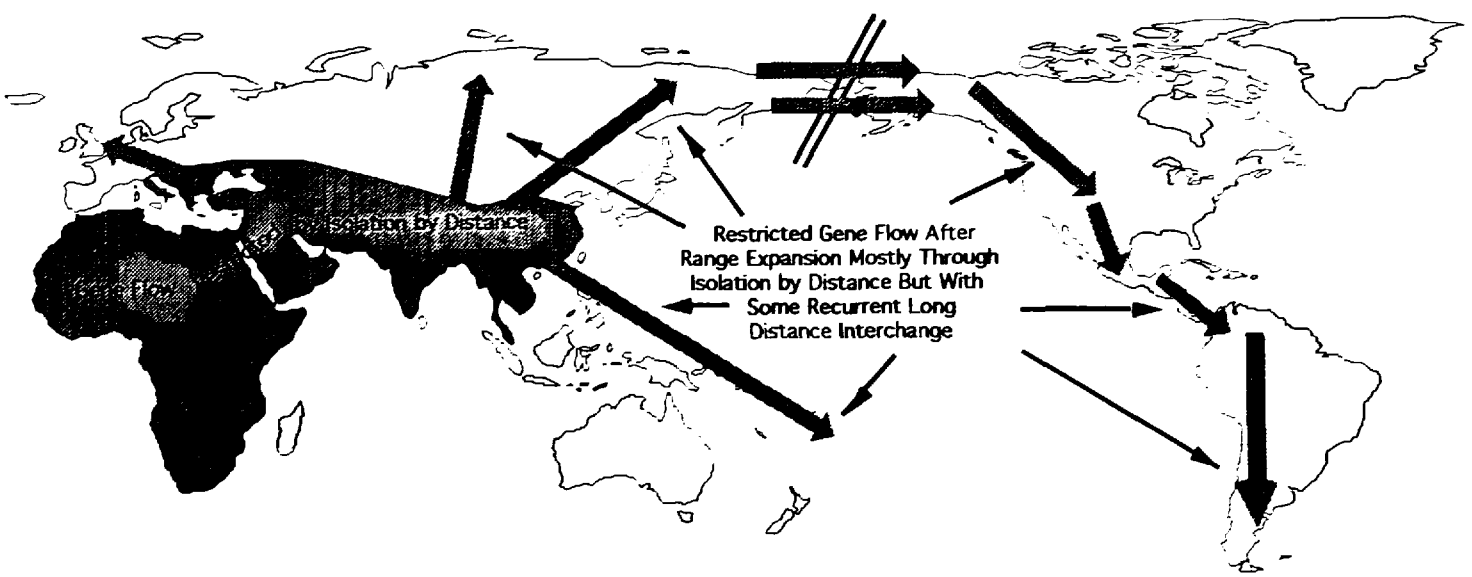

Figure 6. Statistically significant inferences from geographical analyses of human mtDNA haplotype trees. As far back as is observable with mtDNA, there was gene flow restricted by isolation by distance in human populations living in Africa and southern Eurasia. More recent statistically significant range expansion events are indicated by wide arrows. There were expansions into Europe, northern Asia, the Pacific, and the Americas. Two arrows are indicated going into North America because this expansion either involved a colonization event with a large number of people, an extended colonization, or at least two separate colonization events. The lines drawn through these arrows indicate that after the colonization there was a significant reduction, perhaps cessation, of gene flow between Asia and North America. After the colonization of North America, there were further significant expansions into the remainder of the Americas. After these expansion events, there is statistically significant gene flow once again. Most of this postexpansion gene flow fits the expectations of isolation by distance, but some postexpansion gene flow occurred through long-distance interchanges.

this recent European expansion event was also a replacement event. The other recent expansions (into northern Asia, the Pacific, and the Americas) appear to be range expansions into previously unoccupied areas.

Genetic interchange between Africans and Eurasians over long periods of human evolutionary history is also strongly suggested by a hemoglobin beta locus tree (Harding et al. 1997). The coalescence of an autosomal gene is expected to be about four times as old as that of mtDNA or Y-DNA, and this seems to be the case for the beta locus (Harding et al. 1997). Consequently, the patterns of widespread gene flow across Africa and Asia observed with the hemoglobin locus predate the hypothesized "replacement" event of the recent candelabra model (Harding et al. 1997). Obviously, if such a replacement had occurred, these earlier genetic signatures of gene flow should have been obliterated.

To reinforce these conclusions, the hemoglobin beta locus data of Harding et al. (1997) were subjected to a nested clade analysis of geographical associations (Templeton et al. 1995). First the estimated haplotype tree is converted into a series of nested branches (clades) (Templeton et al. 1987; Templeton and Sing 1993). Figure 7 shows the hemoglobin haplotype network of Harding et al. (1997), along with the nested statistical design. Once the haplotype tree has been converted into a nested statistical design, the geographical data are quantified in two main fashions (Templeton et al. 1995): the clade distance, D_c, which measures the geographical range of a particular clade; and the nested clade distance, D_n, which measures how a particular clade is geographically distributed relative to its closest evolutionary sister clades (i.e., clades in the same next higher-level nesting category). Contrasts in these distance measures between older and younger clades are important in discriminating the potential causes of geographical structuring of the genetic variation (Templetonet al. 1995), as discussed above. In this case, temporal polarity is determined by an outgroup analysis that indicates that haplotype B3 in Figure 7 is the root (Harding et al. 1997) in addition to the polarity inherent in the nested design itself. The statistical significance of the different distance measures and the old-young contrasts are determined by random permutation testing that simulates the null hypothesis of a random geographical distribution for all clades within a nesting category given the marginal clade frequencies and sample sizes per locality. Figure 8 presents the results of this nested clade analysis of geographical distributions.

The statistically significant patterns shown in Figure 8 need to be interpreted biologically. In order to make inference explicit and consistent, a detailed inference key is provided as an appendix to Templeton et al. (1995) (hereafter

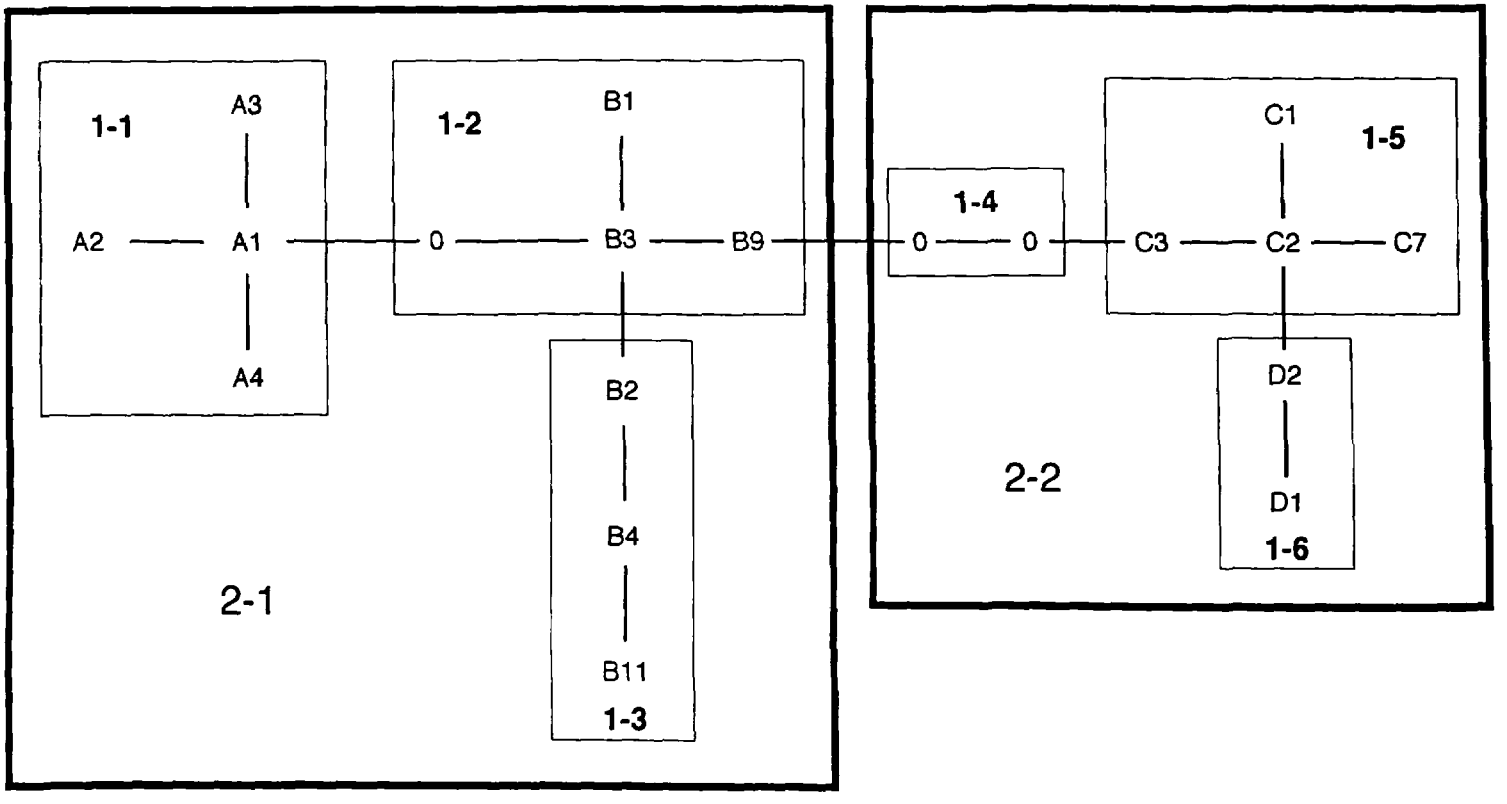

Figure 7. The hemoglobin haplotype network of Harding et al. (1997), alone with the nested statistical design. Haplotype designations are those given in Harding et al. (1997). Nested groupings above the haplotype level are designated by "C-N," where C is the nesting level of the clade and N is the number of a particular clade at a given nesting level. Boxes with thin lines nest together haplotypes into 1-step clades, and boxes with thick lines nest together 1-step clades with 2-step clades.

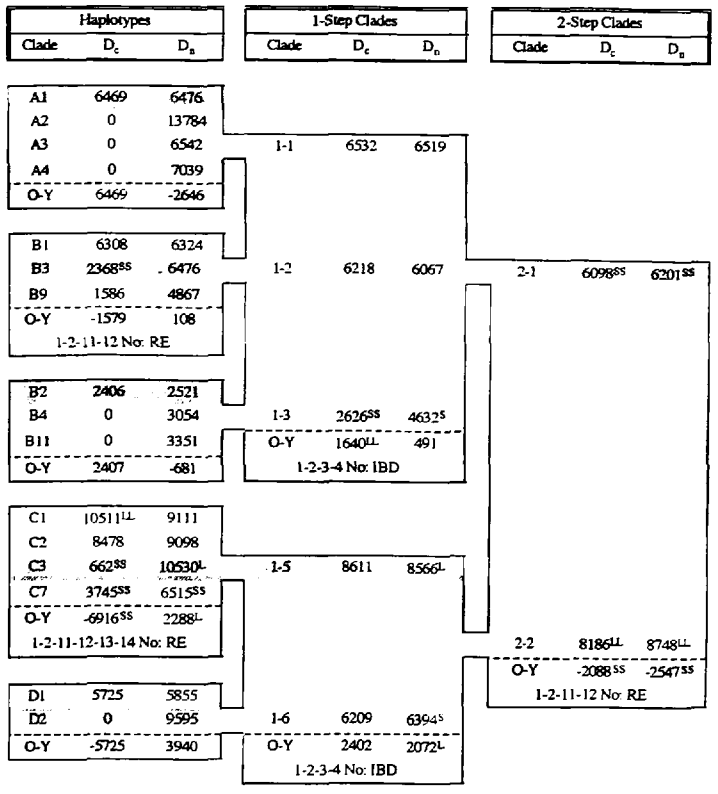

Figure 8. Results of the nested geographic analysis of the human beta chain hemoglobin haplotypes. The nested design is given in Figure 7, as are the haplotype and clade designations. Following the name or number of any given clade are the clade and nested clade distances. The oldest clade within a nested group is indicated by shading. The average difference between the oldest and younger clades within a nesting category (as determined by B3 being the root) for both distance measures is given in the row below a dashed line labeled "O-Y." A superscript S means that the distance measure is significantly small at the 5% level, and SS, at the 1% level. Similarly, a superscript L means that the distance measure is significantly large at the 5% level, and LL, at the 1% level. At the bottom of the boxes that indicate a nested set of clades in which one or more of the distance measures is significantly large or small is a line indicating the biological inference. The numbers refer to the sequence of questions in the TRP key that the pattern generated, followed by the answer to the final question in the TRP key. Following this answer is the biological inference generated by use of the TRP key, where RE is range expansion and IBD is recurrent gene flow restricted by isolation by distance.

referred to as the TRP key). Templeton (1998a) gives an empirical validation of this key. This key provides for the objective and systematic identification of the distinct signatures associated with isolation by distance, fragmentation, and range expansion that were described qualitatively above. Moreover, the key also identifies the artifacts that can emerge from inadequate geographical sampling. Consequently, not all rejections of the null hypotheses can be interpreted biologically. Figure 8 shows the resulting inferences.

In comparing the mtDNA (Figure 6) and hemoglobin (Figure 8) inferences, it is important to keep two factors in mind. First, these two haplotype trees are detecting events on different time scales. In particular, the time depth of the hemoglobin network has a 95% confidence interval of 400,000 to 1,300,000 years ago (Harding et al. 1997). Once ultimate coalescence has occurred in a haplotype tree, there is no information about previous events or evolutionary forces. Therefore, the older events and forces detected in the hemoglobin analysis would be completely invisible to the mtDNA analysis. The oldest event detected in the hemoglobin analysis is an out-of-Africa range expansion found among 2-step clades as nested within the entire haplotype tree, and which therefore must have occurred close to the time depth of the entire tree. This out-of-Africa expansion event is obviously too old to be the one postulated by the recent candelabra model. Because it spans the entire time depth of the hemoglobin haplotype tree, there is no information at all about the pre-expansion population. Hence, this old out-of-Africa expansion could have been a colonization event of empty areas, a replacement event, or a hybridization event in which new migrants interbred with previous Eurasian inhabitants. There is simply no way of knowing. After this expansion, gene flow clearly occurred among Africans and Eurasians as constrained by isolation by distance as shown by the 1-step clades nested within both 2-step clades (Figure 8). The mutations defining these mid-level clades are expected to be $\geq$ 200,000 years old (Harding et al. 1997). Given that the mtDNA shows recurrent gene flow with isolation by distance certainly for times $<$ 200,000 years ago (Figure 6), the two data sets jointly imply a long time span of recurrent genetic contact among the major Old World human populations.

An out-of-Asia expansion event is detected within clade 1-5 in the hemoglobin analysis (Figure 8). One of the critical mutations defining this expansion event (the mutation on the branch between C3 and C2) has an estimated age of 137,000 $\pm$ 81,500 years and a second critical mutation (the one defining C7) of 69,000 $\pm$ 48,000 years (Harding et al. 1997). If this out-of-Asia expansion is older than 100,000, then it would be impossible for a complete genetic replacement of the ancestral Asian population to have occurred by Africans 100,000 years ago. If this out-of-Asia expansion is younger than 100,000, then there was genetic interchange between Asians and Africans, and therefore no "split" between Africans and Eurasians 100,000 years ago. Another range expansion is found within clade 1-2 (Figure 8), and the geographical distribution of the haplotypes implies that this is an out-of-Africa expansion. Because clade 1-2 includes the very oldest haplotypes, this may simply be a reflection of the old out-of-Africa range expansion detected among the 2-step clades. However, the significant effect of the old haplotype B3 may in this case be due in part to the nonsignificant but widespread distribution of haplotype B1. The mutation defining B1 has an estimated age of about

152,000 years, but its confidence interval spans virtually the entire past 300,000 years (Harding et al. 1997). Hence, the clade 1-2 inference may represent a more recent out-of-Africa expansion occurring sometime in the last 300,000 years. Even if clade 1-2 represents a recent out-of-Africa expansion event, it certainly *is not* a replacement event. A true replacement event at about 100,000 years ago would have obliterated all evidence for older gene flow; yet the clade 1-2 out-of-Africa event is nested-*within* a pattern of significant gene flow with isolation by distance (clade 2-1). There is no obvious way to reconcile the hemoglobin data with a recent out-of-Africa replacement event.

The second factor to keep in mind when comparing the mtDNA with the hemoglobin analysis is the level of dynamic resolution. The nested clade analysis can only detect population events and recurrent forces that are marked by mutational changes (Templeton 1998a). MtDNA is evolving much more rapidly than the hemoglobin locus, and the attendant haplotype trees are far more resolved for mtDNA than for hemoglobin. Consequently, the hemoglobin analysis is on both an older and a coarser time scale than the mtDNA. Therefore, the most recent events and forces detected in the mtDNA analysis would be invisible to the hemoglobin analysis. This explains why the hemoglobin analysis does not detect the more recent range expansions revealed by the mtDNA (Figure 6): there are simply no or too few mutations in the hemoglobin data to mark these recent expansion events. Hence, the hemoglobin and mtDNA analyses are complementary, not contradictory.

Finally, genetic interchange between Africans and Eurasians is additionally suggested by a nested clade analysis of a Y-DNA haplotype tree (Hammer et al. 1998). Interestingly, a range expansion out of Africa and into Eurasia is detected in this nested analysis. However, in light of the mtDNA and hemoglobin results, this expansion was not a replacement event, at least for the maternal demographic component. Following this out of Africa expansion, the nested analysis reveals a pattern of significant recurrent gene flow restricted by isolation by distance, including interchange between African and Eurasian populations. Moreover, there was a subsequent range expansion out of Asia and into Africa, as was also detected in the hemoglobin analysis. The Y-chromosome therefore shows more evidence of long-range population movements than the mtDNA. One possible explanation for this pattern is that males dispersed more than females during long-range population movements. However, both mtDNA and Y-DNA show recurrent gene flow with isolation by distance interconnecting African and Eurasian populations, indicating that both males and females have dispersed during short-range migrations. Regardless, there is clearly genetic interchange between Africans and Eurasians due to a mixture of gene flow mediated by isolation by distance and population movements. No genetic split between Africans and Eurasians is found in the Y-DNA, as was also true for the mtDNA and hemoglobin beta region.

Combined, the mtDNA, Y-DNA, and hemoglobin data sets reveal that human evolution from about a million years ago to the last tens of thousands of years has been dominated by two evolutionary forces: (1) population movements and associated range expansions (perhaps with some local replacements, but definitely with no global replacement within the last 100,000 years), and (2) gene flow restricted by isolation by distance. The only evidence for any split or fragmentation event in human evolutionary history within this time frame is the one detected with mtDNA (Figure 6) involving the colonization of the Americas (Templeton 1998a). However, this colonization was due to either multiple colonization events or involved movements by large numbers of peoples (Templeton 1998a), resulting in extensive sharing of genetic polymorphisms of New World with Old World human populations. Moreover, the genetic isolation between the Old and New Worlds was brief and no longer exists. Other than this temporary fragmentation event, the major human populations have been interconnected by gene flow (recurrent at least on a time scale of the order of tens of thousands of years) during the last one to two hundred thousand years. Gene flow may have been more sporadic earlier, but multiple genetic interchanges certainly occurred among Old World populations $\geq$ 200,000 years ago. Hence, the haplotype analyses of geographical associations strongly reject the existence of evolutionary sublineages of humans, reject the separation of Eurasians from Africans 100,000 years ago, and reject the idea of "pure races" in the past. Thus, human "races" have no biological validity under the evolutionary lineage definition of subspecies.

Conclusions

The genetic data are consistently and strongly informative about human races. Humans show only modest levels of differentiation among populations when compared to other large-bodied mammals, and this level of differentiation is well below the usual threshold used to identify subspecies (races) in nonhuman species. Hence, human races do not exist under the traditional concept of a subspecies as being a geographically circumscribed population showing sharp genetic differentiation. A more modern definition of race is that of a distinct evolutionary lineage within a species. The genetic evidence strongly rejects the existence of distinct evolutionary lineages within humans. The widespread representation of human "races" as branches on an intraspecific population tree is genetically indefensible and biologically misleading, even when the ancestral node is presented as being at 100,000 years ago.

Attempts to salvage the idea of human "races" as evolutionary lineages by invoking greater racial purity in the past followed by admixture events are unsuccessful and falsified by multilocus comparisons of geographical concordance and by haplotype analyses. Instead, all of the genetic evidence shows that there never was a split or separation of the "races" or between Africans and Eurasians. Recent human evolution has been characterized by both population range expansions (with perhaps some local replacements but no global replacement within the last 100,000 years) and recurrent genetic interchange. The 100,000 years ago "divergence time" between Eurasians and Africans that is commonly found in the recent literature is really only an "effective divergence time" *in sensu* Nei and Roychoudhury (1974, 1982). Since no split occurred between Africans and Eurasians, it is meaningless to assign a date to an "event" that never happened. Instead, the effective divergence time measures the amount of restricted gene flow among the populations (Slatkin 1991).

Because of the extensive evidence for genetic interchange through population movements and recurrent gene flow going back at least hundreds of thousands of years ago, there is only one evolutionary lineage of humanity and there are no subspecies or races under either the traditional or phylogenetic definitions. Human evolution and population structure have been and are characterized by many locally differentiated populations coexisting at any given time, but with sufficient genetic contact to make all of humanity a single lineage sharing a common, long-term evolutionary fate.

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