Population Bottlenecks and Pleistocene Human Evolution

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We review the anatomical and archaeological evidence for an early population bottleneck in humans and bracket the time when it could have occurred. We outline the subsequent demographic changes that the archaeological evidence of range expansions and contractions address, and we examine how inbreeding effective population size provides an alternative view of past population size change. This addresses the question of other, more recent, population size bottlenecks, and we review nonrecombining and recombining genetic systems that may reflect them. We examine how these genetic data constrain the possibility of significant population size bottlenecks (i.e., of sufficiently small size and/or long duration to minimize genetic variation in autosomal and haploid systems) at several different critical times in human history. Different constraints appear in nonrecombining and recombining systems, and among the autosomal loci most are incompatible with any Pleistocene population size expansions. Microsatellite data seem to show Pleistocene population size expansions, but in aggregate they are difficult to interpret because different microsatellite studies do not show the same expansion. The archaeological data are only compatible with a few of these analyses, most prominently with data from Alu elements, and we use these facts to question whether the view of the past from analysis of inbreeding effective population size is valid. Finally, we examine the issue of whether inbreeding effective population size provides any reasonable measure of the actual past size of the human species. We contend that if the evidence of a population size bottleneck early in the evolution of our lineage is accepted, most genetic data either lack the resolution to address subsequent changes in the human population or do not meet the assumptions required to do so validly. It is our conclusion that, at the moment, genetic data cannot disprove a simple model of exponential population growth following a bottleneck 2 MYA at the origin of our lineage and extending through the Pleistocene. Archaeological and paleontological data indicate that this model is too oversimplified to be an accurate reflection of detailed population history, and therefore we find that genetic data lack the resolution to validly reflect many details of Pleistocene human population change. However, there is one detail that these data are sufficient to address. Both genetic and anthropological data are incompatible with the hypothesis of a recent population size bottleneck. Such an event would be expected to leave a significant mark across numerous genetic loci and observable anatomical traits, but while some subsets of data are compatible with a recent population size bottleneck, there is no consistently expressed effect that can be found across the range where it should appear, and this absence disproves the hypothesis.

Introduction

The paleodemographic history of humanity has classically been studied as a problem of archaeology (Birdsell 1972; Hassan 1981; Wobst 1993), with largely theoretical contributions from mathematical modeling (Yellen and Harpending 1972; Weiss 1973; Buikstra and Konigsberg 1985). However, in the past several years, an increased availability of data on human genetic variation, coupled with advances in theoretical population biology, have allowed us to further examine human demographic history from a genetic perspective. These data have addressed some of the earlier problems but have also created others, because genetic hypotheses about the past are largely a reflection of the paleodemographic models assumed (Brookfield 1997).

Large-scale genetic studies have assessed the worldwide pattern of variation in human mtDNA (Cann, Stoneking, and Wilson 1987; Vigilant et al. 1991; Takahata 1993; Easteal, Harley, and Betty 1997), Y chromosomes (Dorit, Akashi, and Gilbert 1995, 1996; Hammer 1995; Hammer and Zegura 1996; Underhill et al. 1997; Hammer et al. 1998), β-globin (Harding et al. 1997), and HLA alleles (Klein et al. 1993; Ayala 1995; Takahata and Satta 1998). Other studies have analyzed systems comprising multiple loci interspersed throughout the genome, including microsatellites (Di Rienzo et al. 1997; Jorde et al. 1997; Kimmel et al. 1997; Calafell et al. 1998; Reich and Goldstein 1998; Stephan and Kim 1998), single-nucleotide polymorphisms (Mountain et al. 1992; Mountain and Cavalli-Sforza 1994, 1997; Wang et al. 1998), and human-specific *Alu* insertions (Batzer et al. 1992; Harpending et al. 1993; Rogers and Jorde 1995; Sherry 1996; Sherry et al. 1997). When these sources of data have been compared, they have sometimes yielded contradictory results (Ruvolo 1996; Hey 1997; Wise et al. 1997). Methods of population genetic analysis have begun to address these contradictions in the context of testing hypotheses of past demographic change (Jorde et al. 1995; Hey 1997).

Contradictions also occur between genetic and other, more traditional, sources of data addressing past human evolution (Bower 1999; Pennisi 1999). Unlike indirect methods based on population genetics, archaeological and paleontological sources provide direct evidence about the past that can be independently compared with genetic inferences. Recent debates have pitted such evidence against genetic interpretations (e.g., Thorne and Wolpoff 1992 vs. Wilson and Cann 1992), simplifying the controversy to dueling slogans about

Abbreviations: MYA, million years ago; Myr, million years; MSA, Middle Stone Age; N_c, census population size; N_e, effective population size.

Key words: human evolution, bottlenecks, paleoanthropology, paleodemography.

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which source of evidence is ''better'': e.g., ''fossils are the only direct evidence of evolution,'' and ''all of the living have ancestors while it may be that no fossils have descendants.'' This is not a useful way to proceed, and the use of simulations provides the possibility of using such evidence quite differently, to test models of demographic evolution rather than to emphasize the incompatibilities of different data sources.

Here, we provide a broad application of the simulation approach to examine both genetic and nongenetic sources of information concerning the most fundamental demographic issues—the population size of the human lineage in the past, and how it has changed during the last 2 Myr. The different reconciliations of paleoanthropological data and recombining genetic systems, nonrecombining systems, or systems with low rates of recombination all have one thing in common: the expectation that small population size bottlenecks (reductions in population size followed by population size increases) played an important role in the Plio-Pleistocene evolution of our lineage. No evidence contradicts the contention that one of these bottlenecks took place at the time of the speciation at the beginning of our lineage, at the end of the Pliocene some 2 MYA. This early population size bottleneck has great explanatory power and important implications for understanding genetic variation and its relationship with past population size. The question we address is whether this bottleneck is compatible with any other more recent ones.

In this paper, we review the anatomical and archaeological evidence for an early population size bottleneck and bracket the time when it could have occurred. We outline the subsequent demographic changes that the archaeological evidence of range expansions and contractions address, and we examine how estimates of inbreeding effective population size from genetic data may provide an alternative view of past population size change. We discuss the possibility of more recent population size bottlenecks, and we review nonrecombining and recombining genetic systems that may reflect them. We examine the constraints that these genetic data place on the possibility of significant population size bottlenecks (i.e., of sufficiently small size and/or long duration to minimize genetic variation in autosomal and haploid systems) at several different critical times in human history. Different constraints appear in nonrecombining and recombining systems, and among autosomal loci most are incompatible with any Pleistocene population size expansions. Microsatellite data can be construed as showing Pleistocene population size expansions but are difficult to interpret because different microsatellite studies do not show the same expansion. The archaeological data are only compatible with a few of these analyses, most prominently with data from *Alu* elements, and we use these facts to question whether the view of the past from analysis of inbreeding effective population size is valid. Finally, we examine the conditions under which inbreeding effective population size can be expected to provide any reasonable measure of the actual past size of the human species.

A 2-Myr Bottleneck

There are many reasons to believe that there may have been a number of severe population size bottlenecks on the lineage leading to living humans, principally because of the many speciation events that must have occurred. The diversity of the Pliocene hominid fossil record, beginning with the large samples from Aramis and Kanapoi 4.0–4.4 MYA (White, Suwa, and Asfaw 1994; Leakey 1995; Leakey et al. 1998), indicates that ours is just the most recent of a wide array of hominid species that once existed. The demographic effects of such speciations can be expected to have been intense, probably involving significant founder effects due to small population sizes, and they eradicated evidence of earlier speciations, such as the chimpanzee-hominid divergence. In turn, we expect that any genetic evidence of these early hominid speciations would have been covered up by the most recent significant bottleneck. We believe this bottleneck could have been the speciation event at the beginning of the lineage leading to living human populations.

There are two issues to consider here: what is the paleoanthropological evidence of a Late Pliocene hominid speciation, and what is the evidence that this speciation was cladogenic and involved a small population size bottleneck? In later sections, we will explore the question of whether this was the most recent significant bottleneck.

A hominid speciation is documented with paleoanthropological data at about 2 MYA by significant and simultaneous changes in cranial capacity and both cranial and postcranial characters. This marks the earliest known appearance of our direct ancestors. The new species has been called *Homo erectus* or *Homo ergaster* by some authors. Following others (Jelínek 1978; Aguirre 1994; Wolpoff et al. 1994), we call this emerging evolutionary species early *Homo sapiens,* as it begins an unbroken lineage leading directly to living human populations. The first specimens are humanity's earliest known direct ancestors.

We, like many others, interpret the anatomical evidence to show that early *H. sapiens* was significantly and dramatically different from earlier and penecontemporary australopithecines in virtually every element of its skeleton (fig. 1) and every remnant of its behavior (Gamble 1994; Wolpoff and Caspari 1997; Asfaw et al. 1999; Wood and Collard 1999). Its appearance reflects a real acceleration of evolutionary change from the more slowly changing pace of australopithecine evolution. For instance, *Australopithecus afarensis, Australopithecus africanus,* and the earliest *H. sapiens* sample are three species that are generally thought to be an ancestral-descendent line, although with cladogenesis between them. There certainly is cladogenesis between the last two, as *H. sapiens* and the penecontemporary habiline species now attributed to *Australopithecus* (Wolpoff 1999; Wood and Collard 1999) must have a recent common ancestor later than *A. africanus.* These consecutive species samples are about half a million years apart, but the amounts of change between them are quite different. From the

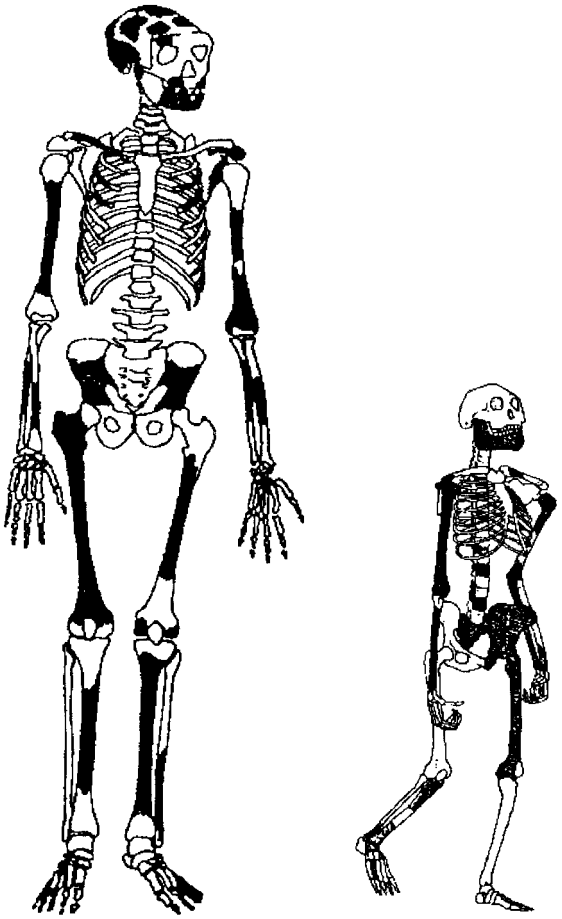

FIG. 1.—The first members of early *Homo sapiens* are really quite distinct from their australopithecine predecessors and contemporaries. Perhaps the most fundamental dissimilarity, a dramatic size difference, is shown here in this correctly scaled comparison of the reconstructed skeletons of two women: ''Lucy,'' a 3-Myr-old australopithecine (Wood 1992), and ER 1808 (Walker, Zimmerman, and Leakey 1982), a woman of our species about half that age. Australopithecine contemporaries to ER 1808 were as small as Lucy. Other differences lie in skeletal proportions and brain size (fig. 2), both absolute and relative to body size.

earlier to later australopithecine species, cranial capacity (approximate midsex average) goes from 450 cm^3 to 475 cm^3, while from *A. africanus* to the earliest African *H. sapiens* sample the change is much greater: 860 cm^3. Supporting this, a newly named 2.5-Myr-old australopithecine species that is argued to be a direct ancestor of *H. sapiens, Australopithecus garhi,* has a male cranial capacity of 450 cm^3 (Asfaw et al. 1999). The significant change to the cranial size of *H. sapiens* is greater than could be explained by body size alone (fig. 2), which also greatly increases as discussed below.

Yet, brain size is only one of the evolving systems reflected in early *H. sapiens* anatomy. There are four interrelated complexes of changes at the very beginning of *H. sapiens* (Wolpoff 1999): (1) changing brain size (larger, especially longer vault, with a broad frontal bone and an expanded parietal association area; neural canal expansion); (2) changing dental function (more anterior tooth use, greater emphasis on grinding and less on crunching) as reflected in broader faces and larger nuchal areas; (3) development of a cranial buttressing system to strengthen the vault, including vault bone thickening and prominent tori; and (4) dramatic expansion of body height (estimated average weights double) and numerous changes in proportions (fig. 1). These, and other changes involving the visual and respiratory systems, reflect significant adaptive differences for the new species and give us important insight into the mode of speciation because they seem to happen all together, at the time of its origin.

The anatomy of the earliest *H. sapiens* sample indicates significant modifications of the ancestral genome and is not simply an extension of evolutionary trends in an earlier australopithecine lineage throughout the Pliocene. In fact, its combination of features never appears earlier; some of its characteristics are unique, such as the very large body sizes and long legs described below, while others can be found in isolation in various different Pliocene and penecontemporary hominid species.

A Genetic Revolution

If we assume these earlier australopithecines are a group of very closely related species, for instance, nearer to each other than *Pan* and *Homo,* we can expect that they differ much more in allele frequencies than in the presence or absence of specific genes for these features. Therefore, a reshuffling of existing alleles could result in the frequencies of features we observe in early *H. sapiens.* Thus, our second question is about this reshuffling, whether early *H. sapiens* is a consequence of rapid speciation with significant founder effect or the result of a long, gradual process of anagenic change. The first explanation, cladogenesis, is suggested by the fact that no gradual series of changes in earlier australopithecine populations clearly leads to the new species, and no australopithecine species is obviously transitional. This may seem to be an unexpected statement, because for 3 decades habiline species have been interpreted as being just such transitional taxa, linking *Australopithecus* through the habilines to later *Homo* species. But with a few exceptions, the known habiline specimens are now recognized to be less than 2 Myr old (Feibel, Brown, and McDougall 1989) and therefore are too recent to be transitional forms leading to *H. sapiens.*

Our interpretation is that the changes are sudden and interrelated and reflect a bottleneck that was created because of the isolation of a small group from a parent australopithecine species. In this small population, a combination of drift and selection resulted in a radical transformation of allele frequencies, fundamentally shifting the adaptive complex (Wright 1942); in other words, a genetic revolution (Mayr 1954; Templeton 1980).

This interpretation is also supported by the fact that several different adaptive complexes changed significantly (as noted above) and together, and that evidences of these changes is found in the earliest specimens. These earliest remains exemplify the significance and magnitude of the newly evolved differences, although not exhaustively, as not all body parts are represented. The most ancient finds are the KNM-ER 3228 innominate (Rose 1984) and the KNM-ER 2598 occipital bone

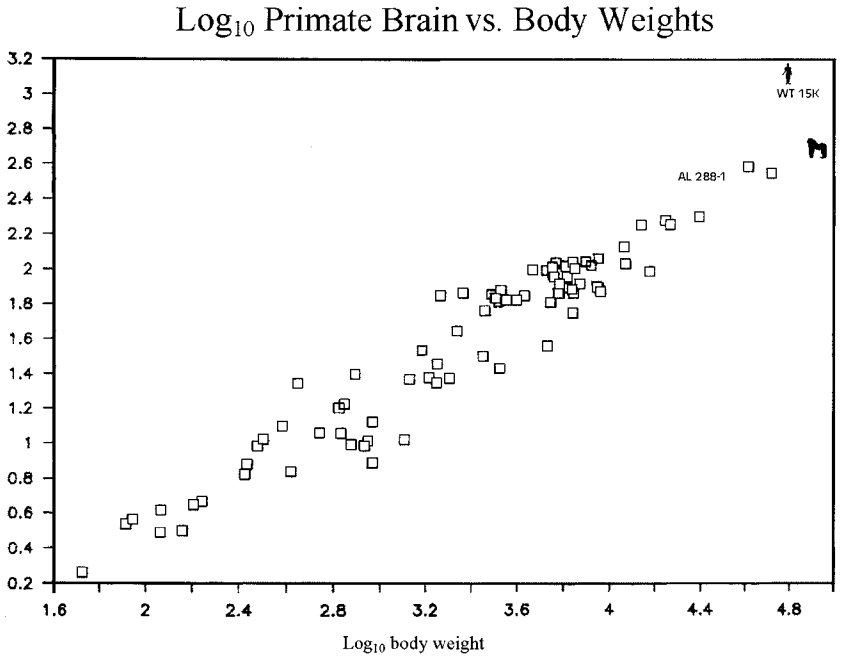

FIG. 2.—Plot of mean $\log_{10}$ brain weights and body weights for 85 living primate species (Holloway 1988). Two early hominids complete enough for estimates of brain and body weight are inserted in position: the Hadar australopithecine female AL 288-1 (''Lucy'') and the early *Homo sapiens* Turkana boy ER 15000 (adult estimates for the parameters are plotted). Note that the australopithecine is within the nonhuman primate distribution, while ER 15000 is beyond their ellipsoid of variation and is like the human above it (the figurine represents the population means for living *H. sapiens*). The gorilla value (the largest body size for any living primate) is also shown as a figurine. These and other data show that cranial capacity in living and fossil *H. sapiens* is beyond the expectations of primate allometry. This expansion is the case only for *H. sapiens*, even the earliest, and it is one of the most dramatic and important distinctions of the species.

(Wood 1991), dated, respectively, at 1.95 ± 0.05 and 1.89 ± 0.01 Myr (Feibel, Brown, and McDougal 1989). It was noted in their descriptions, and we found in our comparisons, that each of these bones closely resembles its later (what we refer to as) early *H. sapiens* counterpart and differs markedly from australopithecines.

KNM-ER 2598 is the upper portion of a big, thick occiput with a broad, vertically tall, backward-projecting and thick nuchal torus (bone thickness is 18 mm at inion) and a flexed occipital angle (108°). Internally, there are large cerebral fossae. None of these features, reflecting complexes 1 and 3 above, are found on earlier hominid occiputs. For instance, bone thickness at inion averages 10.3 mm for *A. afarensis* and 12.8 mm for *A. africanus.* The midline vertical height of the ER 2598 nuchal torus is 23.5 mm, compared with an *A. afarensis* mean of 12.5 mm and an *A. africanus* mean of 13.9 mm.

KNM-ER 3228 is a very large right male innominate that exceeds the size of the largest male australopithecine bones (Stw 431, SK 50). It differs from them in features such as the relatively large acetabulum and strongly developed iliac pillar (fig. 3). These reflect complex 4, above. The emerging anatomy shows that there were increases in the hip joint reaction and gluteal abductor forces from the australopithecine condition and is compatible with Ruff's (1995) model of postaustralopithecine pelvic changes. As he reconstructs this specimen and the more complete ER 15000 pelvis from 400,000 years later (both males), the transverse breadth of the pelvis was constrained by climatic adaptation to the tropics, while the pelvic aperture's breadth increased in response to larger head size at birth (with the male condition presumably reflecting the female responses). The more vertical orientation of the iliac blade that resulted from these changes, combined with the very long legs of early *H. sapiens,* created more bending stress in the ilium and higher joint reaction force on the acetabulum.

Ruff (1995) believes increasing head size at birth during the australopithecine-like birth process (reflecting complex 1, above) controlled the pelvic aperture shape (cf. Tague and Lovejoy 1986). Birth in the earliest *H. sapiens* did not involve a second rotation during the trip through the pelvic aperture to bring the baby into the sacrum-facing position of today's births, because pelvic outlet shape appears to have matched the inlet shape in being transversely broad and anterior-posteriorly narrow. Ruff thereby contends that many of the pelvic features in the early *H. sapiens* males, including pelvic aperture shape, are related to the birthing problems faced by women. His interpretation of this shape implies a significant change to relatively premature (altricial) births in earlier *H. sapiens,* because, in spite of markedly greater cranial capacity, fetal heads were too small at birth to influence pelvic aperture dimensions and shape constraints and select for the changes in aperture shape that characterize women today (and in the Late Pleistocene).

Figure 3 shows the basis for this interpretation, with the earliest known specimen of *H. sapiens,* the male innominate discussed above. The australopithecine

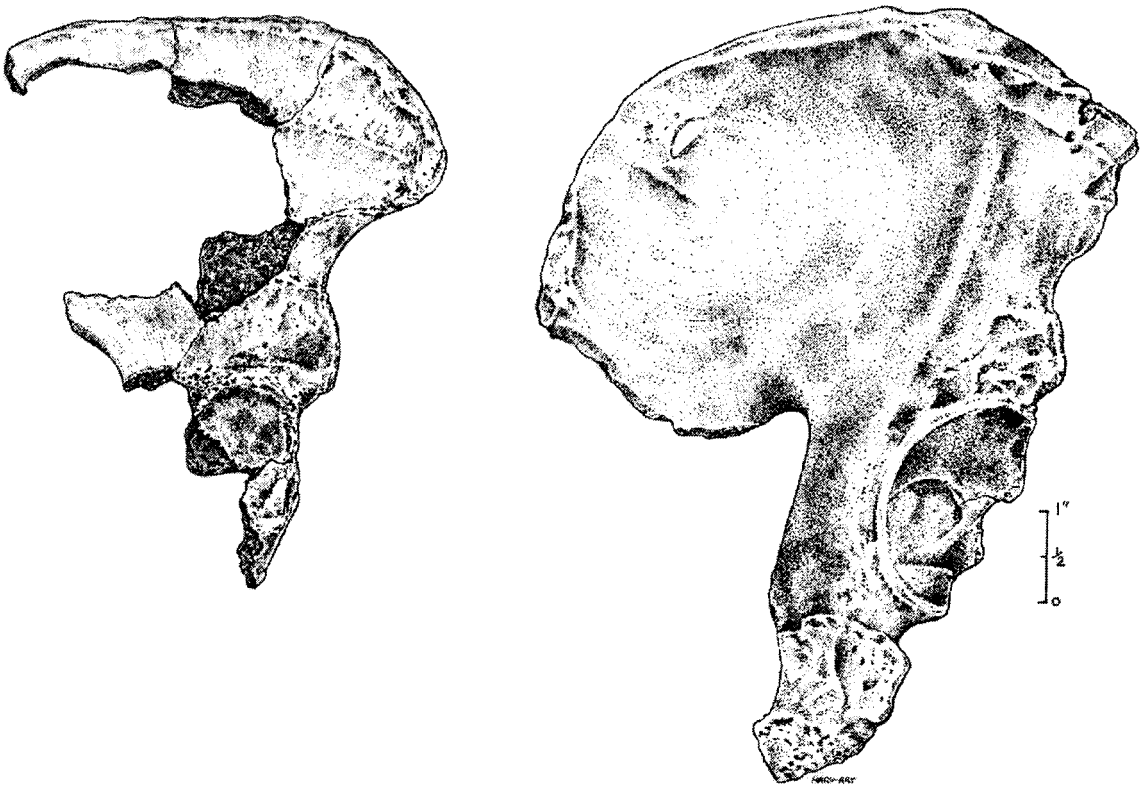

FIG. 3.—Comparison of the Stw 431 australopithecine (left) and KNM-ER 3228 early *H. sapiens* male innominates (drawings by Karen Harvey). ER 3228, dated at 1.95 ± 0.05 Myr, is the earliest specimen that can unquestionably be attributed to the earliest known direct ancestor of living human populations in the genus *Homo.* The Sterkfontein innominate is at least 200,000 years older (Schwarcz, Grün, and Tobias 1994).

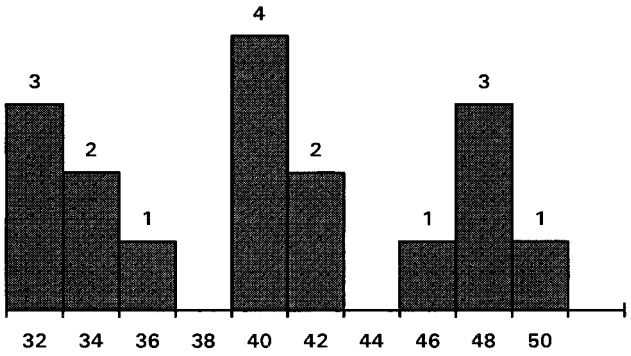

FIG. 4.—Frequency distribution of Late Pliocene and Early Pleistocene (approximately 1.9–1.6 Myr) Koobi Fora femur lengths in centimeters, actual or as estimated by McHenry (1991) and Ruff and Walker (1993). The total range exceeds the variation in Africa today, where the world's shortest and tallest populations are found. The larger mode is the size of very tall populations such as Tutsi or Nuer, and the middle mode is approximately Khoisan-sized. All specimens associated with crania in the large group are attributed to early *H. sapiens* (both sexes are represented), and all associated specimens in the small group are australopithecines. There are no cranial associations for the femora in the middle-sized group, but the oft-made suggestion that they represent the larger habiline species (or sex) is not unreasonable. The middle group are not likely to be females of early *H. sapiens,* because the only demonstrable female, KNM-ER 1808, is in the large group. This distribution indicates that early *H. sapiens* was quite large and had a human-like magnitude of sexual dimorphism in body size.

that is illustrated in the comparison is the most complete male innominate of this genus. It is a much smaller, lighter biped with a large pelvis relative to his body size. This reflects the fact that body size itself is a very significant aspect of change (complex 4, above). Early *H. sapiens* is considerably taller and markedly heavier than earlier australopithecines or penecontemporary habilines. In fact, all large-sized postcranial remains from the Koobi Fora and Olduvai deposits found with diagnostic cranial material are associated with early *H. sapiens,* and no early *H. sapiens* crania are associated with anything but the largest postcranial remains. The frequency distribution for femur length (fig. 4) shows this quite unequivocally. The distribution appears to have three modes, with the large mode including all femora attributed to early *H. sapiens,* such as male specimens ER 736 and the estimated adult length for the WT 15000, and ER 1808, which other skeletal evidence shows to be a female.

In sum, the earliest *H. sapiens* remains differ significantly from australopithecines in both size and anatomical details. Insofar as we can tell, the changes were sudden and not gradual.

Behavioral Changes

This section addresses a second reason for suspecting there was a bottleneck and a genetic reorganization at the beginning of *H. sapiens* evolution. The characteristic early *H. sapiens* features denote a new adaptive pattern that many describe as the first true hunt-

ing, gathering, and scavenging adaptation and that we believe may be uniquely associated with the Oldowan archaeological occurrences. These facts provide insight into what some of the sources of selection promoting the new species might have been.

Body size is a key element in the behavioral changes reflected at the earliest *H. sapiens* archaeological sites because of the locomotor changes that large body size denotes and the increased metabolic resources it requires. Moreover, the marked increase in brain size for early *H. sapiens* has significant metabolic consequences, because the human brain, which is 2% of the body weight, uses some 20%–25% of its metabolic energy. Larger brain size evolved in spite of these increased energy requirements, but the additional energy had to come from somewhere, and the answer must certainly lie in meat (Milton 1999). Larger body size in nonhuman primates is associated with the consumption of increasing amounts of low quality foods, and an increase in the amount of time and energy spent eating. The greater human body mass, and especially the longer legs, reflected a new foraging strategy related to this, in which, as Leonard and Robertson (1996) note: ''large day ranges, increased meat consumption, division of foraging activities, and sharing of resources . . . may have both necessitated and allowed for a higher-quality diet.'' These authors estimate that the body size increase from the australopithecines would require a 40%–45% increase in the total energy expenditure of early *H. sapiens.* They suggest that if this evolutionary change were associated with a shift to a more human-like foraging strategy, it would mean that the energy expenditure increase may have been even greater, perhaps as much as 85% greater than that for australopithecines, because of the locomotor requirements. The payoff for early *H. sapiens* populations, and the source of the additional energy, was in the higher-quality diet with its concentrated energy sources and the predictable use of more resources provided by the newly developed hunting, gathering, and scavenging strategy.

These behavioral changes are far more massive and sudden than any earlier changes known for hominids. They combine with the anatomical evidence to suggest significant genetic reorganization at the origin of *H. sapiens,* and from this genetic reorganization, we deduce that *H. sapiens* evolved from a small isolated australopithecine population and that small population size played a significant role in this evolution.

Population History After the Bottleneck

We have no way of directly estimating with any certainty the size of the human species immediately after the bottleneck at its origin. Archaeological sites from this time are widely scattered, but their sampling is too incomplete for a direct assessment. The problem is that significant range expansion out of Africa occurred a half million years or more later than the first *H. sapiens.* Population size before then may have remained small, and this is not an insubstantial time span, being one quarter of the time *H. sapiens* has existed. An important date in behavioral evolution is 1.5 MYA because it is marked by the earliest appearance of the Acheulean (Asfaw et al. 1992), the ubiquitous hand-axe industry of the Early and Middle Pleistocene. The appearance of the Acheulean involves dramatic behavioral changes. The earliest-dated Acheulean site is also the earliest site with significant butcher marks on the limb bones of megafauna and occurs just before the time of significant human colonization of the Old World tropics and semitropics. Before this time, humanity was limited to Africa and immediately adjacent sections of Asia such as the Levant. These are major changes in human paleoecology and paleodemography, and it is possible that in the half million or more years between the origin of *H. sapiens* and these changes, the human population was quite small and restricted to only a narrow ecological and geographic range.

Following these first significant range expansions, population size estimates are increasingly accurate for more recent times (cf. Birdsell 1972; Weiss 1984). Today, the human species numbers approximately 6 billion individuals, although as recently as the Early Holocene there may have been as few as 6 million (Coale 1974; Weiss 1984; Eldredge 1998). The pattern of population size change across the Pleistocene has come to be of critical interest, linking paleodemography with population genetics, paleoecology, and paleoanthropology.

Exponential expansion of the human species has certainly been ongoing since the inventions of agriculture and domestication early in the Holocene (Pennington 1996). It seems likely that this expansion began even earlier, as reflected by increasing site densities and complexity of material culture during the Late Pleistocene (Birdsell 1972; Gamble 1987; Klein 1989). Humans became a colonizing species early in the Pleistocene; humanity was first restricted to some parts of Africa, but by 1 MYA, populations had spread widely and occupied the tropics and some temperate regions of the Old World. The archaeological record shows that these range expansions have continued since (Butzer 1971; Ward and Weiss 1976; Soffer 1987; Gamble 1994; Lahr and Foley 1994). In spite of oscillating population sizes across the temperate zones everywhere, perhaps corresponding to the glaciations and their effects (Gamble 1987; Jochim 1987; Roebroeks, Conrad, and van Kolfschoten 1992; Mussi and Roebroeks 1996), the archaeological record reflects increased habitat specialization and continually larger population numbers worldwide. However, the oscillations were significant. For instance, both central/western Europe and southern Africa were largely depopulated in the Late Pleistocene, Europe several times, according to Klein (1989, 1994).

Because of the pattern of population increase suggested by the distribution of dated archaeological sites, traditional estimates of past population size have been based on assumptions of long-term exponential growth (Keyfitz 1966; Coale 1974; Biraben 1979). Weiss (1984), in his modeling of past population parameters, postulates that the often-observed hunter-gatherer population density of 0.28 per km^2 (Tindale 1940; Birdsell 1958; Hassan 1981) can be applied to estimating population size from the areas of habitation in the Pleisto-

cene. From this, and the distribution of archaeological sites, his interpretation of Pleistocene paleodemography implies that peoples who inhabited the Paleolithic world lived in small groups with low population densities and a slow average rate of growth, an interpretation that has been continually confirmed (e.g., Stiner et al. 1999). Weiss (1984) estimates a population of about 0.5 million between a half million and a million years ago, and about 1.3 million in the Middle Paleolithic. However, all of these estimates have high probable errors (Petersen 1975), not only because of the difficulties in applying archaeological information to demographic questions, but also because of the evidence of significant population size fluctuations.

Effective Population Size

Analysis of genetic evidence taken from large numbers of individuals may provide a different avenue of information about human paleodemography. Under selective neutrality and mutation-drift equilibrium, we might expect the genetic diversity within a population to be related to the size of the population. Ideally, we might be able to interpret what the population size has been in the past from the level of current genetic variation. In reality, however, many different factors can affect the relationship between genetic variation and population size, so populations of the same actual, or census, size (N_c) may have very different levels of genetic variation. Humans are nonideal in many ways, including overlapping generations, population subdivisions with sizes that vary both over time and across space, local population extinctions and recolonizations, and different reproductive patterns between sexes. These factors combine to make the relationship between the level of genetic variation and the census population size very complex.

To account for the many factors other than population size that affect genetic variation, population geneticists replace census population size with a surrogate they can calculate, the effective population size (N_e). N_e is the number of individuals in an ideally behaving, random-mating population that has the same magnitude of genetic drift as the actual population of interest (Wright 1938; Crow and Kimura 1970; Hartl and Clark 1997). Its calculation always assumes that the genes concerned are neutral and unlinked to genes that may be perturbed by selection (Caballero 1994). Unfortunately, there is no single effective population size (Chesser et al. 1993; Templeton and Read 1994). Rather, its definition varies in accordance with the kind of diversity of interest and the factors thought to disturb it. For studies of past population, the measure of magnitude of genetic drift that we are interested in is the change in average inbreeding coefficient, which is itself the probability of identity by descent of two randomly chosen alleles (Crow and Dennison 1988). Using this measure of genetic drift in calculations of N_e yields the inbreeding effective size. It is the inbreeding effective size that is addressed throughout this paper.

Finding Other Population Size Bottlenecks

It is unreasonable to assume that the human population either has been constant or has changed in a smooth, continuous manner throughout the past 2 Myr. The issue we examine is whether these oscillations and variations in the size of the human population ever again attained a magnitude sufficient to be observable as a bottleneck. Genetic drift reduces variation at a rate proportional to the effective size of the population, such that for a population size bottleneck to be observable, its duration must be long relative to the effective size of the population. Therefore, only in the extreme case, in which the number of generations of reduced size during the bottleneck approaches the number of individuals at the reduced size, does the long-term effective population size approach the bottleneck size.

If a population size bottleneck is followed by a population expansion, we might expect to see evidence of this in the pattern of genetic diversity (Tajima 1989). The principal effect of a postbottleneck expansion in population size is to increase the number of low-frequency genetic variants, since individuals are much more likely to share common ancestors during the bottleneck than at times after the bottleneck. This effect will be more pronounced after longer and more severe bottlenecks, which leave less ancient genetic variation in the population. Tajima's *D* statistic, which may be significantly negative for severe past bottlenecks, may be used to detect this effect. In contrast to selection, which may affect one genetic locus independently of others, these population size changes are expected to affect all genetic loci.

Thus, traditional methods of interpreting patterns of past population size changes based on paleontology and archaeology have been joined by new methods of interpreting current patterns of genetic diversity. The use of genetic methods requires that certain assumptions are met, and the accuracy of these methods reflects the extent to which the required assumptions have been the case. As Brookfield (1997) notes, interpretations of ancient demographic events based on genetic evidence are sensitive to, and in many cases stem from, our assumptions about the characteristics of those events. Because we must base our interpretations on the present pattern of genetic diversity, which is a product of multiple competing demographic and selective forces, our choices about which factors are important will influence our conclusions and may render them inaccurate at best or meaningless at worst. When examining genetic data for evidence of ancient population size and structure, then, it is important to aim for consistency with other sources of evidence, including those based on more traditional methods.

Nonrecombining Haploid Systems

The question of whether there have been population size bottlenecks within the past million years was raised by the application of genetic data to human paleodemography, with the finding that human mtDNA has little variation relative to the current size of the hu-

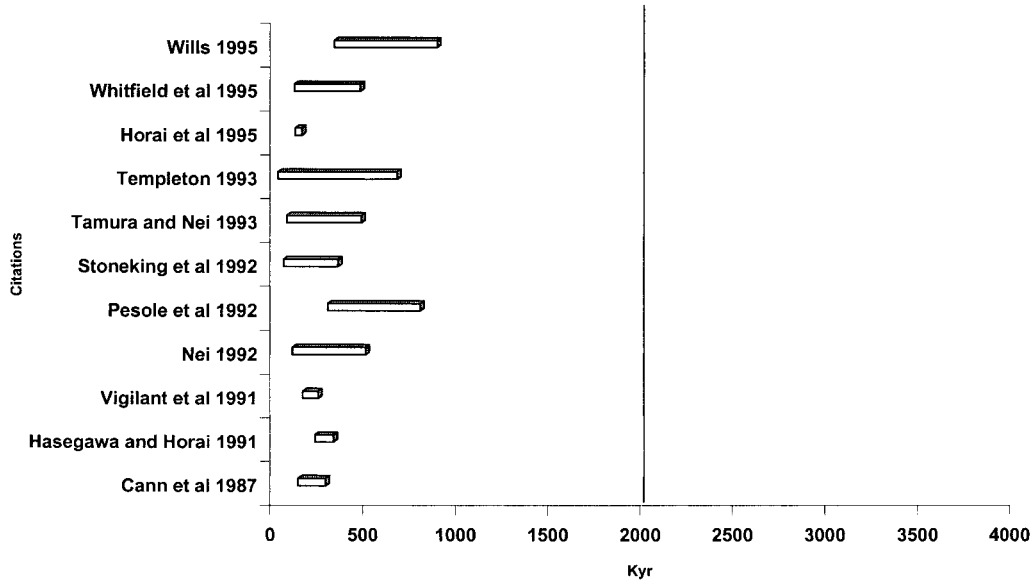

FIG. 5.—Distribution of coalescence estimates for mtDNA, arranged in order of publication date. Methods of range estimation vary; see specific sources for details. It would be fair to say that the uncertainty of this information has been increasing over time (and for further uncertainty see Parsons and Holland [1998]).

man population (Cann, Stoneking, and Wilson 1987; Excoffier 1990; Vigilant et al. 1991). Many researchers used mtDNA diversity to estimate the time to the most recent common ancestor, or coalescence time, of human mtDNA. A wide range of estimates was obtained (fig. 5); 200,000 years is a widely accepted median estimate. This estimate allows an estimate of inbreeding N_e of about 8,800 individuals (table 1). The effective human population size estimated from mitochondrial diversity is therefore far removed from traditional estimates of the census population size of our species in the past (Weiss 1984).

The small effective size of mtDNA led to the hypothesis that the human lineage had undergone a recent

Table 1
Estimated N_e Values for Nuclear Systems

Genetic System	Published N_e Estimate	95% Range of Estimate	Sources
Human-specific *Alu* polymorphisms	17,500	14,000–35,000	Batzer et al. (1992), Harpending et al. (1998), Sherry (1996)
β-globin	10,000	10,000–55,000	Harding et al. (1997)
ψη-globin	—	9,000–68,000	Bailey et al. (1992)
γ-globin	—	7,000–57,000	Bailey et al. (1992)
δ-globin	—	18,000–160,000	Maeda, Bliska, and Smithies (1983)
HLA intraallelic data	10,000	—	Takahata and Satta (1998)
HLA interallelic data	100,000	—	Ayala (1995)
Single-nucleotide polymorphisms	10,000–100,000	—	Wang et al. (1998)
ZFY	3,000–28,000	0–96,000	Dorit, Akashi and Gilbert (1995)
YAP	2,000–26,000		Hammer (1995)
ZFX	3,000–15,000	1,000–18,000	Huang et al. (1998)

NOTES.—We obtained these ranges using a coalescent simulation approach (Hudson 1990). For polymorphic *Alu* insertions, a simulation technique was developed that was similar to those of other studies (Sherry et al. 1997). Our technique required that we assume a constant population size for the human lineage, an assumption shared by all other means of estimating N_e, because N_e is a long-term average over the time period to the most recent common ancestor of a genetic locus. We also assume a date of 5 Myr for the chimpanzee-human species divergence (Takahata, Satta, and Klein 1995), a chimpanzee generation length of 19.6 years (Teleki, Hunt, and Pfiffering 1976), and a human generation length of 23.1 years for the period of coalescence. The long-term human generation length of approximately 23 years is midway between the observed chimpanzee value of 19.6 years and the generation length osteologically estimated for a recent, precontact human hunter-gatherer sample, 26.6 years (from Lovejoy et al. 1977). Finally, we assume a population size of the chimpanzee-human ancestor species of 100,000 (Ayala 1995; Takahata, Satta, and Klein 1995), as assumed in other studies (Sherry 1996; Sherry et al. 1997). For each locus, 1,000 simulations were performed for each of a range of possible population sizes in order to determine a confidence interval for N_e estimation. The range of population sizes tested began at zero and was increased in increments of 500 until an upper bound on population size was reached. For polymorphic *Alu* elements, the estimated confidence interval includes those values of N_e that produced numbers of polymorphic sites as extreme as or more extreme than the observed value in at least 5% of the simulations. For haplotype data discussed in the text, we used the same assumptions to simulate the gene genealogies consistent with the loci under study. For these genes, either the average pairwise difference or the maximum pairwise difference was used as the test statistic. Values of population size are included in the confidence interval if at least 5% of simulations produce test statistics as extreme as or more extreme than the observed value. Other assumptions and techniques are the same as those for the *Alu* procedure. In some cases not enough published data were available for these procedures, but either N_e estimates or coalescence time estimates have been published. In these cases, published estimates of coalescence times have been converted to long-term average N_e estimates for purposes of comparison.

bottleneck in population size. It was suggested that at the time of mtDNA coalescence, the entire human species was limited to one thousand to several thousand individuals (Cann, Stoneking, and Wilson 1987; Vigilant et al. 1991). To account for the mtDNA data, such a bottleneck would have to have been of sufficient duration to allow the fixation by drift of a single ancestral mtDNA variant. Presumably, this bottleneck was followed by expansion to the current population size. The postbottleneck population expansion could have resulted in a relatively increased number of low-frequency genetic variants. This would explain the departure of mtDNA from neutral mutation-drift equilibrium (Excoffier 1990; Merriwether et al. 1991; William, Ballard, and Kreitman 1995; Nachman 1996; Hey 1997; Loewe and Scherer 1997; Parsons, Muniec, and Sullivan 1997; Wise, Sraml, and Easteal 1998). Proceeding from this expectation, several researchers have examined the possibility of recent population expansions, such as those that would follow a bottleneck, using the distribution of pairwise genetic differences in human mtDNA (Harpending et al. 1993; Sherry et al. 1994; Rogers and Jorde 1995). This distribution appears to be consistent with a massive Late Pleistocene population expansion.

The hypothesis of a recent population size bottleneck is also supported by some analyses of the human Y chromosome (Dorit, Akashi, and Gilbert 1995, 1996; Hammer 1995; Whitfield, Sulston, and Goodfellow 1995; Underhill et al. 1997; Hammer et al. 1998). For the parts of the Y chromosome with observed variation, coalescence time estimates vary from 37 to 516,000 years (Hammer 1995; Donnelly et al. 1996; Fu and Li 1996; Weiss and von Haeseler 1996; Hammer et al. 1998). The antiquity of Y-chromosomal variation is not significantly different from that of mtDNA (Hammer 1995). As in the case of human mtDNA, estimated N_e for the human Y chromosome is low and is consistent with a recent period of small population size. However, if this is the result of a recent bottleneck, such a bottleneck would have to have been of sufficient duration to cause the fixation of a single Y chromosome variant. As with mtDNA, this bottleneck would be expected to cause a departure from equilibrium in the Y chromosome data. This expectation is apparently met by the frequency spectrum of Y chromosome variants (Harpending et al. 1998).

The interpretation that the departure from neutral mutation-drift equilibrium reflects population size expansions assumes selective neutrality for these gene systems. However, several geneticists have suggested that selection may influence the distribution of mtDNA and Y chromosome variation in humans (Whitfield, Sulston, and Goodfellow 1995; Hey 1997; Templeton 1997; Wise, Sraml, and Easteal 1998). This has been a persistent interpretation from studies examining haploid and autosomal variation in the same individuals. Within nonrecombining systems such as mtDNA and parts of the Y chromosome, all the alleles are linked, so selection on any portion reduces variability in the entire genome (Spuhler 1989; Braverman et al. 1995; Templeton 1997; Nachman et al. 1998). Genetic systems with little or no recombination are consistently biased toward low levels of variation in *Drosophila.* Selection is the only reasonable explanation for the pattern of interlocus variance in *Drosophila* (Nurminsky et al. 1998; McAllister and Charlesworth 1999), where regions with low rates of recombination retain greater intraspecific diversity than those with higher rates of recombination (Begun and Aquadro 1991, 1992; Hudson 1994, 1995; Stephan et al. 1998). The same pattern of variation is found on the human X chromosome (Nachman et al. 1998) and may characterize other parts of the human genome.

The suggestion that selection has occurred many times in human evolution is not unexpected, and it is consistent with the pattern of great morphological change in humans during the past 2 Myr. Selection could take several forms. Hitchhiking (Kaplan, Hudson, and Langley 1989; Johnson 1999) would help explain the small N_e calculated for these nonrecombining systems because of their linkage. Background selection (Charlesworth, Morgan, and Charlesworth 1993) is an alternative explanation for reduced variation that is related to selective sweeps, since hitchhiking during a selective sweep could be followed by background selection (Nachman et al. 1998). An explanation for low N_e based on selection is more compatible with the lack of ancient genetic variation in these systems than a short-duration ($<$2,000 generations) bottleneck of very small population size. The possibility that there has been selection in these nonrecombining systems (Hudson 1994, 1995; Stephan et al. 1998; Whitehead 1998) points to the necessity of considering autosomal diversity in humans for further evidence of whether the hypothesis of a severe recent bottleneck that some interpretations of haploid variation suggest can be refuted.

Autosomal Loci

Data are available from a number of autosomal gene systems to address the effective population size of the human lineage and the possibility of bottlenecks as explanations of genetic diversity. It is imperative to compare these with data from haploid systems (Hey 1997; Wise et al. 1997). Autosomal systems studied include those interspersed throughout the genome: microsatellites, *Alu* insertions, and single-nucleotide polymorphisms (SNPs), as well as single genetic loci, including β-globin, dystrophin, and ZFX.

When considered together (Table 1), these gene systems provide substantial evidence with regard to the limits of ancient population size changes. All of the autosomal systems examined to date are consistent with a long-term average N_e on the order of 10^4 to 10^5 for the human species (table 1). Moreover, they are all consistent with earlier analyses of protein polymorphisms (Nei and Graur 1984) and of nucleotide polymorphisms (Li and Sadler 1991; Takahata, Satta, and Klein 1995) that estimated the long-term effective human population size as on the order of 10^4.

The striking agreement of all autosomal sources of data on a relatively small N_e for the human lineage is inconsistent with the hypothesis that a recent short pop-

ulation size bottleneck explains it. Such a bottleneck, even if very severe, would leave ancient variation in many gene systems from the prebottleneck period of large population size. Such ancient variation is not observed. This lack of ancient variation also cannot be explained by recurrent ancient bottlenecks that also limited variation. If these had occurred, we expect they would have left some signs of the population expansions between them. While some gene systems are compatible with the interpretation of such expansions, others reject them (Harris and Hey 1999, and see below). These observations indicate that there is no recent severe bottleneck in human prehistory. Our results agree with those of others who have examined both nuclear and mitochondrial genetic evidence (Ayala 1995; Jorde et al. 1995; Whitfield, Sulston, and Goodfellow 1995; Hey 1997; Wise et al. 1997; Hammer et al. 1998; Harpending et al. 1998; Wise, Sraml, and Easteal 1998; Harris and Hey 1999).

Certain estimates of autosomal N_e values and values determined for mtDNA can potentially be reconciled, because under neutrality, the autosomal N_e is expected to be four times the haploid value (Takahata 1993). However, this reconciliation is not compatible with the explanation of low diversity in the haploid genes based on a recent bottleneck. Such a bottleneck would have predictable effects on the combined pattern of nuclear and mitochondrial DNA diversity, effects that have not been observed. The mtDNA coalescent is not expected to be one fourth that of nuclear genes following a small population size bottleneck that eradicates variation in both. Instead, because of its smaller effective population size, mtDNA should return to mutation-drift equilibrium more rapidly after a small population size bottleneck than would nuclear DNA, since drift is stronger in a smaller population. However, what we actually observe is mitochondrial DNA that is relatively invariant and out of equilibrium (Excoffier 1990; Merriwether et al. 1991; William, Ballard, and Kreitman 1995; Nachman et al. 1996; Templeton 1996; Hey 1997; Parsons, Muniec, and Sullivan 1997; Wise, Sraml, and Easteal 1998), while equilibrium cannot be disproved for most nuclear systems. This is clearly inconsistent with a severe recent population size bottleneck.

Long-Term Small Effective Size: the Long-Necked Bottle

An alternative reconciliation of these contradictions is found in the hypothesis that current human genetic variation is the product of a very long history of small population size in equilibrium (Takahata 1993; Donnelly et al. 1996; Weiss and von Haeseler 1996; Fu and Li 1997; Harding et al. 1997, 1998; Hammer et al. 1998; Harpending et al. 1998; Zietkiewicz et al. 1998). In this long-necked-bottle model, either N_e remained constantly small, or it oscillated frequently to low levels due to periodic events such as glaciations. This hypothesis differs from a single, short-term bottleneck explanation in that the population size is posited to be small for a long enough period for an equilibrium to be reached in most, if not all, neutral gene systems. This could account for differences in coalescence between recombining autosomal and haploid genetic systems. The fact that N_e in haploid systems is expected to be one quarter of that in recombining autosomal systems predicts that we will calculate a fourfold difference in coalescence times if small ancestral population size, and not a single population size bottleneck, is the cause of the variation (Takahata 1993).

The long-necked bottle model was developed by Harpending et al. (1998) as part of their analysis of *Alu* variation. It addresses the implications of an N_e value on the order of 10^4–10^5 for a long period in humans. If the N_e calculated from *Alu* variation (17,500 according to Harpending et al. 1998) is a significant fraction of the number of breeding adults in the human species (as Harpending et al. [1998] assume, following Wood [1987]), there must have been far too few people to occupy all of the continents inhabited during the Pleistocene, or even to inhabit a significant part of one continent. Such a population spread around the world would have a density so low that there would be only about 22 breeding couples in Germany and 35 in France (Takahata and Klein 1998). To account for this problem, Harpending et al. (1998, p. 1967) conclude that a population on the order of 10^4 could not have occupied the entire Old World, but lived for a million years or more ''in an African area the size of Rhode Island or Swaziland'' as a separate species. This species would presumably be the direct ancestor of modern humans, *H. sapiens.*

If correct, this would mean that the vast majority of known archaeological sites represent the remains of the activities of extinct human species. These sites are direct evidence of *somebody's* behavior, and they show that expansions of the geographic range of humans from Africa to the rest of the Old World may have begun shortly after the appearance of significant changes in human mobility. These changes are suggested by the much larger size, particularly the longer legs, of our earliest direct ancestors some 2 MYA. An early range expansion, with the implication of increasing population size, is indicated by Late Pliocene/Early Pleistocene dates published for the first Indonesian hominids (Swisher et al. 1994) and by the early dates variously suggested for the Yuanmou incisors from China (Qing 1985) and the Dmanisi mandible from Georgia (Gabunia and Vekua 1995). These dates range between 1.9 and 1.6 Myr and are compatible with range expansions that might have quickly followed the 2 Myr African appearance of our lineage. The sites involved are far from Africa and are more likely to be lucky findspots within a large range of new habitations than isolated migrant populations that moved from Africa to the places where they were found. Even if these earliest dates of colonization are incorrect, significant habitation in many areas of the Old World were certainly established by 1.4 and 1.2 MYA (Liu and Ding 1983; DeVos 1985; Hyodo et al. 1993; Wu and Poirier 1995). Colonizations at this later time were range expansions that may reflect the adaptive changes in human populations marked by the

Acheulean industry, which first appears abruptly in eastern Africa some 1.4 MYA (Asfaw et al. 1992). Important behavioral changes are reflected at these earliest sites, where bifaces and picks (rare tools in earlier industries) dominate the Acheulean, and the first case of butchering of mature adults of large mammalian species is found. After these early colonizations, archaeological evidence shows that the range of humans continued to expand into more marginal habitats, and despite significant fluctuations, occupation densities appear to have steadily increased (Klein 1989).

But is this archaeological picture of human paleodemography actually shown to be incorrect by the long-bottleneck interpretation? There are some specific reasons to believe that living human populations have multiple roots in widespread past populations. For example, nested cladistic analyses of mtDNA (Templeton 1993) and β-globin (Templeton 1998) indicate a long-term occupation of different areas of the Old World over the past 200,000 years or more. The contradiction between a geographically limited ancestral population and the worldwide habitation indicated by both archaeological distributions and some genetic analyses must be resolved.

We examined the consequences of a small population size bottleneck at the beginning of the human lineage to see whether the *Alu* analysis really requires that human ancestors lived in a very restricted geographic area for a million years. To do so, we developed a compound growth equation to model the paleodemographic history of humanity, much as it has been modeled in the past (Coale 1974; Hassan 1981; Keyfitz 1966). Our exponential growth equation is of the form:

$$N_t = (N_0 + N_0 i)^t,$$

where N_0 is the initial population size, i is the rate of increase, and t is time. We determined parameters for this equation from the small population size bottleneck that subsequently expanded quickly to an initial species size of 10,000 individuals at the time of humanity's origins some 2 MYA, and from the onset of the Neolithic some 10,000 years ago, when paleodemographers (such as Weiss 1984) estimate a population of 6 million. Assuming an average generation length of 23 years, as above, we calculated a generational growth rate of 7×10^{-5}. An estimate of effective size from this equation will be conservative in being an overestimate, since inbreeding effective size is smaller than variance effective size in a growing population. This calculation takes into account only the effects of growth common to both effective sizes, so using it to estimate inbreeding effective size establishes base conditions that we can examine deviations from.

The question of interest is what long-term average N_e the simple growth model describes. To calculate the long-term effective population size implied by this simple exponential model, we summed the population sizes over the period from 2 Myr to 10,000 years in 23-year generational intervals. The harmonic mean of the human population, calculated at these generational intervals, is approximately 64,000. If we assume a 1:3 ratio of effective to census population size, as observed over the short term in some human groups (Wood 1987) and as assumed by Harpending et al. (1998), the long-term effective population size over the past 2 Myr can be estimated at about 21,000. This cannot be significantly different from the estimate Harpending et al. (1998) give for the effective population size for humans determined from *Alu* insertions: 17,500; as noted (and see below), our assumptions generally maximize the N_e estimate.

Population Expansions

If such a growth model approximates the actual pattern of human paleodemography, we should expect to find evidence of population size growth. The archaeological record shows persistent range expansions and increases in population density; for all intents and purposes, this record begins at the same time *H. sapiens* originated, some 2 MYA. Pleistocene range expansions have been discussed for some years, and we examined how well the simple growth model fits the archaeological record of these expansions. We compared predictions of the equation with data from Weiss (1984; see also Birdsell 1972), who gives population estimates based on the observed distribution of archaeological sites across the Old World. These estimates consider the inhabited area of the world at various times as indicated by the range of distribution of these sites and an observed hunter/gatherer population density of 0.28 per km^2 (Birdsell 1958, from Tindale 1940) to derive population sizes. Weiss estimated a population of about 0.5 million ''at any time, from 1 million to 500,000 years ago.'' The curve generated by our simple model passes through 0.5 million at 777,000 years ago. He suggests a population of about 1.3 million in the Middle Paleolithic; this model estimates this population size at 478,000 years ago.

These are far from the smallest past population size determinations that have been published. For instance, Harpending et al. (1993) used archaeological site distributions and a lower estimated population density to calculate a world population as small as 125,000 over the time range from 1 million to 500,000 years ago, the period for which the Weiss approximation is 500,000. Thus, our model is not extreme, because it provides estimates well above this minimum. We may conclude that our simple growth model provides a rough fit of population estimates from archaeological site distributions under the assumption that the people described by the model created the archaeological sites.

There is also evidence of continued gradual increases in population density. In Middle Paleolithic Africa, the presumed homeland of modern humans according to both the recent-bottleneck and the long-bottleneck formulations, there is significant evidence for increasing population numbers and density. This is reflected in both site numbers and distributions (Clark 1992) and the observations that during the later Middle Paleolithic, African sites show a pattern of increasing regionalization and specialization (Allsworth-Jones 1993). This was a time of important changes in African stone tool indus-

tries (Klein 1989; Clark 1992). All across Africa, the Middle Paleolithic industries, called the Middle Stone Age (MSA), developed out of then local Acheulean. Large bifacial cutting and chopping tools dropped out of assemblages, while small flake component predominated. Clark (1992) attributes this change to the development of hafting, attaching stone (or other) cutting edges to wood.

The African MSA is as early as or earlier than the other Middle Paleolithic variations (McBrearty, Bishop, and Kingston 1996), and it is certainly equally or more complex. Some of its distinct qualities include grindstones for the preparation of plant foods; use of marine resources such as shellfish and seashells transported over 100 km or more; use of bone, including barbed bone points; and the hafting of the spear and other projectile points. These are marked regional differences within Africa. Early variants from the southernmost part feature long blades and woodworking tools such as burins. In East Africa, the Kenyan site of Baringo has an MSA layer just below a tuff dated to 250,000 years, with long, thin blades that were struck from a preshaped core. Similar blades are reported from the lowest Mousterian in the Hayonim cave in Israel. Blades like these have historically been taken as a marker of modern human behavior. They should not be (Bar-Yosef and Kuhn 1999). Blades are not different from other flakes taken off of prepared cores, the hallmark of Middle Paleolithic industries everywhere. Central African sites combine Levallois-based tools and more traditional Acheulean bifaces. At Katanda, along the Semiliki river near where it flows into Lake Albert in Zaire, barbed bone points and grindstones dated to about 80,000 years (with an almost 25% probable error range) have been discovered (Yellen et al. 1995). North Africa is more dominated by Levallois-based technologies.

Each of these elements was short-lived and narrowly distributed, and none spread throughout the entire African MSA range. They did not prevail, as similar attributes did persist and spread widely much later. Moreover, on the whole, they do not reflect particularly more progressive behaviors. These and other similarities to much later industries and technologies are short-lived and disappear, not the pattern we would expect if they were heralding a new, superior pattern of behavior. We believe that they indicate significantly higher population densities and greater population numbers in Africa through much of the Middle Paleolithic. These result in more technologically diverse samples, and with more population interactions, they reflect the increasing importance of isolating mechanisms.

Later, Klein (1998) finds evidence of increasing population density in southern Africa, beginning some 50,000 years ago, in the decreasing size of tortoises and mollusks at the Late Stone Age sites. Moreover, recent changes in population density are also reported from the analysis of different data during the later Middle Paleolithic of Eurasia. Stiner et al. (1999) examined archaeological sites on the northern and eastern rims of the Mediterranean and found that in the late Middle Paleolithic, much earlier than 20,000 years, as well as in more recent periods, there were pulses of demographic increases reflected in the increased reliance on small, agile game species. These studies record the continued increases in population density right through to the latest portion of the Pleistocene.

The *Alu* elements have fairly low resolution for detecting ancient or very recent population growth (Sherry et al. 1997; Harpending et al. 1998). Perhaps for this reason, but perhaps also because of the growth model's validity, their analysis is compatible with these archaeological data.

Problems with Population Expansion Markers

However, the simple growth model and archaeological evidences of past population sizes are contradicted by analyses of other autosomal systems. We are aware that the smoothed growth curve of this model could not reflect the detailed model of human population growth for all prehistory. Evidence of oscillating climate and dramatic habitat shifts across the Pleistocene shows that some areas were depopulated for significant periods, and so the history of the human population and its structure cannot be simple. However, there are some autosomal genes that indicate that there was no significant growth of the human population in the Pleistocene. These include single genetic loci such as β-globin, dystrophin, and ZFX. Analysis of these autosomal systems combine a low average population size and positive values of Tajima's *D* statistic. Therefore, their variation is not compatible with constantly increasing population size. In fact, they are not compatible with any population size increase of a magnitude greater than 50%, earlier than some 10,000 years ago; that is, at any time during the span of the Pleistocene (Hawks 1999).

The value of Tajima's *D* for the human worldwide β-globin data is 1.158, where significantly negative numbers are expected in cases of large past expansions. This statistic shows no evidence of ancient population expansion, nor do others (Harding et al. 1997). A similar situation is found for the human dystrophin locus, with Tajima's *D* being equal to 0.962 for the worldwide human sample (Zietkiewicz et al. 1998). Likewise, the distribution of variation at the lipoprotein lipase locus (Clark et al. 1998), with a Tajima's *D* statistic of 0.909, shows no evidence of expansion, although this sample is not as evenly distributed geographically as those for other loci. Hawks (1999) investigated the power of these loci to detect recent population expansions by simulations of different demographic scenarios. He found that while recent population expansions are unlikely to show significantly negative values of Tajima's *D*, they are also highly unlikely to show positive values for this statistic. The observation of positive values of Tajima's *D* at multiple autosomal loci therefore has great statistical power to reject hypotheses of population expansion. Using this observation, Hawks (1999) used simulation methods to test whether the observed pattern of autosomal diversity is compatible with recent population expansions. That study tested expansion times from 0 to 150,000 years and expansion magnitudes, from no expansion to 100-

fold expansion. Unlike mtDNA, which could be interpreted as showing an expansion around 70,000 years (Harpending et al. 1993; Sherry et al. 1994; Rogers and Jorde 1995; Relethford 1998), the distributions of these autosomal loci apparently rule out population expansions of an order of magnitude or more earlier than 10,000 years ago.

Other autosomal data also show no signs of significant population expansions during the Pleistocene. Li and Sadler (1991) present a study of 48 human genes for which at least two human sequences are available. This data set shows no evidence of mutation-drift disequilibrium. Takahata and Satta (1998), in a study of intraallelic variation among HLA haplotypes, also show no evidence of mutation-drift disequilibrium. Furthermore, Hey (1997), in a comparison of a single X chromosome locus and mtDNA diversity, found disequilibrium in mtDNA that was not present on the X chromosome, an observation that is clearly inconsistent with population expansion. While these loci do not have sufficient resolution to detect recent population expansion events, none of them indicate any sign of population expansions and are consistent with the larger sets of data that reject them.

The problem is that these same loci determine a very small long-term average human N_e for the Pleistocene. Combined with the absence of evidence for population size expansions noted here, interpreting N_e as a measure of census population size means, effectively, that the ancestors of modern human populations did not first emerge from their homeland and expand significantly enough to be archaeologically visible until the beginning of the Neolithic. If these interpretations are valid, one must assume that a great replacement of indigenous populations around the world, including the far peripheries such as the Americas and Australia, took place at this time or later.

This is an unusual reading of human prehistory (and history), and we question whether there might be a better explanation of the genetic data. As we have noted, such observations on nuclear DNA call the assumption of mtDNA neutrality into question. They raise other questions because they are not compatible with archaeological data that suggest much earlier expansions through evidence of range and density increases (Klein 1998; Stiner et al. 1999). It is difficult to argue that these archaeological data can be dismissed as the record of behavior in other human species, because significant parts of it are African or are found in western Asia at times when the archaeological remains are associated with so-called ''modern humans.'' Therefore, it would be these ''modern humans'' whose populations did not expand.

It is more reasonable to conclude that these autosomal genes are under selection. If so, the absence of evidence for recent expansion would be explained, but then these genes could no longer be used for valid N_e estimation (Caballero 1994; Rogers 1997).

Microsatellites

The other source of information about past human population size increases is found in studies of microsatellite variation. A number of analyses support some sort of population expansion or expansions in the past. Population size expansions should affect all neutral genes the same way, except as may be dictated by differences in mutation rate. Therefore, to interpret variation in microsatellite loci as the consequence of population size expansions, these loci must be selectively neutral, and our expectation is that all microsatellite loci should show, more or less, evidence for the same pattern of expansion.

However, studies of microsatellites contradict each other in several ways. Reich and Goldstein (1998), using within-site and among-sites methods that depend on allele size variance, find that some African populations (but not others) show patterns of microsatellite diversity consistent with a population expansion. They hypothesize that a bottleneck happened everywhere, but that other populations, including both African and non-African populations, do not show signs of this bottleneck because of a later founder effect in their history. This founder effect, in their view, artificially increased the variance of some loci because it sampled distantly related alleles due to chance.

Yet, an excess of allele size variance was not detected in a study by Kimmel et al. (1997). In fact, this study found an excess of heterozygosity relative to allele size variance. Kimmel et al. (1997) found that this effect was related in computer simulations to population expansions. Human populations varied in this characteristic of microsatellite variation, with Asians showing the strongest pattern of excess heterozygosity, less heterozygosity in Europeans, and the lowest heterozygosity in Africans. Kimmel et al. (1997) interpreted these results as being possibly due to earlier expansions in Asia and later expansions in other regions. However, if these results do reflect population expansions, it is unclear what the timing of such expansions was. In particular, expansions as recent as 10,000 years ago may have created the same effect as more ancient expansions in their tests. Whatever the case, this study contradicts the findings of Reich and Goldstein (1998).

Di Rienzo et al. (1997) found evidence in microsatellite data for an expansion in a low deviation from the regression line between the square of mean mutation size for microsatellite loci and allele size variance. Such deviation is lower in the case of an expansion because, Di Rienzo et al. (1997) assumed, the allele size variance is a simple function of time. It is high in the case of a constant population because of the large expected variance in coalescence times of independent loci (Kingman 1982; Hudson 1990). However, the relationship of small deviation to population expansions can only hold if we ignore the population size of the population prior to the expansion and assume it to be zero. If we allow this population size to be greater than zero, the expected deviation increases. In particular, if the preexpansion N_e is on the order of 10,000, the figure indicated by both autosomal and nonrecombining loci, both an expansion scenario and a constant population size scenario will produce the same variance around the regression line. Using estimates of population size from other genetic

data in this way indicates that population expansions cannot be identified by this method.

Population expansion following a bottleneck or founder event for non-African populations has also been suggested by the work of Tishkoff et al. (1996, 1998) and Calafell et al. (1998), who found the presence of many private alleles in Africa and few outside of Africa and argue that this reflects the habitation of the rest of the world by a small subset of Africans. A similar conclusion is reported by Liao (1999) from his study of concerted evolution at the RNU2 locus, which consists of multiple tandemly arrayed 6.1-kb repeats. These studies agree in reasoning that this pattern must reflect a founder effect that limited variation outside of Africa. The private alleles would be distributed much more widely if there subsequently were high interregional gene flow over the past hundred thousand years. Instead, the distribution of the non-African alleles and linkage disequilibrium of non-African RNU2 loci suggest low rates of gene flow. This, it is argued, disproves multiregional evolution because low rates are said to be inconsistent with ''the relatively high levels of migration needed to synchronize evolution across the human range'' that multiregional evolution requires (Calafell et al. 1998, p. 47).

But multiregional evolution does not require maintaining high levels of gene flow. On the contrary, only very low levels of gene flow could account for the observed F_{st}, which today is between 0.05 and 0.15 among continents (Relethford 1995; Harpending, Relethford, and Sherry 1996; Templeton 1998), and these levels are compatible with the multiregional interpretation (Relethford and Harpending 1994; Templeton 1998). In addition, microsatellite data may not even be able to provide specific evidence for a founder event, since the F_{st} estimated for these gene systems is not different from that of most other loci (Cavalli-Sforza, Menozzi, and Piazza 1994; Zietkiewicz et al. 1998). For none of these loci is non-African diversity a simple subset of the diversity within Africa. These observations open the door for other explanations of the data, the most important of which are differences in ancient population size among regions, particularly a larger population size in Africa than elsewhere (Relethford 1995, 1999).

Further difficulties for any interpretation of microsatellite variation involving a population size bottleneck lie in the fact that the various sources of genetic data for populations leaving Africa do not reflect the same bottleneck. For that matter, combined with other genetic information such as YAP+ chromosome variation (Altheide and Hammer 1997), they do not even agree on the same direction of population movement.

One final complication to estimating population history from microsatellite diversity is the effect of chromosome position (Nachman et al. 1998), which has not yet been incorporated into microsatellite models. The relationship between recombination rate and magnitude of selection makes microsatellite comparisons very difficult, because with selection, diversity no longer necessarily reflects population expansions. While selection has not been demonstrated for these loci, the fact that their variation, in aggregate, is not explained by a single pattern of population size increase does raise suspicions. Although interpretations from different microsatellite studies have supported population expansions, the microsatellites studied thus far cannot reflect consequences of the same expansion, and this inherent contradiction reduces our confidence in the results.

Effective and Census Population Sizes

Returning to the question of human population size in the past, haploid systems and autosomal genes with low rates of recombination prove to be unreliable sources of information because of selection, microsatellites give detailed but conflicting information, and *Alu* variation lacks resolving power. We may therefore question the extent to which we can obtain valid information about ancient human population size by calculating the long-term inbreeding N_e. Even if we could estimate it validly, comparison with other animal taxa indicates that it is almost certainly unjustified to assume that our N_e determination would be a constant significant fraction of the number of breeding adults in our species (Nei and Graur 1984). Among other species, this relationship rarely if ever is true. N_e has varying connections with census population size for many reasons (Caballero 1994; Barton and Whitlock 1996; Whitehead 1998). For instance, both directional selection and background selection act to depress N_e relative to N_c. In larger species ($N_c > 10^6$), the ratio of these two in living populations can be quite small (Pray et al. 1996). It is not just humans, with N_c recently expanded to a size on the order of 10^9, who have small N_e estimates for nuclear gene systems (on the order of 10^4–10^5 as noted above). For instance, in Whitehead's (1998) study of mtDNA variation in whales, N_e for the various species ranges between 10^4 and 10^5, ''with no relation between effective population size and the order of magnitude estimated for current population size.'' He dismisses a recent severe bottleneck explanation for this long-lived widespread group (as we do for humans) and instead posits that the female transmission of traditions with different survival values, along matrilines or from matrigroup to matrigroup, has a significant effect on mtDNA variation because of molecular hitchhiking, as we have discussed for the human haploid systems. Whitehead shows that a fitness advantage of as little as 10% for a matrilineally transmitted tradition devastates mtDNA diversity in a period compatible with even the highest mtDNA mutation rate estimates. We need not comment on how this model could be applied to Pleistocene human evolution. It may also be important in explaining the variation noted in N_e in chimpanzee subspecies (Wise et al. 1997).

No large mammalian species has N_e greater than 10^5, and even *Drosophila* species with census population sizes on the order of 10^{11}–10^{14} do not have N_e exceeding 10^6 (Kaplan, Hudson, and Langley 1989). There is ample evidence from many species that ''long-term effective population size is vastly smaller than present-day population size'' (Avise, Ball, and Arnold 1988). There are good reasons to expect that the effect is great-

ly amplified in hominids and other large mammals relying on information established in traditions.

Further complicating the N_e and N_c relationship in hominids, there are other demographic factors apart from the census population size that are important in the long-term human N_e calculation (Templeton and Read 1994). The details and complications of Pleistocene colonizations and range expansions are significant, because if we cannot assume Pleistocene population size has been constant, in expanding populations ''inbreeding effective size can be orders of magnitude smaller than census size'' (Templeton 1980). There is also the issue of population structure and its consequences. In describing a situation much like what we reconstruct for human populations in temperate regions during most of the Pleistocene, Wright (1940) notes that when ''local populations are liable to frequent extinction, with restoration from the progeny of a few stray immigrants . . . the line of continuity of large populations may have passed repeatedly through extremely small numbers even though the species has at all times included countless millions of individuals in its range as a whole.''

N_e can be very small relative to census size when populations are subdivided (Chesser et al. 1993; Marjoram and Donnelly 1994; Whitlock and Barton 1997) and local extinctions and recolonizations are frequent (Maruyama and Kimura 1980; Giplin 1991). This genetic model of human population structure (Takahata 1994; Whitlock and Barton 1997) is important for paleoanthropologists because it could explain the paleontological and archaeological observations noted above. In regional populations, there could be some threads of survivorship, even as rates of local extinctions and replacements for their subdivided populations are substantial. This pattern would account for the apparently contradictory roles of extinction and continuity by showing how our species could at the same time (1) be widely dispersed, (2) have enough populations in contact for sufficient genic exchanges across the species range to promote isolation by distance, (3) retain long-lasting regional genetic continuity for features shared with many populations, and (4) have a small enough N_e for significant genetic drift.

When significant colonizations out of Africa began, changes in population structure and rates of extinction were more likely to have been common in colonists in temperate regions out of Africa than in the populations that remained there. This is because population sizes were smaller toward the peripheries of the human range (Wolpoff, Wu, and Thorne 1984), and peripheral populations are more likely to vary in size and be subjected to oscillating sources of selection (especially climatic and ecological), both of which reduce N_e. These initial conditions contributed to a pattern of difference between population density and population structure at the center and the edges of the human range that persisted through most of the Pleistocene. There would be a larger N_e in Africa and smaller values elsewhere for reasons independent of census size differences, and we expect that there were systematic census size differences as well (Thorne, Wolpoff, and Eckhardt 1993).

For these reasons, we conclude that in practice the long-term average N_e for the human species, even if it could be validly determined, cannot be taken as an estimate of actual past population sizes.

Discussion: Bottlenecks in Human Evolution

A population size bottleneck early in the evolution of the *H. sapiens* lineage, perhaps at its origin some 2 MYA, has significant explanatory power in resolving some of the contradictions between different sources of data addressing past human population size. This bottleneck is well supported paleontologically, but what about genetically? The long-term inbreeding effective population size of humans is on the order of 10^4–10^5 taken over the last 1–2 Myr. The limited amount of genetic variation reflected by this small N_e implies that ancient population size changes, predating 1 Myr, will be difficult to detect using genetic methods. Methods of appraising population bottlenecks from genetic evidence rely on the effects of such bottlenecks on the rate of genetic drift. But if the bottleneck is very ancient, if genetic drift has been powerful at times since the bottleneck, or if there has been selection, then any of the processes that erode genetic diversity may have erased any evidence for a population bottleneck.

Minimally, we may expect to place a lower time limit on the possibility of severe population bottlenecks, such as those that might be associated with a speciation or a period of rapid adaptation. Based on autosomal evidence from several gene systems, we may rule out such a bottleneck at times more recent than 1.5 Myr (this date, the time when significant expansion of the human range out of Africa first began, can be estimated from the autosomal data presented in table 1). No date more recent than this is compatible with known neutral nuclear variation. However, nonmolecular sources of information must become more important as we consider demographic events far in the past.

Therefore, considered together, nuclear data allow bottlenecks within a narrow range around 2 MYA, a range of possibilities that is fully compatible with the fossil and archaeological records. We may try to refute the hypothesis of a bottleneck at this time from other genetic data by using the expectation that if there were no bottleneck early in our history, we should expect some ancient variation, older than 2 Myr, to remain at neutral loci in the human population today. This should be true even if forces that erode diversity have been powerful since the bottleneck, as would be reflected by a small long-term average N_e. For example, if N_e has been equal to its lower bound, 10^4, then the expected coalescence time of a neutral locus should be exponentially distributed with a mean of 4×10^4 generations (Hudson 1990). Assuming 23-year generations as before, the mean coalescence time will be about 920,000 years. We can expect from this distribution that 11% of loci will have coalescence times greater than 2 Myr. Likewise, for an N_e of 2×10^4, 34% of loci will coalesce earlier than 2 Myr without a bottleneck. Since a bottleneck would be expected to truncate this distribu-

tion at or around 2 Myr, the presence of diversity older than 2 Myr can be reasonably expected if the hypothesis is wrong, and would be a clear disproof that such a bottleneck occurred.

However, while all the genetic systems that have been examined to date are compatible with a population size bottleneck at the origin of *H. sapiens*, no genetic system for which neutrality has been claimed has been found to have a minimum coalescence time estimate significantly more ancient than 2 Myr. Those analyses based on elements interspersed throughout the genome, such as the human-specific *Alu* insertions, yield some of the oldest estimates, but all are compatible with the occurrence of a 2-Myr bottleneck. Therefore, although there probably are many factors limiting human genetic diversity, no diversity reasonably interpreted as neutral (and the *Alu* insertions are the best example of this) has yet been detected that must unquestionably extend from the period before our last speciation.

A second potential for refutation comes from nonneutral systems, such as those under balancing selection, because these address whether the bottleneck sizes noted above are consistent with other data. The most prominent example is the HLA gene system that diverges from neutrality and is likely subject to balancing selection (Klein et al. 1993). This system should be expected to retain ancient variation through a population size bottleneck because of the mechanism of balancing selection (Ayala 1995). The HLA complex genes have the largest amount of variation studied thus far (Klein 1986). As it turns out, retention of a large number of ancestral HLA alleles precludes effective population sizes of much less than 1,000 at any particular point in time during human prehistory (Ayala 1995; Ayala and Escalante 1996; Takahata and Satta 1998). This minimum bottleneck number, 1,000, also seems to be the minimum effective population size compatible with the maintenance of species viability and adaptability (Lande 1995). The HLA data, then, do not preclude a speciation bottleneck of minimal population size.

However, this is the only bottleneck not ruled out by the confluence of these data sources. Considerable genetic data are inconsistent with a recent bottleneck in the human lineage, as are data from prehistoric archaeology and paleoanthropology (Jelínek 1982; Wolpoff, Wu, and Thorne 1984; Eckhardt 1987; Kramer 1991; Pope 1992; Frayer et al. 1993; Kennedy 1994; Clark 1997; Wolpoff and Caspari 1997). Information from additional genetic systems will no doubt continue to increase our understanding of the population size of our species at its origin and help further clarify these issues of subsequent population change, but at the moment such studies rest on the horns of a dilemma. If we assume neutrality for the autosomal loci well known at this time, they preclude any recent population size bottleneck for two reasons: (1) they are in equilibrium while mtDNA is not, and (2) they are not consistent with any significant population expansion as must follow such a bottleneck earlier than 10,000 years ago. If we do not assume neutrality, these loci do not give us information about past population size.

Conclusions

While it is clear that paleontological, archaeological, and genetic approaches are potentially rich sources of hypotheses about human demographic history, each alone has a considerable disadvantage when applied as a test of paleodemographic questions. The weaknesses of fossil and archeological approaches lie in their incompleteness and poor sampling. While paleoanthropologists have learned much about human phylogeny and adaptation, it has been a challenge to obtain any but the roughest estimates of past population size from site distributions, distributions of technologies or traits, or evidence of morphological evolution. Geographically clustered sampling and taphonomy bias the samples, and their sizes are very small. The weakness of genetic data is inaccuracy, especially in the sense of low levels of resolution, as there are many factors other than population size that affect genetic diversity and do so in ways that are largely not quantifiable. Perhaps the most significant of these is selection, and its main effect is to remove the element of predictability from these relationships because the details of past selection are unknown, and perhaps unknowable.

All the currently available genetic, paleontological, and archaeological data are consistent with a bottleneck in our lineage more or less at about 2 MYA. At the moment, genetic data cannot disprove a simple model of exponential population growth following such a bottleneck and extending through the Pleistocene. Archaeological and paleontological data indicate that this model is too oversimplified to be an accurate reflection of detailed population history, and therefore we conclude that genetic data lack the resolution to validly reflect many details of Pleistocene human population change.

However, there is one detail these data are sufficient to address. Both genetic and anthropological data are incompatible with the hypothesis of a recent population size bottleneck. Such an event would be expected to leave a significant mark across numerous genetic loci and observable anatomical traits. Genetic and anatomical traits, after all, are the raw data the hypothesized bottleneck is meant to explain. But while some subsets of data are compatible with a recent population size bottleneck, there is no consistently expressed effect that can be found across the range where it should appear, and this absence disproves the hypothesis. There are better ways to explain the data.

Although significant population size fluctuations and contractions occurred, none has left a singular mark on our genetic heritage. Instead, while isolation by distance across the network of population interactions allowed differences to persist, and with selection, local adaptations were able to develop, evolution through selection, along with gene flow, has promoted the spread of morphological and behavioral changes across the human range. It is this pattern of shared ancestry that has left its signature in the variation that we observe today. We know this from many sources of data and argue that no single source can suffice. If the evidence of a population size bottleneck early in the evolution of our lin-

eage is accepted, most genetic data by themselves either lack the resolution to address subsequent changes in the human population or do not meet the assumptions required to do so validly.

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