

Genetic Evidence for Long-Term Population Decline in a Savannah-Dwelling Primate: Inferences from a Hierarchical Bayesian Model

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The purpose of this study was to test for evidence that savannah baboons (*Papio cynocephalus*) underwent a population expansion in concert with a hypothesized expansion of African human and chimpanzee populations during the late Pleistocene. The rationale is that any type of environmental event sufficient to cause simultaneous population expansions in African humans and chimpanzees would also be expected to affect other codistributed mammals. To test for genetic evidence of population expansion or contraction, we performed a coalescent analysis of multilocus microsatellite data using a hierarchical Bayesian model. Markov chain Monte Carlo (MCMC) simulations were used to estimate the posterior probability density of demographic and genealogical parameters. The model was designed to allow interlocus variation in mutational and demographic parameters, which made it possible to detect aberrant patterns of variation at individual loci that could result from heterogeneity in mutational dynamics or from the effects of selection at linked sites. Results of the MCMC simulations were consistent with zero variance in demographic parameters among loci, but there was evidence for a 10- to 20-fold difference in mutation rate between the most slowly and most rapidly evolving loci. Results of the model provided strong evidence that savannah baboons have undergone a long-term historical decline in population size. The mode of the highest posterior density for the joint distribution of current and ancestral population size indicated a roughly eightfold contraction over the past 1,000 to 250,000 years. These results indicate that savannah baboons apparently did not share a common demographic history with other codistributed primate species.

Introduction

The occurrence of past vicariant events can often be inferred from geographically congruent patterns of phyletic subdivision within populations of codistributed species (e.g., Patton and da Silva 1998). Similarly, past environmental changes can be inferred from patterns of demographic history (i.e., population expansion or contraction) among codistributed species with similar or dissimilar ecological requirements (Storz and Beaumont 2002). Thus, information from multiple species about the direction, magnitude, and timing of past changes in population size can provide a basis for testing hypotheses about regional zoogeographic history.

Fortunately, genetic data can now be used to test such hypotheses, thanks to recent advances in theoretical population genetics and computational statistics (Emerson, Paradis, and Thébaud 2001). In particular, coalescent-based modeling has provided a powerful new means of estimating demographic and mutational parameters from patterns of DNA variation in contemporary populations (Hudson 1990; Donnelly and Tavaré 1995; Nordborg 2001). A typical approach is to infer parameters by comparing summary statistics calculated from an empirical data set with a distribution generated by Monte Carlo simulations of the coalescent process. When using sequence data to test for evidence of population expansion or contraction, one of the most commonly used summary statistics is Tajima's (1989a) D ,

which measures whether the observed frequency distribution of segregating sites is consistent with a neutral-equilibrium model. But as pointed out by Hey and Harris (1999), Tajima's D and other related statistics generally provide inadequate summaries of the data for the purpose of testing complex parameter-rich models of demographic history (such as those considered in theories of human origins; Relethford 2001). For such models, likelihood analysis of the raw sample configuration generally permits a much broader scope of inference (Donnelly and Tavaré 1995; Stephens 2001). Specifically, coalescent simulations can be used to calculate the likelihood of the observed sample configuration under the stationary distribution of a specific demographic model, thereby permitting full use of the data in a maximum likelihood or Bayesian framework.

Inferences about the biogeographic history of East Africa during the late Quaternary are of special interest because of the implications for the evolution of anatomically modern humans and other hominoid primates. Archaeological evidence indicates that the expansion of the African human population coincided with the development and spread of Upper Paleolithic technology during the late Pleistocene, suggesting a causal role for cultural innovation in driving the expansion (Klein 1989). An alternative hypothesis is that the human population expansion in Africa was primarily attributable to climatically induced environmental change at or before the glacial-interglacial transition that marked the beginning of oxygen isotope stage three (~60,000 years BP; Rogers and Jorde 1995; Ambrose 1998). Such a broad-scale environmental change would be expected to affect other codistributed mammals (Rogers and Jorde 1995; Ambrose 1998; Harpending and Rogers 2000). As stated by Ruvolo (1996, p. 211), "Any significant environmental

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or climatological event producing dramatic genetic effects within humans should have affected chimpanzees and gorillas, as well as a diverse array of other species.”

Genetic inferences about the timing of the human population expansion remain highly controversial (Harpending and Rogers 2000; Wall and Przeworski 2000). Much of the debate centers on the effects of nonequilibrium demographic processes and the potentially confounding influence of selection at linked loci (Hey 1997; Fay and Wu 1999; Hey and Harris 1999; Wakeley 1999; Wall and Przeworski 2000). But available genetic data generally present a more consistent picture of late Pleistocene human history when attention is restricted to Africa alone. Data based on mtDNA variation generally suggest that the expansion of the African human population started ~30,000–130,000 years ago (Rogers and Harpending 1992; Hasegawa, Di Rienzo, and Wilson 1993; Sherry et al. 1994; Rogers 1995, 1996; Rogers and Jorde 1995; Watson et al. 1997; Harpending et al. 1998; Excoffier and Schneider 1999; Harpending and Rogers 2000; Ingman et al. 2000). Similarly, mtDNA data for chimpanzees (*Pan troglodytes*) suggest that this species underwent a demographic expansion in equatorial Africa during this same approximate time interval (~20,000–60,000 years ago; Goldberg and Ruvolo 1997; Gagneux et al. 1999). The apparent similarity in the mismatch distributions of homologous mtDNA sequences from chimpanzees and African humans has been interpreted as evidence for a simultaneous response to a common environmental event in the late Pleistocene (Rogers and Jorde 1995; Ambrose 1998; Harpending and Rogers 2000). The purpose of this study was to evaluate this hypothesis by analyzing data from another codistributed African primate, the savannah baboon (*Papio cynocephalus*). We used a coalescent-based analysis of multilocus microsatellite data to test for evidence of population expansion or contraction. Specifically, we used a hierarchical Bayesian model to test for evidence that savannah baboons underwent a population expansion in concert with the hypothesized expansion of chimpanzees and African humans.

Methods

Sampling and Genotyping

Whole blood was obtained from a total of 100 baboons that were sampled from a contiguous portion of the species range in East Africa (Altmann et al. 1996; Storz, Ramakrishnan, and Alberts 2002). Genomic DNA was isolated from blood samples according to the protocol described by Bruford et al. (1992) or by using QIAamp extraction columns (Qiagen, Valencia, Calif.). The genetic analysis was based on a total of 14 autosomal microsatellites (10 di- and 4 tetranucleotide repeat loci). Baboon microsatellites were amplified using primers designed from flanking sequences of homologous loci in the human genome. Locus names and chromosomal assignments (in parentheses) are as follows: D7S503 (3), D13S159 (17), D6S311 (4), D6S271 (4), D16S402 (20), D4S431 (5), D2S141 (13), D16S420 (20), D11S925 (14), D17S791 (16), D5S1457 (6),

D10S611 (9), D14S306 (7), and D4S243 (5). Chromosomal assignments of microsatellite loci (following karyotypic nomenclature of Cambefort, Mounie, and Colombies 1976) were based on linkage map data from Rogers et al. (2000). Although the markers were originally selected in humans on the basis of polymorphism levels, there is no correlation in levels of allelic diversity at homologous microsatellite loci between baboons and humans (Morin et al. 1998). Thus, there is no reason to expect that ascertainment bias has affected the observed frequency spectra (Beaumont 1999; Wakeley et al. 2001).

PCR protocols were reported previously (Storz, Ramakrishnan, and Alberts 2002). Allele sizes were quantified using an ABI 3700 automated sequencer and analyzed using GENESCAN software (PE Biosystems, Foster City, Calif.).

The Model

We consider the demographic history of a closed population that increases or decreases exponentially from an initial size N_1 to the current size N_0 over a time interval x_a . The population size at any time x is given by

$$N_x = N_0 \left(\frac{N_1}{N_0} \right)^{x/x_a}, \quad (1)$$

where time is increasing into the past. The data consist of frequency counts of chromosomes scored for microsatellite allele length at a number of unlinked loci. The loci are assumed to have independent genealogies and are evolving according to a strict single-step mutation model, with mutation rate μ . The distribution of allelic frequencies is assumed to arise from a genealogical history, G , consisting of the genealogy and the sequence of mutation laid down on the genealogy. Given the demographic parameters and mutation rate, results of coalescent theory can be used to calculate the probability of obtaining any genealogical history consistent with the allelic-frequency data, as described in Beaumont (1999).

We infer the parameters using the hierarchical Bayesian model of Storz and Beaumont (2002). In this model the mutational and demographic parameters are allowed to vary among loci. Although there are empirically justified reasons to expect interlocus variation in mutation rate (e.g., Chakraborty et al. 1997; Di Rienzo et al. 1998; Deka et al. 1999; Ellegren 2000a; Schlötterer 2000; Renwick et al. 2001), there would not seem to be any theoretically justified reason to expect interlocus variation in demographic parameters. This is because all genes have been transmitted through the same organismal pedigree and have therefore experienced the same demographic history. But the joint effects of linkage and selection can produce variation in effective population size across different regions of the genome (Hill and Robertson 1966; Barton 1995). Thus, allowing demographic parameters to vary makes it possible to detect aberrant patterns of variation at individual loci that may arise from genetic hitchhiking (Maynard-Smith and Haigh 1974) or background selection (Charlesworth B., Morgan, and Charlesworth D. 1993), either of which

could make the demographic history of a single locus appear different from that of other unlinked loci. This approach should be viewed as a heuristic approximation to a full analysis in which the locus-specific effects of selection are modeled explicitly. The robustness of this modeling approach stems from the fact that likelihoods from separate loci are not combined in a multiplicative fashion, as in the model described by Beaumont (1999). Thus, aberrant loci will not strongly influence the results.

The hierarchical model is built as follows. There are separate parameters for each of k loci, giving a set of parameters $\Phi = \{N_{0i}, N_{1i}, x_{ai}, \mu_i\}_{i=1,k}$. The parameters for each locus are assumed to be drawn from log-normal distributions, each with means (on a log scale) of $\mathcal{M} = \{M_{N0}, M_{N1}, M_\mu, M_{xa}\}$ and standard deviations (SDs) of $\mathcal{V} = \{V_{N0}, V_{N1}, V_\mu, V_{xa}\}$. These distributions were then used to calculate the probability density $p(\Phi|\mathcal{V}, \mathcal{M})$. Prior distributions for the means were assumed to be specified by normal distributions with means $\alpha_{N0}, \alpha_{N1}, \alpha_\mu$, and α_{xa} and SDs $\sigma_{N0}, \sigma_{N1}, \sigma_\mu$, and σ_{xa} . Priors for the SDs were taken to be normal distributions truncated at zero with means $\beta_{N0}, \beta_{N1}, \beta_\mu$, and β_{xa} and SDs $\tau_{N0}, \tau_{N1}, \tau_\mu$, and τ_{xa} . This set of parameters is designated as \mathcal{H} . The use of log-normal priors was motivated by the observation that posterior distributions for demographic and mutational parameters are generally skewed. It is therefore preferable to model the parameter distributions using log-transformed priors on a log scale (Beaumont 1999; Storz and Beaumont 2002) or skewed priors on a natural scale (Wilson and Balding 1998; Pritchard et al. 1999).

The above distributions were then used to calculate the probability density $p(\mathcal{V}, \mathcal{M}|\mathcal{H})$. We used Metropolis-Hastings simulation, as described in Beaumont (1999) and Storz and Beaumont (2002), to estimate the joint posterior distribution of the parameters and the genealogical history:

$$p(\Phi, \mathcal{M}, \mathcal{V}, G|D) \propto p(G|\Phi)p(\Phi|\mathcal{V}, \mathcal{M})p(\mathcal{V}, \mathcal{M}|\mathcal{H}), \quad (2)$$

where D denotes the observed sample configuration (for a thorough discussion of this type of analysis, see Stephens and Donnelly 2000 and Stephens 2001). In the Metropolis-Hastings algorithm, parameters are updated by choosing trial values and deciding whether or not they should be accepted. The simulated sequence of parameter values tends to the joint posterior distribution of the parameters as the sequence length becomes large. The goal of the analysis is to report marginal posterior distributions for \mathcal{M} and \mathcal{V} , which can easily be obtained from the simulation output by analyzing the values of these parameters independently of the others.

For the hierarchical model, the acceptance probability was calculated as:

$$P = \frac{p(\mathcal{V}', \mathcal{M}'|\mathcal{H}')}{p(\mathcal{V}, \mathcal{M}|\mathcal{H})} \times \frac{p(\Phi'|\mathcal{V}', \mathcal{M}')}{p(\Phi|\mathcal{V}, \mathcal{M})} \\ \times \frac{p(G'|\Phi')}{p(G|\Phi)} \times \frac{p(\mathcal{V}, \mathcal{M}, \Phi, G|\mathcal{V}', \mathcal{M}', \Phi', G')}{p(\mathcal{V}', \mathcal{M}', \Phi', G'|\mathcal{V}, \mathcal{M}, \Phi, G)}, \quad (3)$$

where the prime denotes a trial updated value chosen

from an updating schedule given in Storz and Beaumont (2002). The last term in the expression is the Hastings correction, which ensures that there is no bias in the updating procedure toward any particular region of parameter space. The details of the Hastings correction are given in Beaumont (1999) and Storz and Beaumont (2002). For $P \geq 1$, the trial value was accepted, otherwise it was accepted with probability P .

Specification of the Priors

Simulations were based on the following assumptions. Prior means for the current and ancestral population sizes (α_{N0} and α_{N1}) were set equal to a \log_{10} -transformed value of 5.9. This value was obtained by estimating the total area of the distributional range of savannah baboons ($\sim 3.0 \times 10^6$ km²), the population density (0.80 baboons/km²; Samuels and Altmann 1991), and the ratio of effective population size to census number (0.33; Storz, Ramakrishnan, and Alberts 2001, 2002). We allowed for a large variation in this mean, $\sigma_{N0} = \sigma_{N1} = 3$, to allow for uncertainty in these estimates. The prior mean time since the population started changing in size, α_{xa} , was taken to be 60,000 years BP, to match the hypothesized date of population expansion for African humans and chimpanzees (Rogers and Jorde 1995; Ambrose 1998; Harpending and Rogers 2000), giving $\alpha_{xa} = 4.8$. Although savannah baboons, chimpanzees, and archaic humans surely had somewhat different ecological requirements, the types of environmental catastrophe envisioned by previous authors (Rogers and Jorde 1995; Ambrose 1998; Harpending and Rogers 2000) are expected to have caused population bottlenecks (and subsequent expansions) in all three species. The SD of the mean around the hypothesized time of expansion ($\sigma_{xa} = 2$) was chosen such that more recent and more ancient dates also had support under the prior. We assumed a point prior of $g = 10.15$ years per generation (=average of male and female generation times; Storz, Ramakrishnan, and Alberts 2002). We chose priors for the mean mutation rate that supported values between 10^{-3} and 10^{-4} : $\alpha_\mu = -3.3$ and $\sigma_\mu = 0.25$. This gives good support for a mean mutation rate among loci of 5×10^{-4} , a value widely assumed in demographic models (e.g., Goldstein et al. 1995), but which also allows for the somewhat higher rates indicated by pedigree-based estimates for autosomal microsatellites in humans (Brinkmann et al. 1998; Ellegren 2000b).

The priors specified above are for the means of the demographic parameters and mutation rate, $\mathcal{M} = \{M_{N0}, M_{N1}, M_\mu, M_{xa}\}$. To model the variation in parameters among loci, $\mathcal{V} = \{V_{N0}, V_{N1}, V_\mu, V_{xa}\}$, we assumed in all cases that zero variation was most likely, so that $\beta_{N0} = \beta_{N1} = \beta_\mu = \beta_{xa} = 0$. In the case of the demographic parameters, we assumed that aberrant loci would be sufficiently rare that there would be relatively little variation among loci. Consequently, we chose $\tau_{N0} = \tau_{N1} = \tau_{xa} = 0.05$. By contrast, it is reasonable to expect substantial variation in the mutation rate among loci, so we

chose a vague prior $\tau_\mu = 1$, which allows the SD in the \log_{10} mutation rate among loci to vary from 0 to ~ 2 .

Implementation

To obtain convergence in a reasonable amount of time with 14 loci, a subset of 100 chromosomes was sampled for each locus. The chain was run for 4×10^9 steps, recording parameter values every 2×10^5 steps to give 20,000 draws from the posterior distribution. Five independent chains were run for each analysis (see *Results*). The output was checked for convergence using the Gelman-Rubin statistic calculated in CODA (Best, Cowles, and Vines 1995), as implemented in R (Ihaka and Gentleman 1996; <http://www.r-project.org/>). Posterior densities from individual runs were also examined to check for overall consistency in shape. The last half of each run was then combined to produce an overall set of 50,000 points. Each run took ca. 70 h on a 700 MHz Pentium (a small “Beowulf” cluster of machines was used to run chains in parallel). Density estimation was carried out using the program Locfit (Loader 1996), as implemented in R. This was used to estimate modes and highest probability density (HPD) limits (Gelman et al. 1995). The HPD limits specify points of equal probability density enclosing a region (or possibly disjoint regions in multimodal data), with probability equal to some specified value. For example, in a bivariate plot, the 90% HPD limit is represented as a contour enclosing a region (or regions) within which the parameter values are expected to lie with 90% probability. The strength of evidence of population decline versus population growth was assessed using Bayes factors, as described in Beaumont (1999). The Bayes factor is a ratio where the numerator is the posterior probability of one model (e.g., population contraction) divided by its prior probability and the denominator is the posterior probability of another model (e.g., population expansion) divided by its prior probability. The Bayes factor gives the relative likelihood of the two different models. Bayes factors greater than $\exp(2)$ are generally considered significant. The ratio of posterior probabilities can be estimated from the simulated chain by counting the proportion of iterations in which the population has expanded and then dividing this by the proportion of iterations in which it has contracted.

Results

For the total sample of savannah baboons, the number of alleles per locus averaged 7.7 (range = 3–11) and expected heterozygosity averaged 0.678 (range = 0.271–0.830). No departures from Hardy-Weinberg equilibrium were observed at any loci (Storz, Ramakrishnan, and Alberts 2002). A significant degree of genetic subdivision would have been reflected by a heterozygote deficit. No such Wahlund effect was detected in our population sample as the average inbreeding coefficient for all 14 loci ($f = 0.011$) was not significantly different from zero.

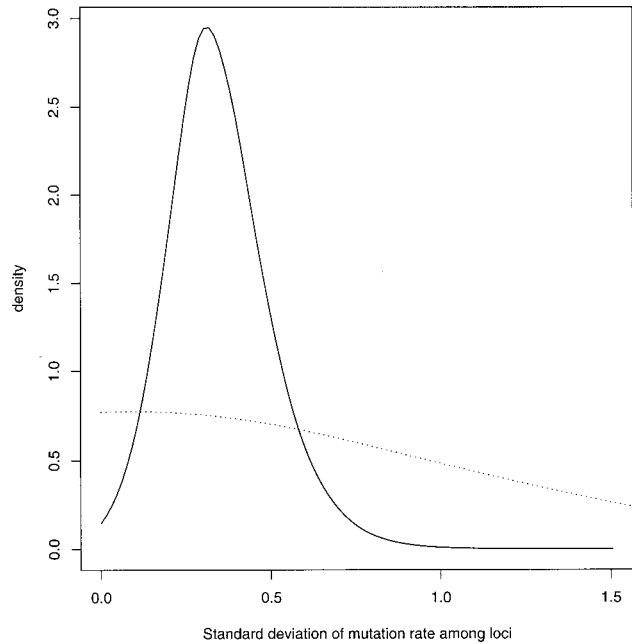


FIG. 1.—The posterior distribution (on a \log_{10} scale) of the SD of mutation rate among loci (V_μ). The prior is shown as a dotted line.

Variation in Parameters Among Loci

There was no evidence for substantial variation in the demographic parameters among loci, but there was evidence for variation in mutation rate. The five independent runs of the Markov chain Monte Carlo (MCMC) showed good convergence of the posterior distributions of $\mathcal{V} = \{V_{N0}, V_{N1}, V_\mu, V_{xa}\}$, the SDs of the parameters across all 14 loci. Neither the Gelman-Rubin statistic nor its 0.975 quantile was greater than 1.02 for any parameter. The posterior distributions for V_{N0} , V_{N1} , and V_{xa} were very similar to the priors. The posterior density at zero was always high, and the estimated modes were at or near zero. Although we cannot rule out some variation in the demographic parameters, the results are consistent with zero variation. By contrast, there was strong evidence for interlocus variation in mutation rate (fig. 1). The estimated HPD limits of the prior distribution were 0–1.3 with a mode at zero. The estimated HPD limits of the posterior distribution of V_μ were 0.10–0.59 with a mode at 0.31, indicating that there is little support for $V_\mu = 0$. The mode of 0.31 was consistent with a 10- to 20-fold difference in mutation rate between the most slowly and most rapidly evolving loci.

Convergence of MCMC Simulations

The five independent simulations show reasonable convergence for the means of the parameter values, although the degree of convergence for M_{N0} and M_{xa} was less than ideal. The Gelman-Rubin statistics (with 0.975 quantile in parentheses) for each parameter were M_{N0} , 1.15 (1.39); M_{N1} , 1.00 (1.01); M_μ , 1.00 (1.00); and M_{xa} , 1.11 (1.28). As a rule of thumb, values of the Gelman-Rubin statistic less than 1.2 indicate reasonable conver-

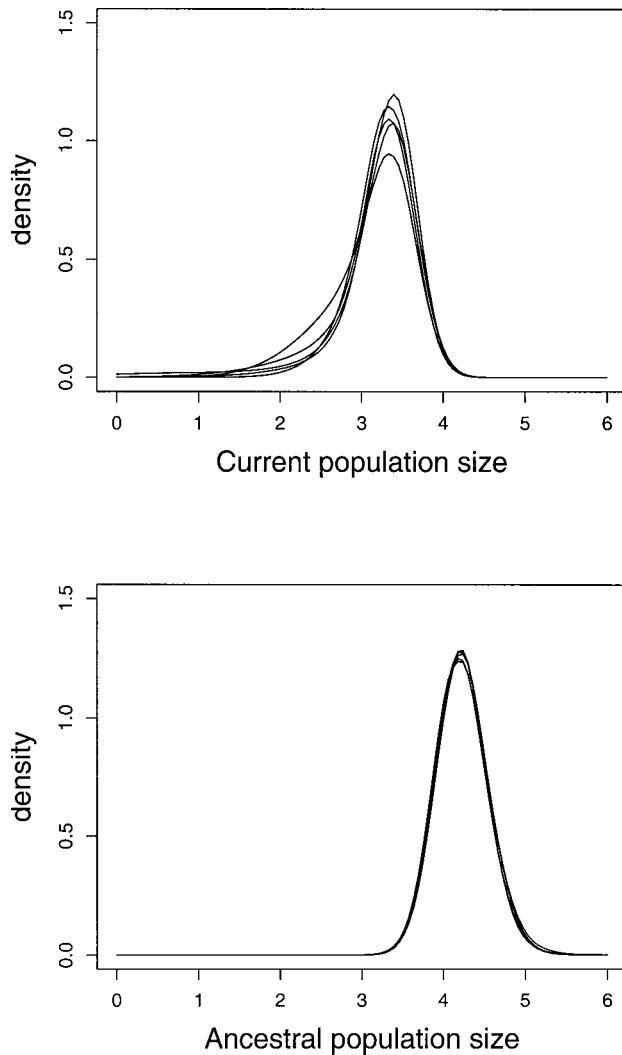


FIG. 2.—Posterior distributions for current population size (M_{N0} ; top) and ancestral population size (M_{N1} ; bottom) estimated from five independent MCMC simulations.

gence (Gelman et al. 1995). The reason for poor convergence for M_{N0} and M_{xa} is that there was a thick tail for low values of M_{N0} and M_{xa} , and this was sampled to different degrees among the independent simulations. Differences in the degree of convergence corresponding to different values of the Gelman-Rubin statistic are illustrated in figure 2.

Evidence for Historical Population Decline

The data indicate that *P. cynocephalus* has undergone a pronounced population decline (fig. 3). The 90% HPD limits for the joint distribution of the ancestral and current population size lie well above the line of equality. The Bayes factor for contraction versus expansion was 9,999 (in only 5 out of 50,000 points was the current size greater than the ancestral size). The mode of the joint distribution was $M_{N0} = 3.36$, $M_{N1} = 4.24$, indicating an eightfold contraction in population size. The summaries of the marginal posterior distributions for each parameter are given in table 1. Marginally, the an-

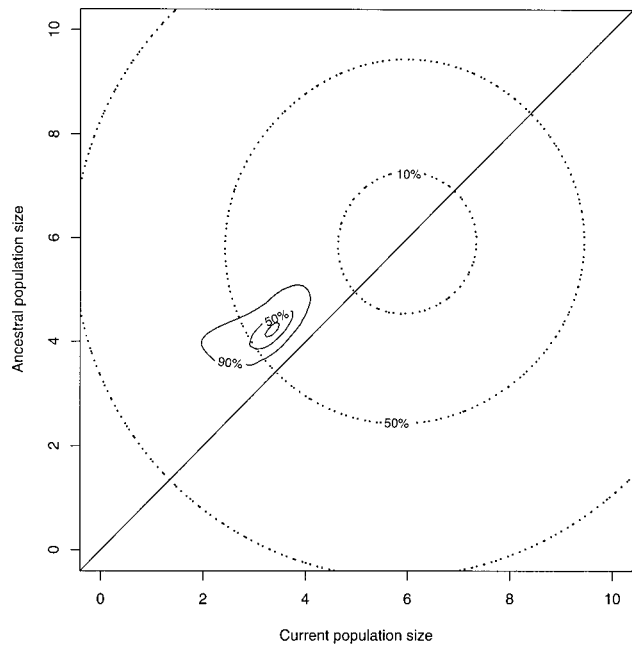


FIG. 3.—Joint posterior distribution (on a \log_{10} scale) of the mean current population size (M_{N0}) and the mean ancestral population size (M_{N1}) of the savannah baboon, *P. cynocephalus*. The 90%, 50%, and 10% HPD limits are plotted as continuous lines. The HPD limits for the prior are plotted as dotted lines. The diagonal line corresponds to $M_{N0} = M_{N1}$.

cestral effective population size was estimated to be between 5,000 and 60,000, and the current effective population size was estimated to be between 200 and 10,000.

Timing of the Population Decline

The data were not very informative about the possible time scale of population decline. The posterior distribution of the time since the population started to decline (conditional on having declined rather than expanded) is plotted in figure 4, and the summary of this distribution is given in table 1. The distribution is skewed with a long tail to the left. The estimated mode for the time since the population started to decline was around 30,000 years, and it is unlikely to have occurred

Table 1
Posterior and Prior Distributions of the Means of the Parameter Values Used in the Model

		Lower HPD Limit	Mode	Upper HPD Limit
M_{N0} ..	Posterior	2.34	3.36	3.98
	Prior	0.97	5.90	10.83
M_{N1} ..	Posterior	3.69	4.21	4.75
	Prior	0.97	5.90	10.83
M_{μ} ...	Posterior	-3.95	-3.54	-3.14
	Prior	-3.91	-3.50	-3.09
M_{xa} ..	Posterior	3.07	4.51	5.40
	Prior	1.51	4.80	8.09

NOTE.—The distributions are characterized by the 90% upper and lower highest posterior (or prior) density (HPD) limits, as defined in the text. The modes of the distributions are also given.

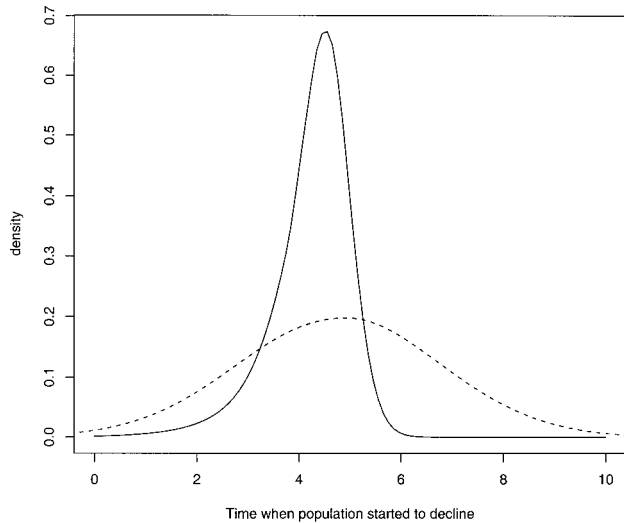


FIG. 4.—The posterior distribution (on a \log_{10} scale) of the mean time since the population started to change in size (M_{xa}). The prior is shown as a dashed line.

more than 250,000 years ago or more recently than $\sim 1,000$ years ago. It can be seen from figure 5 that the joint posterior distribution of M_{N0} and M_{xa} was highly correlated, and short times since the population has declined imply that the current effective size is quite small. If we had used more informative priors for the population size, the tail in M_{xa} would be reduced, supporting a more ancient date for the onset of the population decline. An additional caveat is that the information on times comes from the prior chosen for M_{μ} , and if higher (or lower) values had been chosen, the times would be shorter (or longer) in direct proportion. It can be seen from table 1 that there is negligible information on M_{μ} , and the posterior distribution is almost identical to the prior.

Discussion

Results of the coalescent analysis of microsatellite variation provide strong evidence that savannah baboons have undergone a historical decline in population size. The data suggest that the onset of the decline occurred in the late Pleistocene or early Holocene. A previous analysis of microsatellite allelic frequencies in savannah baboons revealed no evidence for a recent genetic bottleneck (Storz, Ramakrishnan, and Alberts 2002). The test used to detect a bottleneck was based on theory developed for neutral loci that relates the expected heterozygosity at mutation-drift equilibrium to the observed number of alleles in the population sample (Nei, Maruyama, and Chakraborty 1975; Watterson 1984; Maruyama and Fuerst 1985; Cornuet and Luikart 1996). Because allelic diversity is reduced more rapidly than heterozygosity during a bottleneck (Nei, Maruyama, and Chakraborty 1975), an abrupt reduction in population size is expected to produce a transient excess of heterozygosity, relative to the expected value at mutation-drift equilibrium. The fact that this test revealed no significant departure from mutation-drift equilibrium suggests

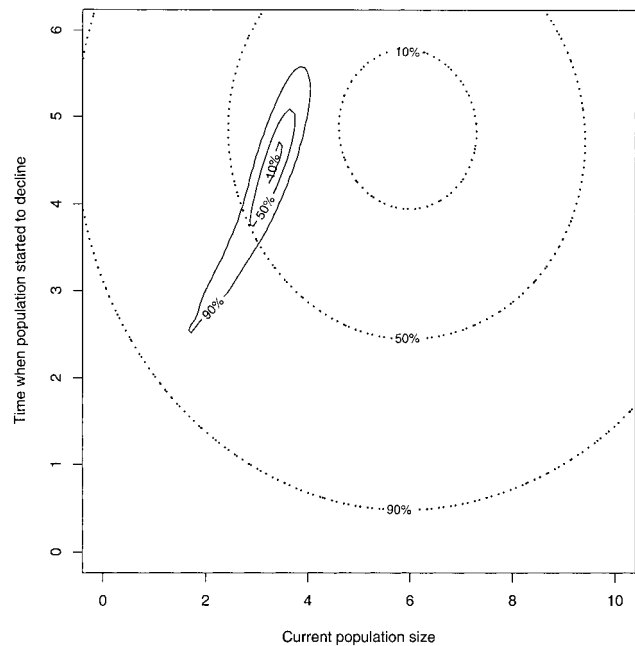


FIG. 5.—Joint posterior distribution (on a \log_{10} scale) of the mean current population size (M_{N0}) and the mean time since the population started to change in size (M_{xa}). The 90%, 50%, and 10% HPD limits are plotted as continuous lines. The HPD limits for the prior are plotted as dotted lines.

that the savannah baboon population has remained relatively stable in recent history. This supports the results of the likelihood-based coalescent analysis, which indicated that the onset of population decline occurred well over 1,000 years ago. It thus appears that the size reduction of the baboon population is attributable to a long-term decline and not to a recent bottleneck.

The evidence for a relatively ancient onset of population decline also suggests that the inferred distribution of coalescence times cannot be attributed to a recent change in the degree of population subdivision (Wakeley 1999; Wakeley et al. 2001). A more recent onset of population decline would have been more difficult to distinguish from the effects of subdivision because shorter coalescence times could simply reflect rates of drift within partially isolated local demes rather than in the population as a whole.

Disentangling the Effects of Demography and Selection

Using genetic data to make inferences about demographic history is complicated by the potentially confounding influence of selection at linked sites (Nachman et al. 1998; Przeworski, Hudson, and Di Rienzo 2000). Departures from expectations of the standard neutral-equilibrium model can result from the direct or indirect effects of selection or from changes in the size or spatial contiguity of the population under study. For example, negative values of Tajima's D indicate an excess of low-frequency variants relative to null expectations and may be caused by population expansion or positive selection at linked sites. Positive values of D indicate an excess

of intermediate-frequency variants relative to null expectations and may be caused by population contraction, population subdivision, or balancing selection at linked sites (Tajima 1989*a*, 1989*b*). With regard to marker-based inferences about historical demography, the confounding influence of selection may be especially problematic in studies based on variation in mtDNA and the nonrecombining portion of the Y-chromosome. Because of the absence (or near absence; Awadalla, Eyre-Walker, and Maynard-Smith 1999) of recombination, positive selection at linked sites or purifying selection against mildly deleterious mutations could have produced the excess of low-frequency variants observed in mtDNA surveys of human populations (Excoffier 1990; Nachman et al. 1996; Wise, Sraml, and Easteal 1998).

Global surveys of human genetic variation have revealed profound differences in the frequency spectra of mitochondrial and nuclear sequence variation (Hey 1997). It seems likely that the observed discrepancy is attributable to the effects of selection on one or both classes of sequence variation. Whatever the underlying cause, the disparate patterns of variation have led to conflicting inferences about human demographic history. Harpending and Rogers (2000) argued that mtDNA variation preserves a faithful record of human demographic history, whereas the frequency spectrum of nuclear sequence variation often reflects a history of balancing selection that has acted independently on multiple loci. According to Harpending and Rogers (2000), the pervasive effects of balancing selection may explain why nuclear sequence data are often characterized by an excess of intermediate-frequency variants relative to neutral-equilibrium expectations (see Przeworski, Hudson, and Di Rienzo 2000; Nachman 2001). By contrast, Wall and Przeworski (2000) suggested that the consensus pattern of sequence variation across multiple, unlinked nuclear loci may often provide the most reliable basis for inferring aspects of human demographic history and that the frequency spectrum of mtDNA variation likely reflects a history of selective sweeps or purifying selection on mildly deleterious mutations. According to Wall and Przeworski (2000), the effects of either positive or negative selection may explain why mtDNA data typically exhibit an excess of low-frequency variants relative to neutral-equilibrium expectations (see also Hey 1997).

Although any given nuclear locus is potentially subject to the direct or indirect effects of selection, the potential for selection to confound marker-based inferences about demographic history can be minimized by combining data from multiple unlinked regions of the genome. Comparison among unlinked markers can be used to distinguish between the effects of selection (which are locus specific, at least to a degree determined by local recombination rate; Maynard-Smith and Haigh 1974; Kaplan, Hudson, and Langley 1989) and the effects of demographic processes (which are expected to have relatively uniform effects across the genome). One of the chief virtues of using microsatellite markers for the estimation of neutral parameters is that a large number of allelic length polymorphisms can be assayed across disparate regions of the genome. Moreover, data

for humans indicate that recombination rates exhibit no significant association with levels of microsatellite polymorphism (Payseur and Nachman 2000).

But even if information is combined from many microsatellite loci, the effect of selection on a single locus can potentially bias the results of a multilocus analysis. In a model where demographic parameters are not allowed to vary among loci, aberrant patterns of variation at loci under selection can have a strong influence if likelihoods for individual loci are combined in a multiplicative fashion. In our hierarchical model, the likelihoods are combined in a more additive fashion. Thus, results will not be unduly affected by loci that deviate from the baseline level of neutral variation. One of the chief virtues of the hierarchical model is that it provides a means of identifying aberrant loci that could potentially bias the estimation of neutral parameters (cf. Beaumont and Nichols 1996; Vitalis, Dawson, and Boursot 2001).

Our results provide strong evidence for interlocus variation in some parameters. Given our prior assumption that heterogeneity in mutation rate is the most likely cause of such variation, we conclude that there is no evidence for substantial interlocus variation in demographic parameters. The posterior distributions most strongly support SDs close to zero and are generally indistinguishable from the priors. This suggests that there is insufficient power to detect differences among loci, most likely because each individual locus conveys relatively little information about demographic history.

Disentangling the Effects of Demography and Mutation

Compared with single-nucleotide polymorphism, standing levels of microsatellite variation generally will be less strongly affected by the interaction of linkage and selection because loci with high mutation rates are expected to undergo a more rapid return to equilibrium after a selective sweep (Wiehe 1998). But uncertainty about the mode of mutation presents more of a problem for microsatellite analysis. Convergent or parallel mutations that produce allelic size homoplasy can potentially obscure the signal of past demographic events (Di Rienzo et al. 1998; Gonser et al. 2000). As an example, consider the genealogical history of a sample under a model of population expansion. Looking backward in time, coalescence rates will be lowest near the branch tips (closer to the present when the population is large) and will be highest near the root of the tree (closer to the start date of the expansion when the population was small; Donnelly and Tavaré 1995). At any given locus, the inferred relationship between two randomly sampled alleles will depend on the depth of the tree (i.e., the number of generations since the most recent common ancestor). Because mutations are expected to occur independently along the branches leading from the root (i.e., common ancestor) to the sampled alleles, branch lengths should be proportional to the number of mutational steps separating the alleles. Thus, inferences about a past history of population expansion or contraction

may be sensitive to the assumptions of the mutation model (Donnelly 1999).

The relative frequency of multistep mutations remains a subject of considerable debate (Di Rienzo et al. 1994, 1998; Estoup and Cornuet 1999; Ellegren 2000b; Renwick et al. 2001). Pedigree data from humans suggest that >90%–95% of microsatellite mutations involve single-step changes in allele size, and the remainder typically involve a small number of steps (Brinkmann et al. 1998; Kayser et al. 2000). Moreover, analyses of Y-chromosome microsatellites based on the stepwise mutation model have provided strong evidence for demographic expansion of the human population, corroborating inferences from other markers (Pritchard et al. 1999; Thomson et al. 2000). If multistep mutational changes are infrequent relative to single-step changes, as suggested by the available pedigree evidence, then only a small number of loci should be affected. Our choice of priors for the mutational parameters allowed for a considerable degree of interlocus variation in μ . In a similar manner, the model accounts for some degree of variation in the mode of mutation (occasional multistep changes) by allowing interlocus variation in demographic parameters. Overall, the hierarchical model will tend to give less weight to loci that exhibit aberrant patterns of variation, thereby ensuring that our conclusions are not overly sensitive to violations of the strict stepwise mutation model.

Discordant Patterns of Demographic History Among Codistributed African Primates

The main objective of this analysis was to test for evidence that savannah baboons underwent a population expansion in concert with the hypothesized expansion of African human and chimpanzee populations in the late Pleistocene (Harpending and Rogers 2000). The rationale is that any type of environmental event sufficient to cause simultaneous population expansions in African humans and chimpanzees would also be expected to affect other codistributed mammals (Rogers and Jorde 1995; Ruvolo 1996; Goldberg and Ruvolo 1997; Ambrose 1998; Harpending and Rogers 2000). Although the microsatellite data indicate that savannah baboons actually underwent a pronounced population contraction during the late Pleistocene, our results do not necessarily refute the hypothesis that the expansions of African humans and chimpanzees were driven by a single environmental event. Several authors (Rogers and Jorde 1995; Ambrose 1998; Harpending and Rogers 2000) have suggested that the population expansions occurred as a result of recovery from some form of environmental catastrophe, such as the volcanic winter that followed the eruption of Mt. Toba (which occurred ~73,500 years BP; Rampino and Self 1992, 1993). If the expansions were preceded by a population bottleneck (for example, due to a climatically induced range contraction into one or more refugia), the nature of the subsequent recovery would depend on whether the populations expanded from a single refugium (as suggested for African humans and chimpanzees; Ambrose 1998; Harpending and

Rogers 2000) or several. As stated by Harpending and Rogers (2000, p. 370): "... a few species that showed a different pattern would not refute the hypothesis of a Pleistocene bottleneck, but a few showing the same pattern would greatly strengthen it." Data from a more diverse array of codistributed mammals should eventually provide a clearer picture of the zoogeographic history of East Africa and the possible role of environmental catastrophes in the evolution of anatomically modern humans and other hominoid primates.

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