
Elucidating Population Histories Using Genomic DNA Sequences

by Linda Vigilant

In 1993, Cliff Jolly suggested that rather than debating species definitions and classifications, energy would be better spent investigating multidimensional patterns of variation and gene flow among populations. Until now, however, genetic studies of wild primate populations have been limited to very small portions of the genome. Access to complete genome sequences of humans, chimpanzees, macaques, and other primates makes it possible to design studies surveying substantial amounts of DNA sequence variation at multiple genetic loci in representatives of closely related but distinct wild primate populations. Such data can be analyzed with new approaches that estimate not only when populations diverged but also the relative amounts and directions of subsequent gene flow. These analyses will reemphasize the difficulty of achieving consistent species and subspecies definitions by revealing the extent of variation in the amount and duration of gene flow accompanying population divergences.

Access to complete genome sequences from humans and a growing list of primates represents an exciting opportunity for evolutionary anthropology. The recently completed macaque genome represents a particularly important advance because the three-way comparison among humans, chimpanzees, and macaques should improve our ability to identify important differences in the lineage leading to humans (Rhesus Macaque Genome Sequencing and Analysis Consortium 2007). The quest to identify what makes us human is a fascinating, ongoing story filled with early breakthroughs (Enard et al. 2002; Zhang 2003), sobering reconsiderations (Mekel-Bobrov et al. 2007; Woods et al. 2006), and an emerging recognition that a lot of work remains to be done, particularly in the identification of adaptive traits in humans and our closest relatives (Bakewell, Shi, and Zhang 2007). Another major area of inquiry facilitated by primate genome sequences is the evolution of genome structure. While much early attention was devoted to the ~1% of the genome exhibiting single-nucleotide differences between humans and chimpanzees (Chimpanzee Sequencing and Analysis Consortium 2005; Nielsen et al. 2005), increasing attention is now being paid to the many structural changes in gene number and order (Cheng et al. 2005; Harris, Rogers, and Milosavljevic 2007; Perry, Tito, and Verrelli 2007; Popesco et al. 2006). Another important use of genome information is for elucidating pop-

ulation histories, including estimating ancestral population sizes and the manner and timing of population divergences. This paper focuses on how an increasing amount of information available through use of genome sequences, high-throughput sequencing, and new analytical approaches is shedding new light on such topics as how the divergence that led to humans and chimpanzees occurred, as well as more general aspects of how populations diverge.

The entities that we commonly recognize as species ultimately began as populations that diverged and eventually ceased to exchange genes. Species may be distinguishable by morphological characters, but such differences are likely to represent responses to ecological or sexual selection and are thus less useful for the reconstruction of population relationships (but see Ackermann, Rogers, and Cheverud 2006). Researchers have therefore turned to the use of genetic markers evolving in a neutral or nearly neutral fashion to address the question of how and when present-day populations diverged from a common ancestor. This is done by surveying genetic variation at one or many loci in representatives of the populations in question, with the expectation that the inferred gene trees reflect the evolutionary relationships of the populations. Here, I first briefly review the uses and limitations of analyses of mitochondrial DNA (mtDNA) and the Y chromosome, markers that reveal the histories of females and males, respectively. I then discuss the advantages and insights that come from analysis of multiple autosomal loci and end by describing some future prospects for understanding the evolutionary histories of populations. Throughout, I will use

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examples from studies of genetic variation in humans and other primates to illustrate general points.

Inferences from Mitochondrial DNA

A much-used tool to study population histories is the maternally inherited mtDNA molecule. Because of its useful properties of high abundance in cells relative to nuclear DNA, rapid rate of evolution, and lack of recombination, a vast number of studies of mtDNA variation in wild populations have been carried out since the late 1980s. These studies have been the backbone of phylogeography, the study of the genealogical and spatial relationships of populations (Avice 2000). The mode of inheritance of mtDNA means that the variants seen in the present day can be readily traced back to a single common ancestor living in the past. The geographical distribution of the lineages in the present-day descendants of the common ancestor can offer information about where the most recent common ancestor occurred. For example, the deepest branches on trees describing modern human mtDNA variation consist exclusively of individuals of African origin, supporting an African origin of human mtDNA (Cann, Stoneking, and Wilson 1987; Ingman et al. 2000; Vigilant et al. 1991).

Examples from other African primates illustrate both the power and the limitations of population-relationship inferences based on mtDNA. Several subspecies of chimpanzees have been distinguished on the basis of their geographical distribution and are accordingly termed “western,” “central,” and “eastern” chimpanzees (Hill 1969). Phylogenetic trees relating the mtDNA variants in these subspecies generally accord with these distinctions and depict the deepest divergence between western chimpanzees and the other subspecies (Gagneux et al. 1999; Morin et al. 1994). However, the central and eastern subspecies are not reciprocally monophyletic; rather, some individuals of different subspecies are closely linked in tree analyses (Gagneux et al. 2001). Two possible explanations are that the divergence between eastern and central chimpanzees is too recent to be detected even by this rapidly evolving marker and that female-mediated gene flow continues between these populations.

Baboons offer even more interesting examples of the challenges inherent in describing population relationships. A series of studies by Jolly and coworkers have brought a combination of ecological, morphological, and genetic data to bear on the evolutionary relationships between baboon taxa (e.g., Jolly 1993; Phillips-Conroy and Jolly 1986; Phillips-Conroy et al. 1992; Szmulewicz et al. 1999). Among these, a recent mtDNA phylogeny provides some molecular traces of hybridization among morphologically distinct baboon taxa (Newman, Jolly, and Rogers 2004). In contrast to expectations, the mtDNA sequences in the olive and yellow baboons show rather low diversity and were intermixed in the phylogenetic tree. This, along with patterns of morphological variation among the taxa, suggests the occurrence of hybrid-

ization among taxa rather than just retention of recent ancestral mtDNA variation. This is supported by extensive documentation of hybridization at the borders of baboon taxa (hamadryas-anubis: Phillips-Conroy, Jolly, and Brett 1991; Phillips-Conroy et al. 1992; gelada-hamadryas: Jolly et al. 1997).

Nonetheless, many studies of mtDNA find monophyletic splits and no hint of gene flow, in accordance with expectation for closely related populations or species (e.g., Sterner et al. 2006). However, the above examples of mtDNA trees that fail to describe the monophyletic patterns expected from morphology or geography raise the question of whether interpopulation migration might be more common than generally assumed. There are at least three reasons why studies of mtDNA variation might underestimate gene flow among populations. First, mtDNA evolves rapidly, and so more ancient episodes of interpopulation migration might be overlooked or ascribed to variation in the common ancestral population. Second, sampling schemes could obscure migration. If individuals have limited dispersal, variation within the population might be clinal, and sampling far from current or previous population contact zones might miss evidence of introgression. Third, mtDNA is limited to depicting female population histories, and the majority of mammal species are characterized by male dispersal (Greenwood 1980; Lawson Handley and Perrin 2007). This last point, the exclusively maternal inheritance of mtDNA, has led researchers to explore patterns of population variation of its paternally inherited counterpart, the Y chromosome.

The Y Chromosome and Primate Population Histories

Although the nonrecombining portion of the Y chromosome would, in principle, offer appropriate data for genealogy construction, several factors have limited the study of patterns of population variation in Y chromosomes in nonhuman taxa (but see Stone et al. 2002). The first difficulty has been the limited availability of sequence information and the limited success experienced when using markers developed in one species even in a closely related species (Erlar, Stoneking, and Kayser 2004). This problem will be remedied as genome sequences of various organisms are completed, but another difficulty concerns the levels of variation observed in the Y chromosome. In many species analyzed thus far, the levels of sequence variation (nucleotide diversity) are very low (Hellborg and Ellegren 2004; Kuroki et al. 2006; Lawson Handley et al. 2006). Possible reasons for this are a low mutation rate relative to mtDNA, negative selection, and small male effective population sizes (Charlesworth 2001; Lawson Handley, Berset-Brandli, and Perrin 2006). Recent work has particularly highlighted male effective population sizes that are small because of variance in male reproductive success as a likely cause of the low variation (Eriksson et al. 2006; Lawson Handley, Berset-Brandli, and Perrin 2006), although others argue that

selection plays a key role (Boissinot and Boursot 1997; Hellborg and Ellegren 2004; Hughes et al. 2005). Assessment of the relative importance of various factors in causing low levels of intraspecific diversity on the Y chromosome has been hampered by the fact that low variation itself limits the ability to test for evidence of selection. However, one approach to assessing the effect of variance in male reproductive success would be comparisons of the relative levels of variation at autosomal, X-linked, and Y-linked loci among taxa known to vary in the extent of male reproductive skew.

When technically feasible, comparisons of patterns of DNA sequence variation seen in the mtDNA molecule and Y chromosome can be a particularly effective way of elucidating sex-specific aspects of population divergences. Tosi and colleagues have used this approach in an impressive series of studies focusing on macaque population histories, and they have shed light on the evolutionary relationships of macaque species (Tosi, Morales, and Melnick 2000), described evidence of introgression among macaque species (Tosi, Morales, and Melnick 2002), and investigated the origin and phylogeography of the long-tailed macaque (Tosi and Coke 2007).

Although displaying low nucleotide diversity, the Y chromosome also harbors rapidly evolving microsatellite loci. In a recent study, Eriksson and colleagues sequenced mtDNA control regions and genotyped 12 Y-chromosome microsatellite loci in DNA from wild male bonobos from across the species range (Eriksson et al. 2006). The networks relating the Y-chromosome haplotypes were much more structured according to sample origin than were the mtDNA networks (fig. 1), a result consistent with predominantly female gene flow in this species. Similar results have been obtained in a study of eastern chimpanzees (*Pan troglodytes schweinfurthii*), where a comparison with data from humans suggests that even human populations described as practicing patrilocality (male philopatry) exhibit much weaker genetic signals of patrilocality than do chimpanzees (Langergraber et al. 2007). Assessment of Y-chromosome genealogies has great potential for uncovering population relationships, particularly in species featuring male migration. When comparisons involve groups or populations that have been separated for a significant length of time (on the order of tens or hundreds of thousands of years), microsatellite genotypes should ideally be complemented by characterization of slower-evolving single-nucleotide polymorphisms (SNPs) on the Y chromosome in order to guard against false inferences due to the presence of independently arising yet identical alleles at microsatellite loci. However, discovering variable nucleotides on the Y chromosome is time-consuming and particularly difficult in organisms lacking a genome sequence (but see Hellborg and Ellegren 2003), and polymorphisms may still not be found even after several kilobases (kb) are analyzed (Lawson Handley, Berset-Brandli, and Perrin 2006; Lawson Handley et al. 2006).

Population History Inferences Using Genomic Data

Analysis of multiple unlinked loci on autosomes (as well as the X chromosome) is preferable to analysis of single loci (such as the mtDNA or Y chromosome) because it allows many more realizations of the evolutionary process to be seen. Factors such as selection, migration, gene duplication, and simple chance can result in gene trees that differ from population trees, and so it is important to examine information from many loci from multiple individuals per population (Degnan and Salter 2005; Edwards and Beerli 2000; Knowles and Carstens 2007). For practical reasons, until recently this has mostly been achieved through analysis of microsatellites, which are highly variable and easily characterized nuclear loci.

Bowcock and colleagues provided an early demonstration that analysis of multiple microsatellite loci from many individuals could reveal the geographic origins of individuals and describe population relationships (Bowcock et al. 1994). This study found that the deepest roots of the trees relating either individuals or populations led to samples of African origin and were thus consistent with an African origin of human genetic variation. More recently, tree-based approaches to describing individual variation at microsatellite loci have been supplanted by model-based clustering programs that sort individuals without regard to previous information regarding population affinities (Pritchard, Stephens, and Donnelly 2000). Application of such an approach to large data sets describing variation found in a worldwide sampling of humans has led to some interesting findings. While confirming that nearly all genetic variation found in humans consists of within-population differences among individuals and that only a small proportion of variation distinguishes populations (Lewontin 1972), a study by Rosenberg and colleagues also partitioned the total variation found into six clusters (Rosenberg et al. 2002). Five of these clusters corresponded to large geographic regions, and some subclusters coincided with geographically and culturally delimited populations. This is of interest, for example, for studies of disease associations because it suggests that the self-reported ancestry of an individual would very often correspond to the genetically defined ancestry (Rebbbeck and Sankar 2005). More controversially, such corroboration by genetic analysis of categories of self-reported geographic or ethnic ancestry can be seen as contributing to a general overemphasis on racial distinctions and classification in modern human society (Kittles and Weiss 2003).

The pattern of geographic clustering of human genetic variation found by Rosenberg and colleagues was surprising because earlier studies had consistently found a more continuous pattern of human genetic geography (Cavalli-Sforza, Menozzi, and Piazza 1994). In fact, earlier studies ascribed apparent geographic structuring of human genetic variation to discontinuous sampling of individuals from geographically disparate populations and predicted that a geographically random sample would give a more complex, less disjunct pattern

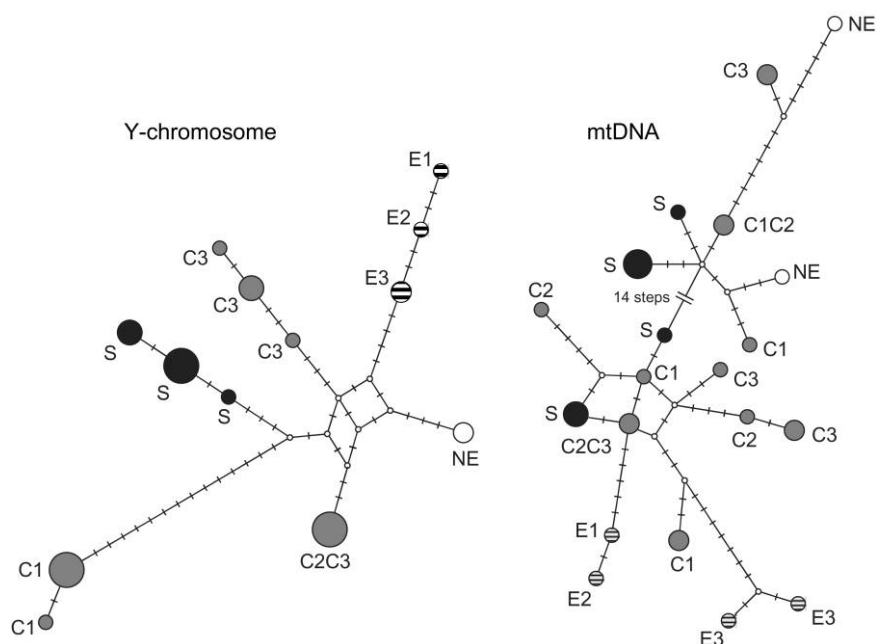


Figure 1. Networks of bonobo Y-chromosome and mtDNA variants collected from the same set of individuals. Shading in the circles indicates the collection locality, as indicated by the letter codes. The size of the circles is proportional to the number of individuals sharing the haplotype. (Figure reprinted from Eriksson et al. 2006, with permission.)

(Bowcock et al. 1994). This argument was developed in a reanalysis of the Rosenberg data in which it was demonstrated that random sampling of the original data led to gradients of human genetic variation within and among continents (Serre and Pääbo 2004). Further analysis of a still larger data set suggested that human genetic variation does indeed follow a clinal pattern, but the authors argued that, given sufficient data, small discontinuities corresponding to geographic barriers can be detected (Rosenberg et al. 2005). Lately, a consensus has been emerging in the clusters-versus-clines debate that emphasizes the clinal nature of the vast majority of human global genetic variation, with clusters explaining only 2% of the variance in pairwise differentiation measures (Lawson Handley et al. 2007 and references therein).

Relationships of Nonhuman Primate Populations

Patterns of variation in nonhuman primates should provide a valuable perspective for attempts to study the correspondence between geographic and genetic variation in humans. A recent study employed an approach analogous to those used in the just-mentioned studies of human global genetic variation to examine the distribution of genetic variation among the three geographically defined subspecies of chimpanzees

(Becquet et al. 2007). Results corroborated previous findings based on mtDNA (see above) of a close relationship between eastern and central chimpanzees and an earlier divergence of western chimpanzees. There is a hint of population substructure within western chimpanzees, but this is difficult to evaluate in the absence of a more dispersed sampling of individuals from known localities. Thus, this study, along with the studies on humans mentioned above, suggests that sampling schemes can have profound effects on the results obtained, with random or grid sampling more likely to lead to suggestions of clinal variation than the disjunct samples typically available.

As discussed above, the interpretations of clustering approaches to the analysis of genetic variation can be problematic when applied to taxa that have not been sampled continuously across their distribution. However, such clustering approaches can be particularly helpful in elucidating the population structure of taxa living in a fragmented environment. Richard Bergl scoured forest patches on the border of Nigeria and Cameroon to collect fecal samples for microsatellite analysis of noninvasive DNA from up to one-third of the remaining highly endangered and elusive Cross River gorillas. Analyses suggested the presence of three population clusters roughly consistent with geography but displaying no simple isolation-by-distance effects (Bergl and Vigilant 2007). In an

encouraging result for conservation efforts aimed at preserving or improving connections among forest fragments, possible migrants and admixed individuals were also identified.

New analytical methods and access to complete genome sequences offer new opportunities to understand relationships among populations and in particular to use estimated genetic divergences to infer the manner and timing of population or species divergences (Hey 2006; Patterson et al. 2006). Thus far, complete genome sequences of humans (International Human Genome Sequencing Consortium 2001; Venter et al. 2001), chimpanzees (Chimpanzee Sequencing and Analysis Consortium 2005), and macaques (Rhesus Macaque Genome Sequencing and Analysis Consortium 2007) have been published. Genome sequences soon to be finished include those of the orangutan, the marmoset, the gibbon, and the gorilla. While much attention has been paid to interspecific comparisons—which can, for example, reveal whether certain genes have been positively selected in particular lineages (e.g., Bakewell, Shi, and Zhang 2007)—genome sequences are an important resource for subsequent analysis of variation within species or closely related species. Once a reference sequence exists, it is a simple matter to resequence targeted regions or genes in multiple individuals and to detect any differences by comparing the sequences.

The recent completion of the rhesus macaque genome illustrates the usefulness of genomic sequences for understanding population histories. The evolutionary relationship between rhesus macaque populations in China and India has long been enigmatic, and genetic analysis of single loci, such as mtDNA (Smith and McDonough 2005), or even small amounts of genomic data have offered limited insights (Ferguson et al. 2007). Knowing whether there are significant genomic differences between individuals of Indian and Chinese origin is especially important in view of the macaque's role as a model organism for research. Hernandez and colleagues reported the results of a comparison of about 1,500 SNPs located in >150 kb of noncoding DNA (Hernandez et al. 2007). The data fit a model in which the two populations split about 162,000 years ago, with the Chinese population then expanding threefold and the Indian population decreasing by three-fourths about 50,000 years ago. These demographic inferences, along with estimates of effective population sizes, offer a more nuanced view of macaque population history than was previously available. In addition, the patterns of linkage disequilibrium (nonrandom associations between polymorphisms at different loci) vary, with Indian macaques having more and Chinese macaques having less linkage disequilibrium than humans. Such information aids in the design of studies in rhesus macaques aimed at mapping gene variants associated with human disease.

Histories of Humans and Great Apes

A topic of enduring interest is the relationship between humans and our closest living relatives, the chimpanzees. Nearly

40 years ago, Vincent Sarich and Allan Wilson elicited controversy by suggesting, on the basis of immunological studies of proteins, that humans and apes diverged only 4–5 million years ago (Mya), in contrast to the prevailing view that they separated at least 10 Mya (Sarich and Wilson 1967). This recent date has garnered consistent support over the years (Horai et al. 1992; Sibley and Ahlquist 1987; Takahata, Satta, and Klein 1995), and eventually enough data accumulated for a statistically reliable determination of whether the gorilla or the chimpanzee was the closest relative of humans, with chimpanzees and humans found to be most closely related (Ruvolo 1997). However, a subsequent study examining 53 segments totaling ~24 kb from a human, a chimpanzee, a gorilla, and an orangutan found that nearly half of the segments examined support other topologies (such as human and gorilla being most closely related). This pattern of “incomplete lineage sorting” is thought to reflect large effective population sizes of the human-chimpanzee and human-chimpanzee-gorilla ancestors and a very short interval (~1 million years) separating the split leading to gorillas and the split of humans and chimpanzees (Chen and Li 2001).

A more recent study used vastly more data, avoided demographic assumptions, and considered recurrent mutation in order to infer the timing as well as the nature of the human-chimpanzee divergence (Patterson et al. 2006). This study received much attention for suggesting that the speciation occurred less than 6 Mya, with an initial separation followed by hybridization among protohumans and protochimpanzees. The hybridization scenario is invoked to explain the wide range of divergence times for humans and chimpanzees at various loci and the particularly low divergence observed on the X chromosome. The hybridization scenario also reconciles the recency of these speciation events with the interpretation of the 6.5–7.4-million-year-old Toumai fossil as representing an ancestor of humans but not of chimpanzees. A recent date for human-chimpanzee speciation (4 Mya) was also suggested by another study, which argued that a large ancestral population size was adequate to explain the varying divergence times across the genome and that selection and/or a gradual speciation process, rather than hybridization, might explain the patterns found on the X chromosome (Hobolth et al. 2007).

Recent results from studies of African apes highlight how recently major population divisions have occurred. Using ~30 kb of sequence data from a variety of studies, Won and Hey (2005) investigated the relationships between chimpanzees and bonobos and between western and central chimpanzees. Results from a model allowing migration found a divergence time of 0.86–0.89 Mya for the split between chimpanzees and bonobos, with no suggestion of gene flow. However, a clear signal of unidirectional gene flow from the western chimpanzees to the larger population of central chimpanzees was seen, and a divergence time of 0.420 Mya was estimated. Although mtDNA does not hint at gene flow between western and central chimpanzees, it is supported by the majority (37 of 47) of the nuclear loci analyzed. Because they are based

Table 1. Time estimates for great ape population divergences

Taxa and split time	Gene flow
Chimpanzee-bonobo:	
0.80 million years ago (Mya) ^a	Not allowed in model
0.86–0.89 Mya ^b	No
0.79–0.92 Mya ^c	No
Western chimpanzee–central chimpanzee:	
0.43–0.65 Mya ^a	Not allowed in model
0.26–0.64 Mya ^b	Yes, west to central
Western gorilla–eastern gorilla:	
0.9–1.6 Mya ^d	Yes, primarily east to west
0.8–1.4 Mya ^c	Yes

^aFischer et al. (2004).

^bWon and Hey (2005).

^cBecquet and Przeworski (2007).

^dThalmann et al. (2007).

on data from multiple loci and models that take into account variation in the ancestral population, the dates obtained for the population divergences tend to be more recent than those previously suggested (table 1). For example, the genetic divergence of chimpanzees and bonobos was previously estimated at 2.5 Mya from mtDNA data (Horai et al. 1992) and 1.8 Mya from nuclear sequence data (Yu et al. 2003).

Few attempts have been made at using genetics to uncover the evolutionary history of gorillas. One reason is the difficulty of analyzing gorilla mtDNA. Because of numerous translocations of gorilla mtDNA to the nuclear genome, investigators of gorilla mtDNA run the risk of inadvertently analyzing non-organellar copies of mtDNA rather than, or along with, authentic organellar mtDNA (Bensasson et al. 2001; Thalmann et al. 2004, 2005; but see Anthony et al. 2007; Clifford et al. 2004). However, the impression from the limited amount of mtDNA control-region sequence analysis has been that western and eastern gorillas, two geographically disjunct populations only recently considered to represent species (Groves 2001), had a split time comparable to that of chimpanzees and bonobos and hence on the order of 2.5 Mya (Garner and Ryder 1996).

To gain a better perspective on gorilla evolutionary history, Thalmann and colleagues sequenced 16 noncoding autosomal segments totaling ~14 kb from 15 western and three eastern gorillas (Thalmann et al. 2007). These two gorilla species are currently separated by about 1,000 kilometers, and the eastern populations are particularly small and fragmented. The results did not fit a model with a simple divergence or even a limited amount of gene flow, but they do suggest an initial split about 1 Mya, with gene flow until as recently as 0.1–0.2 Mya. Gene flow appeared to occur in both directions, but predominantly from east to west. Thus, these results suggest that, like chimpanzees and bonobos, western and eastern gorillas diverged about 1 Mya, but that the gorilla split was accompanied by persistent migration, unlike the chimpanzee-bonobo split. It is possible to speculate whether both divergences were initi-

ated by climatic or ecological changes occurring about 1–2 Mya in central Africa, particularly in regard to the formation of the Congo River (Beadle 1981), which currently presents an impassable barrier to chimpanzees and bonobos.

Conclusions and Prospects

Complete genome sequences facilitate studies designed to determine the evolutionary history of primate populations by surveying genetic variation in several representatives per population. These data can then be tested against models that allow populations to exchange migrants while in the process of diverging. Because they allow for gene flow during the process of divergence, the models currently used are an improvement over models assuming a simple divergence. However, more dynamic and complex models that include aspects such as intralocus recombination (Becquet and Przeworski 2007), ancestral population structure, the incorporation of multiple ancestral populations, and the movement of populations across landscapes are needed (e.g., Currat and Excoffier 2004). More studies of natural populations are needed in order to evaluate how typical migration during divergence might be, as well as to estimate and compare the duration and extent of periods of migration. Genetic analysis of both chimpanzee and gorilla populations have found evidence of migration predominantly or exclusively from a small peripheral population to a large central one. This gives a hint as to how population divergence and eventual speciation might occur despite gene flow, as the small peripheral population might diverge via drift (Charlesworth, Lande, and Slatkin 1982; Garcia-Ramos and Kirkpatrick 1997). Not all divergences are accompanied by gene flow, however, and the DNA sequence data from bonobos and chimpanzees best fit a model of isolation, perhaps linked to a time of ecological change. Interdisciplinary study of populations with a well-studied history of hybridization can help fill the gap in our understanding of the demographic, ecological, or other processes favoring divergence or introgression. For example, patterns of local climatic fluctuation have been linked to changes in the long-term structure of the baboon hybrid zone in Awash National Park, Ethiopia (Phillips-Conroy and Jolly 1986).

It is impossible to overstate the impact that the new high-throughput sequencing technologies currently being introduced will have on all fields using genetic information (Bentley 2006; Margulies et al. 2005). The massively parallel sequencing systems offered by 454 Life Sciences or Solexa/Illumina rapidly produce many orders of magnitude more data than could have been previously generated at reasonable speed or cost. The last change of this significance to the field of molecular anthropology occurred in the 1980s, just as I was beginning my graduate studies. At that time, the invention of the polymerase chain reaction (Mullis and Faloona 1987) and sequencing of complete mitochondrial genomes (Anderson et al. 1981) greatly facilitated study of mtDNA variation. For perspective, as part of his dissertation research, a student

in my laboratory, Olaf Thalmann, recently generated a total of about 220,000 bp of DNA sequence information from gorillas (Thalmann et al. 2007). This is not very much more than the approximately 144,000 bp that I sequenced for my dissertation research in a survey of human mtDNA variation some 16 years earlier (Vigilant et al. 1991). However, Thalmann's current project uses the 454 sequencing platform and plans to generate—in two sequencing runs—about 2,300,000 base pairs (2.3 megabases) of DNA sequence to investigate how varied social systems in the great apes are reflected in patterns of variation on the X and Y chromosomes.

A major challenge facing molecular anthropologists seeking to use the new sequencing technologies is acquiring appropriate samples. For addressing questions on population histories, samples of known origin collected according to a particular scheme, such as grid sampling, are most appropriate. However, most captive primates are of uncertain or vaguely defined origin, limiting the ability to draw more than broad conclusions regarding population relationships, structure, or histories (e.g., Becquet et al. 2007). Samples can be obtained in the field, but particularly for researchers studying great apes, noninvasive samples, such as feces, are often the only material available from wild individuals. Even for researchers studying taxa, such as baboons, that can be darted for collection of blood samples and other information, noninvasive sampling may be used for sampling unhabituated individuals or young offspring (Bayes et al. 2000). The DNA obtained from noninvasive samples is typically of lower quality than that obtained from tissue or blood, which hampers the use of noninvasive DNAs in typical sequencing protocols. DNA extracts from noninvasive fecal samples contain DNA not only from the individual but also from whatever it had eaten, as well as bacterial and fungal DNA (Bradley and Vigilant 2002; Bradley et al. 2007). Research on quantifying the constituents of such fecal DNA extracts is needed, as are approaches for excluding extraneous DNA from downstream analyses.

Finally, studies of historical population genetics by definition focus on the evolutionary past of populations, but they can inform discussions on speciation (Losos and Glor 2003). The conflict between species as taxa designations and species as evolutionary entities is long-standing (Groves 2001; Kimbel and Martin 1993). However, it has been argued that increasing quantities of data from multiple disciplines, including an improved historical perspective, are leading to a more dynamic view of species as taxonomic designations for real entities in nature (Hey et al. 2003). Such a dynamic view of what constitutes a species will be necessary to accommodate accumulating information on the myriad nuances of gene flow between populations over evolutionary time. Thus, while we may still need to avoid getting lost in taxonomic distinctions, with large-scale genomic data, we are poised to make a leap in our understanding of the evolutionary history of natural populations.

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Comment

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The latter half of the 1960s was a heady time for the study of genetic variation in populations. Using protein loci, Harris (1966) and Lewontin and Hubby (1966) demonstrated a high level of heterozygosity in natural populations of humans and *Drosophila pseudoobscura*. How widespread was this variation in other animal populations? What evolutionary forces had led to this variation? Even though he was just beginning his career, Cliff Jolly was an active participant in this exciting search. Jolly's early work in genetics, done in conjunction with Nigel Barnicot (Barnicot et al. 1965; Jolly and Barnicot 1966) was among the first to firmly establish that protein polymorphisms were widespread in primate species, particularly baboons. While Jolly's very early work was based on captive animals, he soon moved to demonstrating that wild populations of baboons in the Awash exhibited polymorphisms that produced gene frequency differences between local groups (Jolly and Brett 1973; Brett et al. 1976). When the Awash work began in 1972, population biologists were in the middle of the selectionist/neutralist debate and were trying to work out whether these polymorphisms were the result of drift or selection as well as the amount of gene flow between populations.

Times changed. Different theoretical questions and models appeared. Different technologies were developed. The drift/selection debate faded into the background. New technologies based on DNA differences, as opposed to protein polymorphisms, became the norm and provided a wealth of new information. Questions concerning sociobiology and the relationship between genetics and behavior were paramount. Could we tell whether a high-ranking male made a skewed contribution to the number of offspring in a social group? Could we determine whether and why a female was choosing her mate? Could we prove this using genetic information? While Jolly did not focus on these intragroup behavioral questions per se, he was concerned with behavior and genetics on a somewhat different level. For Jolly and colleagues, the questions concerned behavior and genetics in the Awash hybrid zone. Who was contributing to the Awash baboon hybrid zone; where were males and females coming from? How open

or closed were communities of animals? On the broadest scale, what did this population movement mean for baboon systematics? Over the years, in the search for answers to these questions, there was a move toward inclusion of new genetic information from mtDNA and Y-chromosome markers to elucidate the effects of both males and females on the genetic structure of populations (Wildman et al. 2004).

Vigilant's paper is another step along the path of the study of genetic variation, gene flow, and the systematics of primate populations. As she so clearly demonstrates, it is now possible to survey a much larger part of the genome. More sophisticated statistical techniques can be used to test these new data against migration models and to determine the time since the separation of populations and the clustering of individuals into groups. She argues strongly that this new information will be crucial for answering questions about population history that have occupied primatologists for decades.

Over the past 40 years, the genetic data have changed. Protein polymorphisms gave way to DNA sequences, which in turn gave way to full genome amplification. Statistical techniques have changed from *F* statistics to Bayesian clustering techniques. Many of the underlying questions, however, have remained the same. How do we understand population variation, and how do we use this variation to understand population history not only in terms of the time since separation but also in terms of the behavior of animals in populations that can lead to the patterns of variation observed? Futuyma (1986) made the distinction between process and product in the study of evolution. Some scholars use genetic information to work out the taxonomic relationships among organisms, the product of evolution. The goal, often unrealized, is to use this product information to describe the process by which the product was formed. It has always been Jolly's intent to have product inform process and process inform product. And the way in which he has done this is to concentrate on widely distributed populations.

Many primatologists concentrate on highly endangered small populations of animals. One of the most important contributions Jolly has made to primatology is to draw attention to what can be learned from widely distributed populations. It is with these wide-ranging species that questions of evolutionary process can more closely be followed. Jolly and his students have worked with three of the most widely ranging primates: baboons, macaques, and vervets. In all these groups, Jolly and his students have used a sampling strategy that is both extensive and intensive, that has both breadth and depth. Significant proportions of local social groups are sampled, and these groups range over significant geographic areas. With current technology, both genetic and statistical, we can, as Vigilant suggests, begin to approach answers to questions that Jolly has investigated for more than 40 years.

Anyone working with genetics and population biology recognizes that we remain in heady times. We are on the cusp of having the information that will allow us to answer questions that have interested us for decades. I expect Jolly to

continue to be a central player in this new and unfolding discussion.

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