Anthropological Genetics in the Genomic Era: A Look Back and Ahead

ABSTRACT The use of genetic methods and data has a long history in anthropology. Following dramatic growth in anthropological genetic field studies in the 1960s and 1970s, the revolution in molecular genetic methods during the 1980s spurred another period of growth and expansion. The earlier emphasis on examination of the role of alternative evolutionary mechanisms in structuring allele frequency variation within and between populations is reflected today in a renewed focus on unraveling demographic history using highly informative molecular markers. The existence of large, publicly available molecular genetic databases, coupled with advances in analytical methods, makes it possible to tackle a wide variety of problems in human evolution not possible with classical markers and traditional analytical methods. These recent advances will help frame the nature of research in the discipline in the near term. [Keywords: human evolutionary genetics, phylogenetics, molecular markers, genetic variation, population structure]

GENETIC DATA, AND INFERENCES that can be drawn from these data, have become commonplace in modern society. With the advent of genetics as “big science” through the Human Genome Project and subsequent efforts to sequence the genomes of other organisms, it is nearly impossible to read the daily popular press without seeing at least one or two references to genetics. From in vitro fertilization methods to forensic applications in criminal proceedings, genetics is now a part of popular culture as well as part of the culture of science. Given its dramatically expanding scope, it is useful to recall that the beginnings of the modern field of genetics originated barely a century ago with the rediscovery of Mendel’s seminal experiments (Orel 1996). The physical structure of the hereditary material, deoxyribonucleic acid (DNA), was elucidated only 50 years ago (Watson and Crick 1953). Between these two critical events, studies of genetic variation and evolution on a variety of organisms were initiated, a rich and powerful mathematical theory of the evolutionary genetics of populations was developed (Wright 1969), and anthropologists began using genetic data and analytical methods to investigate patterns of human biological variation and evolution (see Crawford 2000a for brief historical review).

References to human genetic variation in the American Anthropologist (AA) began appearing relatively early, although some of the early entries were unencumbered by genetic data or analysis and may best be considered fanciful, speculative, and inferential. C. B. Davenport’s (1945) treatment of cross-cultural dietary differences and mobility patterns as a result of underlying genetic differences between populations is one such example. However, shortly thereafter, R. Singer (1953) reviewed the then-available data on the distribution of the sickle-cell trait in Africa and its possible locus of origin. Just a year earlier, Theodore D. McCown (1952) had noted the importance of genetics training in the education, especially at the graduate level, of physical anthropologists.

Discussions of race and racial taxonomy, as well as genetic data, have been prevalent in AA over the years (e.g., Keita and Kittles 1997; Templeton 1999; see also Caspari this issue). Similarly, the journal has been an outlet for discussing the role of genetic data and analytical methods in inferring the origins of modern humans (e.g., D’Andrade and Morin 1996; Stoneking 1994; Templeton 1993, 1994). More regionally focused studies on genetic variation have also appeared that explore both ecological (Clark and Kelly 1993) and social determinants of patterns of genetic diversity (e.g., Boster et al. 1998; Fix 1995; Jackson 1986) within and among defined populations.

While few in number, the genetic studies appearing in AA cited above do reflect the diversity of applications of genetic data and analyses in anthropology, encompassing human origin debates, the role of ecological and disease processes in human adaptability, and local-regional issues of population structure, origin, and migration. The comparatively small number of anthropological genetics articles that have appeared in AA over the past several decades...
is perhaps not surprising. Many authors choose to place their research reports in more specialized journals whose readership reflects a higher proportion of readers with genetic and evolutionary interests. It is worth noting, however, that as research in anthropological genetics expanded with the molecular biology revolution of the 1980s (Crawford 2000a), the number of genetics-oriented articles appearing in AA also increased. It is also worth noting that many nongenetics articles published in AA use methodological and analytical approaches derived from evolutionary genetic and population biology models (e.g., Borgerhoff Mulder et al. 2001; Moore 1994b, 2001) to address fundamental questions of human behavioral or cultural variation.

EVOLUTION, POPULATION STRUCTURE, AND PATTERNED GENETIC VARIATION

The earliest example of the use of genetic data to assess population variation was Leopold Hirszfeld and H. Hirszfeld's survey of ABO types among World War I recruits (Hirszfeld and Hirszfeld 1919), providing the first evidence for geographic structure in genetic variation. Subsequently, the recognition that population differences existed for the earliest studied classical genetic markers led to their use in the construction of a variety of human typologies and classifications. The role of genetics and anthropology in the history of racial classification and its ramifications is beyond the scope this article. (These issues are dealt with in detail in this issue by Rachel Caspari.) The broader abuses of anthropology and genetics as part of the "Final Solution" in 1930s Nazi Germany are discussed by Benno Muller-Hill (1988). Similarly, the ethical issues raised not only by these historical events but also by the dramatic expansion of genetic methods in the last two decades are reviewed elsewhere (e.g., Anderlik and Rothstein 2001; Greely 2001; Juengst 1998; O'Rourke et al. in press).

Early studies of genetic variation by anthropologists include the classic work on natural selection on human polymorphisms by Alice R. Brues (1963, on ABO and maternal-fetal incompatibility) and Frank B. Livingstone (1960, on sickle hemoglobin and malaria). However, by 1964, Derek F. Roberts argued that biological anthropology in the United States suffered from a notable malaise that did not characterize the other life sciences. Less than a decade later, he identified what may be characterized as at least a partial cure for that malaise: "a great stimulus by human genetics" (1973:1). The effective integration of human genetic methods into biological anthropological studies of human variation and evolution marked the florescence of anthropological genetics in the 1970s. The advent of the molecular biology revolution of the 1980s (Crawford 2000a), the number of genetics-oriented articles appearing in AA also increased. It is also worth noting that many nongenetics articles published in AA use methodological and analytical approaches derived from evolutionary genetic and population biology models (e.g., Borgerhoff Mulder et al. 2001; Moore 1994b, 2001) to address fundamental questions of human behavioral or cultural variation.

and inference, and by the undertaking of long-term population studies.

The focus of most anthropological genetic studies beginning in the late 1960s was to document local patterns of genetic variation within and among populations and to examine the relative effects of evolutionary mechanisms that gave rise to the observed patterns. In addition to the difficult quest to document the action of natural selection in the human genome, this meant a greater emphasis on investigating the effects of gene flow (admixture), genetic drift, and mutation in specific human populations. This represented a shift away from the traditional classification and taxonomy of human groups to an investigation of evolutionary mechanisms at the genetic level in human populations.

Taking advantage of known population histories, Michael H. Crawford and colleagues investigated the relationship between migration, population movement and resettlement, and admixture in Tlaxcaltecan populations of Central Mexico (Crawford 1976) and among Garifuna (Black Carib) communities in Belize and Guatemala (Crawford 1983, 1984). Numerous investigators also utilized knowledge of the historical sizes of populations, and initial founding of individual communities to assess the role of drift in structuring allele frequency variation in contemporary populations. Roberts (1967, 1968) analyzed the historical demography and changing genetic structure of the island of Tristan da Cunha, while L. Luca Cavalli-Sforza (1969) studied the effects of reduced population size and relative isolation on the genetic structure of Alpine isolates in Italy. Communities whose identities are related to specific religious traditions such as the Dunkers (Glass 1953), Amish (McKusick et al. 1964), Mennonites (Crawford 2000b; Crawford et al. 1989), and Mormons (O'Brien et al. 1994; O'Brien et al. 1996) have also been helpful in elucidating the relationship between demographic structure and dynamics, and the generation of the pattern of genetic variation within and between populations.

Detailed population histories and records are not absolutely essential to the study of human population genetics. Based on the mathematical treatment of isolation by distance and identity by descent (Malécot 1948), Newton E. Morton et al. developed analytical methods, termed "bioassay of kinship," to study the genetic structure of many populations and regions, including Micronesia and the Middle East (e.g., Morton et al. 1982; Morton and Lalouel 1973). Similar population genetic models and methods were employed by Jonathan S. Friedlaender (1975) in his original study of Bougainville Island, and James V. Neel (e.g., Neel and Weiss 1975) and colleagues in an influential series of human population genetic studies among the Yanomama and other groups in lowland South America.

In addition to studies of individual, local populations, or groups of historically related populations, some anthropological genetic studies sought information on broader patterns of variation. Cavalli-Sforza et al. (1994) pioneered
studies seeking regional or continental level patterns of genetic variation through the use of synthetic gene frequency maps. Several such studies also examined the relationship between patterns of genetic variation and the distribution of linguistic groups (e.g., Cavalli-Sforza et al. 1988). Similarly, Brian K. Suarez et al. (O’Rourke et al. 1992; Suarez et al. 1985) examined the effects of geography and local ecology on gene frequency variation in a large sample of populations in the Americas.

The attention to the dynamics of individual populations in anthropological genetic studies was based not only on the body of theory in evolutionary population genetics but also on the anthropological interest in population history. In 1972, Lewontin demonstrated that 85 percent of observable genetic variation in the allele frequencies of 15 protein loci was found within local populations. A mere six percent of genetic variation could be accounted for by differences between continental-level groups. If the study of evolution was the study of changes in variation over time, then understanding the roles of evolutionary mechanisms in the structuring of allele frequency variation within individual populations was a likely starting point. Like the majority of anthropological genetic studies, Richard C. Lewontin’s (1972) demonstration was based on the examination of allele frequencies of classical markers—such as red cell antigens, enzymes, and serum proteins. Recently, Guido Barbujani et al. (1997) replicated Lewontin’s earlier work using a large suite of newer molecular markers. Analysis of 30 microsatellite markers and 79 restriction site markers in 16 populations from around the world revealed again that 85 percent of the variation was represented by individual diversity within populations, while only about 11 percent of the variation was distributed between major groups.

Results from variation in the mitochondrial genome (mtDNA) are in essential accord with the nuclear data (Jorde et al. 1998; Seielstad et al. 1998), as are cranio metric data (Relethford 2002). Mark T. Seielstad et al. (1998) report 81 percent of the variation in mtDNA single nucleotide polymorphisms (SNPs) and 85 percent of autosomal (nuclear) SNP variation are found within populations, while approximately twelve percent and eight percent of the variation in these genomes, respectively, are found between continental populations. In contrast, only 35 percent of the variation in Y-chromosome SNPs is found within local populations, while over 52 percent is accounted for by differences between major groups. This difference in the distribution of genetic variance across maternally and paternally derived markers is consistent with an inference that over time females are far more likely to migrate than males. Indeed, the inferred migration rate for females is approximately eight times that for males (Seielstad et al. 1998; Stoneking 1998). The inference of greater mobility for females than males is consistent with the anthropological observation that most agricultural and foraging societies are patrilocal. Thus, at marriage women leave their natal communities and move to the place of residence of their mate. The displacement between birthplaces of parents and offspring, then, is primarily the result of mothers moving, not fathers (Seielstad et al. 1998).

Hiroki Oota et al. (2001) tested the hypothesis that mtDNA and Y-chromosome marker variation are correlated to either patrilocality or matrilocality. These investigators obtained mtDNA hypervariable sequence data and Y-chromosome Short Tandem Repeats (STR) haplotypes on three matrilocal and three patrilocal groups of northeastern Thailand. STRs are short segments of DNA that are repeated a variable number of times at specific locations in the genome. Different numbers of repeats at a locus are analogous to alleles, and variation in repeat number defines the polymorphism. As expected, patterns of genetic population differentiation in these haploid genetic systems were strongly correlated with residency practice. Genetic distances of the mtDNA sequence data were more than twice as large as the Y-chromosome-based distances for the matrilocal communities. The pattern was reversed for the patrilocal groups. Here, the genetic distance based on the Y-chromosome STRs was over three times as large as the distance based on mtDNA sequence variation. At least over short temporal spans, the demographic signal in molecular genetic data, such as those just described, seems clear and the relevance to anthropological inquiry obvious.

THE MOLECULAR REVOLUTION

The molecular revolution is essentially a technical one. The ability to generate large quantities of specific DNA segments for analysis through the Polymerase Chain Reaction (PCR), automated sequencing technology for DNA sequences and high-throughput genotyping, as well as the development of microarray technology, has revolutionized the way in which data on genetic variation in populations may be obtained. Classical marker antigens, proteins, and enzymes have been replaced by SNPs, restriction site polymorphisms (RSPs), STRs, insertions and deletions (indels, e.g., Alus), and direct DNA sequence. The result is data richness unknown for classical markers. The embarrassment of riches afforded by the new molecular genetic techniques in anthropological genetics led Henry Harpending and Elise Eller to observe that, “Today a single publication can present more and better data than the sum of everything available in the literature before 1985 or so” (1999:301). Not only is heterozygosity substantially greater for many of the new molecular markers but they also exhibit a range of evolutionary rates and alternative mechanisms for the generation of new variants. The surfeit of data has resulted in a complementary development of new analytical methods in phylogenetics, linkage and linkage disequilibrium analyses, statistical genetics, and coalescent models. Not only the data but also the methods of data analysis in population genetics, including anthropological genetics, have undergone dramatic expansion in recent years (e.g., Bandelt et al. 1999; Hudson 2000; Wall 2000).
Despite the growth in the number and variety of molecular genetic markers available for analysis, comparatively few populations have been screened for most of them. It is still the case that many more populations have been characterized for classical markers than molecular markers. Conversely, for those populations that have been the subject of molecular genetic study, many more genetic markers have typically been determined in each individual sample studied. Thus, the geographic coverage of world populations is greater for classical markers, while many more loci are available for study in those groups that have been characterized by the newer molecular methods. One difficulty encountered in studying global, or even regional, patterns of variation with classical markers has not changed with the advent of the rapid typing of molecular markers. This difficulty is the lack of standardization with respect to which genetic systems to use to characterize genetic variation in individual populations. While many populations were characterized for classical marker variation during the latter half of the 20th century, comparative studies were hampered by the fact that in most populations studied, few systems were uniformly typed. Such comparative studies were frequently reduced to using red cell antigen (blood group) variation as the primary data, solely because blood groups were the most common early genetic markers and had been typed in more populations than more polymorphic, and, hence, more informative markers such as those of the human leukocyte antigen (HLA) system. The lack of comparability remains a challenge in the molecular era, where now hundreds of SNPS, STRs, indels, etc. are available, with little effort being made to establish a common set of markers useful for population screening for comparative evolutionary studies.

Nevertheless, the increase in molecular methods for obtaining genetic data, and the expanded analytical armamentarium, has facilitated genetic analysis of both human genomes—nuclear and mitochondrial. The nuclear genome is characterized by approximately three billion bases; is biparentally inherited; has editing functions, both introns (noncoding regions of DNA) and exons (coding regions that underlie gene expression); and exhibits recombination. In contrast, the maternally inherited mitochondrial genome is only about 16.5 kb in size (kb = kilobase, or 1,000 nucleotide bases in length); it is almost complete exonic with the exception of the Control Region; and it lacks both transcription editing and recombination. As a result, the evolutionary histories of the nuclear and mitochondrial genomes need not be concordant. Indeed, they often are not (Hey 1997; cf. Jorde et al. 1998). One reason for possible discordances is the temporal window to evolutionary change afforded by different markers in the two genomes. Lacking editing capabilities, the noncoding region of the mitochondrial genome accumulates sequence changes at a much faster rate than that typically found in the nucleus, thus providing an opportunity to examine differentiation between lineages, and perhaps populations, over a relatively recent time frame. Alternatively, nuclear coding regions, characterized by transcription editing and purifying selection, evolve at a much slower rate, providing a window onto much more ancient evolutionary changes. Noncoding regions of the nucleus may well evolve at even different rates, constrained by selection only to the degree they are linked to conserved coding regions.

Evolutionary rates of nucleic acid sequences are constrained by much more than selection and molecular editing machinery. The evolutionary history of genetic markers is a reflection of the demographic history of the population under study. Although the action of specific evolutionary mechanisms was inferred from genetic data on populations whose demographic histories were basically a matter of record as described above, the power of the new molecular data and analytical techniques is in inferring unknown demographic histories from genetic data (Harpending and Eller 1999). Thus, changes in the demographic structure of a population over time, a change in the shape of the gene genealogy, may also result in changes in phylogenetic inference.

Much of the uncertainty regarding evolutionary inferences of populations relates to the ephemeral nature of populations and the often arbitrary nature of population definitions (Moore 1994a, 1994b). This difficulty stems from the fluidity of individual and group identities in time and space. Individuals may change ethnic identities, and, hence, group membership, at will, complicating assumptions of demographic continuity over time. It is clear that regional patterns of genetic variation for some genetic systems (e.g., mitochondria) may exhibit temporal stability over time, and therefore be indicative of ancestral-descentant relationships (O’Rourke et al. 2000a). It is not clear how long such regional patterns remain temporally and spatially stable, or that the same result would obtain for genetic systems in the nuclear genome.

The difficulty of precisely and accurately defining human populations in the genetic sense may be one reason that early anthropological genetic research was conducted on comparatively isolated, founder populations.

**GENETICS AND HUMAN ORIGINS**

In no other area have genetic approaches generated more controversy than in human origins research. Vincent M. Sarich and Alan C. Wilson (1967) were among the first to use genetic methods and data to address questions of human origins. Based on differences in albumin variants among humans and nonhuman primates, they concluded that the observed differences would have accumulated in approximately five to eight million years. This divergence date was much more recent than the paleontological record indicated, stimulating a lively debate on the timing of the appearance of the hominid lineage. The more recent date for hominid origins suggested by the genetic data was ultimately supported with newer paleontological data and is uniformly acknowledged today.
More recently, Rebecca L. Cann et al. (1987) used variation in mitochondrial DNA to infer that the diversity in the modern human gene pool is also of very recent vintage, perhaps 200,000 years or less. This view of modern human origins, too, was at variance with the general paleontological picture, which placed human origins much further back in time. The two alternative views of human origins crystallized around two competing models, a recent African origin model and the multiregional, or continuity, model. Predictions regarding patterned genetic variation in modern human populations, and the demographic processes that gave rise to them, are quite different between the two models. The recent African origin model predicts an origin from a single ancestral population in the relatively recent past. This requires a signature of a population bottleneck in the demographic history of our species followed by a dramatic population expansion, and the generation of specieswide variation over a relatively short period of time. The latter inference suggests we should see an excess of rare variants in many human populations since there has been insufficient time for neutral markers to drift to high frequency. Alternatively, the multiregional model predicts comparatively larger populations of early humans distributed throughout Eurasia and supposes at least moderate gene flow between them. This model does not require a recent population expansion, but such an expansion might not be incompatible with the model.

Using genetic data to test the predictions of these alternative models has been problematic. Initially, the only molecular marker with sufficient comparative data to be useful was mtDNA. From the early work of Cann et al. (1987) and others (e.g., see Jorde et al. 1998), it seemed clear that there was greater mtDNA variation in African populations than non-African populations; not an unexpected result if modern human populations derive from a single African ancestor relatively recently. Indeed, as mtDNA sequence data accumulated it appeared that the human population had experienced a population expansion within the last 100,000 years from a comparatively small starting population (e.g., 10,000 individuals; data reviewed in Rogers 2001). However, mtDNA is a single, haploid molecule, and markers derived from it constitute a haplotype, which are not truly independent markers. As such, its robusticity for inferring demographic events may be questioned. For example, if the inference of a population expansion is incorrect, the greater genetic variation in African populations may reflect larger, long-term population sizes, weakening the inference of a recent African origin (e.g., Relethford and Harpending 1994; Relethford and Jorde 1999). Nuclear markers have yielded more heterogeneous results (Harpending and Rogers 2000; Rogers 2001).

One difficulty in using molecular data to evaluate alternative demographic histories is that it is difficult to distinguish population expansion from a selective sweep. That is, strong selection driving rare variants to higher frequencies produces the same effect and is frequently indistinguishable from rapid population growth without selection. Selection, of course, is expected to affect only a few, perhaps closely linked, loci while population growth is expected to have uniform effects on the entire genome. Thus, distinguishing selection in a stable, constant population from population growth in a small founder population using genetic data requires examination of multiple independent loci. Wall (2000) recently concluded that 50–100 independent nuclear loci will be required to distinguish between the alternative demographic scenarios of the recent African origin model and the multiregional model. As more molecular data become available, this will soon become a reality.

Like mtDNA, the limited data available on the Y-chromosome (e.g., Underhill et al. 2000) and widely dispersed autosomal STR loci show evidence for a population expansion in the late Pleistocene epoch (Rogers 2001). However, other nuclear sequences present patterns of variation that are not so uniformly clear. Studies of nuclear DNA sequences outside known functional genes show evidence of a population expansion, as do some intronic sequences. Other intronic sequences, along with many sequences in coding regions do not provide evidence for a population expansion in our species history. Several investigators now view these results as an indication that while much of the genetic data is consistent with a late Pleistocene population expansion of the species, it is also overlain by patterns of variation structured by selection to a greater degree than previously suspected (Harpending and Rogers 2000; Rogers 2001; Wall and Przeworski 2000). Thus, while contemporary genetic data cannot yet reject either of the competing models for modern human origins (Relethford 1998, 2001), the growing body of molecular evidence increasingly supports a recent African origin and provides insight into the nature of natural selection pressures on the maintenance and patterning of variation in the human genome.

One additional form of genetic data has been used to address the problem of modern human origins, ancient DNA (aDNA). Matthias Krings et al. (1997, 1999) extracted mtDNA from the Neandertal-type specimen and demonstrated that it differed from a series of over nine hundred modern humans by an average of 27 nucleotide differences (N = 22–36 substitutions). The range of differences among the large modern human series was 1–24 substitutions with a mean of eight. This dramatic difference in mtDNA hypervariable sequence between modern humans and an archaic European was taken as evidence that the Neandertals had not contributed to the modern human gene pool and, thus, provided evidence in favor of the recent African origin model. However, as a single sample, it alone is insufficient to reject the multiregional model with finality (e.g., Relethford 2001). More recently, additional archaic humans have been studied with respect to ancient mtDNA variation producing similar results (Krings et al. 2000; Ovchinnikov et al. 2000). Thus, while the aDNA analyses are also not sufficient to resolve the competing models for the origin of modern humans, the aDNA data
appear to provide less support for multiregional evolution than for a single, recent origin.

The role of genetic analyses in human origin research is illustrative. By focusing on measurement of population variation and detailing demographic histories from genetic variation, these methods bring an independent line of inquiry to the problem of human origins that can not be addressed by paleontological data. Bringing independent sets of data and methods of analysis to bear on a common problem is a strength of science, not a weakness.

We are still experiencing a dramatic increase in the generation of molecular genetic data on the world's populations, and increasing numbers of paleontological specimens are yielding genetic data (reviewed in O'Rourke et al. 2000b). This suggests that the increase in data on human genetic diversity is rapidly bringing an unprecedented level of resolution and analytical power to the problem of modern human origins. Unfortunately, the nature of paleoanthropological research is such that we cannot anticipate a comparable increase in available information from new fossil forms. This means that the import of genetic methods and approaches to the study of human origins is likely to grow rather than be diminished.

However, inferences on human origins from genetic data are not without problems. It seems generally accepted that the transition from archaic to modern humans occurred relatively recently (200,000 years ago). The question of interest is whether this transition was rapid, stemmed from a single source population, and, therefore, could be characterized as a speciation event; or whether the transition was rather more gradual over time and space. The extreme versions of these two alternatives, the replacement model and the multiregional model, were used for illustrative purposes above. The reality of our evolutionary history may be less clear-cut. If, for example, modern Homo sapiens originated in Africa, and during migrations to other continental regions interbred with existing archaic populations, the distinctions between the replacement and multiregional models become blurred, and the predictions about patterns of genetic variation based on such models also become more complex. If, as I have just argued, existing genetic data are not yet sufficient to distinguish between the extreme forms of the models with finality, the data are even less adequate to disentangle the more subtle differences expected from intermediate models. This emphasizes the need for appropriate analytical methods and close attention to model building. Such observations are not novel (cf. Harpending and Rogers 2000; Hawkes and Wolpoff this issue; Hawkes et al. 2000). It is worth repeating, however, that greater attention to developing appropriate models, for example incorporating selection, gene flow, and alternative (or dynamic) demographic histories, is necessary to realize the potential of the emerging genetic data to aid our understanding of human evolutionary history.

**QUANTITATIVE VARIATION**

Historically, biological anthropologists have also used quantitative traits as more indirect measures of genetic variation within and between groups. The assumption is that quantitative (metric as well as discrete) biological characters (e.g., anthropometrics, skin reflectance, discrete dental traits), owe their expression to underlying genes and reflect genetic differences and similarities between both individuals and populations in the same way that classical genetic markers do. Unfortunately, until recently it has been difficult and perhaps impossible to know the genetic architecture of quantitative traits, although elegant models for the genetic analysis of quantitative variation have been developed (Konigsberg 2000; Rogers 1986; Rogers and Harpending 1983; Williams-Blangero and Blangero 1992). Alan R. Rogers and Henry Harpending (1983) showed that the genetic information content of a quantitative character was equivalent to that of a single, biallelic locus if the quantitative character were normally distributed, fully heritable, and neutral with respect to selection. Neutrality and 100-percent heritability are far more difficult to demonstrate for a quantitative, morphological character than, for example, DNA markers. These constraints impose limitations on the utility of quantitative characters in the study of the evolution of human variation.

The recent advances in molecular genetics are now being applied to quantitative traits. Developments in linkage analyses to identify quantitative trait loci (QTLs), coupled with the wealth of genetic polymorphisms covering the human genome, now make possible the analysis of specific quantitative traits to identify and characterize loci contributing to expression of the quantitative phenotype (Almasy and Blangero 1998; Rogers et al. 1999). The genetic architecture of traits as stature (Hirschhorn et al. 2001; Perola et al. 2001), body mass index (Feitosa et al. 2002; Hanson et al. 1998; Perola et al. 2001), obesity (Commuzie et al. 1997), the physiology of altitude adaptation (Beall 2000), and human pigmentation (Akey et al. 2001; Bastiaens et al. 2001a; Bastiaens et al. 2001b; Harding et al. 2000) are now being elucidated by gene function studies and linkage analyses using whole genome scans.

A single example will suffice to illustrate the emerging complexity of quantitative genetic variation in a simple, well-known continuous trait, skin color. Skin color is determined in large measure by the concentration of melanin in the skin. The number of genes that influence melanin production and concentration has been estimated to be as small as four to six and as large as several dozen. At present we have no clear evidence to suggest which is the more likely in humans, but the 100 known genes for mouse coat color suggests the system may well be genetically complex (Jobling 2001). The one known gene involved in normal skin color variation is the melanocortin-1 receptor, MC1R. This gene is a peptide receptor that helps in the regulation of production of eumelanin, the dark pigment contributing to skin color (Harding et al. 2000).
Maarten T. Bastiens et al. (2001a, 2001b) have shown that variation in MC1R is also responsible for freckling in the majority of cases, independent of skin and hair color, and that variants in this gene are also associated with fair skin, red hair, and elevated risk to nonmelanoma skin cancers. Joshua M. Akey et al. (2001) measured skin reflectance in a Tibetan sample and found that variation in reflectance was influenced by the interaction of specific alleles at MC1R and P, which is another gene involved in eumelanin synthesis. If pleiotropy and epistasis are common in quantitative variation, as they seem to be in this simple example for only two loci affecting skin color, then the genetics of quantitative variation may be complex, indeed. Identifying the phylogenetic signal from noise in such complex systems may be more of a challenge than expected.

Until the advent of aDNA methods (O’Rourke et al. 2000b), paleoanthropological inferences of the fossil record were dependent on morphological and morphometric characters. Yet the phylogenetic information content of these characters is unknown, since we have information on quantitative genetic variation for few if any such characters, much less knowledge of individual genes affecting the expression of the trait. With the advent of the rich molecular genetic database now being developed, coupled with new analytical procedures for maximizing the utility of the molecular database, the future looks brighter for clarifying the nature of genetic variation in many human quantitative traits.

CONCLUSION

If anthropogenetics developed from the productive intersection of biological anthropology and human genetics three decades ago, its modern descendant is a subdiscipline that melds not only these two disciplines but also portions of molecular biology and bioinformatics. This new hybridity for the field has two fundamental results: One, the way in which we will approach questions of human evolution and variation in the future is likely to change, and, two, the way in which we prepare students for careers in the discipline must change.

Given the dramatic increase in our understanding of genetic variation at the molecular level, it seems inevitable that future studies will focus less on descriptive studies of frequency variation than on the role of gene function on the distribution of key phenotypes, functional genomics. As we learn more about gene expression, we will require more precise information regarding the timing of expression and developmental genetic studies will be incorporated into our research arsenal, including making use of the developing technologies of micro and expression arrays. Certainly, molecular quantitative genetics, already in evidence in our research literature, as noted above, has much to contribute. Finally, the molecular innovations that have fueled the recent increase in genetic data have also spawned the development of numerous new analytical methods and techniques.

Exploring of the malaise in U.S. physical anthropology 40 years ago, Roberts warned that “Subjects do not continue to live merely because they have a history, or because of their content. They survive because they are part of the intellectual climate of the moment” (1966:165). In this genetic era (Weiss 1998), I think the prospects for growth and prosperity of the discipline are as encouraging as they have ever been.

DENNIS H. O’ROURKE Laboratory of Biological Anthropology, University of Utah, Salt Lake City, UT 84112

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McCown, Theodore D.

Mckusick, Victor, John A. Hostetler, Janice A. Egeland, and R. Eldridge