1. Introduction: structure and function in the biology of human populations

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Traditionally, physical anthropologists were concerned with describing and interpreting the patterns of geographical variety which are found to be so striking in the human species. The characteristics first examined were, naturally enough, the visually obvious ones, such as body and head shape and size, pigmentation of skin, hair and eyes and hair form; and for their detailed study a variety of increasingly refined anthropometric and anthroposcopic techniques were devised. Many of these characters show rather striking geographical patterns, with populations being differentiated on a broad continental basis. This permitted and indeed encouraged the drawing up of racial taxonomies, an activity which received a great deal of attention. The activity, however, was not merely one of classification, for on the Darwinian premise that similarity indicates phylogenetic affinity, it was taken that the taxonomies attempted to express the evolutionary history of the species. Ascertaining this history has always been and remains one of the main goals of physical anthropology.

It was well recognised that for this purpose the characters first available for examination had a number of disadvantages. Most of them, for instance, are influenced in their expression by the immediate environment in which the individual develops. Similarities and differences, therefore, are to some extent determined by non-genetic factors which are not relevant to establishing evolutionary affinities. At least as important is the fact that such genetic basis as there is to anthropometric variation, both within and between populations, is typically complex. Within any one population, and in groups that are hybrids between two or more, it generally displays, normal or Gaussian form, without the appearance of discrete classes. Such variation has so far remained intractable to precise genetic analysis and, in particular, although caused by particulate inheritance, has not in any case been reduced to the level of identification and localisation of responsible genes. This means not only that individuals of similar or identical phenotype may be genetically very different but also that, even if each phenotype is genetically unique, there may be no linear relationship on the particular scale of measurement between the magnitude of phenotypic difference and the magnitude of genotypic difference.

The situation changed radically with the discovery of an ever increasing

number of characters which show discrete variation within and between populations. The development of these characters is not affected by immediate environmental factors and, because the mode of inheritance has been precisely established, it is possible to identify – and to some extent locate – responsible genes. Many of these characters have been identified in blood, mainly because this tissue is easy to collect and handle, and the variants often reach polymorphic proportions within populations. They include the various blood group systems, haemoglobins, serum proteins and a rapidly increasing number of enzymes. For them, populations can be characterised for gene frequencies, and in population comparisons of these frequencies it is found, typically, that what varies is the level at which the polymorphism is set. On the whole the pattern of geographical distribution is less distinct than for many of the quantitative traits, and changes in gene frequency with distance tend to be clinal. Also, there is rarely close concordance in the distribution of the different characters. Having said that, it is nevertheless true that broad continental patterns emerge, and taxonomies of man, based on polymorphic systems, are broadly in harmony with those based on anthropometric traits.

Prior to the IBP, an extensive body of information had gradually accumulated concerning the world distribution of polymorphic systems. For some which had been known for a long time and were easy to test, e.g. the ABO blood group system, quite detailed information was already available, but for recently discovered systems there was a dearth of data. The IBP offered an excellent opportunity for extending knowledge and on the whole this was seized. Many investigators in the HA project throughout the world collected blood samples for genetic analysis and the results have been compiled by Dr A. E. Mourant and his colleagues who acted as the International Reference Centre for genetic surveys. Dr Mourant summarises this work in an extensive paper in this volume.

Although, through survey work, the broad patterns of genetic variation in man have become known, the causes for these patterns remain obscure and controversial. Essentially the issue of debate is whether genetic differentiation of populations is dominated by the stochastic processes which are bound to occur in small populations – and Mendelian populations have been small throughout most of human evolution – or whether it is dominated by natural selection, which can be seen primarily as a set of deterministic processes. Views about the relative importance of these two types of process have fluctuated over the past 50 years. Today the stochastic view tends to hold greatest sway, partly because of evidence produced by biochemists and biophysicists that many gene mutations do not affect, or affect only in a trivial way, protein structure; partly because of some refined mathematical theory, demonstrating that the genetic load in populations would be too great to permit population persistence if every polymorphic genetic locus affected fitness; and partly because there is a dearth of empirical evidence for the action of

selection. There is of course a selectionist answer to each of these points. The biochemists have not yet taken into account the comparative efficiency of gene substitution on the economy of cellular biosynthesis, and in particular the relative availability of bases, and amino acids. Mathematical approaches, focussing directly on genes, overlook the fact that selection operates on the overall phenotype of individuals and that fitness is a relative thing – many phenotypes would survive if they were not in competition with other phenotypes. And the fact that, with a few notable exceptions, selection has not been demonstrated to act, certainly doesn't mean that it is not acting; it is well recognised that in natural situations, even strong selection is difficult to detect.

The position is, thus, in a state of considerable flux, but the point of importance here is that concern with the question of what are the causes of genetic variety has led biological anthropologists and human population geneticists to concentrate increasingly on unravelling the detailed genetic structure that exists within populations and population systems, since the diversity which exists between populations is the consequence of forces which operate within them. This has necessitated the development of refined and sophisticated techniques and procedures for field studies and the modern human biologist has to spend many months or years working with a comparatively small group of people, whereas his predecessor could quite quickly and easily sample the physical variety which existed in a population. The modern approach, and the types of problem, both logistic and academic, that have to be overcome are well exemplified in many of the contributions to this volume.

An important development in human population genetics, which has followed this increasing concern with within-population phenomena, is the incorporation of demographic studies with the genetic ones. It has long been recognised that the forces determining the genetic structure are, or are manifest in, demographic conditions. Population size and changes in it affect the magnitude of stochastic processes and the probabilities of inbreeding; migration and fission and fusion, influence genetically effective population sizes and are the vehicles of gene flow; and natural selection classically operates through genetically determined differences in fertility and mortality. Until recently, however, the concern with demography in genetics has largely been theoretical, but in the course of many HA IBP studies considerable attention has been given to elucidating the demographic structure of real populations. Not unexpectedly the real situations turn out to be vastly more complicated than any of the theoretical models but the use of these models has certainly added insight to our understanding of particular situations.

Another area which has attracted the concern of population geneticists is the social structure of populations. This not only influences demography but also genetic structure directly, through the prescribed mating systems. Although genes are often distributed as though mating were at random, such

mating is in fact rare, especially in any extended population; and the form and nature of deviations need to be known. Assortative marriage is particularly a function of social systems. These systems also frequently determine the actual definition of populations. What may, at first sight, appear to be a single Mendelian unit is often a set of multiple units separated by social breeding barriers. Then, understanding of the social anthropology of a population can be vital in recognising biological kin as compared with social kin.

These considerations of demography and the social sciences are well exemplified in the case studies reported in this book which focus primarily on genetic structure – in the Russian investigations of isolates in North Asia and the American studies of the Yanomama. But they are also evidenced, as indeed genetics itself is, in the other contributions. These can, rather broadly, be said to be concerned with function, and deal with such issues as adaptation, health and ecology.

The distinction of course between structural and functional studies is blurred. Typically, knowledge of a population's structure is critical to understanding questions of function. Indeed such knowledge can be vital in devising the most penetrating design for a functional study, as a number of the case histories show. Contrariwise, one can see the structure of any population as the historical product of the ways in which it has functioned in the past, and both types of study are ultimately concerned with explaining the nature and form of human variety. But once central attention moves from concern with genetic structure and population affinities to the ways individuals and populations adapt, or fail to adapt, to their environments, priorities for attention change. In particular, concern with the effects of variation is at least as important as concern with its causes, and interest is as much levelled at variation that may have no genetic basis (or at variation whose causation is not understood) as at variation which is clearly genetic. Interest in adaptive processes has provided a new impetus to classical anthropometric and other quantitative traits because, whatever their determination, many of them clearly affect or reflect the capacity to survive and reproduce, i.e. fitness.

There are many components to adaptation: individual adaptability in development, physiology and behaviour; genetic adaptations produced by classic Darwinian natural selection; and group adaptations, which may be biological, cultural or bio-cultural and which in man are especially important. Analysis of these components and the way they interact to determine fitness has been a central theme in many of the HA studies.

Although distinctions are again not clear-cut, a number of different approaches to investigations of adaptation are exemplified in the contributions to this book. One strategy is to single out for special attention some condition or variation in a trait which has a complex determination, and use contrasting ecological conditions to identify the relative importance of the various de-

terminants. It can broadly be called the epidemiological approach and is well exemplified in the way the Solomon's study is presented here, with its special concern for the analysis of blood pressure determinants. Another approach to analysing components of individual adaptability and fitness is to focus on a marked environmental contrast and examine the various biological effects of this contrast. This is usually done by comparison of 'sedentes' in one environment with recent migrants to another. Such comparison affords a means of controlling for many genetic differences, though, as is well shown in the study of Tokelau migrants to New Zealand, migrants are often not fully representative of the populations from which they come. A most important problem which is only beginning to be considered by human biologists is what biological attributes predispose individuals to migrate.

While studies of recent migrants allow analysis of individual adaptability, investigations of peoples who are known to have moved in the more distant past from one environmental situation to another, provide an opportunity for determining the genetic adaptations to the new environment which have been produced by natural selection over the generations since colonisation. The approach is particularly rewarding when, as Professor Hiernaux does, one considers a number of populations in each of two major ecosystems such as the African savanna and the African rain forest. Systematic differences between the various groups in the contrasting environments are unlikely to be products of drift. Clearly, reasonably accurate dating of the times of separation are also useful.

Knowledge of the ontogenetic effects of an environmental change, obtained from the study of recent migrations, is obviously useful in interpreting the nature of the difference between long-separated peoples. In the simplest situation, subtraction of the components of individual adaptability and environmentally produced effects on fitness from a total difference should reveal the genetic components of that difference. This relationship is particularly important in considering classical anthropometric and anthroposcopic traits where, as already mentioned, there are usually both environmental and genetic components of the observed variation.

A third type of migrant study is exemplified by the investigations in Israel. Here one of the essential features of the design was to compare groups who had long been separated but who had recently returned to common environments in Israel. Thus there was the possibility of examining the effects of such genetic divergence as had occurred since the separation, in a situation which was at least partly controlled to avoid environmental effects. This type of design would seem to be particularly appropriate where investigations focus, as the Israel study did, on physiological characteristics. These characteristics are typically highly environmentally labile, and if there is any genetic basis to between-population differences it will surely be detectable only when environmental effects are standardised as much as possible. And in such stan-

dardisation one is as much concerned with an individual's previous environmental experience as with the environmental circumstances under which physiological tests are conducted.

Little is as yet known about the genetics of physiological variation within populations let alone between populations – a regrettable state which, unfortunately, the IBP did not do much to improve – but the increasing interest in issues of adaptation and ecology has led to the incorporation of ever more physiology in human biological field investigations (a development which owes a great deal to the IBP). Of the case studies reported here, a central concern with physiology is evidenced not only in the Israel study, but also in the New Guinea and central Africa investigations.

These last two studies, and the one of the Pygmies, especially exemplify a fifth type of approach to functional studies. In this some particular population or population group is selected, either because of its ethnic or environmental uniqueness, or, contrariwise, because it well represents general features of a particular economy, or stage of development, and all the biological elements which might conceivably bear on the overall determination and measurement of fitness are examined. The strategy is sometimes termed the 'total ecological approach', and the aim, apart from providing much-needed descriptive information, is to develop a holistic view both of the complex inter-relationships that exist between the various biological attributes and of the ways populations are biologically organised to exploit environmental opportunities and obviate environmental hazards.

Both of these major objectives present many technical and conceptual difficulties. Describing the total phenotypes of individuals necessarily requires multi-disciplinary operations at the moment. The techniques of physiology, nutrition, epidemiology and genetics are so specialised and different that it is impossible for one person to practise them all. And when experts in each discipline work together on the same population it is all too easy for general aims to become subordinated to disciplinary objectives. Truly interdisciplinary approaches are rare, though one can detect the beginnings of them in various of the case studies described here.

Then there is the complex problem of how the different types of data can be combined into overall estimates of the fitness of individuals. It is this fitness which is of primary ecological concern, and the genetic component of its variation which is of essential evolutionary concern. But integrating the functional effects of nutritional, physiological, anthropometric and polymorphic variety raises many difficulties, including ones of scale. One scale, which is comparatively easy to use is morbidity experience, i.e. a direct test of somatic fitness, but in traditional societies without written records it is almost impossible to do more than ascertain morbidity patterns at the time of the study itself. A better scale, certainly from the evolutionary point of view, is the demographic one of comparative fertility and mortality. By

observation and questionnaire it is possible to gain information on the reproductive success not only of individuals themselves but also of their relatives, and clearly this can span some considerable time period. It is an approach which is mentioned in a number of studies and should surely be developed. Whether or not there are genetic components, it would be interesting to know the extent to which variation in physiological fitness affected reproductive fitness in a population. One would surely expect such an affect, especially in man, where it could be expressed indirectly through status and general socio-economic conditions. But studies of this kind require very patient and careful collection of the demographic data and are extremely time consuming in a traditional society where even a subject's age can usually only be estimated at all accurately after a great deal of questioning. The approach also requires the physiological testing of all categories of subjects: women as much as, if not more than, men; the aged as well as the young; and the chronically sick as well as the healthy. Often the physiological tests themselves preclude this, and there is an urgent need to devise simple tests of physiological fitness which can then be applied to large numbers of subjects and, without risk, to the sick. All too often, from an ecological viewpoint, physiologists in their disciplinary concern for elucidating physiological mechanisms, have confined their attention to healthy young adult males.

It is evident that demographic and ethnological data are as important in functional studies as in structural ones, and most of the case studies reported here recognise this. Even, however, when these data are not available, there is still great value in collecting biological data on the same individuals. This is particularly well shown in the New Guinea project, where not only have important inter-relationships between different physiological characteristics become evident from having such data but also a variety of associations between the genetic polymorphic variety and biochemical concentrations and disease states have been revealed. It is of course by such association that natural selection may be acting on gene marker systems, though the final proof of this requires the demonstration that the association affects demographic performance. Certainly it would seem from the New Guinea work that much further work is urgently required, examining the possible relationships between polymorphic variety and quantitative variables which affect fitness in societies still exposed to the sorts of natural environment which have prevailed throughout most of human evolution. It is here that ecological and genetic-structure studies tie up and where the controversy over neutral or adaptive genes may be resolved.

On the other major concern of the 'total ecological approach' – the way in which human populations as whole populations are biologically organised – a start is only beginning to be made. This problem, perhaps more than any other, demands a bio-social approach and is awaiting the development of a substantive and coherent body of ecological theory. It can be tackled through

systems theory, applied, for example, to patterns of community energetics, but no examples of it are available for inclusion in this book. It is, however, evinced in some of the high-altitude IBP studies, which are reported on elsewhere and has become a central concern in much post-IBP work.

It has been customary for human biologists to confine their attention to aspects of physical variation. It is, however, in mental traits that man shows his most remarkable characteristics and behaviour is often the main component of adaptation. Likewise, mental health is a critical aspect of fitness. It is therefore gratifying that studies of behaviour have been included in some IBP studies, as is well evidenced in the final contribution in this book on South African populations. This study also represents, as does work in the Solomon Islands and New Zealand, another pioneering development in human biology field work – concern with the impacts of modern advanced technology and living conditions. Traditionally, human population biologists have worked with societies which have simple economies and are exposed to the rigours of natural environments, and, as has already been argued, there is a good case for this, since these are the environments under which most of human evolution occurred. But ever increasingly people are living in essentially man-made environments, particularly urban ones, and the effects of these conditions, which from the evolutionary point of view are very new, are in great need of investigation in both the developed and developing world. This need is as much practical as academic. It is a further tribute to the IBP that it played a role, both directly and indirectly, in initiating studies of urban biology, and it may not now be long before we know as much about the biological structure and function of urban populations as of more exotic ones.

2. The genetic markers of the blood

A. E. MOURANT

The initial concept of the HA section of IBP implied a study of the interaction, in human populations, between the genotype, in its broadest sense, and the environment. This, in turn, called for a study of gene distribution in human populations.

The most obvious human genetic systems having a possible effect on adaptation to the environment are those which directly cause diseases such as haemophilia and phenylketonuria, and those determining such visible characters as physique and skin colour which demonstrably interact with the environment.

Relatively rare diseases of genetic origin were regarded as lying outside the scope of IBP. The external characters of the body, on the other hand, are of the greatest concern to IBP and have been studied extensively as part of the Programme. However, despite the rapid and almost explosive advance of human genetics in recent years, the analysis of these characters in terms of genes has advanced very little. It has long been recognised that each character is the result of the combined action of numerous genes belonging to several separate allelic systems. There has, however, been very little advance in the identification of the separate genes and systems of genes involved. Part of the difficulty has lain in the complexity of the interactions between the genes themselves, and part in the unknown extent to which the environment interacts with the genotype to determine the final phenotype.

Thus the study of these characters, which has formed a large part of the HA investigations, has been carried out almost exclusively on a phenotypic basis.

Meanwhile very rapid advances have been taking place in the study of the so-called marker genes. With the possible exception of the vast number of genes each responsible for some very rare hereditary disease, by far the greatest number of known human genes are those which determine sets of biochemical characters most easily studied in the blood, though most of the gene products involved are present in other tissues as well.

The marker genes nearly all fall into four main classes, determining respectively the blood groups or red-cell agglutinogens, the plasma proteins, the red cell enzymes and haemoglobins, and the histocompatibility antigens.

The blood groups have been known since 1900; their study has been fostered by their vital importance in transfusion therapy and the prophylaxis and treatment of haemolytic disease of the newborn. A dozen or more major genetic systems of blood groups are known, determining well-defined poly-

morphisms characterised by two or more genes each having frequencies of several per cent, frequencies which in nearly all cases have been shown to vary significantly between different ethnic groups. There are, in addition, a very large number of systems within each of which nearly all individuals are of a single homozygous type, but in which there exist rare persons of a different hereditary type. Techniques of study are now highly standardized and reagents widely available, so that the blood groups remain even now the most widely used of marker systems in family studies, forensic paternity testing, and population investigations. Unfortunately, apart from their negative function of causing haemolytic disease of the newborn, very little is known of the normal role in the body of the blood group antigens and the nature of any possible interaction with the environment, and it has been one of the objects of HA work to search for such interactions.

Large numbers of the proteins of the plasma, hitherto characterised by their broad physical and chemical properties, are now recognised by more sophisticated tests as the products of a number of distinct systems of allelic genes. The functions of most of these proteins in the body's economy are known and in some cases differential physiological effects of different alleles have been ascertained. There are about a dozen useful plasma protein polymorphisms; by far the most valuable of these is that of the Gm groups, detected by antigenic differences arising from variations of the amino-acid sequence in immunoglobulin molecules.

Gm investigations require a rather laborious type of immunological test; tests on populations have been fairly numerous but far less in number than for some of the blood group systems. It is clear, however, that if Gm tests were more widely used they would be of greater value in discriminating between populations, and in showing relationships between them, than any one of the classical blood group systems.

The principal protein of the red cells is haemoglobin, but they also contain a very large number of distinct enzymes. Haemoglobin polymorphisms are of great importance in certain regions, especially Africa. More and more of the enzymes are being shown to be polymorphic; polymorphisms are detected mainly by means of different migration speeds during gel electrophoresis. For many of the enzyme systems there are substantial allele frequency differences between ethnic groups but, chiefly because characteristic world patterns are only beginning to be recognisable, the enzymes have not yet contributed greatly to the taxonomic side of population studies. However, since the functions of the enzymes are well understood and are vitally important in the functioning of the body, and since in many cases the different gene products differ measurably in their chemical activity, there is every prospect of these polymorphisms proving important in giving rise to differential responses to the environment, as has already been proved for glucose-6-phosphate dehydrogenase.