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EDITORIAL

The tropics today are undergoing massive changes, with destruction of the natural environment, the impact of monocultures expanding and contracting according to external economic pressures, with colonisation and settlement from outside, and urbanisation. Too little attention is being given to the effect of this change in natural environment on the ability of indigenous peoples to maintain themselves by their traditional activities, their productivity, their very survival. They demonstrate only too clearly growing susceptibilities to the effects of drought, deforestation, soil compaction, demographic shifts, urbanisation and changing occupational activities which erode socio-economic structure and health. As a consequence, people in the tropics are facing growing challenges in self-sufficiency and are increasingly forced to subsist under truly marginal conditions. In return, they themselves are contributing to the problems. As a consequence also, large proportions of tropical groups are failing to survive, genepools so delicately evolved and balanced over centuries disintegrating. The real problems are accumulating very quickly in the tropics, and to document the change, an immediate research effort is required to examine baseline material now, to allow comparison with similar material at some time in the future.

When the Decade of the Tropics Programme was approved by the IUBS General Assembly in Ottawa in 1982, it was immediately apparent that the biological features and problems of man in the tropics would be a fundamental research component. Facts were necessary in order to plan this, and the Section of Human Biology of IUBS, via the Council of the International Association of Human Biologists, was requested for opinions on topics regarded as of most urgency and for information on relevant work in hand. As a result, a list of some 50 projects was drawn up and discussed. From these, two main themes were finally identified, (1) the maintenance of genetic diversity in tropical populations, and the factors by which this is achieved, and (2) variations in working capacity and factors affecting it in tropical populations. For each of these a working party was convened to review the present state of knowledge, and their proceedings are in course of publication. As a result, the working parties were able to draw up recommendations for research to be carried out as part of the programme.

From the working party on genetic variation it was clear that though there has been enormous expansion of new genetic knowledge with the many new techniques that have recently become available, this mostly relates to temperate populations and the tropical have so far been virtually ignored. Many tropical environments are intrinsically hostile to man, and the genetic mechanisms evolved to help combat this hostility represent major evolutionary triumphs, yet there must be others awaiting discovery. Exploration of the vast reservoir of genetic heterogeneity that exists amongst tropical populations is particularly urgent in many instances, not only to establish its extent but also to understand and learn from its function before the populations disintegrate or become extinct and it will be too late.

The recommendations of the working party on genetic variation are published here.

D.F. ROBERTS
Treasurer, IUBS
Introduction

The initial recommendations for the Decade of the Tropics programme (21st IUBS general Assembly, Ottawa 1982, p 45) included as a major theme «An undying understanding of human populations as traditional and changing components of tropical ecosystems». Fundamentally that understanding is the knowledge of their genetic constitution and structures. What are the genetic features that distinguish tropical populations and facilitate their continuing existence in the face of the challenges of tropical environments? How do these relate to other variables of their biotopes? To provide that knowledge, a programme of collaborative research on the genetics of tropical human populations is here proposed. The objects of the programme are as follows:

To gain an understanding of the true extent of genetic variability within and between human populations in the tropics; of the biological significance of that variation; and of the factors responsible for its origin and maintenance.

It is unlikely that in the short period of ten years the objects will be fully achieved. However, it is hoped that in this programme some of the new knowledge and techniques that have recently become available and are being applied in sophisticated populations will be applied to tropical populations, hitherto virtually ignored in this respect, as a first sampling of the vast reservoir of genetic heterogeneity that exists amongst them. In many instances there is particular urgency since some of the peoples themselves are verging on extinction, or are being crowded from their traditional equilibrium situation by the pressures of colonial expansion and settlement, and increased contact. Besides the descriptive analysis, establishing which variants are present and their frequencies, it is envisaged that in selected instances these will be compared with data from other types of biological enquiry, genetic, physiological, morphological, epidemiological, demographic, and ecological to give some indication of the contribution of genetic variation to man's survival and success in tropical environments. Thus an interdisciplinary approach is recommended, involving a diversity of biological inputs.

A number of research units already exist that utilise the various new techniques. It is expected that many of these units would be willing and able to divert some of their time and expertise to dealing with material from tropical samples. So that although field investigations will be an integral part of the present programme, one of its aims should be to encourage or assist working teams interested in such research on tropical peoples. It is hoped to foster a greater degree of communication between units, and especially to strengthen local research centres, through interchange of scholars and students; seminars and workshops; literature exchange; and publication outlets, in accordance with the general principles of the «Decade of the Tropics» (Solbrig & Golley, 1983).

Background

Much of the present information on human genetic variation in the tropics derives from investigations carried out under the auspices of the International Biological Programme some two decades ago. Information on genetic constitution was collected with the intention of using it as a variable to be controlled in comparisons of groups inhabiting different environments, and also in its own right a view to understanding the evolution of the communities investigated. That, however, was
the time when the enormous increase in knowledge of human genetic variability was yet to occur. Although most of the polymorphic blood group systems had been established, the usefulness of electrophoresis as a technique for distinguishing genetic variants was just beginning to be understood and applied (Giblett, 1969; Brock & Mayo, 1972). Hence from the surveys of that period genetic information is restricted to gene frequencies in most polymorphic blood group systems, and a few serum and red cell enzymes and other proteins (Mourant et al, 1976).

Since that time, however, knowledge of genetic variability in man has increased enormously. Older laboratory techniques have been refined and new ones devised (e.g. two dimensional electrophoresis, isoelectric focusing, use of monoclonal antibodies) so that what were formerly thought to be single Mendelian variants have been found to consist of a number of subtypes, as for example with red cell phosphoglucomutase or serum Vitamin D binding protein. Entirely new polymorphic systems have been discovered and exploited, and particularly those of the major histocompatibility complex and the enzyme systems. At one extreme, variation in the detailed morphology of the human chromosomes has been revealed by differential staining procedures. At the other, full aminoacid and base pair sequencing of alleles has been carried out in a number of polymorphisms, and the fundamental differences between variants established, so that again what appeared at the first level of analysis to be a single entity proved to conceal considerable heterogeneity. The thalassemias provide an illustration of such heterogeneity. Here, with the establishment of the molecular structure of haemoglobin, first there came the differentiation of those affecting the alpha and beta chains. The thalassemias were recognised as due to the reduced or absent synthesis of the affected globin chain, in the presence of the continuing synthesis of the unaffected chain. But then sequence analyses demonstrated a variety of mutations. some affected the chain terminator of the coding region, others consisted of deletions or changes of single or multiple nucleotides; in general, deletions were found to account for most of the alpha thalassemias, and point mutations producing defects in transcription or in mRNA processes to account for most of the beta variants.

Moreover, sequence analysis has been extended to the DNA itself, showing the existence of intervening sequences between the codons within the coding sequence, of flanking sequences, of pseudogenes. Development of restriction endonucleases and their use to identify the presence or absence of particular sequences and so to give restriction fragment length polymorphisms has revealed another enormous source of variability within these flanking sequences. These have begun to be applied in clinical genetics for presymptomatic and prenatal diagnosis, but at the population level are already promising to be of enormous utility. The first hint of this was in 1980, when use of a single restriction enzyme (Hpal) showed that the gene responsible for the beta chain of HbS was different in West and East Africans. Now, for example, in the beta globin chain cluster, some 60 kb in length, eleven polymorphic restriction sites, identified by eight restriction enzymes, give three distinct haplotypes associated with the βγ gene. In western Africa these are geographically specific, associated with Benin, Senegal, and Central Africa. Clearly these extremely powerful polymorphisms are of relevance in demonstrating local and regional variation, but they indicate the occurrence of discrete mutations at different localities and therefore something of the origin and movement of the populations in whom they occur. Moreover, they suggest that older estimates of mutation rates are likely to be inadequate, and so are all the estimates of genetic variability and the uses to which they have been put in quantification of evolutionary rates, genetic distances between populations, genetic relationship, and similarly.

These discoveries mean that the current descriptions of genetic constitution of tropical populations are merely skeletons. The time is now ripe to put flesh on these, and to give the additional dimensions that will allow fuller interpretation and understanding of human genetic variability in the tropics.

**Outline**

A principal feature of human tropical populations is their distribution in discrete geographical areas (South America, Africa, India, South-East Asia and Indonesia, Oceania and Australia), separated by oceans. These areas have been settled at different times by different populations. This distribution provides the framework for the proposed programme. One principal object is to establish the extent of genetic heterogeneity among these continental groups, to compare it with that among major populations within each continental group. This is the prerequisite to understanding its biological significance. Moreover, there occur in each continent smaller more isolated populations, differentiated by language, culture, ways of life, as well as biologically, from the more numerous major populations. Their inclusion is of particular
importance, for not only is their existence threatened but they also contribute disproportionately to the overall heterogeneity, for they appear to be reservoirs of rare alleles.

The following topics should be included:

1. The restriction fragment length polymorphisms (RFLPs of nuclear DNA).

Their identification and frequencies in the major continental populations and their subdivisions, and particularly in small populations who have long been isolated, call for urgent attention. Little has so far been done in the tropics, yet from what is known of classical gene markers, tropical populations make a predominant contribution to the total genetic heterogeneity that exists in man. Estimates so far suggest that the RFLPs will reveal genetic heterogeneity ten times that revealed by classical genetic markers. This is due to the fact that the new recombinant DNA technology makes it possible to detect polymorphisms which are not evident by studying the protein gene product. They may be (a) single-base changes which alter a codon, but the new codon codes for the same aminoacid (so-called synonymous mutation as far as the protein is concerned); (b) single-base changes which alter the 5' or 3' regions of the gene, which, although transcribed into mRNA, are not translated into protein; (c) changes which occur in the intervening sequences (introns) which, although transcribed into precursor mRNA are removed during processing and are not reflected in the mRNa. These mutations will, of course, be detected by direct studies on the DNA.

There are several estimates of the number of RFLPs. Jeffreys (1979), investigating the beta globin gene region, estimated that there was one variable restriction enzyme site every 100 nucleotides, but Ewens revised the figure to 1 in 200. Recent work on the albumin gene suggests a higher figure, namely 1 in 85 (Murray et al., 1985). Bowcock (1984) in southern African populations estimated heterogeneity at regions of the genome identified by four single copy DNA probes, and concluded that the frequency of basepair substitution was 1 in 200. Using 19 cloned DNA segments derived from at least five different chromosomes, Cooper et al. (1985) estimated a frequency of heterozygous base pairs in the human genome of about 1 in 300. On the Y chromosome five polymorphic sites are already detectable in the region shared by the X and Y using several dozen probes, two further clones define RFLPs in the non-pairing region, and there appear to be population differences in the variant frequencies in Europe.

Whether the RFLPs are neutral or subject to the influence of natural selection is a key issue. For if their frequencies are to be used in the same way as classical markers for studies of genetic affinity, genetic distance, or kinship, then they would obviously be of greater value if they were neutral than if they are subject to the influence of natural selection. Cooper and Schmidt (1984) conclude that most DNA variation exists in non-coding regions. The fact that RFLPs are likely to have arisen as a result of changes in non-coding DNA sequences suggests that they are neutral, but there is interesting relevant evidence from the distribution of restriction endonuclease sites throughout the genome. If RFLPs are randomly distributed throughout the coding sequences (exons) of average-sized structural genes, then at one per 200 nucleotide pairs there should be six polymorphic sites in the average structural gene. In the absence of linkage disequilibrium, 26 haplotypes would be expected. But of the 12 RFLPs identified in the beta globin cluster by Kazazian et al. (1983), seven were in flanking DNA, three in intervening sequences, one in a pseudogene, and only one in a coding sequence. The complete sequence of a 16.5 kb region of the beta globin cluster (Poncz et al., 1983) showed two polymorphic sites in the 886 nucleotides of six exons of the delta and beta genes (0.25 %) but 36 sites in the 6216 nucleotides of the introns and flanking sequences (0.58 %). There is therefore a non-random or uneven distribution of RFLPs in these sections of the human genome; and if this occurs throughout, then it must reflect the effect of selection, on the assumption that mutation is fairly random distributed throughout the DNA.

There is no reason to expect the linkage of RFL polymorphisms to be constant over all populations, and there may be differences in linkage groups and linkage disequilibria from one population to another which should be sought. This work will be of direct relevance in the utilisation of linkages of the RFLPs to disease loci. Associations of these polymorphisms with environmental factors and particularly disease, their role in susceptibility to disease, and hence their selective advantages and disadvantages deserve scrutiny.

RFLPs in tropical populations

The most recent and most comprehensive published compilation of loci of the human genome is that prepared by the Seventh International Workshop on Human Gene Mapping, 1983 (HGM7). Its report, especially the chapter prepared by Skolnick, Willard and Menlove, is the basis of this review on restriction fragment length polymorphisms (RFLPs). It will
be seen from Table I that 159 RFLPs were reviewed, 47 associated with human structural genes and 112 with, so-called, arbitrary DNA probes. The distribution of these RFLPs according to individual chromosomes is presented in Table II, from which it will be seen that at least one RFLP is situated on every chromosome: the greatest number on any autosome is to be found on chromosome 6 (there are 14 RFLPs) and there are no fewer than 26 on the X chromosome.

**Table I**: Comparison of the number of DNA clones listed in 1982 and 1984.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>RFLPs Genes</td>
<td>22</td>
<td>132</td>
</tr>
<tr>
<td>Arbitrary</td>
<td>7</td>
<td>47</td>
</tr>
<tr>
<td>Other arbitrary DNA segments</td>
<td>18</td>
<td>112</td>
</tr>
</tbody>
</table>

All the references cited in this report have been scanned together with a dozen or so other communications which RFLPs had been reported in tropical populations. There were very few. The search for RFLPs has been virtually confined to Western Europeans, and individuals descended from them and from former inhabitants of the Mediterranean region (Greeks and Italians), and American blacks. The reason for this choice of population is straight-forward. DNA has been extracted from individuals who, in the main, had presented for prenatal diagnosis of thalassaemia or sickle cell anaemia and this material was then used for the more extensive studies.

In the absence of studies on populations inhabiting tropical areas, the next approach was to locate any studies conducted on populations which have until relatively recently lived in the tropics. American blacks, Asians and Orientals, now living in the USA, would, in this way, qualify for inclusion. Again the search was largely unrewarding but the scope of the available studies is summarised in Table III.

**Table III**: DNA clones identifying one or more RFLP

<table>
<thead>
<tr>
<th>Assigned loci</th>
<th>Unassigned loci</th>
</tr>
</thead>
<tbody>
<tr>
<td>In one population</td>
<td>126</td>
</tr>
<tr>
<td>In more than one population</td>
<td>13 *</td>
</tr>
</tbody>
</table>

* includes \( \alpha \) - and \( \beta \) - globin clusters.

**Table II**: DNA segment distribution by chromosome

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Genes</th>
<th>Arbitrary sequences</th>
<th>RFLPs</th>
<th>Repetitive sequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>2</td>
<td>6</td>
<td>1</td>
</tr>
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<td>2</td>
<td>6</td>
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<td>15</td>
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</tr>
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<td>3</td>
<td>1</td>
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<td>10</td>
<td>3</td>
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<td>18</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>19</td>
<td>6</td>
<td>3</td>
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<td>0</td>
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<tr>
<td>22</td>
<td>2</td>
<td>8</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>X</td>
<td>7</td>
<td>75</td>
<td>26</td>
<td>2</td>
</tr>
<tr>
<td>Y</td>
<td>1</td>
<td>10</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

An indication of the RFLPs which have been given in Table IV. The results of these various studies are presented in Table V.

Table IV: RFLPs defined in more than one population.

<table>
<thead>
<tr>
<th>Chromosome and region</th>
<th>Gene name</th>
<th>Populations studied</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Caucasians</td>
</tr>
<tr>
<td></td>
<td></td>
<td>USA</td>
</tr>
<tr>
<td>3q28</td>
<td>Somatostatin</td>
<td>+</td>
</tr>
<tr>
<td>4q11-q22</td>
<td>Albumin</td>
<td>+</td>
</tr>
<tr>
<td>7q21-q22</td>
<td>Pro a2 (1) collagen</td>
<td>+</td>
</tr>
<tr>
<td>9q34-pter</td>
<td>Argininosuccinate synthetase</td>
<td>+</td>
</tr>
<tr>
<td>11pter-p11</td>
<td>Parathyroid hormone</td>
<td>+</td>
</tr>
<tr>
<td>11p15</td>
<td>Insulin</td>
<td>+</td>
</tr>
<tr>
<td>11</td>
<td>Globin β cluster</td>
<td>+</td>
</tr>
<tr>
<td>14q32</td>
<td>D14S1 (pAV101)</td>
<td>+</td>
</tr>
<tr>
<td>16pter-p12</td>
<td>Globin α cluster</td>
<td>+</td>
</tr>
<tr>
<td>17q22-q24</td>
<td>Growth hormone</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>human chorionic somatomammotropin</td>
<td>+</td>
</tr>
<tr>
<td>Xp22.3-p21</td>
<td>DX59 (RC8)</td>
<td>+</td>
</tr>
<tr>
<td>Xp11.3-p11</td>
<td>DX57 (L1.28)</td>
<td>+</td>
</tr>
<tr>
<td>Xq13-q22;Yp</td>
<td>DXYS1</td>
<td>+</td>
</tr>
<tr>
<td>Xq13-q22;Yp</td>
<td>λHAB006</td>
<td></td>
</tr>
</tbody>
</table>

* refers to South African and English Caucasoids; † South African Caucasoids.

2. Mitochondrial DNA

The unique properties of mitochondrial DNA give a different perspective on human genetic variation. In these organelles of the cytoplasm, closed circles of about 16.5 kb of DNA code for a small number of proteins and components of the translation apparatus. The mitochondrial genome is therefore much smaller and simpler than the nuclear genome. It contains sequences that occur only once per mitochondrial genome, there are no spacer sequences between genes and no intervening sequences within transcribed genes. It appears to be much less susceptible to sequence rearrangements than is the complex, more labile, sequence organisation and structure of the nuclear genome. Unlike most genes which are contributed to the offspring by both parents, mitochondrial genes are apparently transmitted exclusively by the female, with no recombination. Since biparental inheritance is absent, all the genetic variation that arises from sexual inheritance is absent. Therefore many of the complexities that obscure the interpretation of nuclear data are reduced or absent from the mitochondrial. Its evolution appears to be simpler and more straightforward.

Several hundred individuals have now been studied, mainly by restriction endonuclease cleavage, and it appears that each individual is homogeneous for one mitochondrial genotype. Microevolution between individuals appears to be of the order of relatively few base pairs, and mtDNA sequence comparison indicates that transitions (A → G or C → T) are much more frequent than transversions (A or G → C or T); substitutions predominate over deletions or additions. However, there is considerable potential for population studies to establish the extent of mitochondrial variation among and within populations. So far, in the human mtDNAs examined in a series of 112 individuals who were tested with 12 different restriction endonucleases, there are known 163 polymorphic sites due to point mutations by comparison with 278 constant. Most mutations which are fixed in human mtDNA are single-base changes, and most of these do not cause aminoacid substitutions. However, mutations which alter the protein sequences in mitochondria have been detected, and so have polymorphisms caused by small additions and deletions.

As with the nuclear RFLPs, the majority of individuals studied come from outside the
tropics, though they do represent several different continents. The few tropical, subjects include aborigines from Australia and New Guinea, sub-Saharan Africa, and south-east Asia. But the orientation of the work so far seems to have been more towards evolutionary than interpretative issues, for which the identification and frequencies of the mtDNA polymorphisms in the major continental populations and their subdivisions are fundamental. The results to date indicate that while particular variants characterise particular populations, sufficient are common to all as to suggest that there must have been extensive movement throughout the old world. The ancestors who eventually reached Australia carried an appreciable part of the total mitochondrial pool, and not just those genes restricted to south-east Asia. The time depth of the human mitochondrial gene pool appears to be some 200,000 years.

For such studies of evolutionary rates and the divergence dates, a proper calibration of dating by the use of mitochondrial DNA is required. Hence it is important to examine populations who have moved into their present habitats at known times, and here American Indian, Polynesian and other Pacific island populations and hybrids of known later dates will be particularly important. From a theoretical viewpoint, hybrid populations will also be critical, for they may provide information on the breakdown of co-adapted gene complexes and the subsequent burst of mutation rates that is thought to occur. The strictly maternal mode of inheritance means that the mtDNA results will be particularly useful for clarifying the process by which past hybridisation occurred, e.g. whether invaders or colonisers consisted of both sexes or males only. They will also provide valuable information on the evolution of polygamous and especially polyandrous societies, and will thus provide the obverse, as it were, of the Y chromosome RFLP's.

There is no information yet on the association of mtDNA polymorphisms with human disease other than mitochondrial cytopathy, but it is to be expected that some of the mutations may be slightly deleterious.

3. Established polymorphisms re-examined by new techniques

The considerable advances that have been made in refining older laboratory techniques and devising new ones means that a great deal more information on population variation can be obtained from gene product studies, particularly enzymes and proteins. To very few of the populations examined by the older methods, compiled by Mourant et al (1976), have any of the new techniques (such as isoelectric focussing, use of monoclonal antibodies) been applied. Many tropical populations still remain unexamined even by classical variables, and this too should be done as a matter of urgency. For very few tropical populations is there knowledge of the frequencies of genes of the major histocompatibility complex, and nothing of the D and related loci, yet these play a critical role in susceptibility to a number of diseases, as well as providing estimates of genetic affinity, independent of those by blood groups, serum protein and red cell enzyme genes. Where these have been examined in non-tropical populations, curious parallelisms in distributions occur. Certainly all subjects in whom nuclear and mitochondrial DNA studies are carried out should be fully characterized by these longer known polymorphisms.

There still remain many problems of how the gene frequency differences are maintained, especially in relation to the biological and cultural variation that occurs in the tropics, sufficient to warrant a major endeavour.

4. Chromosome variation

At the level of microscopically detectable variation, there is very little information available on chromosomal polymorphisms in tropical populations. Yet the few studies of populations elsewhere suggests that there are differences in frequency and morphology of variants, e.g. in the total content of heterochromatic bands in populations living under different environmental conditions. To follow up this suggestion, population comparisons of heteromorphisms are required. The Y chromosome and nucleolar organiser regions appear especially interesting in this respect. The proposed work should incorporate C, Q and special banding procedures, especially the use of multiple stains. The possibility that there may be differences in fragile site frequencies should not be overlooked.

Since chemical and physical mutagens may cause microscopically detectable chromosome damage, the observation of the frequencies of, e.g. sister chromatid exchange, chromosome and chromatid breaks, dicentrics, minutes, may give important clues to mutagenic environmental factors.

The repetitive DNA sequences that occur in the bands are presumably not translated, and the constitutive heterochromatic regions are regarded as genetically inert. The band variation may thus represent neutral polymorphisms, and so be of relevance, e.g. in questions of population affinities.

In view of the technical variation between laboratories, investigations should include arrangements for duplicate analysis, as a cross-laboratory control.
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There is no information yet on the association of mtDNA polymorphisms with human disease other than mitochondrial cytopathy, but it is to be expected that some of the mutations may be slightly deleterious.

3. Established polymorphisms re-examined by new techniques

The considerable advances that have been made in refining older laboratory techniques and devising new ones means that a great deal more information on population variation can be obtained from gene product studies, particularly enzymes and proteins. To very few of the populations examined by the older methods, compiled by Mourant et al (1976), have any of the new techniques (such as isoelectric focussing, use of monoclonal antibodies) been applied. Many tropical populations still remain unexamined even by classical variables, and this too should be done as a matter of urgency. For very few tropical populations is there knowledge of the frequencies of genes of the major histocompatibility complex, and nothing of the D and related loci, yet these play a critical role in susceptibility to a number of diseases, as well as providing estimates of genetic affinity, independent of those by blood groups, serum protein and red cell enzyme genes. Where these have been examined in non-tropical populations, curious parallelisms in distributions occur. Certainly all subjects in whom nuclear and mitochondrial DNA studies are carried out should be fully characterized by these longer known polymorphisms.

There still remain many problems of how the gene frequency differences are maintained, especially in relation to the biological and cultural variation that occurs in the tropics, sufficient to warrant a major endeavour.

4. Chromosome variation

At the level of microscopically detectable variation, there is very little information available on chromosomal polymorphisms in tropical populations. Yet the few studies of populations elsewhere suggests that there are differences in frequency and morphology of variants, e.g. in the total content of heterochromatic bands in populations living under different environmental conditions. To follow up this suggestion, population comparisons of heteromorphisms are required. The Y chromosome and nucleolar organisser regions appear especially interesting in this respect. The proposed work should incorporate C, Q and special banding procedures, especially the use of multiple stains. The possibility that there may be differences in fragile site frequencies should not be overlooked.

Since chemical and physical mutagens may cause microscopically detectable chromosome damage, the observation of the frequencies of, e.g. sister chromatid exchange, chromosome and chromatid breaks, dicentrics, minutes, may give important clues to mutagenic environmental factors.

The repetitive DNA sequences that occur in the bands are presumably not translated, and the constitutive heterochromatic regions are regarded as genetically inert. The band variation may thus represent neutral polymorphisms, and so be of relevance, e.g. in questions of population affinities.

In view of the technical variation between laboratories, investigations should include arrangements for duplicate analysis, as a cross-laboratory control.
### Table V: Frequencies of RFLP Alleles or Haplotypes in various populations some of which originate in the tropics.

<table>
<thead>
<tr>
<th>CHR Region</th>
<th>Gene name</th>
<th>Name</th>
<th>Enzyme</th>
<th>Length (kb)</th>
<th>Caucasian t</th>
<th>Negroid t</th>
<th>Asian</th>
<th>Other</th>
<th>Other</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 q28</td>
<td>Somatostatin (SST)</td>
<td>A1</td>
<td>Eco RI</td>
<td>12.0</td>
<td>91 ± 0.2</td>
<td>98 ± 0.2</td>
<td>95 ± 0.3</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>A2</td>
<td></td>
<td>6.4</td>
<td>09 ± 0.2</td>
<td>02 ± 0.2</td>
<td>05 ± 0.3</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>B1</td>
<td></td>
<td>14.5</td>
<td>87 ± 0.0</td>
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<tr>
<td></td>
<td></td>
<td>B2</td>
<td></td>
<td>7.8, 7.7</td>
<td>13 ± 0.3</td>
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<tr>
<td>4 q11-q22</td>
<td>Albumin (ALB)</td>
<td>H1</td>
<td>8 sites</td>
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<td>12 ± 0.3</td>
<td>30 ± 0.0</td>
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<td></td>
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<td>H2</td>
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<td></td>
<td>09 ± 0.5</td>
<td>35 ± 0.9</td>
<td>32 ± 0.10</td>
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<td></td>
<td>H3</td>
<td></td>
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<td>32 ± 0.04</td>
<td>46 ± 0.10</td>
<td>32 ± 0.10</td>
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<td>H4</td>
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<td></td>
<td>14 ± 0.01</td>
<td>00 ± 0.0</td>
<td>00 ± 0.0</td>
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<td></td>
<td></td>
<td>H5</td>
<td></td>
<td></td>
<td>00 ± 0.0</td>
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<td>H6</td>
<td></td>
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<td>08 ± 0.05</td>
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<td></td>
<td>H7</td>
<td></td>
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<td>01 ± 0.1</td>
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<td>7 q21-q22</td>
<td>Pro α 2 (1) collagen (COL 1A2)</td>
<td>A1</td>
<td>Eco RI</td>
<td>9.5, 3.5</td>
<td>38 ± 0.0</td>
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<td>E2</td>
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<td>9 q34-pter</td>
<td>Argininosuccinate synthetase (ASS)</td>
<td>A1</td>
<td>Hind III</td>
<td>2.7</td>
<td>30 ± 0.5</td>
<td>A2 &gt; A1</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>A2</td>
<td></td>
<td>3.9</td>
<td>70 ± 0.5</td>
<td>A2 &gt; A1</td>
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<td></td>
<td></td>
<td>B1</td>
<td></td>
<td>8.1</td>
<td>66 ± 0.05</td>
<td>B1 &gt; B2</td>
<td>B1 only</td>
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<td></td>
<td></td>
<td>B2</td>
<td></td>
<td>8.1</td>
<td>44 ± 0.05</td>
<td>C1 &gt; C2</td>
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<td></td>
<td>C1</td>
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<td>10.1</td>
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<td></td>
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<td>5.3</td>
<td>87 ± 0.05</td>
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<td>11 pter-p11</td>
<td>Parathyroid hormone (PTH)</td>
<td>A1</td>
<td>Pst I</td>
<td>2.2</td>
<td>28 ± 0.05</td>
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<td>A2</td>
<td></td>
<td>2.7</td>
<td>72 ± 0.05</td>
<td>46 ± 0.07</td>
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<td>11 p1205-p1208</td>
<td>β-globin gene cluster (HBB)</td>
<td>H1 1-A</td>
<td>5'3' several</td>
<td></td>
<td>34 ± 0.4</td>
<td>10 ± 0.6</td>
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<td>H2 1-B</td>
<td></td>
<td></td>
<td>18 ± 0.3</td>
<td>03 ± 0.3</td>
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<td></td>
<td>H3 1-C</td>
<td></td>
<td></td>
<td>10 ± 0.3</td>
<td>03 ± 0.3</td>
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<td></td>
<td></td>
<td>H4 1-other</td>
<td></td>
<td></td>
<td>01 ± 0.01</td>
<td>03 ± 0.3</td>
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<td></td>
<td></td>
<td>H5 2-A</td>
<td></td>
<td></td>
<td>07 ± 0.02</td>
<td>03 ± 0.3</td>
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<td></td>
<td></td>
<td>H6 2-B</td>
<td></td>
<td></td>
<td>02 ± 0.01</td>
<td>03 ± 0.3</td>
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<td>H7 2-C</td>
<td></td>
<td></td>
<td>03 ± 0.02</td>
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<td></td>
<td></td>
<td>H8 2-other</td>
<td></td>
<td></td>
<td>13 ± 0.03</td>
<td>10 ± 0.6</td>
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<td></td>
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<td>H9 3-A</td>
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<td>06 ± 0.06</td>
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<td>H10 3-B</td>
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<td></td>
<td>06 ± 0.06</td>
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<td></td>
<td>H11 3-C</td>
<td></td>
<td></td>
<td>19 ± 0.10</td>
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<td></td>
<td></td>
<td>H12 3-other</td>
<td></td>
<td></td>
<td>13 ± 1.11</td>
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<td></td>
<td></td>
<td>H13 4-A</td>
<td></td>
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<td>19 ± 10</td>
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<td></td>
<td></td>
<td>H14 4-B</td>
<td></td>
<td></td>
<td>06 ± 0.06</td>
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<td></td>
<td>H15 4-C</td>
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<td>06 ± 0.06</td>
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<td></td>
<td></td>
<td>H16 4-other</td>
<td></td>
<td></td>
<td>13 ± 11</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td>H17 5-A</td>
<td></td>
<td></td>
<td>19 ± 10</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>H18 5-B</td>
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<td>06 ± 0.06</td>
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<td></td>
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<td>06 ± 0.06</td>
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</table>

**Notes:**
- Ref. refers to the source of the data.
- Frequencies are rounded to two decimal places.
- Alleles are indicated by the presence or absence in various populations.
<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Region</th>
<th>Genes</th>
<th>Frequencies</th>
<th>References</th>
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</thead>
<tbody>
<tr>
<td>11 p15</td>
<td>Insulin (5')</td>
<td>A1, A2, A3</td>
<td>Pvu II, Sac I</td>
<td>Ref 18</td>
</tr>
<tr>
<td>14 q32</td>
<td>D14SI (pAW 101)</td>
<td>A1, A2, A3, B1, B2</td>
<td>Eco RI</td>
<td>Ref 18</td>
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<tr>
<td>16 pter-p12</td>
<td>α-globin gene cluster</td>
<td>A1 (αα), A2 (-α), A3 (ααα)</td>
<td>Bam HI</td>
<td>Ref 18</td>
</tr>
<tr>
<td>17 q22-q24</td>
<td>Growth hormone - human chorionic somatomammotropin (hGH-hCS) gene cluster</td>
<td>A1, A2, B1, B2, C1, C2, D1, D2, E1, E2</td>
<td>Hind III</td>
<td>Ref 18</td>
</tr>
<tr>
<td>X p11.3-p11</td>
<td>DXS7 (L1.28)</td>
<td>A1, A2</td>
<td>Taq I</td>
<td>Ref 18</td>
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<td>X p22.3-p21</td>
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<td>XY Xq13-q22</td>
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<td>Yp</td>
<td>λHAB006</td>
<td>H1, H2, H3, H4</td>
<td>Taq I</td>
<td>Ref 18</td>
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</table>

1 unless stated to the contrary the frequencies are those found in U.S. populations; * Greek individuals were shown to have frequencies as follows: A1 = • 88 ± 0.03; A2 = • 07 ± 0.03 and A3 = • 05 ± 0.02 (Ref 18).

1 Naylor et al. (1983); 2 Murray et al. (1984); 3 Junien et al. (1984a); 4 Junien et al. (1984b); 5 Grobler-Rabie et al. (1985); 6 Grobler-Rabie et al. (1985) personal communication; 7 Brebner et al. (1985); 8 Deiger et al. (1984); 9 Antonarakis et al. (1983); 10 Antonarakis et al. (1984); 11 Ramsay (unpublished); 12 Bell et al. (1984); 13 Elbein et al. (1985); 14 Bowcock (1984); 15 Wyman & White (1980); 16 Ramsay & Jenkins (1984); 17 Embury et al. (1980); 18 Goosens et al. (1980); 19 Chakravarti et al. (1984); 20 Davies et al. (1983); 21 Lester (unpublished); 22 Bhattacharya et al. (1984); 23 Rahuel et al. (1984); 24 page et al.
5. Multifactorial characters

The characters so far discussed provide a useful basis for and control in broader biological studies. In these, the grosser phenotypic variants, covering a range of degrees of genetic determination, from frequencies of different genetic diseases, colour vision defects, dermatoglyphics, to physique and growth also can usefully be included. Naturally occurring poor environmental conditions reduce the expression of the genetic potential for each individual, with effects particularly noticeable if deprivation occurs prenatally and in childhood. Variations in growth rate and achievement can be seen as reflecting other biological challenges during development; compared within and across populations, they are particularly informative in this respect, especially if studied in parallel with disease susceptibility, immunological profiles, physique and body composition. But for their analysis control of the genetic constitution is essential. It is in this type of enquiry that parallel investigation of the broader ecology is likely to be particularly rewarding.

6. Special situations

On account of the great diversity of society and environment of man in the tropics, there are many situations where nature seems to have arranged an almost experimental situation, in which particular biological problems can be investigated. Thus, one may find a population that is a single genetic entity occupying two locations differing in one or more major environmental features, an ideal situation for disentangling the effect of genetic selection from physiological and ontogenic adaptation. Hybridisation occurs widely, representing the opportunity for examination of the breakdown of co-adapted gene complexes. Parts of some populations may unwittingly have been particularly exposed to the effects of radiation, and here mutation may be sought. There is a wide range of mating patterns, allowing the examination of the effects of inbreeding. Populations are arranged in a whole variety of hierarchical structures, which again affects their genetic constitution. Opportunities for the investigation of all these and other factors making for the maintenance of genetic variability should be within the scope of the proposed programme.

Attention should therefore be directed particularly to the following:

i. the smaller, more isolated populations, differentiated from the main stream. Their inclusion is of particular importance, for they are the more threatened and also contribute disproportionately to the overall heterogeneity; they appear to be reservoirs of rare alleles, and are informative for elucidating the effects of inbreeding, of demographic bottlenecks, and of the founder principle.

ii. situations where hybridisation is currently in progress, or occurred at known historical dates, in order to calibrate assessment of the rate of differentiation obtained by DNA studies.

iii. situations of extreme background radiation, high and low, to monitor the variation in mutation rate.

iv. situations where particular selective stresses occur at high level, so that the selective effects can be identified and measured.

v. situations where disease foci of high incidence prevail, to assess genetic susceptibility.

vi. where new polymorphisms are discovered, family studies for the establishment of linkage relationships.

IMPLEMENTATION

1. Populations

At least three populations are required in each of the six major tropical regions, and in addition small isolates wherever possible, and other populations presenting situations of special interest. Remoteness need be no bar, for specimens obtained in the field can be satisfactorily analysed if flown back to the laboratory within 24-48 hours of collection. If an air service is not available, then a generator-operated centrifuge may be used in the field to separate the cells and sera and preserve them in portable liquid nitrogen containers, or DNA may be extracted direct. Special situations may allow the collection of other tissues, e.g. placenta for mtDNA. Sites of present research are as follows:

i. New Guinea. For a number of years interdisciplinary research has been pursued amongst the aboriginal peoples of New Guinea from centres in Goroka and Port Moresby, in collaboration with the John Curtin School of Medical Research (Canberra), the University of Oxford, the
distributing these to laboratories with different specialties. The advantages are obvious of locating investigations among populations whose habitat is under investigation in other themes of the Decade of the Tropics programme.

To help organisation and advise on content and methods of enquiry, and to facilitate information exchange among groups, a steering committee has been set up. It consists of Dr. R. Cann (U.S.A.), Professor T. Jenkins (South Africa), Dr. R. L. Kirk (Australia), Dr. P. LeFevre Wittier (France), Dr. S. S. Papiha (India), Professor D. F. Roberts (United Kingdom), Professor G. De Stefano (Italy), and Dr. J. Schmidtke (Germany).

References


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Microevolution in the Amazon - a Global Perspective
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For about two decades now our group of researchers, in collaboration with other Brazilian and foreign centers of investigation, have been studying Amazonian human populations. Some of them are forest-dwellers, but others live in small or large towns. Their racial constitution is also variable; some are Amerindians, but populations of mixed (White/Indian/Black) descent have also been studied. The research involves the acquisition of demographic, socio-cultural and medical information, that has been correlated with the genetic variability present in 20-40 genetic systems that are expressed in blood; in some cases the morphological variation of these individuals has also been evaluated. A large quantity of scientific papers, reviews and books have been published describing these results, but the unpublished material is also considerable, involving 12 Indian tribes and two admixed communities. Plans for the future include the extension of the genetic studies to loci determinable by isoelectric focusing techniques and restriction fragment length polymorphisms, as well as new applications of multivariate techniques to old and new data. The ultimate objective is to understand the factors involved in the origin and maintenance of genetic variability.

Genetic Effects of Inbreeding and Isolation in the Tuti Islanders, Sudan
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It is proposed to study an endogamous island community, Gezirat Tuti, Sudan. The population, the Nubian Mahas, numbers approximately 10 000. Previous research on the island demonstrated an unusually high level of preferential first cousin marriage, especially patrilateral parallel cousins. The aim of the project is A. to establish the frequencies of genetic variants, namely the blood groups, red cell enzymes, serum proteins, restriction fragment length and mitochondrial DNA polymorphisms, B. construct pedigrees, C. examine the effects of the inbreeding on the variation in these polymorphic systems, and particularly to determine the effect of patrilateral cousin marriage on the distributions of the sex chromosome polymorphisms, D. to compare the island results with a control sample drawn from the Sudanese capital population.

Genetic Relationships Between Ethiopian and Yemenite Jews by Means of Mitochondrial DNA Polymorphisms
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The purpose of the proposed investigation is to use mt DNA polymorphisms in order to assess the extent of genetic diversity within each group and to estimate the genetic distances between the two populations.

The haploid nature of the mt DNA molecule, its maternal inheritance and the lack of variations for mt DNA types within individuals make the mt DNA an excellent marker for the reconstruction of lineages and for clarification of evolutionary relationships among species, populations and individuals.

Several different theories about the origin of these populations and their possible migrations exist. The proposed investigation aims to provide new insight on these questions of ethno-historical relationships.

Furthermore, it is hoped that comparing the genetic profiles based on classical polymorphisms with those obtained from the proposed mt DNA analysis will improve the distinction between evolutionary factors such as selection or admixture, and the identification of their relative contributions to their gene pools.
The question of universally acceptable and agreed methods for assessing working capacity in populations has often been debated. Much discussion of this topic was indeed generated at the I.U.B.S. Symposium (Dec. 1984, London) but because of the constraints of time it was clearly understood that the group were not charged with making agreed decisions on methodology. It was recognised, however, that an early priority in the « Decade » programme would be to establish a concordance on methodology.

Fundamentally there was general approval of the methodology established by the International Biological Programme based on a spectrum of tests to measure aerobic power directly and indirectly, anaerobic power, respiratory function and to assess habitual activity. There have been major methodological advances since I.B.P. including more sophisticated methods of ambulatory monitoring, telemetry and more accurate instrumentation and methods. Determinants of explosive effort in anaerobic work are principally those of muscle strength and skill, and of sustained effort in aerobic work factors of structural and functional dimensions and of the oxygen transport chain; so there is clearly a need to measure both components in population studies.

A strong case can be made for abandoning direct measurements of maximum aerobic power (n O2 max) and for adopting an agreed submaximal exercise index e.g., n O2 at a respiratory exchange rate of unity, when making comparisons between population groups. Although n O2 max is theoretically a better standard and has a smaller coefficient of variation it has limited absolute value in normal working practices and a major criticism is that it can only be attained by direct measurement on a small proportion of even a well-motivated population sample.

Standardisation of tests of performance which measure capability, function and performance related to a particular task may follow the EEC recommended pattern (Testing Physical Fitness, Strasbourg, 1983). Agreed methods should be applicable to population studies at different levels of sophistication and expertise and should include:

1) Standard test for submaximal exercise (both arm and leg exercise).
2) Standard test for maximal exercise capacity (in selected groups).
3) Standard test for anaerobic power.
4) Tests of performance related to everyday tasks.
5) Measurement of 24-hr energy expenditure by ambulatory monitoring.

Recently, an important advance in energy-expenditure monitoring in free-living people has recently been introduced (doubly labelled water method) and the use of this method will be discussed with a view to implementing such studies as part of the Decade of the Tropics programme.
Protein-Synthesizing Structures of Prokaryotic and Eukaryotic Cells

by Alexander S. Spirin

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Introduction

Creation of the protein biosynthesis machinery was undoubtedly among the first evolutionary events. Genes were invented by evolution in order to maintain the conservativity of a protein biosynthesis pattern in generations. The principally basic significance of the protein biosynthesis machinery for life has resulted in its universality among the very different taxonomic groups of organisms, including eubacteria, archaeabacteria, fungi, plants, and animals.

The general simplified scheme of protein biosynthesis is shown in Fig. 1.
The DNA serves for the storage of genetic information. Realization of the genetic information proceeds through the process of transcription where RNA is synthesized on DNA as a template. The RNA molecules, formed during this process, are spread in the cytoplasm and serve as templates for the protein biosynthesis. The process of translation of these messenger RNA molecules proceeds in the specialized particles called ribosomes.

Proteins consist of amino acids. Free amino acids, however, are not used by the ribosome. To become a substrate for protein synthesis, an amino acid must be activated by coupling with the adenylic moiety of ATP and then accepted by a special RNA molecule called transfer RNA. The resulting aminoacyl-tRNA is used by the ribosome as a substrate for protein synthesis. Using mRNA as a program and aminoacyl-tRNAs as energy-rich substrates, the ribosome translates genetic information from the nucleotide language of mRNA into the amino acid language of polypeptide chains.

Ribosomes are abundant in cells involved in an intensive protein synthesis. In the bacterial cell they are dispersed throughout the cytoplasm and account for up to 50% of its dry weight. In the eukaryotic cells with an active protein secretion and a developed network of endoplasmic reticulum, a marked proportion of cytoplasmic ribosomes are attached to the endoplasmic reticulum membrane, specifically to the surface facing the cytoplasmic matrix. These ribosomes synthesize proteins which are directly transported into the membrane lumen for subsequent secretion. Protein synthesis for intracellular needs takes place on the free cytoplasmic ribosomes that are not associated with the membrane.

**Ribosomes**

The ribosomes in living nature can be divided into two main principal groups (Fig. 2). All prokaryotic organisms, including gram-positive and gram-negative eubacteria, actinomycetes, blue-
green algae and chloroplasts, contain prokaryotic type ribosomes, which exhibit a sedimentation coefficient of about 70S. The cytoplasm of all eukaryotic organisms, including animals, fungi, plants, and protozoans, contains somewhat larger 80S ribosomes. The 70S ribosomes of archaebacteria form a special subgroup. These ribosomes exhibit a sedimentation coefficient of prokaryotic type ribosomes, but in some morphological features they are closer to the eukaryotic type ribosomes. There are also two other small subgroups of ribosomes: mitochondrial 75S ribosomes of fungi and mitochondrial 55S ribosomes, or «miniribosomes», of mammals.

When examined by electron microscopy, the isolated ribosomes look like compact rounded particles with a linear size of about 200-250 Å in the case of prokaryotic ribosomes and 250-300 Å in the case of eukaryotic ones. On the whole, all ribosomes are characterized by the basic universality of their structural organization. Ribosomes from different organisms and cells, whether prokaryotic or eukaryotic ones, have a strikingly similar appearance and only minor morphological differences.

The ribosome consists of two subparticles, or ribosomal subunits, which can be easily separated and then studied individually. The prokaryotic 70S ribosome dissociates into subunits with sedimentation coefficients of 50S and 30S. The eukaryotic 80S ribosome dissociates into 60S and 40S subunits.

The morphological model of the bacterial 30S ribosomal subunit reconstructed from different electron microscopic projections is given in Fig. 3. The subunit may be subdivided into lobes which are referred to as the «head», «body», and «side bulge» or «platform» [1,2]. The eukaryotic 40S subunit has a similar morphology, although two additional details of the structure may be mentioned [3]. The first is a protuberance, or «bill», located on the head of the side opposite to the bulge. Second, the end of the body distal to the head appears to be bifurcated due to the presence of some additional mass; this bifurcation is referred to as the «eukaryotic lobes». The shape of the large subunit is virtually identical in prokaryotic and eukaryotic ribosomes [4]. The morphological model of the bacterial 50S subunit is shown in Fig. 4 [2,5].

This subunit is more isometric than the smaller one. Three peripheral protuberances can be distinguished: the central one may be termed the head; the lateral fingerlike protuberance is called the L7/L12 stalk; and still another lateral protuberance, located on the other side of the central protuberance, is referred to as the side lobe. In an intact ribosome the two ribosomal subunits are joined in a very specific «head-to-head
and the side lobe-to-side lobe manner (Fig. 5) [2,6].

![Fig. 5. - Schematic representation of the model of the 70S ribosome made of the 30S subunit and 50S subunit in their head-to-head and side lobe-to-side lobe association [6].](image)

The next important question in studying the ribosomal structure is that about the mutual arrangement of ribosomal RNA and proteins. In prokaryotic ribosomes the ribosomal RNA predominates. Two-thirds of the prokaryotic ribosome consists of RNA, and only a third is comprised of protein. The eukaryotic ribosome is more loaded with proteins which make up 50 % of its mass.

The principle of mutual arrangement of RNA and protein was first deduced from experiments conducted to measure the radii of gyration of ribosomal subunits. The radius of gyration measured by the diffuse small-angle X-ray scattering was found to be markedly lower than expected on the basis of the size of the subunit, assuming that it was a uniformly dense body. It followed from this observation that a more electron-dense component of the particle (e.g., RNA) lay nearer to the center of gravity of the particle, while a less dense component (e.g., protein) tended to be closer to the periphery [7]. Neutron scattering experiments in solvents with a different ionic conditions it is possible to remove ribosomal proteins from the subunit without any distortion in the compactness of the ribosomal RNA. It was found that the ribosomal RNA from the small ribosomal subunit looks like a Y-shaped structure with arms of unequal length (Fig. 3) [11]. The 23S RNA from the large ribosomal subunit appears much more rounded, having only small protuberances (Fig. 4) [12]. From these studies a conclusion can be made that a crude morphology of the ribosomal subunits is determined mainly by the specific self-packing of ribosomal RNA.

Electron microscopy can extend our knowledge on the ribosomal RNA structure. In special ionic conditions it is possible to remove ribosomal proteins from the subunit without any distortion in the compactness of the ribosomal RNA. It was found that the ribosomal RNA from the small ribosomal subunit looks like a Y-shaped structure with arms of unequal length (Fig. 3) [11]. The 23S RNA from the large ribosomal subunit appears much more rounded, having only small protuberances (Fig. 4) [12]. From these studies a conclusion can be made that a crude morphology of the ribosomal subunits is determined mainly by the specific self-packing of ribosomal RNA.

When the core position of the ribosomal RNA and its shape are determined, elucidation of the protein distribution on the surface of the particle, i.e. of the protein topography, becomes the next crucial step toward the quaternary structure of the ribosome. A large number of experimental approaches to the study of protein topography have been developed. Some information regarding the protein neighbours can be obtained from the data on protein binding sites upon the primary and secondary structures of the ribosomal RNA. Indeed, if the binding sites of proteins on RNA are located close to each other, it is clear that these proteins are neighbours in the ribosome. A more universal approach makes use of crosslinking neighbour proteins with each other. After a treatment of ribosomal subunits with such reagents, the identification of proteins in the crosslinked pairs provides the means of establishing that the corresponding proteins are neighbours in the ribosome.

The above approaches provide evidence for the arrangement of proteins with respect to each other, but without reference to the morphology of the ribosomal particle. The use of the immuno-electron microscopy allows the
location of a protein on a morphologically visible contour of the ribosomal particle. A bivalent specific antibody against an individual ribosomal protein may interact with two identical ribosomal particles, yielding their dimer through the bridge of the antibody molecule. By observing dimers in the electron microscope, one may identify sites on the surfaces corresponding to the location of a given protein.

Proceeding from the data outlined above, one can attempt to construct tentative models which account for the mutual arrangement of proteins and RNA in the ribosome. These models may reflect, to some extent, the quaternary structure of the ribosomal subunits at low resolution. Model-building studies are particularly appropriate for the 30S ribosomal subunit, since there is far more information on this subunit than on the 50S subunit. A tentative model accounting for the arrangement of the Y-shaped 16S RNA molecule and 21 ribosomal proteins approximated by spheres with diameters corresponding to their molecular masses is presented in Fig. 6 [13].

At present the main problem for biologists is the mode of functioning of the ribosome as a protein-synthesizing machinery. An examination of the electron microscopic images of the 70S ribosome and of its model reveals a pocket or cavity at the base of the L7/L12 stalk. From a number of indirect data it follows that one of the functionally most important regions is this pocket or cavity which is delimited by the non-covered concave surface of the 50S subunit and the lateral concave surface of the 30S subunit. It is tempting to think that is the pocket that accommodates the two tRNA sites [14]. Indeed, both the grooves separating the 30S subunit head from the body of the 50S subunit open out into this pocket or cavity. These grooves were shown to be the site of mRNA location. Furthermore, the L7/L12 stalk seems to be important for the movement of both the mRNA and tRNA during the process of protein synthesis. All these indications may be promising for further elucidation of the structure-function relationships in the ribosome.

**Polyribosomes**

A ribosome begins to read mRNA from a strictly definite point of its sequence, i.e. from the beginning of its coding region. It should in some way identify the readout origin, bind to it, and then begin the translation. The series of events that provide for the beginning of the translation is called initiation. After initiation the ribosome consecutively reads mRNA codons in the direction of the mRNA 3'-end. The mRNA readout implies concomitant synthesis of the polypeptide chain coded by the mRNA. Throughout the course of the protein synthesis, the ribosome is associated with a limited section...
of the template polyribonucleotide. Such a section has been found to have a length of 30 to 60 nucleotide residues. It must be noted that the length of the mRNA coding sequence usually exceeds 300 nucleotides. While moving along the template polynucleotide from the 5'-end to the 3'-end, the ribosome, after some time, moves away from the 5'-terminal section of the template. As a result, this section becomes exposed and is capable of binding with another free ribosome. The second ribosome will start the readout, and, moving away from the 5'-terminus, will give the third ribosome an opportunity to bind and start reading, etc. In this way, moving along the template one after another, a number of ribosomes simultaneously perform a readout of the same information and, hence, synthesize identical polypeptide chains. This process is schematically presented in Fig. 7. The

structure in which the template polynucleotide is associated with many translating ribosomes is called the polyribosome. Under the electron microscope, both in the cell cytoplasm and in the cell-free system, polyribosomes resemble superunits created by ribosomes clustered in groups. All this is typical of both the prokaryotic and the eukaryotic protein-synthesizing machinery.

Informosomes

At the same time, a very striking difference between prokaryotes and eukaryotes exists. In contrast to prokaryotic mRNA, eukaryotic mRNA is complexed with proteins of unknown functions and exists as messenger ribonucleoprotein (mRNP). The nucleoprotein form of the existence of mRNA was discovered in cytoplasmic extracts of embryonic fish and sea urchin cells. Firstly, free non-ribosomal articles revealed as mRNA-protein complexes of a defined stoichiometry (protein to RNA mass ratio of about 3 : 1, buoyant density in CsCl of about 1.4 g/cm³) were found and called informosomes [15,16]. Similar particles were later detected by various workers in all animal cells and in the higher plants. Later, the cytoplasmic mRNA which is involved in the process of translation and is localized in polyribosomes was found to exist in the form of mRNA-protein complexes as well. As compared with free informosomes, the polyribosome-bound messenger ribonucleoproteins are somewhat less loaded with proteins (protein to RNA mass ratio is about 2 : 1, buoyant density in CsCl is about 1.45 g/cm³). The protein composition of polyribosomal mRNPs does not coincide with that of free informosomes, though some components may be common.

![Fig. 7. - Schematic representation of a polyribosome.](image)

Loose compartmentation of proteins on RNA

Besides, when studying the ribosome-free and informosome-free cytoplasmic extract, it was found that eukaryotic cells are characterized by the existence of special groups of proteins and protein complexes with strong non-specific activity for high molecular weight RNA, the so-called RNA-binding proteins [17]. They are absent in the cytoplasm of prokaryotic cells. For a long time these proteins were suspected to compose a pool of free informosomal proteins in the cytoplasm. More recently, however, it was found that the major components of free RNA-binding proteins do not coincide with the main polypeptides of free or polyribosomal informosomes [18]. In other words, only a smaller fraction of free RNA-binding proteins can be considered as a pool of informosomal proteins, whereas a predominant part of them appears to have a different destination.
The sets of RNA-binding proteins in the cytoplasm depend on cell types. But there are two major polypeptides with molecular masses of 95,000 daltons (for the homologous 70,000 daltons in plants) and 49,000 daltons which occur universally in all types of animal and plant cells. These two proteins have been identified as elongation factors of translation, EF-2 and EF-1, respectively [19]. Correspondingly, the isolated eukaryotic elongation factors EF-1 and EF-2, behave as typical RNA-binding proteins in all standard tests, in contrast to their prokaryotic analogs, EF-Tu and EF-G [20]. It is interesting that aminoacyl-tRNA synthetases have been also found among RNA-binding proteins of the eukaryotic cytoplasm (bacterial aminoacyl-tRNA synthetases lack such non-specific RNA-binding capability) [21]. The question arises as to the biological significance of the non-specific RNA-binding capability of elongation factors, aminoacyl-tRNA synthetases and a number of other proteins in the cytoplasm of eukaryotic cells.

In addition to ribosomal proteins and the proteins more or less firmly bound with mRNA (i.e. the proteins of polyribosomal mRNPs), the polyribosomal fraction of eukaryotic cells has been found to contain a large amount of loosely associated proteins [22]. An analysis has shown that almost all proteins loosely associated with polyribosomes are identical to the RNA-binding proteins present in the cytoplasm in the free state. In connection with this the association of translation factors (primarily of both the elongation factors EF-1 and EF-2) and aminoacyl-tRNA synthetases with eukaryotic polyribosomes has been demonstrated. Thus, there are grounds to believe that the RNA-binding proteins of the eukaryotic cytoplasm have a tendency to be localized on polyribosomes; evidently the proteins loosely associated with polyribosomes are in a dynamic equilibrium with the RNA-binding proteins. The result can be the formation of an increased local concentration (i.e. clouds) of these proteins around polyribosomes. A summarized scheme of the compartments of messenger ribonucleoproteins and RNA-binding proteins in the cytoplasm of the eukaryotic cells is presented in Fig. 8 [23].

It has been proposed that the non-specific affinity for RNA of a number of proteins serving translation is an evolutionary acquisition which provides for their increased local concentration or partial compartmentation near the sites of their functioning, i.e. around polyribosomes, in a big and complex volume of the eukaryotic cell [24]. The relatively low affinity of the proteins for mRNA and ribosomal RNA may result in the formation of such loose dynamic equilibrium constellations.

Since the proteins controlling translation are complexed with mRNA (informosomes) or loosely clustered around polyribosomes (dynamic constellations), protein synthesis can be regulated through alterations of the affinities of these proteins to RNA. For example, the removal of a repressor protein from the non-translatable mRNA may be a result of some modification of the protein, reducing or abolishing its affinity for RNA, on the other hand, the decrease of the non-specific affinity of a translation factor or an aminoacyl-tRNA synthetase for RNA as a result of a modification could induce deceleration of the total protein synthesis. Though a direct evidence in favour of such regulatory mechanisms is not yet available, a number of recent observations, such as phosphorylation of elongation factor 1 and ADP-ribosylation of EF-2 resulting in the loss of their affinity for RNA and release from the polyribosome fraction, are in good accordance with this hypothesis [25-27].

Fig. 8. Scheme of compartmentation of messenger ribonucleoproteins and RNA-binding proteins in the cytoplasm of the eukaryotic cell [23].

**Conclusion**

In conclusion it is necessary to emphasize some general peculiarities in the structural organization of eukaryotic cells. The cytoplasm of eukaryotic cells appears to be much more organized structurally than that of bacteria and other prokaryotes. The internal membrane network subdivides the eukaryotic cytoplasm into specific compartments, such as nucleus, endoplas-
mic reticulum, mitochondria, chloroplasts, etc. More dynamic polymer protein structures, such as microtubuli, microfilaments and intermediate filaments, form the so-called «cytoskeleton». The tendency to form multi-enzyme complexes and aggregates is especially displayed in eukaryotes. The messenger RNA and dynamic mRNA-ribosome complexes (polyribosomes) of the eukaryotic cytoplasm are accompanied by a large amount of bound proteins with both known and unknown functions. The RNA-binding capability of many proteins involved in mRNA biogenesis and its translation is a special evolutionary acquisition of eukaryotes. Their binding to high molecular weight RNAs ensures compartmentation of these proteins near the sites of their functioning in the big volume of the eukaryotic cell. Phosphorylation and ADP-ribosylation of the proteins may be a way for regulation of their RNA-binding activity and thus their compartmentation on nucleic acids. Effective regulation of translation in eukaryotes can be done through changes of the RNA-binding activity of aminoacyl-tRNA-synthetases and translation factors in this way.

References

The World Federation for Culture Collections met during the Vth International Conference on Culture Collections in Bangkok in December 1984, the theme of which was « International Resources for Biotechnology ». A new Executive Board and Committees were appointed. The Federation expressed itself much aware of the developments in Biotechnology and the need to respond to the requirements of workers in this expanding field. Accordingly the Executive Board and Committees have been active, meeting again in Helsinki in 1985 during GIAM 7, and ned in Manchester in 1986 during the ICM XIV.

Particular interest and activity has been in microbial information systems with special concern for the future of the World Data Centre following the retirement of Professor V.B.D. Skerman. The offer of the Life Science Research Information Section of the Institute of Physical and Chemical Research (RIKEN) Japan to take over this important resource has been accepted and a Steering Committee appointed to work with the relocated WDC on behalf of the Federation.

WFCC has also agreed to co-sponsor with CODATA the Microbial Strain Data Network and is thus strongly linked with developments in international computer data systems. To facilitate these developments a number of WFCC Executive Board members have been linked to DIALCOM, the electronic communication system to be used by MSDN, CODATA and the MIRCEN network and WFCC is anxious to join all Board members to the system.

There is concern that valuable genetic material may be lost through withdrawal of support from established collections and the Endangered Collections Committee has started a fund for assessing and relocating important collections of micro-organisms that are endangered. Start up funds have been received from IUMS.

The Education Committee has been particularly active. It has negotiated an agreement with Cambridge University Press to prepare a series of handbooks with the generic title « Living Resources for Biotechnology ». Royalties will go to the WFCC. Additionally, an educational video film is being made jointly with the Audio-Visual Centre at the University of East Anglia. The film (called « Back-up : Services from Culture Collections ») will be available in all video systems and translated into a number of languages. It is appropriate for final year microbiology degree students throughout the world and will be shown publicly at ICM XIV. Funds for these two projects have been made available from UNESCO and IUMS. Royalties from the video film will be shared between WFCC and UEA. The Education Committee is additionally preparing an on-line bibliography, a list of teachers for training courses, and Advisory Sheets. The latter will be of particular value to developing countries.

The Patents Committee and the Postal and Quarantine Committees have built up valuable working relationships with regulatory authorities. The WFCC has been represented by the Patents Committee at World Intellectual Property Organization meetings and is advising on the development and implementation of the Budapest Treaty.

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The Vth ICCC will be held in Maryland USA in 1988.

International Genetics Federation : IGF
Peter R. Day, Secretary General

The Federation exists to encourage cooperation and collaboration among geneticists of the world. It does this by planning and supporting international and regional congresses.

Planning for the 16th International Genetics Congress in Toronto, August 20-27, 1988 is now well underway. An international programme committee has been appointed and is considering symposium topics. The Congress President, Professor R. H. Haynes, has suggested that its theme should be « Human Control of the Germplasm ».

There are 40 member societies, representing geneticists in more than 33 countries.
International Commission on Microbial Ecology: ICONE
David Pramer, Secretary General

ICOME functions both as an International Commission on Microbial Ecology of the International Union of Biological Sciences (IUBS) and an International Committee on Microbial Ecology of the International Union of Microbiological Societies (IUMS). The Chairman and Executive Committee of ICOME maintain strong links with its parent organizations as well as with national microbiological societies throughout the world. Twenty-six national committees have named representatives to ICOME, and the International Association for Ecology (INTECOL) has appointed an ex-officio member to ICOME. The Executive Committee of ICOME presently includes Drs. W.D.P. Stewart (U.K.) Chairman, T. Rosswall (Sweden) past-Chairman, D. Pramer (U.S.A.) Secretary, V. Sundman (Finland) Member, and D. Toerien (South Africa) Member.

ICOME sponsors the Publication by Plenum Press of an annual series of books entitled «Advances in Microbial Ecology». The initial volume appeared in 1977 under the editorship of Dr. Martin Alexander of Cornell University. In 1981, Dr. Kevin Marshall of the University of New South Wales became editor. He works in collaboration with a Board that includes Drs. Ronald Atlas of the University of Louisville (U.S.A.), B.B. Jorgensen of the University of Aarhus (Denmark), and J.H. Slater of the University of Wales (U.K.). Available at the IUBS Secretariat are copies of the Table of Contents of the most recent volumes in the series. The individual papers are prepared by experts representing the highest standard of activity in the field.

ICOME also sponsors a series of International Symposia on Microbial Ecology which convenes at three year intervals. Previous conferences have met in Dunedin, New Zealand, Warwick, U.K., East Lansing, Michigan, U.S.A. and in Ljubljana, Yugoslavia. At the last conference, 1984, there have been more than 1,000 responses from 55 different countries.

ICOME, as a Commission or Committee or through its individual membership, has numerous interactions with various governmental and non-governmental organizations and international activities. It has in the past and will continue for the future to co-sponsor with other international organizations colloquia and workshops of a scholarly nature with regional or worldwide significance. An example of this type of event is the co-sponsorship by ICOME of the International Society of Limnology Third Workshop on the Measurement of Microbial Activity in the Cycling of Carbon in Aquatic Ecosystems, which took place in 1986.

ICOME met during the Symposium in Yugoslavia in August 86. Among the business conducted were the election of officers, the selection of a for the Fifth International Symposium on Microbial Ecology in 1989, that will take place in Maryland, USA.

International Committee on Plant Protection Congresses
E. Magallona, President

The 11th International Congress on Plant Protection (11th ICPP) will be held at the Philippine International Convention Center and the Philippine Plaza Hotel on October 5-9, 1987.

The following activities are envisioned for the 11th ICPP.

Four plenary sessions have been identified. In the opening plenary, an invited keynote speaker shall address the issue, «International Plant Protection : Focus on the Developing World». In the next three symposia, three or four experts of international reknown shall speak on the following topics.
1. International Plant Protection Efforts in Developing Countries;
2. International Challenges to the Agrochemical Industry;

Six regular symposia topics have been identified:
1. Crop Losses, Pest Biology and Ecology;
2. Pest Management Systems with Emphasis on Low Input Technology;
3. Conventional and Novel Pesticides : Action, Residues and Metabolism;
4. Plant Resistance to Pests;
5. Crop Protection in the Tropics;
6. Quarantine and Seed Health.

The Manila Declaration shall seek to address the issue of relevance. It shall identify a course of action for international cooperation against major pests especially those in the developing part of the world.
The International Association of Human Biologists
D.F. Roberts, Secretary General

1. Efforts have continued during the year for the development of contributions by human biologists to the Decade of the Tropics programme. A symposium was organised at Frascati, Rome, April 1st-4th 1985, on the theme of genetic variation and its maintenance in tropical human populations. (cf. page 2).

2. Newsletter No. 17 (January 1986) was distributed, giving information on the activities of the International Association of Human Biologists, the International Union of Biological Sciences, reports on a number of congresses and courses of international interest, and news items.

3. During the year two further Occasional Papers of the IAHB were published, one relating to the history of human biology in Australia and the other in Poland.

4. The Advisory Commission on Research of the IAHB continues to receive requests, particularly from colleagues in under-developed countries, for help in formulating and implementing research plans and analysing material. During the year, members were helped with translation of their articles into English for publication, and assisted in their research in other ways.

5. It is proposed to hold a General Meeting of the IAHB, as well as a business and Council Meeting, during the Lisbon Congress of the European Anthropological Association in October 1986.

A Major New Opportunity to Finance Biodiversity Preservation

by
Robert Goodland, Ecologist
The World Bank

In June, 1986, the World Bank promulgated a policy on the treatment of wilderness in development projects designed to aid significantly conservation in coming decades. The Bank recognizes that while further conversion of some natural land and water areas to more intensive uses will be necessary to meet development objectives, other pristine areas will yield more benefits to present and future generations if maintained in their natural state. These are areas which provide important environmental services or essential habitat for endangered or potentially economic species, among other values.

To prevent the loss of these special wildlands, the policy specifies that the Bank will normally decline to finance projects in these areas and instead prefers projects on already converted lands.

Conversion of even less important wildlands must be justified and compensated by financing the preservation of an ecologically similar area in a national park or nature reserve, or by some other mitigatory measures. The policy provides systematic guidance and criteria for deciding which projects need a wildland measure, which wildlands are in need of protection, and what types of wildland measures should be provided.

Further information may be obtained from the Office of Environmental and Scientific Affairs, the World Bank, 1818 H Street, N.W., Washington, D.C. 20433, USA.
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DIRECTIONS FOR INTERNATIONALLY COMPATIBLE ENVIRONMENTAL DATA — a CODATA Workshop —
This document reproduces position papers as received at the workshop organized by the ICSU Committee on Data for Science and Technology, 19-23 May, 1986, McGill University, Montreal, Canada. Limited number of copies of this document are available from CODATA, 51 Blvd de Montmorency, 75016, France; or in the USA, from the Numerical Data Advisory Board, National Research Council, 2101 Constitution Ave, Washington, D.C. 20418 USA.

GUIDELINES FOR SOIL SURVEY AND LAND EVALUATION IN ECOLOGICAL RESEARCH
By R.F. Breimer, A.J. van Kekem & H. van Reuler
Published by Unesco (MAB Technical Notes 17)
The major aim of this report is to help those working in the tropics on soil survey and pedological studies within an ecological perspective. It has been prepared in cooperation with the International Soil Reference and Information Center (ISRIC), based on studies undertaken by the authors based respectively in the Unesco Regional Offices in Montevideo, Nairobi and Jakarta.

INTEGRATED PLANT PROTECTION IN ORCHARDS
West Palaearctic Regional Section Bulletin of the IUBS Section for Biological Control, 1986 (247 pages).
The proceedings of the 7th Symposium on «integrated plant protection in orchards», held in Wageningen, the Netherlands, 26-29 August, 1985, includes 35 papers focusing on recent developments in the field of pest control. Particularly, the question of how integrated control could be implemented in practice, now that various methods are made available to the fruit growers.

INFLUENCE OF PESTICIDES ON THE BENEFICIAL FAUNA IN FRUIT TREES
West Palaearctic Regional Section Bulletin of the IUBS Section for Biological Control, 1986 (98 pages).
The various papers included in this issue were presented at the meeting held in Colmar, France, 29-30 October, 1985, dealing with the influence of pesticides, some growth regulators and other spraying material on the beneficial fauna in fruit trees.