Human evolution

Ecce Homo — behold mankind

Bernard Wood

We are incorrigibly curious about our origins, yet we are curiously ambivalent when confronted with the prospect of obtaining sound evidence about the emergence of modern humans 250,000 to 150,000 years ago. Developments in molecular biology have made available a new generation of molecular markers that can record events in the evolution of *Homo sapiens* that cannot be detected with conventional methods. In combination with advances that enable whole genotypes to be rapidly screened for distinctive sequences, they promise to provide a much more precise picture of the relationships between regional populations of modern humans. Last month, the Cold Spring Harbor Laboratory hosted a meeting* to take stock of the progress that has been made towards reconstructing our evolutionary history over the past 250,000 years.

The first attempts to recover what Darwin called the 'perfect pedigree of mankind' were based on head shape. However, once the genetic basis of inheritance was understood, and advances in biochemistry enabled researchers to detect variation at the molecular level, attention turned to blood groups, then to plasma proteins and later to enzymes, in the pursuit of what became known as molecular anthropology[1]. The deciphering of the genetic code eliminated the need to rely on phenotypic proxies for information about propinquity, and molecular anthropology was upstaged by direct comparisons between the genomes of individuals sampled from regional populations of modern humans.

The first rigorous attempts to relate regional populations used gene frequencies[2]. These are converted to genetic distances and then the relationships between populations are represented using a variety of 'tree-building' techniques. The variations in gene frequencies of 'trees' that are 'rooted' can be represented as 'surfaces' on maps[3]. When several of these apparently independent genetic systems have their root in the same geographical location this is interpreted as the likely origin of that population[4]. But frequency data are not readily resolved into the type of 'primitive' and 'derived' states that provide reliable evidence about the relationships between populations.

Although this first generation of studies could call upon substantial allelic variation for some of the genetic markers — HLA-A and HLA-B histocompatibility complex antigens, for example — few, if any, of the alleles are exclusive to any of the regional groups. If less widely distributed markers could be found, then these would define the evolutionary relationships between regional populations of modern humans with much greater precision. Such markers would be particularly effective if their own evolutionary history could be traced. Three polymorphic systems with the potential to provide such information are Alu inserts; short tandem repeats (microsatellites); and single-nucleotide polymorphisms.

A substantial part of our genome consists of short interspersed repeated DNA sequences about 300 base pairs in length. These are recognized and cleaved by the restriction enzyme, *Alu*I, and so are known as the Alu family of sequences. They are probably derived from an ancestral RNA gene that has been progressively amplified by a process called retroposition, and are only found in the genomes of primates. Each human genome contains upwards of half-a-million of these sequences, which make up some 5% of our DNA. Alu sequences have several advantages over traditional genetic markers. They are easily screened and stable (that is, newly inserted Alu elements rarely undergo deletion) and they represent unique events. Moreover, it is known that the Alu element is absent in the ancestral state[5].

At the meeting, M. Stoneking (Penn. State Univ.) reported the results of an analysis of eight Alu loci in the nuclear DNA of 1,500 people drawn from populations around the world. From their results, the investigators estimated that the major split between African and non-African populations occurred about 140,000 years ago; this date is consistent with evidence from mitochondrial DNA (mtDNA). Notably, Stoneking found that population samples from Sahul — that is, from Australia and New Guinea — are as close to the presumed ancestral state of the human Alu family as samples from African populations. This suggests that a migration to Southeast Asia may have been one of the first 'out of Africa' excursions of modern humans.

Whereas mtDNA traces phylogeny through the maternal line, evidence from the Y chromosome descends through the male line. The different relationships of the two systems provide the potential to investigate whether one, or other, sex migrated from the founding populations of modern humans. So far, attention has centred on the non-recombining part of the Y chromosome (P. Underhill, Stanford; M. Hammer, Univ. of Arizona). Underhill reported success in separating duplexes between the non-recombin-

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Evolutionary biology

Fungal foray

Some of the homobasidiomycete group of fungi, which includes most of the mushrooms with which we are familiar, have earned exotic names such as bird's nest and puffball because of the appearance of their fruiting bodies (the part of the fungus that produces the spores).

Traditional classification divides this group into the gilled fungi (which have fruiting bodies with a cap and a gilled underpart containing the spores) and the puffballs and relatives (in which the spores are enclosed within variously shaped fruiting bodies). The gilled species expel their spores by an elaborate ballistic mechanism (ballistospory) whereas the puffballs for instance slowly crumble, gently releasing their cargo. Although fruiting bodies are diverse in appearance their anatomy is very simple. This, coupled with the dearth of fossil evidence, has made it difficult to unravel the fungal family tree.

Writing in *The Proceedings of the National Academy of Sciences* (94, 12002–12006; 1997), David Hibbett and colleagues have tackled the complexities of fungal evolution by molecular analyses of

81 species. They compared the nucleotide sequences of various genes and drew up a family tree based on the similarity of sequences between different species.

It turns out that the same gill-and-cap style of fruiting body evolved at least six times. Furthermore, some of the puffballs and their relatives arose from their gilled cousins whereas others, such as the bird's nest fungus (*Crucibulum laeve*; shown here), developed independently. It seems that the group including the puffballs never evolved into gilled mushrooms — the authors surmise that ballistospory can develop into other forms of dispersal, but the reverse has not occurred.

Orla Smith

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ing regions of Y chromosomes using denaturing high-performance liquid chromatography with alkylated particles to exploit the differential retention of homo- and heteroduplex DNA molecules[6]. Although the report presented at the meeting was based on 93 biallelic markers, this group has detected more than 100 novel polymorphisms to date. They screened more than 900 Y chromosomes drawn from populations worldwide and identified 71 haplotypes. These could be broken down into five major haplogroups, upon which substantial regional localization was superimposed.

An ancient A-to-T transversion event determined the earliest branch in the tree, with the ancestral A allele being limited to a subset of modern Africans. All other contemporary peoples across the globe, together with the majority of African populations, display the mutant T allele. This suggests that most modern Y chromosomes are inherited from a single African male individual, a finding that is mirrored in females, as shown by evidence from mtDNA. But, in another presentation, P. de Knijff (Leiden Univ.) suggested that the relatively high recurrent mutation rate limited the effectiveness of Y microsatellite data to the interpretation of genetic affinities over the past 50,000 years. If de Knijff is correct, and if the origin of modern humans was 250,000 to 150,000 years ago, then this high rate would greatly reduce the usefulness of Y-chromosome polymorphisms for determining population relationships at this crucial time in human evolutionary history.

An alternative strategy, adopted by K. Weiss (Penn. State Univ.), is to opt for knowing a lot about a little. His group have concentrated on sequencing 10 kilobases of DNA in 142 alleles of a single gene, which encodes lipoprotein lipase. They found that even in their single gene system there is less 'order' and more recombination than is assumed by conventional models. Thus, the data from traditional and new genetic markers may not be as 'clean' as many researchers are assuming. A global study of mtDNA using restriction analysis and control region sequencing (D. Wallace, Emory Univ.) reaffirmed the relative antiquity of mtDNA samples from modern African populations. This study also points to some discrepancies between phenotypic and molecular evidence because the results show that samples of mtDNA from the Western and Eastern Pygmies of Central Africa are remarkably dissimilar, despite the close physical similarity of the two groups.

Where does all this new information leave us with respect to the origin of modern humans? Although none of the new evidence presented at the meeting contradicted the proposition that Africa is the source of much of modern human genetic variation, it failed to add more precision to the timing of the latest 'out of Africa' diaspora. Many factors, including population size and the degree to which physical barriers affected genetic admixture, influence estimates of the timing of these major population migrations[7]. We must hope that the new, more precise, analytical methods that are being developed will eventually add much-needed accuracy and precision to these attempts to trace modern human evolutionary history. □

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Nuclear physics

Doubly magical gamma decays

Philip Woods

The harmony of the periodic table in chemistry is a manifestation of the underlying quantum shell structure of the atom. Noble-gas elements with full electron shells are unreactive and have high ionization energies. The chemical properties of other elements can be understood in relation to these closed shells, whose location is solely defined by the atomic number Z, the total charge of the atomic nucleus. Similarly, the nucleus can be modelled in terms of neutron and proton shells, closed-shell nuclei having 'magic numbers' of neutrons or protons. But the presence of two varieties of particle leads to more richness and complexity in nuclei than in atoms. This can produce surprises, such as the one that Górska *et al.*[1] have now found in cadmium-98, a relation of the doubly magic nucleus, tin-100.

The first evidence for nuclear shell structure came from measurements of the masses of stable isotopes, and their natural abundances. It was found that nuclei with certain neutron (N) and proton (Z) numbers are abundant, and have high binding energies — they are very stable, in other words. Modern experiments are able to probe shell structures of nuclei very far from stability. Particularly revealing information can be obtained in studies of gamma-ray emission from excited states of nuclei at or near shell closures. Such states should have simple configurations that can be readily interpreted in terms of excitations with respect to a stable core. In general, one expects nuclei with closed neutron or proton shells to have high-lying excited states compared with the ground state, because particles must be promoted across a major shell gap to be excited.

This is indeed the case for the stable isotope ^{40}Ca, which has magic numbers of both neutrons and protons ($N = Z = 20$). ^{40}Ca is the heaviest stable nucleus to have an equal number of neutrons and protons. This stability can be attributed to its doubly magic nature. To remain stable, nuclei heavier than ^{40}Ca must have an excess of neutrons to compensate for the increasingly disruptive long-range electrostatic repulsion between the protons.

Doubly magic nuclei with $N = Z$ should be the ideal testing ground for the nuclear shell model because, to a good approximation, the neutrons and protons occupy the same quantum states. As their wavefunctions overlap, they tend to reinforce one another's structures, and hence shell effects should be amplified. Unfortunately, only two such nuclei exist beyond ^{40}Ca; they are ^{56}Ni ($N = Z = 28$) and ^{100}Sn ($N = Z = 50$). ^{100}Sn lies very far from stability, close to the proton drip-line — the point at which nuclei can spontaneously emit a proton from their ground states[2]. It was discovered three years ago at the GSI and GANIL laboratories, by fragmenting heavier nuclei[3,4] fired at fixed targets. These experiments demonstrated the existence of the ^{100}Sn nucleus, but did not yield insight into its structure. ▶

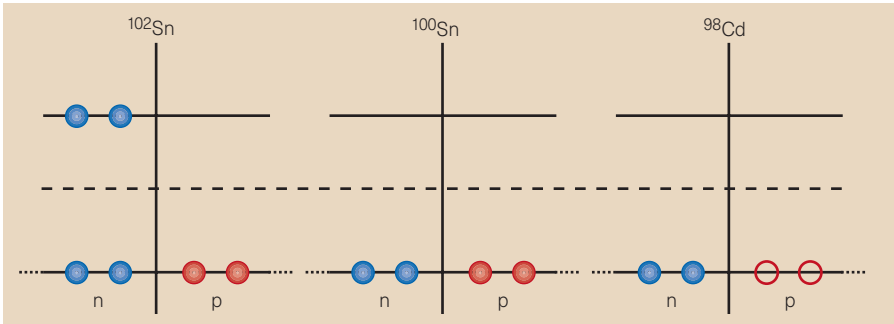

Figure 1 **The neutron and proton shell occupancies of ^{102}Sn and ^{98}Cd in relation to a core of ^{100}Sn, an unstable but symmetrical nucleus with 50 protons and 50 neutrons. ^{102}Sn has two extra neutrons, which must sit at higher energies in the next shell; ^{98}Cd has two proton 'holes' (hollow circles). The opposite behaviours of ^{98}Cd and ^{102}Sn hint at an unexpected breakdown of neutron–proton symmetry.**

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