of cytoskeletal proteins just inside the nucleus — and deform nuclear membranes, perturbing the distribution of nuclear-pore complexes and the ER.

Subsequent perforation of the nuclear envelope occurs not at the sites of invagination but on the opposite side of the nucleus, where tension is greatest. Once torn in this way the nuclear envelope catastrophically loses its shape, and cytoplasmic proteins flood into the nuclear space. It is not clear exactly how the initial perforation comes about. One clue comes from the finding that, in starfish embryos, the envelope becomes permeable to macromolecules (which are normally excluded from the nucleus by nuclear-pore complexes) before it is perforated[6]. So it is possible that microtubule-dependent changes in envelope structure might induce localized disassembly of nuclear pores, creating an epicentre for tearing.

The influx of cytoplasmic molecules that occurs after perforation might facilitate several mitotic processes, including chromosome condensation and spindle formation. Indeed, Beaudouin *et al.* show that chromosome condensation, which begins before nuclear-envelope breakdown, accelerates threefold after perforation. All in all, microtubule-dependent tearing seems to allow cells to tightly coordinate nuclear-envelope breakdown with spindle formation and chromosome dynamics.

Meanwhile Salina *et al.*[3] looked at the molecular basis of microtubule-dependent nuclear-envelope tearing, and find that cytoplasmic dynein becomes redistributed to the cytoplasmic face of the envelope before it invaginates. Once there, dynein associates with dynactin — an activator of dynein-mediated transport processes[9] — and pulls nuclear membranes and other envelope components along microtubules towards the centrosome.

It could prove challenging to work out exactly how dynein binds to the nuclear envelope. This protein is involved in many cellular processes and interacts with many structures and proteins. One possibility is that it associates with membranes through spectrin, a protein that — with dynactin — forms a lattice around organelles[10]. Whatever the case, dynein clearly transmits force across the nuclear envelope, as tearing disrupts both the inner and outer layers. This points to the possibility that dynein interacts with molecules associated with the nuclear-pore complexes, which span both layers. Another issue that needs to be resolved is how dynein is redistributed to the nuclear envelope from its usual cytoplasmic location in a cell-division-dependent way. Such redistribution might be controlled, at least in part, by the phosphorylation of dynein[11].

Might the mechanism described by Beaudouin *et al.*[2] and Salina *et al.*[3] be more generally applicable? The ER, mitochondria and Golgi apparatus all need to partition into daughter cells during mitosis, and a pulling and tearing mechanism dependent on dynein and microtubules could be at work here, too. In fact, the Golgi apparatus does split into two populations that follow centrosomes to different positions in the cell before being absorbed into the ER[12], and mitotic Golgi remnants have been shown to be swept towards centrosomes[13]. It remains to be seen whether or not dynein is involved. But its function in nuclear-envelope breakdown is now clear, and provides a good illustration of how two fundamental cellular processes — motor-driven transport and organelle breakdown — can be coordinated. ■

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Human evolution

Tangled genetic routes

Rebecca L. Cann

It is generally accepted that early human evolution took place in Africa, with human populations spreading from there. Using genetics to trace events in more detail remains a challenging task.

How best can the riches of human genetics be mined for information about our history and geography? In the tradition of human population genetics advanced over the past 50 years[1], the search is on for evidence of the isolation, adaptation and dispersal of populations over time. In this case, there is no digging for fossils, no three-dimensional reconstructions of skulls and such, just the requirement to collect 10-ml samples of blood. However, we are sometimes at a loss to disentangle population structure from population history. The diversity of DNA sequences in a modern population is an accumulation of events in the remote past. But it is unclear that the same forces that change allele frequencies (the incidence with which different gene forms occur) also change the genealogies of genes.

On page 45 of this issue[2], human phylogeographers — who study the geographical distribution of genealogical lineages using DNA sequence variation[3] — acquire a new approach to a recurrent problem. Alan Templeton[2] has analysed 11 different human gene trees with the program GEODIS[4]. His aim has been to assess the strength of the geographical signals they contain, using tests with nested clades (that is, groups of haplotypes — linked alleles — that are arranged by successively increasing numbers of mutations). His analysis provides strong genetic support for describing the geographical centre of our species as African, with at least two major population expansions from that continent about 600,000 and 95,000 years ago. He also establishes a platform to make specific estimates for important parameters of population structure, including the level of gene flow between populations isolated by distance. As a strong supporter of the idea of an African origin for modern people, in the words of Hamlet, "I eat the air, promise-crammed".

Current limitations in the methods used to reliably extract ancient DNA[5] have led molecular geneticists to concede the direct study of the earliest stages of our lineage's history to palaeoanthropology. So events well before 2 million years ago remain the province of those who hunt for and interpret fossil remains. But there is also a contentious debate over modern human origins that centres on the time period from 1.7 million to 20,000 years ago and the emergence of anatomically modern people. Genetic diversity in the human population today is consistent with a model of expansion, predominantly from Africa, between 100,000 and 50,000 years ago. From this breeding population of as few as 10,000 individuals, there followed a second expansion in Europe about 21,000 years ago[6,7].

Oscillations in climate are assumed to have resulted in an increased isolation of different groups, which would have promoted the 'fixation' of local adaptations in morphology, physiology and behaviour. Geographically distinct populations in Europe, Africa, South Asia, China and Australia could have had separate evolutionary trajectories if there were not enough migrants in each generation to spread any new mutations to populations in other regions. Proponents of multiregionalism believe that, after the initial expansion from Africa, populations continued to evolve

in different parts of the world, including Africa. This view places special emphasis on the role of migration in transferring new mutations affecting important human genes arising in geographically isolated groups. More migrants came from Africa, where there were bigger populations, in which greater numbers of new mutations would arise. But do the inferences of differential migration that are essential to this view hold up to scrutiny?

Templeton and other proponents of multiregionalism have criticized Afrocentric interpretations as incomplete, and an inaccurate reflection of how modern populations are and have been structured; they claim that researchers are confusing history with geography. This problem is one of the reasons that an approach incorporating methods known as 'spatial autocorrelation' and 'multidimensional scaling' has gained popularity. Here, patterns of genetic variation are compared with those predicted from theoretical models, and then used to estimate parameters such as levels of inbreeding, natural selection and gene flow[8]. But this approach ignores certain information in the sequences themselves. So it has not been as useful as phylogenetic analysis for identifying a major event in the evolution of allelic lineages within a species — such as a large population 'bottleneck' (in which, at some point in time, comparatively few individuals of a species exist, and so genetic diversity is limited).

In human evolutionary studies, methods that are commonly used to identify differences between species are often extended to the study of variation within a species. Templeton sees this as a major shortcoming in the genetic approach to human evolution. He argues that some morphological traits would fail to show regional continuity between populations over time, if they are not under the strong influence of natural selection, and that gene flow from dispersing and expanding groups is balanced by the presence of random genetic drift (the random loss of alleles over time through small population size). In his view, an estimate[9] that only 90% of the haplotype trees in the nuclear genome demonstrate African roots is clear evidence that regionally isolated, archaic populations were not completely replaced by immigrants of ultimate African origin. Templeton attempts to break this impasse in understanding by showing that what is needed is an analytical tool favouring neither model on an *a priori* basis.

What assumptions lie behind his GEODIS analysis? First, a null hypothesis states that there would no expected association between geography and a tree. Second, a plausible set of trees must be produced. Third, it is essential that the geographical sampling design is adequate. Also, the power of the analysis should increase if sampling includes greater numbers of unlinked regions of the genome — that is, regions inherited independently of others during cell division. Do these assumptions match the application in this analysis?

Gene positions, or loci, on chromosomes 14, 16, 21, X and Y, and those in mitochondrial DNA, were chosen, representing a maximum scan of about 13% of the human genome. Sequences that recombine (those essential to pigmentation, the immune response, oxygen consumption and glycolysis) were considered equally with those that do not (maternal and paternal markers), and with the apparently non-functional pieces of DNA known as microsatellite markers that are inherited from both parents and are presumed to be neutral. Some of the analysis required the pooling of samples from individuals from different locations in order to perform the nested cladistic analysis, and sample size varied from 35 to 1,544 individuals.

It therefore comes as no surprise that evidence for range expansion, long-distance dispersal and isolation by distance varied in strength between the genetic loci sampled. In this respect, Templeton's analysis shows how our current understanding, based on loci that are non-concordant in pattern and process even in the same populations, limits certainty about a global reconstruction of human evolution.

Any tool that helps to clarify the magnitude of genetic drift, population migration or natural selection, and directs the researcher to what is needed (more donors, more sequence), is helpful. But perhaps Templeton was over-ambitious in the scale of his analysis. Most specialists would consider the reconstruction of the human population expansion into Polynesia to be a relatively simple task compared to what Templeton has attempted. But I know only too well that analysis of blood from 35 donors taken from just one island was insufficient to describe the major roots of diversity on that island, although the Polynesian expansion was quite recent. Perhaps we will need a demonstration that GEODIS reveals the composite picture agreed upon by archaeology, genetics and linguistics in this area of the world before we can settle on how to interpret the varied signals uncovered by Templeton's analysis on a global scale. ■

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Daedalus

Solid cooling

The world's domestic refrigerators and air-conditioners all work on the same principle. A liquid is evaporated under low pressure, absorbing the latent heat of evaporation. Elsewhere the vapour is condensed under high pressure, returning that latent heat to a different system. The cycle then repeats. The snag is that the best fluid to use is a halocarbon, which damages the ozone layer. This wouldn't matter except that all refrigerators — especially those in cars — leak. New halocarbon is needed to top them up. So the whole halocarbon problem is merely one of bad plumbing.

Daedalus now has a way out: invent a solid working medium, which cannot leak, and the problem will go away. Most solids are so incompressible that only a small change of temperature with pressure seems feasible. Rubber, of course, warms when you stretch it, as the entropy of the molecules is increased. But Daedalus recalls that carbon nanotube is a valuable probe in an atomic-force microscope. If the force is excessive, the nanotube buckles and folds up totally. This solid collapse destroys the chemically resonant structure of the tube, but is fully reversible — remove the load and it springs straight and true again. Its resonance energy must be absorbed as heat in its collapse, and re-emitted in its recovery.

So DREADCO chemists are packing as much carbon nanotube as possible into a flexible solid, possibly rubber, looking for truly dramatic changes in temperature when the composition is deformed. A small bending or squashing should collapse the nanotubes strongly, so they lose their resonant energy and absorb heat. When the solid relaxes, the nanotubes will reform, lose energy as they reorganize, and deliver it as heat again. The result should be a working solid for a refrigerator.

A solid-state refrigerator poses unusual design problems. A big disc, cylinder or belt will carry the working solid, and will be rotated by a motor. Wheels on the periphery will deform it where cooling is desired, and release it to recover heat. The whole thing will be simple rather than efficient.

The DREADCO team reckon they will be lucky to get more than a few tens of watts of cooling; but with no plumbing to worry about, the new refrigerator should find a useful niche in the market. The automotive market is the obvious one. Efficiency is not very important, the device will not leak or stop working, and cooling power can be increased merely by speeding it up.

David Jones