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Genome sequencing

A grin without a cat

Paul R. Gilson and Geoffrey I. McFadden

In some types of unicellular algae, the chloroplasts have their own nucleus — a legacy of the time when the chloroplast was a free-living cell. The sequence of the genome in one such nucleus is now revealed.

The electronics industry's mania for miniatures has brought us nifty gadgets such as pocket PCs, handheld televisions and wristwatch phones. But these devices are giants compared with what nature can produce. On page 1091 of this issue¹, Douglas and colleagues present an extraordinary case of genetic miniaturization — the genome sequence of an amazingly small nucleus. The nucleus in question is the so-called nucleomorph of a cryptomonad alga, *Guillardia theta*, and its genome weighs in at a mere 0.55 million base pairs. Compared with the human genome (3,200 million base pairs)^{2,3}, this nucleomorph sequence is sub-Lilliputian. How can two blueprints be so different?

In fairness, the nucleomorph is not a complete nucleus but a relic, its genome having been distilled to its essence by hundreds of millions of years of enslavement. Nucleomorphs are the highly reduced nuclei of 'endosymbiotic' algal cells that, in the distant past, set up home within unicellular hosts to mutual benefit. Like their hosts, the endosymbionts were eukaryotic, meaning, loosely, that they had a nucleus. Importantly, they were also photosynthetic, feeding their hosts with the products of this chemical reaction — carbohydrates and oxygen.

Such microscopic gardening arrangements are common. But the cryptomonad endosymbiosis belongs to a special category known as secondary endosymbiosis, whereby the photosynthetic captive becomes an integral, enduring part of the host cell. In the case of *G. theta*, the endosymbiont became what is known as a complex chloroplast. Over time — perhaps as many as 600 million years — the nucleus of this endosymbiont lost most of its genes. Nevertheless, Douglas *et al.*¹ show that the tiny vestige, the nucleomorph, is a bona fide nucleus. It has the usual eukaryotic trappings: several linear chromosomes; introns (sections of DNA that interrupt the coding sequence of genes); possible centromeres (the regions on eukaryotic chromosomes to which the chromosome-separating apparatus attaches during cell division); and histones (proteins that are

swaddled by DNA). Indeed, the nucleomorph is a fairly typical nucleus but for two features — an impoverished complement of genes, and an almost complete lack of non-coding DNA.

Douglas *et al.* find that this cryptomonad nucleomorph has only 531 genes, whereas humans^{2,3} boast at least 31,000. But it is gene density that makes the two genomes so different. Genes make up a mere 1% of the human genome^{2,3}. The other 99% — often referred to as junk or non-functional DNA, which has largely unknown functions — may simply be the accumulated clutter of a system with slovenly housekeeping. Nucleomorphs, on the other hand, are the epitome of neatness and compactness. Many of the *G. theta* nucleomorph's genes have few or no spaces between them, and 44 genes even overlap, parsimoniously using both strands of the chromosomes, rather than the usual one¹. The human genome seems profligate by comparison. Indeed, the entire nucleomorph genome would fit comfortably in one of the many yawning gaps between human genes.

Why are these two genomes so different? Evolutionary forces that shape genome size are not well understood. But we believe that streamlining of the nucleomorph genome is unlikely to be driven solely by natural selection for minimal DNA content. Rather, it may be a result of uncontrolled DNA loss, and it is here that comparison of these two genomes might be enlightening. Unlike other human chromosomes, the Y chromosome has no complementary partner, so it cannot undergo recombination during meiosis (the type of cell division that generates gametes, such as eggs and sperm). Recombination is a process by which mutations — particularly insertions and deletions of sequence — can be weeded out in subsequent generations⁴. The absence of recombination has resulted in wholesale loss of DNA from the Y chromosome, which is now a mere stump with only 50 million base pairs^{2,3}. This chromosome persists, however, because it carries a handful of vital genes, in particular the testis-determining factors.

Nucleomorphs do not have sex chromosomes and each of the three chromosomes is thought to be paired⁵. Nevertheless, nucleomorph chromosomes are probably denied the normal opportunity to recombine because cryptomonad endosymbionts do not seem to undergo meiosis followed by genetic exchange with other nucleomorphs¹. We believe that this genetic isolation and consequent lack of error-correcting mechanisms has caused nucleomorphs to slide into mutational hyperdrive and wholesale DNA loss. But, just as the Y chromosome is maintained because it produces something vital (such as testicles), so too must the nucleomorph genome endure — in this case, because it encodes components of the chloroplast¹.

The interesting question really is not 'How did the nucleomorph genome get so small?', but rather 'Why did it stop where it did?'. Just as the Cheshire Cat in Lewis Carroll's *Alice in Wonderland* faded until only its grin remained, nucleomorphs too appear to have reached an end-point. This applies not only to cryptomonads but also to chlorarachniophyte algae, the nucleomorphs of which also have three chromosomes and similarly small genomes⁶. The nucleomorphs of these two types of algae were derived from different secondary endosymbioses^{1,7}, so why have their genomes condensed to a similar end-point? Douglas *et al.*¹ offer an attractive explanation.

Gene sequences from the *G. theta* nucleomorph indicate that, as in other eukaryotes, the DNA is wrapped around histone proteins, forming 'chromatin'¹. However, in contrast to other eukaryotes, nucleomorph chromatin apparently does not condense into higher-order structures during cell division⁸. Douglas *et al.* calculate that uncondensed nucleomorph chromosomes are only just short enough to fit inside a nucleomorph. If the nucleomorph DNA were packaged into fewer than three chromosomes, then those chromosomes would be too large to segregate during cell division. Conversely, if the DNA were separated onto more than three chromosomes, they might be too small to survive⁹.

As bonsai versions of the nucleus, nucleomorphs provide important genetic and evolutionary lessons. The path taken by cryptomonads and chlorarachniophytes to obtain chloroplasts, namely by engulfing other algal cells, is well worn. Most phytoplankton — the algal backbone of aquatic food chains — also acquired their chloroplasts in this second-hand way¹⁰. But in these phytoplankton, all genes have been transferred to the host nucleus from the engulfed nuclei, which have been lost. Nucleomorphs are kept only while they encode something necessary for survival, probably proteins required to operate and maintain the chloroplast.

Surprisingly, the nucleomorph¹ contains only 30 genes encoding proteins needed to operate the chloroplast, with most such proteins being encoded in the host nucleus. Why are these 30 genes still found in the nucleomorph? Perhaps gene transfer is incomplete, or perhaps (more likely) it is blocked in some way. There is insufficient evidence either way, but again the sequence of the chlorarachniophyte nucleomorph, which also encodes a mere handful of chloroplast proteins¹¹, might be informative. By determining the extent of overlap between these subsets of stranded genes, we will be able to formulate hypotheses about gene transfer from nucleomorphs, just as we have for mitochondria and simple chloroplasts^{12–14}.

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Earth science

Shaken, not stirred

Michael Manga

It is difficult to obtain a dynamic picture of the Earth's mantle. A study involving geophysical observations with geochemical implications shows that compositionally distinct megablobs contribute to the ebb and flow.

The slow and continual deformation of the Earth's mantle is seen in the motion of tectonic plates at the surface. Flow in the mantle is driven by density variations, which are caused by changes in temperature and composition. Unfortunately, the velocity, pattern and driving forces of flow cannot be observed directly in the mantle, as they can in other dynamic parts of Earth such as the oceans and atmosphere. Rather, studies of the Earth's deep interior rely on indirect geochemical and geophysical measurements that are sensitive to the Earth's structure and dynamics.

On page 1049 of this issue, Forte and Mitrova¹ combine a wide range of geophysical observations with mineral physics data — such as density and sound speed in minerals — to develop a model of global mantle flow and structure (Fig. 1a). They show that large-scale heterogeneity in the composition of the deep mantle may provide clues about the long-term evolution of the Earth.

The most tantalizing images of the Earth's interior have been obtained by studying the propagation of seismic waves generated by large earthquakes. Using a technique called seismic tomography — the geophysical analogue of a medical CAT scan — various properties of seismic waves, such as their travel times, can be used to infer the three-dimensional pattern of seismic-wave velocity in the Earth. It is tempting to translate wave propagation speeds into tempera-

ture variations in the mantle, and then to infer a model of flow. For example, waves will propagate slowly through regions that are hot, implying that such regions are less dense and will rise buoyantly. Conversely, faster waves imply a colder, denser region that will sink. Indeed, in the lower mantle the correlation of regions of fast waves with the expected locations of cold, subducted (sunken) oceanic plates (Fig. 1b) is usually used to argue that convection involves the entire depth of the mantle². That is, the mantle cannot consist of distinct, isolated layers that do not mix by convection.

Deducing flow patterns from wave speeds can sometimes be perilous, however. For example, the large, fast anomalies of seismic velocity in the upper mantle below many continents are probably due to differences in composition — the 'tectosphere' in Fig. 1b — rather than regions of sinking mantle³. Recent models based on seismic tomography⁴ also suggest that both compositional and thermal structures exist in the deep mantle⁵.

Forte and Mitrova¹ develop a global convection model based on mineral physics data — specifically, the dependence of density and seismic wave speeds on temperature and composition. Their model incorporates a large number of global geophysics observations, including gravity measurements, the motion of tectonic plates, and deformations at the Earth's surface and core–mantle boundary that are caused by flow. In short, it

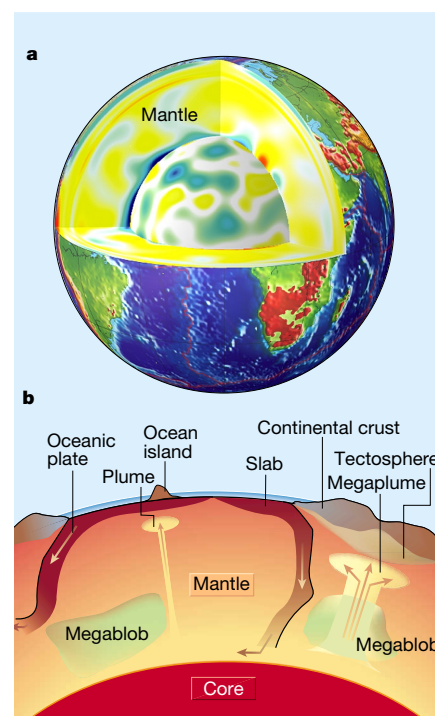


Figure 1 The interior structure of the Earth. a, A cutaway of the Earth, showing temperature variations in the mantle and changes in composition at the core–mantle boundary. (Courtesy of Forte and Mitrova.) b, The structure of the mantle, showing subducted slabs, the tectosphere and megablobs (discovered by Forte and Mitrova¹), which all influence temperature and flow (not to scale).

is the most comprehensive integrated study so far of mantle flow.

Forte and Mitrova verify that the whole mantle appears to act as a single convective system that is driven primarily by thermal anomalies. They also find evidence of large-scale compositional heterogeneity — megablobs — within the lower mantle. The magnitude of the density variations is sufficient to lead to the 'doming' mode of convection, in which large blobs of compositionally distinct mantle 'shake' — that is, the blobs move up and down every so often⁶. This finding is at odds with recent proposals that the deep mantle is convectively isolated from the rest of the mantle⁷.

The results are not definitive, because geodynamic models are limited by the reliability and availability of data. The models of Forte and Mitrova are even further limited by their use of simple assumptions about the composition of the lower mantle. But the new approach does provide a framework for incorporating improved seismic models and mineral physics data. In particular, much of the mineral physics data is extrapolated from measurements made at low pressures and temperatures, and will undoubtedly be refined.

The compositional variations and temperature anomalies mapped by Forte and