

line' of loading devices. This is the first time that systems of nanomachines, rather than individual devices, have been used to perform operations, constituting a crucial advance in the evolution of DNA nanotechnology.

The cargo-carrying DNA walkers² differ from Lund and colleagues' spiders¹ in that they have seven single-stranded DNAs appended: four 'feet' that move along the specially constructed surface, and three 'arms' to pick up nanoparticle cargoes. What's more, the feet are not DNAzymes. Instead, the walker's locomotion depends on single strands of DNA (anchor strands) that join together other single strands on the walker's feet and on the surface. When fuel strands are added to the system, they preferentially hybridize to these anchor strands, displacing the walker's feet and thereby freeing them. The authors thus control the binding and release of their walker's feet simply by adding anchor or fuel strands.

There are several interesting concepts lurking in these papers^{1,2}. Lund *et al.*¹ point out that macroscopic robots generally have to store a fair amount of information to provide "internal representations of their goals and environment and to coordinate sensing and any actuating of [their] components". Molecular robots, however, have limited ability to store such complex information. In both devices^{1,2}, the motion of the walkers is thus programmed into the DNA surface, rather than into the walkers themselves. Similarly, by setting the cargo-donating machines into predetermined loading or non-loading states, Gu *et al.*² also use information stored in the walker's environment to control the outcome of their system.

Another neat idea is Lund and colleagues' use of surface DNA strands¹ to control their spider's direction of movement, without which the spider would only randomly wander around on the surface. With shorter, cleaved binding sites behind it, and longer, uncleaved binding sites in front of it, the spider's time-averaged, net motion is weighted in the forward direction because its legs spend more time on the longer binding sites. The device thus creates a chemical gradient that controls its own behaviour.

Although both papers^{1,2} integrate DNA walkers with origami landscapes, they differ in one important respect. Lund and colleagues' device¹ is autonomous — no external intervention is required for it to execute the program built into the system. By contrast, Gu and colleagues' device² relies heavily on external interventions, most importantly the addition of new DNA strands to drive the movements of the walkers and the operation of the cargo-carrying DNA machines. The reward for this lack of autonomy is greater complexity of behaviour: whereas Lund and colleagues' robot is currently limited to walks along a path, Gu and colleagues' robot can pick up cargo while walking, and can adopt eight states that correspond to different manufacturing possibilities. Future work will seek to maintain autonomy

while ramping up the attainable complexity of behaviour programmed into molecular systems.

Although we remain far away from the possibilities imagined for nanotechnology by science fiction, it is inspiring nonetheless to see such creativity and rapid progress in the development of autonomous molecular systems that can execute complex actions. This is undoubtedly a field to watch. ■

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ORIGINS OF LIFE

Common ancestry put to the test

Mike Steel and David Penny

The question of whether or not all life on Earth has an ultimate common origin is a subtle one, complicated by the phenomenon of lateral gene transfer. It has now been tackled with a formal statistical analysis.

Charles Darwin predicted and biologists accept the theory that all extant life traces back to a common ancestor. But how can we formally test the idea? There is a compelling list of circumstantial evidence — for instance, the 'universal' genetic code. However, addressing the question of common origin by applying formal statistical tests to the vast array of molecular sequences now available from all domains of life has long been a challenge. On page 219 of this issue, Theobald¹ does just this, and concludes that the accepted view holds.

His approach starts with amino-acid sequences from 23 highly conserved proteins taken from groups that span the three domains of life (eukaryotes, bacteria and archaea). He then applies standard programs for inferring evolutionary trees (or networks) from the protein sequences. The third step is to compare the likelihood values of different models of sequence evolution, and thus different ancestry hypotheses, adjusting for the principle that larger numbers of free parameters are expected to give arbitrary improvement to how well a particular model fits the data. However, taking that into account, Theobald finds strong support for the unity of life compared with even two independent origins.

Perhaps the most interesting aspect of Theobald's work¹ is not the conclusion — common ancestry is the default view in science. But a formal test of evolution itself requires considerable ingenuity. Amino-acid sequence similarity alone does not imply common ancestry, because it might be due to convergent evolution. Lateral gene transfer between organisms and uncertainty about the best model of sequence evolution also confound statistical testing of common ancestry.

Theobald's paper reports strong support for the common-ancestry hypothesis over

alternatives proposing that any one of the three domains of life had a separate origin (including, for example, some archaea that seem to be genetically and morphologically distinct from other life forms). The findings are in line with a phrase from the much-quoted final paragraph of *On the Origin of Species* that "probably all organic beings which have ever lived on this earth have descended from some one primordial form".

Does this mean that life arose just once, more than 3.5 billion years ago? Not necessarily — logically, it is possible that life arose more than once, but that only one of these original life forms has descendants that survive today². It is also possible that there could have been more than one origin of life that has extant surviving descendants. The claim is simply that all known life has at least one common ancestor, a last universal common ancestor (LUCA). Such a LUCA may also not have been the first organism on Earth. These subtleties concerning origins have recently been discussed by the philosopher Elliot Sober³.

Theobald's analysis¹ is definitely not an argument for a 'tree of life' in place of a reticulate network that shows extensive lateral gene transfer, particularly in early life and in bacteria and archaea^{4,5}. Indeed, Theobald considers networks, and 9 of the 23 proteins he analyses are thought to have undergone horizontal transfer early in evolution. There is nothing here that is new. Darwin himself always referred to his "theory of descent with modification", a phrase that allows for gene transfer between an endosymbiotic organism (such as the mitochondrion precursor) and its host, or laterally between free-living organisms — it is the test of ultimate common origin that is the important part of the current paper.

For decades, biologists have been using

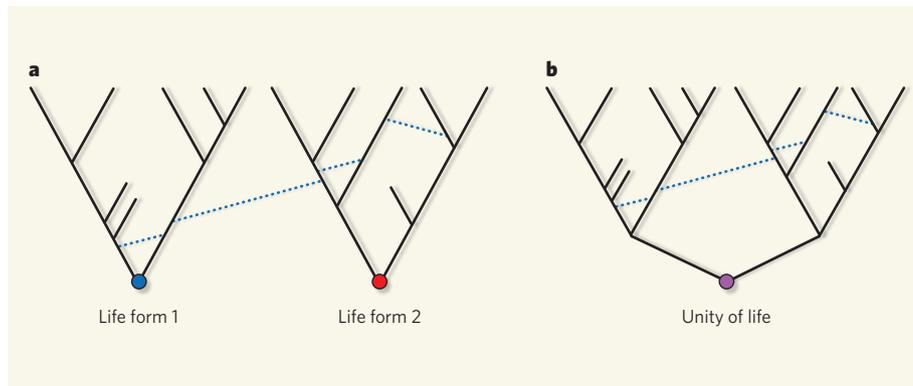


Figure 1 | Does extant life trace back to a common ancestor? **a**, The multiple-ancestry possibility: depicted here is life originating from two separate forms, with proteins with similar functions arising independently. Transfers, by endosymbiosis or by lateral gene transfers, are shown by dotted lines. **b**, A single origin (universal common ancestry), at least after the advent of protein synthesis. Correlations between patterns at different amino-acid positions are used to test between the two possibilities. The approach, as taken by Theobald¹, compares the likelihood values of how well different models of sequence evolution and ancestry fit the data, and compensates for differing numbers of parameters. The results give firm quantitative support for the unity of life.

DNA- and protein-sequence data to build phylogenetic trees and even a ‘tree of life’ that stretches across the eukaryotes, bacteria and archaea. It might be assumed that these trees directly demonstrate common ancestry. After all, the various parts of a tree are all connected, so all species will be descended from some ancestral point in the tree — a hypothetical ‘root’, the position of which may be unknown. The logical problem here is that tree-reconstruction methods will churn out a connected tree for any data, so we need more sophisticated arguments to test common ancestry.

More convincing evidence is the concordance of trees for the same set of taxa across different data sets. This was the basis of the first formal test, performed more than two decades ago, of the process of evolution from a common ancestor in the mammalian tree⁶. However, tree congruence can also be explained by other processes, and the use of model-selection methods such as the AIC (Akaike information criterion) has since been advocated as a way to test common ancestry⁷. This method, used by Theobald, makes it possible to compare the strength of support for different hypotheses across a range of models of sequence evolution. An AIC approach helps to adjust for the fact that, with enough free parameters in a complex model, we can explain just about any data.

So what is the signal in sequence data that provides the evidence for common ancestry? In essence, it is site-specific correlations in the amino acids between different species (Fig. 1). These correlations fall off as the coalescence between lineages in a tree becomes deeper in the past⁸, but if there are sufficient data, the correlations’ cumulative significance becomes statistically strong. Conversely, if two lineages have completely separate origins, correlations between amino-acid site patterns in the corresponding two extant species vanish.

As to how much the ‘tree of life’ is really a tree rather than a tangled network, the jury is still

out. One can see evidence for a dominant tree-like signal by using network-based methods that do not force data onto a tree. By contrast, if we ask people to quantify their subjective distances between different colours and run these distances through phylogenetic network software we get a ‘colour circle’ — nothing like a tree. Yet the same method, applied to distances from many genetic data sets, produces highly

tree-like networks, reflecting an underlying bifurcating evolutionary signal⁹.

Theobald’s work¹ is unlikely to be the last word on common ancestry. It is difficult to exclude all other explanations for correlations, and further work will probably address this problem. In the meantime, there is now strong quantitative support, by a formal test, for the unity of life. ■

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EARTH SCIENCE

Mountains without erosion

Yves Goddérès

Increased erosion associated with the rise of the world’s great mountain ranges has been held to be the cause of a prolonged episode of past climate cooling. That connection is now brought into doubt.

On page 211 of this issue, Willenbring and von Blanckenburg¹ argue that the rise of the Himalaya and other mountain ranges in geologically recent times did not result in a detectable increase in the transfer of eroded material from the continents to the oceans. The broader significance of this conclusion lies in a climatic connection. The implication is that mountain building, in part through oceanic sequestration of carbon-containing sediments, was not responsible for global climate cooling during the late Cenozoic — an interval of time starting about 40 million years ago.

During this time, intense tectonic activity resulted in the uplift of many large mountain ranges, including the Himalaya (Fig. 1, overleaf), the Andes and the Alps. Over the same interval, the climate became progressively colder². The major steps of this global cooling were the onset and growth of the Antarctic ice sheet from 34 million years ago, and the

freezing of the Arctic Ocean some 3 million years ago. A commonly held view is that the build-up of large mountains was responsible for this global cooling trend^{3,4}, the reasoning being as follows. Mountain uplift increases the global flux of eroded material to the sea, with this physical erosion having two consequences. First the dissolution of rock minerals is enhanced by the breaking of rocks into small pieces, and this chemical process consumes atmospheric carbon dioxide. Second, the high sedimentation rates promote the trapping of organic particles, thus sequestering the photosynthetic products of atmospheric CO₂ uptake and further cooling the climate⁵.

Willenbring and von Blanckenburg¹ challenge this widely accepted scenario. They first show that the global flux of eroded material reaching the ocean during the late Cenozoic remained roughly constant, despite the uplift of many mountain ranges. In particular, they