From its origins, life on Earth has been evolving, just not always in the way we thought. **Mark Buchanan** reports

Another kind of evolution

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JUST suppose that Darwin's ideas were only a part of the story of evolution. Suppose that a process he never wrote about, and never even imagined, has been controlling the evolution of life throughout most of the Earth's history. It may sound preposterous, but this is exactly what microbiologist Carl Woese and physicist Nigel Goldenfeld, both at the University of Illinois at Urbana-Champaign, believe. Darwin's explanation of evolution, they argue, even in its sophisticated modern form, applies only to a recent phase of life on Earth.

At the root of this idea is overwhelming recent evidence for horizontal gene transfer – in which organisms acquire genetic material "horizontally" from other organisms around them, rather than vertically from their parents or ancestors. The donor organisms may not even be the same species. This mechanism is already known to play a huge role in the evolution of microbial genomes, but its consequences have hardly been explored. According to Woese and Goldenfeld, they are profound, and horizontal gene transfer alters the evolutionary process itself. Since micro-organisms represented most of life on Earth for most of the time that life has existed – billions of years, in fact – the most ancient and prevalent form of evolution probably wasn't Darwinian at all, Woese and Goldenfeld say.

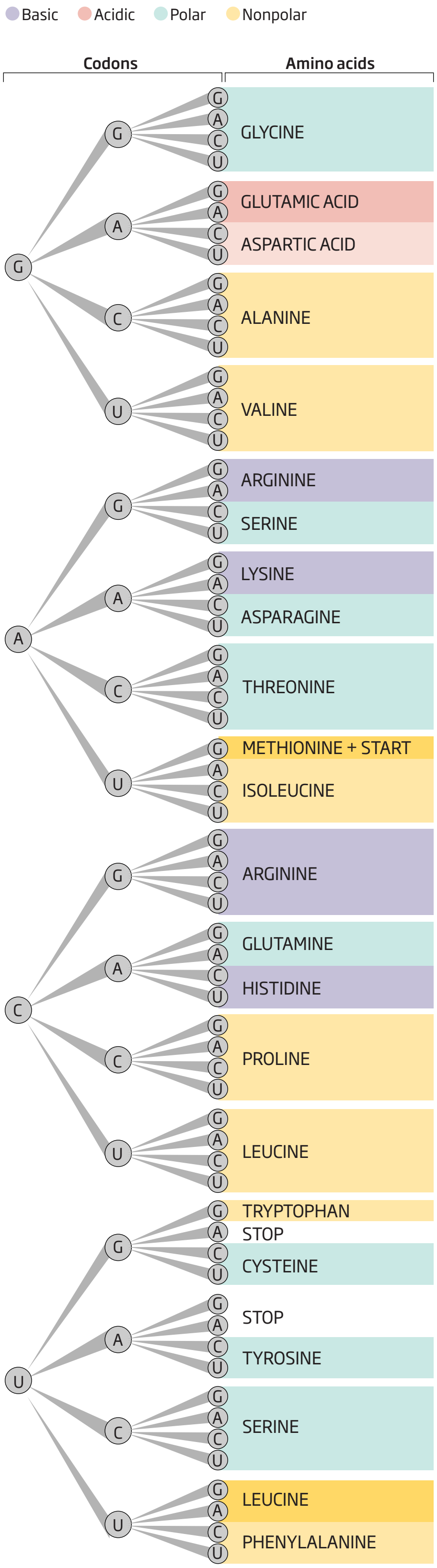
Strong claims, but others are taking them seriously. "Their arguments make sense and their conclusion is very important," says biologist Jan Sapp of York University in Toronto, Canada. "The process of evolution just isn't what most evolutionary biologists think it is."

Vertical hegemony

How could modern biology have gone so badly off track? According to Woese, it is a simple tale of scientific complacency. Evolutionary biology took its modern form in the early 20th century with the establishment of the genetic basis of inheritance: Mendel's genetics combined with Darwin's theory of evolution by natural selection. Biologists refer to this as the "modern synthesis", and it has been the basis for all subsequent developments in molecular biology and genetics. Woese believes that along the way biologists were seduced by their own success into thinking they had found the final truth about all evolution. "Biology built up a facade of mathematics around the juxtaposition of Mendelian genetics with Darwinism," he says. "And as a result it neglected to study the ›

The perfect code

The genetic code is built from four bases - A, U, C and G. They combine in groups of three to make codons, which code for amino acids. There are 64 possible codons, but only 20 amino acids, so there is more than one way to make most amino acids. Consequently, mutations that change a single base tend to produce little or no change in the resulting protein



most important problem in science – the nature of the evolutionary process."

In particular, he argues, nothing in the modern synthesis explains the most fundamental steps in early life: how evolution could have produced the genetic code and the basic genetic machinery used by all organisms, especially the enzymes and structures involved in translating genetic information into proteins. Most biologists, following Francis Crick, simply supposed that these were uninformative "accidents of history". That was a big mistake, says Woese, who has made his academic reputation proving the point.

In 1977, Woese stunned biologists when his analysis of the genetic machinery involved in gene expression revealed an entirely new limb of the tree of life. Biologists knew of two major domains: eukaryotes – organisms with cell nuclei, such as animals and plants – and bacteria, which lack cell nuclei. Woese documented a third major domain, the Archaea. These are microbes too, but as distinct from bacteria genetically as both Archaea and bacteria are from eukaryotes. "This was a enormous discovery," says biologist Norman Pace of the University of Colorado in Boulder. Woese himself sees it as a first step in getting evolutionary biology back on track. Coming to terms with horizontal gene transfer is the next big step.

In the past few years, a host of genome studies have demonstrated that DNA flows readily between the chromosomes of microbes and the external world. Typically around 10 per cent of the genes in many bacterial genomes seem to have been acquired from other organisms in this way, though the proportion can be several times that (*New Scientist*, 24 January 2009, p 34). So an individual microbe may have access to the genes found in the entire microbial population around it, including those of other microbe species. "It's natural to wonder if the very concept of an organism in isolation is still valid at this level," says Goldenfeld.

Lateral thinking

This is all very different from evolution as described by Darwin. Evolution will always be about change as a result of some organisms being more successful at surviving than others. In the Darwinian model, evolutionary change occurs because individuals with genes associated with successful traits are more likely to pass these on to the next generation. In horizontal gene transfer, by contrast, change is not a function of the individual or of changes from generation to generation, but of all the microbes able to share genetic material. Evolution takes place within a complex, dynamic system of many interacting parts, say Woese and Goldenfeld, and understanding it demands a detailed exploration of the self-organising potential of such a system. On the basis of their studies, they argue that horizontal gene transfer had to be a dominant factor in the original form of evolution.

Evidence for this lies in the genetic code, say Woese and Goldenfeld. Though it was discovered in the 1960s, no one had been able to explain how evolution could have made it so exquisitely tuned to resisting errors. Mutations happen in DNA coding all the time, and yet the proteins it produces often remain unaffected by these glitches. Darwinian evolution simply cannot explain how such a code could arise. But horizontal gene transfer can, say Woese and Goldenfeld.

"Early evolution may have proceeded through a series of stages before the Darwinian form emerged"

The essence of the genetic code is that sequences of three consecutive bases, known as codons, correspond to specific amino acids (see diagram, left). Proteins are made of chains of amino acids, so when a gene is transcribed into a protein these codons are what determines which amino acid gets added to the chain. The codon AAU represents the amino acid asparagine, for example, and UGU represents cysteine. There are 64 codons in total and 20 amino acids, which means that the code has some redundancy, with multiple codons specifying the same amino acid.

This code is universal, shared by all organisms, and biologists have long known that it has remarkable properties. In the early 1960s, for example, Woese himself pointed out that one reason for the code's deep tolerance for errors was that similar codons specify either the same amino acid or two with similar chemical properties. Hence, a mutation of a single base, while changing a codon, will tend to have little effect on the properties of the protein being produced.

In 1991, geneticists David Haig and Lawrence Hurst at the University of Oxford went further, showing that the code's level of error tolerance is truly remarkable. They studied the error tolerance of an enormous number of

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hypothetical genetic codes, all built from the same base pairs but with codons associated randomly with amino acids. They found that the actual code is around one in a million in terms of how good it is at error mitigation. “The actual genetic code,” says Goldenfeld, “stands out like a sore thumb as being the best possible.” That would seem to demand some evolutionary explanation. Yet, until now, no one has found one. The reason, say Woese and Goldenfeld, is that everyone has been thinking in terms of the wrong kind of evolution.

Working with Kalin Vetsigian, also at the University of Illinois at Urbana-Champaign, Woese and Goldenfeld set up a virtual world in which they could rerun history multiple times and test the evolution of the genetic code under different conditions (*Proceedings of the National Academy of Sciences*, vol 103, p 10696). Starting with a random initial population of codes being used by different organisms – all using the same DNA bases but with different associations of codons and amino acids – they first explored how the code might evolve in ordinary Darwinian evolution. While the ability of the code to withstand errors improves with time, they found that the results were inconsistent with the pattern we actually see in two ways. First, the code never became shared among all organisms – a number of distinct codes remained in use no matter how long the team ran their simulations. Second, in none of their runs did any of the codes evolve to reach the optimal structure of the actual code. “With vertical, Darwinian evolution,” says Goldenfeld, “we found that the code evolution gets stuck and does not find the true optimum.”

Horizontal is optimal

The results were very different when they allowed horizontal gene transfer between different organisms. Now, with advantageous genetic innovations able to flow horizontally across the entire system the code readily discovered the overall optimal structure and came to be universal among all organisms. “In some sense,” says Woese, “the genetic code is a fossil or perhaps an echo of the origin of life, just as the cosmic microwave background is a sort of echo of the big bang. And its form points to a process very different from today’s Darwinian evolution.” For the researchers the conclusion is inescapable: the genetic code must have arisen in an earlier evolutionary phase dominated by horizontal gene transfer.

Goldenfeld admits that pinning down the details of that early process remains a difficult task. However the simulations suggest that horizontal gene transfer allowed life in general to acquire a unified genetic machinery, thereby making the sharing of innovations easier. Hence, the researchers now suspect that early evolution may have proceeded through a series of stages before the Darwinian form emerged, with the first stage leading to the emergence of a universal genetic code. “It would have acted as an innovation-sharing protocol,” says Goldenfeld, “greatly enhancing the ability of organisms to share genetic innovations that were beneficial.” Following this, a second stage of evolution would have involved rampant horizontal gene transfer, made possible by the shared genetic machinery, and leading to a rapid, exponential rise in the complexity of organisms. This, in turn, would eventually have given way to a third stage of evolution in which genetic transfer became mostly vertical, perhaps because the complexity of organisms reached a threshold requiring a more circumscribed flow of genes to preserve correct function. Woese can’t put a date on when the transition to Darwinian evolution happened, but he suspects it occurred at different times in each of the three main branches of the tree of life, with bacteria likely to have changed first.

Today, at least in multicellular organisms, Darwinian evolution is dominant but we may still be in for some surprises. “Most of life – the microbial world – is still strongly taking advantage of horizontal gene transfer, but we also know, from studies in the past year, that multicellular organisms do this too,” says Goldenfeld. As more genomes are sequenced, ever more incongruous sequences of DNA are turning up. Comparisons of the genomes of various species including a frog, lizard, mouse and bushbaby, for example, indicate that one particular chunk of DNA found in each must have been acquired independently by horizontal gene transfer (*Proceedings of the National Academy of Sciences*, vol 105, p 17023). “The importance of this for evolution has yet to be seriously considered.”

No doubt there will be resistance in some quarters, yet many biologists recognise that there must be a change in thinking if evolution is finally to be understood in a deep way. “The microbial world holds the greatest biomass on Earth,” says Sapp, “but for most evolutionists it’s a case of ‘out of sight, out of mind’. They tend to focus on visible plants and animals.”

If a paradigm shift is pending, Pace says it will be in good hands. “I think Woese has done more for biology writ large than any biologist in history, including Darwin,” he says. “There’s a lot more to learn, and he’s been interpreting the emerging story brilliantly.” ■

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