

A new domain of life | Plenty more bugs in the sea

Tantalising evidence is emerging of a serious gap in biologists' understanding of the diversity of life on Earth

LIFE, like Caesar's Gaul, is divided into three parts. The Linnaean system of classification, with its prescriptive hierarchy of species, genus, family, order, class, phylum and kingdom, ultimately lumps everything alive into one of three giant groups known as domains.

The most familiar domain, though arguably not the most important to the Earth's overall biosphere, is the eukaryotes. These are the animals, the plants, the fungi and also a host of single-celled creatures, all of which have complex cell nuclei divided into linear chromosomes. Then there are the bacteria—familiar as agents of disease, but actually ecologically crucial. Some feed on dead organic matter. Some oxidise minerals. And some photosynthesise, providing a significant fraction (around a quarter) of the world's oxygen. Bacteria, rather than having complex nuclei, carry their genes on simple rings of DNA which float around inside their cells.

The third great domain of life, the archaea, look, under a microscope, like bacteria. For that reason, their distinctiveness was recognised only in the 1970s. Their biochemistry, however, is very different from that of bacteria (they are, for example, the only organisms that give off methane as a waste product), and their separate history seems to stretch back billions of years.

But is that it? Or are there other biological domains hiding in the shadows—missed, like the archaea were for so long, because biologists have been using the wrong tools to look? That is the question asked recently by Jonathan Eisen of the University of California, Davis, and his colleagues. They suspect there are, and in a paper just published in the *Public Library of Science*, they present an analysis which suggests there might indeed be at least one other, previously hidden, domain of life.

What I did on my holidays

The data from which this conclusion was drawn were collected between 2003 and 2007 on one of the most scientifically productive holidays in history. This was a round-the-world cruise taken by Craig Venter on his yacht, *Sorcerer II*, which studied the diversity of micro-organisms in the Atlantic, Pacific and Indian oceans.

Dr Venter was working out his frustrations after having been fired in 2002 from Celera Genomics, a company he helped set up in 1998 with the specific aim of sequencing the human genome faster and better than the public Human Genome Project was managing at the time. In that, it succeeded. In the wider aim of turning such knowledge into hard cash, however, it was nowhere near as successful as its financial backers had hoped. Dr Venter therefore found himself with more time on his hands than he had been planning.

His killer app in Celera's assembly of the human genome was a technique called shotgun sequencing. This first shreds a genome into pieces small enough for sequencing machines to handle, then stitches the sequenced pieces back together by matching the overlaps using a computer. In principle, he realised, that trick could be used on mixed DNA from more than one organism. A good enough program would stitch together only fragments from the same type of creature. This would allow you to see what was living in a sample without having to culture anything. And since a huge majority of micro-organisms (by some estimates, 97%) cannot be cultured, that sounded like a great idea.

Metagenomics, as the new technique is known, has vastly extended knowledge of what bugs live in the sea—and in many other places, from hot springs to animals' guts. It is not perfect. In practice a lot of what emerges are fragments of genomes, rather than complete assemblies. But it has been enormously successful at identifying previously un-



known individual genes.

Dr Eisen wondered if it could be pushed still further. He started combing through the data from the cruise to look for new forms of genes that have, in the past, proved useful in distinguishing bacteria, archaea and eukaryotes from each other, to see if there are any other domains of life out there. After a false start pursuing what are known as ribosomal RNA genes—which are involved in protein synthesis and are believed by some people to be the genetic core around which the rest of life accreted—he lighted on two genes called RecA and RpoB. RecA is involved in DNA recombination. RpoB is involved in translating DNA into RNA. Both, like the genes for ribosomal RNA, are old and ubiquitous. And lo, when he drew trees that tracked the evolutionary relationships between all the RecAs and all the RpoBs found on the cruise, he discovered parts of the trees that did not fit with the pattern established by known versions of these genes in the public genetic databases.

Some of these novel branches were, nevertheless, similar enough to known branches to be accounted for as known unknowns. But both RecA and RpoB had one branch that really was an unknown unknown. Neither of these branches fits in the existing tree of life. And that is a mystery. It may be that they belong to some as-yet-uncharacterised group of viruses (entities classified outside Linnaeus's system, since there is no agreement about whether they are alive or not). Or it may be that they belong to a fourth domain of living organism. Either way, it suggests a profound lacuna in biologists' understanding of the world. The question is, is it a big lacuna as well as a deep one? Is the new group an important part of the biosphere?

That is hard to say at the moment. The genes concerned are rare in the overall metagenomic analysis, so creatures carrying them may not be abundant. On the other hand, those creatures might just be too small to be caught easily by the filters used to winnow life from water for analysis in the first place.

As to importance, when originally identified as distinct, the archaea, too, were regarded as marginal—yet their methane-generating properties are now a factor in climate-change calculations. If the new domain is real, it must have been around for several billion years, and must thus have something going for it. What that something is remains to be seen. ■