Carl Woese

(1928–2012)

Discoverer of life's third domain, the Archaea.

Carl Woese brought a fiercely creative mind, seasoned with rigour, to the biggest questions in biology. By showing almost single-handedly that living organisms fall into three domains — Bacteria, Eukarya and a previously unknown group called the Archaea — he transformed our understanding of how living organisms are related and how they evolved.

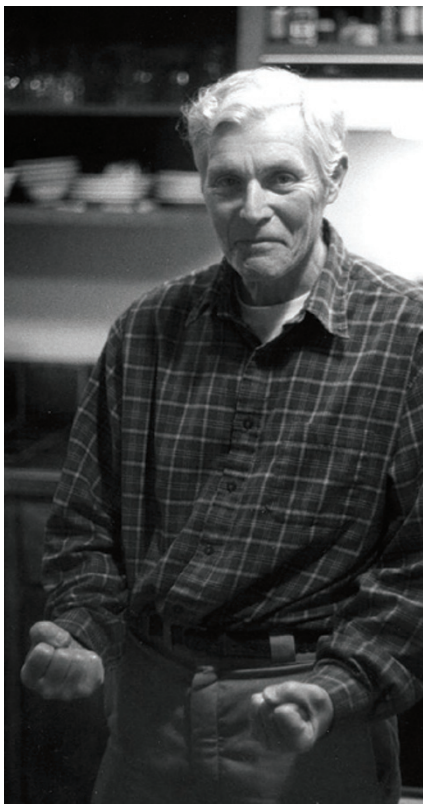
Woese, who died on 30 December, was born in Syracuse in New York in 1928. His undergraduate education was in physics and mathematics at Amherst College in Massachusetts. In 1953, he earned a PhD in biophysics from Yale University in New Haven, Connecticut.

After taking up a research position at the General Electric Research Laboratory in Schenectady, New York, Woese began thinking about the evolution of the genetic code. In 1964, the molecular biologist Sol Spiegelman recruited him to the microbiology department at the University of Illinois in Urbana, where he spent his entire academic career.

At Illinois, Woese examined the nucleotide sequences of 5S ribosomal RNA (a component of ribosomes, which build proteins) from different organisms. He quickly realized that ribosomal RNA is an ideal chronometer for measuring evolutionary distances between living things. It has a slow mutation rate, performs an identical function in all organisms and, because ribosomal RNA interacts specifically with a multitude of proteins, the genes encoding it are unlikely to jump between individuals of different species.

Woese had discovered a window into microbial phylogeny. Until this point, the field had been hopelessly muddy, with identifications of microorganisms based on qualitative characteristics such as differences in shape. In the early 1970s, Woese realized that the sequence of 5S ribosomal RNA contained too few nucleotides (120) to provide a way to classify thousands of organisms. This led him to take on the daunting task of analysing 16S ribosomal RNA, which contains more than 1,500 nucleotides.

Woese began sequencing fragments of 16S ribosomal RNA from every microorganism that he could get his hands on, using RNA 'fingerprinting' — a method developed by British biochemist Fred Sanger. The technique involves separating fragments of RNA in an electric field according to their nucleotide compositions. Woese's enormous undertaking, which involved analysing more than 100 organisms and spanned many years, paid off richly.



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One day, the analysis of 16S RNA from a methane-producing organism gave an astonishing result. The familiar pattern of the 100 or so spots, each containing small stretches of RNA, was altered in an unusual way. Several spots present in all bacterial 16S ribosomal RNAs were missing. New spots had appeared, corresponding to ribosomal RNA sequences never seen before. Woese had captured the signature of a different domain of life.

The ribosomal RNAs of some other microorganisms also produced this strange pattern, including those of 'extremophiles', some of which live at temperatures up to 100 °C and secrete sulphuric acid. In 1977, Woese and his postdoc George Fox published their discovery of 'archaebacteria' (now called Archaea) in the *Proceedings of the National Academy of Sciences*, proposing that these organisms were as distantly related to bacteria as bacteria are to eukaryotes.

As well as transforming our understanding of the relationships between living things, Woese's analysis had an impact on ribosome biology. Woese realized that one could use RNA sequences to determine the double-helical folding, or secondary structure, of RNA molecules. Woese and I used this approach to work out the secondary structures of 16S and 23S ribosomal RNA. These comparisons identified the nucleotides in ribosomal RNA that are universally conserved — and therefore crucial to its function — at a time when many believed that the RNA served merely as a structural scaffold for ribosomal proteins.

Woese's work also spawned a new branch of microbiology: the use of sequence analysis to study natural microbial populations. Combining phylogenetic sequence analysis and the polymerase chain reaction — which amplifies DNA fragments into thousands or millions of copies — makes it possible to identify the microbes in samples from any source, including the ocean and the human body.

At first, Woese's discovery of the Archaea was met with scepticism and even hostility. This, combined with Woese's view of himself as a rebellious outsider, resulted in an often polemical writing style. He took on adversaries as formidable as microbiologist Roger Stanier, taxonomist Ernst Mayr and even Charles Darwin. Yet Woese eventually received the recognition he deserved, including the Crafoord Prize in Biosciences from the Royal Swedish Academy of Sciences in 2003.

Carl once confided to me that a key to his success was "the principle of dynamic incompetence". Visitors to Carl's lab were certainly impressed by his indifference to the mountain of unopened post. His wife Gabriella became so concerned that she persuaded him to let her open the envelopes; among them, she found one with a months-old Dutch postmark. The letter informed Carl that he had been awarded the Leeuwenhoek Medal by the Royal Netherlands Academy of Arts and Sciences — an honour that is given only once a decade and that he shares with Louis Pasteur.

Carl will be deeply missed by colleagues, friends and family. His impact on our understanding of biology is irreversible. ■

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