is often difficult to convince scientists of something revolutionary. Carl Woese was no exception. People dismissed his concepts as crazy. But today, every introductory text book on biology starts with the introduction to kingdoms of life as proposed by Whittaker followed by the three domain classification proposed by Carl Woese.

Most of the genomics work – whether the human genome project or metagenomics or sequencing – being carried out today is the result of exemplary work by this revolutionary scientist who re-constructed the tree of life. Carl Woese passed away on 30 December 2012 after a prolonged illness at the age of 84.

Born 15 July 1928, in Syracuse, N.Y., Carl Richard Woese received his bachelor’s degrees in maths and physics from Amherst College in 1950. There, he was inspired to pursue science as a career by physicist William Fairbank. Later, Woese began doctoral studies in biophysics under the guidance of Yale University physicist Ernest Pollard, whose contributions to the use of radar in World War II earned him a permanent place in the history of radiation physics.

For his doctoral thesis, Woese studied how radiation and heat could inactivate viruses like Newcastle disease virus, which afflicts poultry. Woese graduated from Yale in the year 1953, a standout year in molecular biology’s history that was marked by the discovery of the double helical structure of DNA. He studied medicine for two years at the University of Rochester but discontinued it and returned to postdoctoral research in Pollard’s laboratory, focusing on the molecular changes underlying the germination of dormant spores of the bacterium Bacillus subtilis. In the next five years, Woese documented the formation of parts of the bacterial protein-synthesizing machinery – the ribosome – as the slumbering bacteria emerged from the spores, and studied how radiation could be used to inactivate the spores.

At the end of his postdoctoral period, in the fall of 1960, Woese set up his own laboratory at General Electric’s Research Laboratory in Schenectady, New York, where he continued to explore the molecular biology of spore germination. In 1964, he joined the University of Illinois as professor of microbiology and continued in service till his death on 30 December 2012.

Coming from a physics background, Carl Woese’s early attraction towards molecular biology happened during the 1960s mainly because of his interest in the genetic code and RNA. Woese realized that the ribosomes held the key to the construction of the phylogenetic tree of the main domains of life. Ribosomes interpret the messenger RNA molecules (mRNA) carrying instructions from the DNA of the cell, and together with transfer RNA (tRNA) construct the proteins encoded in the genome. One form of tRNA named 16S turned out to be the yardstick of choice for evolutionary comparison, largely because the molecule forms a part of the protein-making machinery at the heart of all cells.

Woese focused on rRNA as a molecular marker because of its unique biological and molecular attributes. First among these is its universality. Second, is its central role in protein synthesis. The universal role in protein synthesis is expected to constrain sequence variation among the rRNA molecules of different organisms. Likewise, a requirement to interact precisely with many different proteins in the functional ribosome will constrain sequence evolution for rRNA. For these reasons sequence evolution of rRNA is expected to be unusually conservative.

Indeed, evolving proteins in general turn out to be much more “volatile” than rRNA. This, in turn makes the rRNA marker an unusually robust phylogenetic probe for studying long evolutionary distances. Likewise, rRNA genes are most often found in multiple copies in genomes of both prokaryotes and eukaryotes. In other words, horizontal transfer would not be as great a problem for phylogeny based on rRNA as it is for phylogeny based on proteins. This distinction has been verified by the fact that out of all the thousands of sequenced rRNA genes in public databases, no genome has been found to contain alien rRNA sequences completely replacing the original RNA complement. Further, the molecule’s universality meant that it was unlikely to be shuttled laterally among organisms, unlike other genes that were likely swapped freely in a still-evolving evolutionary soup.

In 1966, when Fred Sanger developed the nucleic acid sequencing technology, Woese realized the relevance of this technology in phylogenetic studies. The only thing that confused him was which organism to start with. Ralph Wolfe, his colleague in
the microbiology department at Illinois suggested methanogens. Methanogens are united as a group by their unique biochemistry that involved a set of unusual coenzymes but morphologically this group consists of diverse organisms. Methanogens had been lumped in with the prokaryotes because they 'looked' like bacteria.

Togethers with then-postdoctoral fellow George Fox, graduate students Mitchell Sogin and William Balch, technician Linda Magrum, and others, Woese meticulously assembled a database of differences in 16S rRNA among a long list of microbes that included both eukaryotes and prokaryotes. Ribosomal RNA (16S) has proved to be an excellent molecular chronometer by which to measure the evolutionary distances encountered in the bacterial world. When Woese finished examining their rRNA sequences, he found these methanogens were no more related to prokaryotes than they were to eukaryotes. They were different and they found a third form of life.

In 1977, in one of the most seminal publications in the history of modern biology, Carl Woese and George Fox started the scientific community by announcing the discovery of what would be called Archaea, a category of single-cell microbes genetically distinct from the two groups previously believed to comprise living organisms: prokaryotes, which include bacteria, and eukaryotes, which include plants and animals.

By using ribosomal RNA they demonstrated that it was possible to identify and classify microbes by intrinsic characteristics of their biological sequences.

The paper was published in the Proceedings of the U.S. National Academy of Sciences (PNAS) on 3 November 1977. This marked the birth of molecular phylogeny, a technique that would soon revolutionize studies in the realms of microbiology and evolution.

But their discovery of the third domain was met with stiff opposition. Nobel Laureate Salvador Luria was critical of this discovery and dubbed it a scientific fakery. Woese continued his work with other archaeobacterial groups like Thermoplasma, Sulfolobus acidocaldarius etc. In 1980, he along with Fox published "The phylogeny of prokaryotes" in the journal Science. In this paper he outlined his "Big Tree", a phylogenetic tree that covered all of life.

In 1996, Woese and colleagues (University of Illinois professor Gary Olsen and researchers from the Institute for Genomic Research) published in the journal Science the first complete genome structure of an archaeon, Methanococcus jannaschii. Based on this work, they concluded that the archaea are more closely related to humans than to bacteria. “The Archaea are related to us, to the eukaryotes; they are descendants of the microorganisms that gave rise to the eukaryotic cell billion of years ago,” Woese said at the time.

The publication of the genome helped to suppress ongoing resistance to the idea of a third domain of life. In two papers that were published in 1998 and 2000, Woese proposed a new model to replace the standard Darwinian theory of common descent – that all life on Earth evolved from a single cell or pre-cell. Woese proposed instead that various forms of life evolved independently from as many as several dozen ancestral pre-cells. A 2004 paper further postulated that Darwinian natural selection did not become a factor in evolution until more complex life forms evolved. Woese argued that in the early stages of the development of life, all organisms engaged in horizontal gene transfer and were not in competition.

Before Woese’s revolution, members of the Archaea were considered to be rare, "weird" forms of bacteria which had hardly any relevance to the biosphere. Today, we know that Archaea are present everywhere in the environment and they don’t have much similarity with bacteria.

Carl Woese won many prizes, including election to the National Academy of Sciences (1988) and the Royal Society (2006), MacArthur Fellow (1984), the Leeuwenhoek Medal (the highest honour for microbiologists, given by the Royal Netherlands Academy of Arts and Sciences once every decade; 1992), National Medal of Science (2000), and the prestigious Crafoord Prize by the Royal Swedish Academy of Sciences (2003). Sadly, he and his co-workers were never bestowed a well-deserved Nobel Prize.

As Dr. Nigel Goldenfeld, leader of the IGB Biocomplexity research theme and long-time colleague of Dr. Woese puts it, "It remains one of the 20th century’s landmark achievements in biology, and a rock solid foundation for our growing understanding of the evolution of life."

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