The Empire Underground

Twenty-five years ago, Illinois scientist Carl Woese identified an entirely new form of life. His discovery upended the traditional notion that all living things on Earth fall into five kingdoms and challenged our understanding of evolution and the origin of life. All he had to do was persuade his fellow scientists.

by David W. Wolfe

Late one evening about a quarter-century ago, in a dimly lit laboratory in Urbana, Illinois, a middle-aged scientist sat crouched over a lightbox that illuminated a large sheet of translucent photographic film. Imprinted on the film were rows of dark bands representing the nucleotide sequence of genetic material that had been isolated from several microbes. The bluish glow from the lightbox filled the room, casting giant shadows on the walls and revealing the man's face. His brow was wrinkled as he focused intently on various details of the film. He lifted his head momentarily and shook it as if in disbelief, rubbed his eyes, then looked again.

The bar code-like pattern exposed on the photographic film was the culmination of many days of tedious preparatory work. Each row represented RNA (ribonucleic acid) fragments from a different organism, and by quantifying the similarity in the location and width of the bands in each row, the scientist could gauge the genetic similarity among the organisms. This was in fact the repetition of an analysis he had performed some days earlier. He couldn't believe the results the first time, but here they were again. He had checked and double-checked all aspects of the procedure. This was not some aberration caused by a mix-up in the chemicals he had used or the accidental switching of samples. The results, if they could be confirmed by additional tests, could mean only one thing—he had made one of the most important scientific discoveries of the 20th century: he had identified not merely a new species, but an entire new kingdom, or superkingdom, of organisms.

The scientist was Dr. Carl Woese (pronounced "woes") of the University of Illinois, and the year was 1976. In reality, the discovery unfolded over many days, nights, and weeks. The microbe that revealed its secret and eventually sparked a revolution in biology was considered at the time to be nothing more than an obscure type of bacterium known as a methanogen. The organism draws its name from the methane, or "natural gas," it produces as a byproduct of its metabolism. Indeed, it is now believed that much of the methane gas beneath the Earth's surface has been produced by methanogens. These soil organisms also produce the combustible "marsh gas" that sometimes hovers over swamps and rice paddies.

What Carl Woese conclusively established in 1976 was that, although the methanogens look like common bacteria under a microscope, genetically they are as distinct from bacteria as bacteria are from plants or animals. In fact, on a genetic basis, the methanogens have less in common with bacteria than a redwood

Spirostreptid with Brood *(1999), by Timothy Chapman*

tree or fungus has with you or me. If plants, animals, and bacteria were to be considered separate kingdoms, Woese reasoned, then so must the methanogens.

As Woese expanded his analyses, he soon found that the methanogens were not the only "bacteria" that should fall into the unique genetic category he had discovered. He began referring to the new category as a "domain" and gave it the name "Archaebacteria," or "ancient bacteria." Later this would be changed simply to "Archaea" to more sharply distinguish the domain from bacteria and other forms of life. Woese recognized that these findings would shake our concept of the evolutionary "tree of life" down to its roots. What he could not foresee were the personal and professional battles he would have to fight within the world of science to gain acceptance and understanding of his revolutionary discovery.

I first met Woese in the fall of 1998. I arrived in Urbana on a Sunday afternoon, although our meeting wasn't scheduled until the following morning. I decided to try calling him to confirm the time and get specific directions to his campus office. I had only an office number, but I had a hunch he would be at work. Sure enough, he picked up the phone. As I already knew from his steady stream of publications, he was by no means slowing down, although he was near retirement age.

The next morning, I got up early and found my way to campus. On the lower level of the building that housed the microbiology department, I stopped for a moment to look at a large hallway display dedicated to Woese as recipient of the prestigious Leeuwenhoek Medal, named after Anton van Leeuwenhoek, a pioneer microbiologist of the 17th century. I then continued upstairs to Woese's office, which was actually a small converted laboratory. Much of the bench space held antiquated laboratory equipment—perhaps items he did not have the heart to throw away. There were stacks of papers, journals, and books everywhere, and a few strategically placed computer monitors, keyboards, and printers. As I entered the room, I could see a gray-haired man leaning back in a swivel chair, his feet up on the lab counter, crossed at the ankles. He looked very much at home; it had to be Woese.

One of my first thoughts was how very different a visit to a scientist at the top of his or her profession was from a visit to, say, a successful politician or business leader. There was no penthouse view, no leather chair, no large desk made of exotic woods, and no wet bar (unless the couple of old lab sinks with leaky faucets could serve that purpose). Woese wore old tennis shoes, loose-fitting khaki pants, and a flannel shirt with rolled-up sleeves. Here is someone on the short list for the Nobel Prize, I reminded myself.

As is often the case with revolutionaries, Carl Woese entered the field whose paradigms he would challenge—biology—with a background in another discipline. His undergraduate training during the 1950s was in physics at Amherst College in Massachusetts. He crossed the bridge to biology some years later, earning a doctorate in biophysics at Yale University. After graduate school, a postdoctoral research project revealed to him for the first time the molecular wonders of the microbial world, and the secrets that world might hold for unraveling the origin of the genetic code. After brief periods of employment with General Electric and the Louis Pasteur Institute in France, he landed a tenure-track professorship in the microbiology department at the University of Illinois at Urbana-Champaign in 1964. Finally, with the freedom afforded by the university, Woese could get down to serious work on the questions that most intrigued him.

From the beginning, Woese's major interest was the origin and evolution of life's most important molecules—the DNA (deoxyribonucleic acid) and RNA that make up the genetic code. The double-helix DNA provides the master copy of an organism's genes, and RNA, a single-stranded version of DNA, translates the genetic code into life's essential processes, beginning with the synthesis of protein-enzymes that catalyze life's biochemistry. Woese recognized that the essential first step would be to build a more complete and accurate tree of life, one that encompassed the early evolution of the microbial world. By identifying those present-day microbes that are the most direct descendants of our most ancient ancestors, he was bound to gain insight into the mother of all cells, and into the origin of the genetic code itself. It was clear to Woese that the existing tree, emphasizing plants and animals, was artificially skewed toward large, recently evolved surface organisms such as humans, and so would be of little use to him.

A turning point for Woese came in 1965, when he read a paper titled "Molecules as Documents of Evolutionary History" in the *Journal of Theoretical Biology*. It was written by one of the pioneers in quantum chemistry and molecular biology, Linus Pauling, and a colleague, Emile Zuckerkandl. They had been gathering data on the amino acid sequence of biologically important protein molecules for many years, and they noticed that when they compared the same protein isolated from different species, the similarity of aligned sequences of amino acids of the proteins coincided with the amount of evolutionary time that separated the species. Organisms that evolved at about the same time showed nearly identical sequences, while those that evolved at very different times had noticeable differences.

These proteins, moreover, were like a "molecular clock" because they accumulated random changes in their amino acid sequences over evolutionary time. The changes were apparently "neutral" in that they did not affect the function of the proteins, and so got carried along, harmlessly, generation to generation. Pauling and Zuckerkandl's discovery confirmed the rationale for Woese's plan to determine the evolutionary histories of the bacteria—except that Woese decided to use the nucleotide sequence of genetic material, RNA molecules, rather than the amino acid sequence of proteins, as his molecular clock.

The discovery of such molecular clocks showed that expensive fossil-hunting expeditions, the kind that make such great *National Geographic* covers, are not the only, or even the best, approach to exploring the biological history of life on Earth. Investment in more powerful electron microscopes is not the answer either. Woese and a handful of others at the time were convinced that within every living cell, at a level beyond the view of microscopes, there would be clues to our evolutionary past, tucked away in the structure of long, chainlike molecules such as proteins and genes. This approach could not even have been imagined earlier because scientists did not have the techniques for examining the structure of proteins or genes in detail. Indeed,

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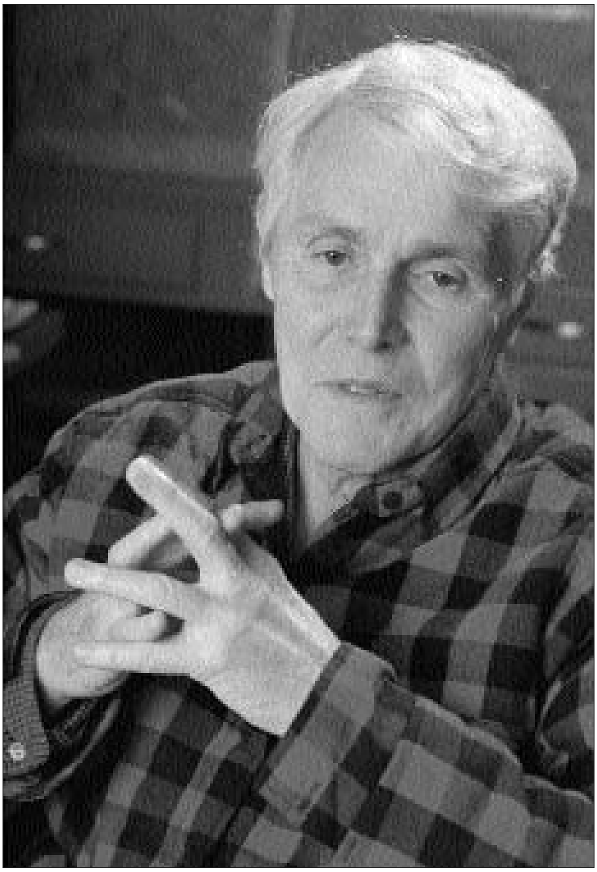
it was only a dozen years earlier that James Watson and Francis Crick had described the structure of DNA. Woese's plan was to use the newly emerging tools of molecular biology to reach back in time, beyond the oldest fossils, to the period when all life was microbial. He would not need to travel to exotic lands to seek out the past; he would do all of his digging in a modest laboratory in Urbana.

Woese decided that a small subunit of a type of RNA called ribosomal RNA (rRNA) would be the best molecular clock for his purposes. Ribosomal RNA draws its name from its association with cellular structures called ribosomes, which are part of the protein-building machinery of every cell. The particular subunit Woese selected is involved in the synthesis of protein-enzymes that no organism can do without. Because of this, it is found in all creatures, from bacteria to begonias, from mushrooms to humans. The ubiquity of rRNA would allow comparisons of all of Earth's genetic diversity on the same terms, and the construction of a truly universal tree of life. Much like the changes in amino acid sequence studied by Zuckerkandl and Pauling, the random neutral changes in nucleotide sequence in rRNA serve as a reliable counting mechanism, the "ticktock" of evolutionary time.


Carl Woese, here at the University of Illinois in 1998, is widely seen as a candidate for the Nobel Prize.

In the early days, Woese worked in almost total anonymity, ignored by most of the scientific community. Many of those who did pay attention considered him a crackpot who used an excruciatingly tedious technique that could never answer the big questions in which he claimed to be interested. But Woese carried on. His first step was to isolate the rRNA subunit from cells. Then he tackled the sequencing problem. Today, with automated equipment, an entire 1,500-to-1,800-nucleotide rRNA subunit might be sequenced in a couple of days. But when Woese began his work in the late 1960s, sequencing would take half a year or more. Sidestepping the problem, he decided to focus on only a few fragments, each some 20 nucleotides long. Although it would be ideal to chart the entire nucleotide sequence, Woese knew it was extremely unlikely that any fragment longer than about six nucleotides would repeat itself within the same rRNA subunit.

The shortcut enabled Woese to compare analogous fragments of rRNA from any two organisms, and quantify their relative evolutionary age and degree of relatedness based on the proportion of nucleotides that matched up. His laboratory shelves became jammed with boxes of the large film sheets containing genetic information for hundreds of organisms. Visually translating these films into "bar codes" that represented nucleotide sequences and evolutionary relationships, he constructed simple "dendrograms," or "trees," and determined which organisms belonged on the same branch or twig, and where the important branching points were located. Gradually, a new universal tree of life began to emerge.

Woese's tree was the first recognition that "invisible" microbes, which constitute much of the genetic diversity and living biomass on our planet, were on an equal footing with multicellular creatures on the tree of life. Indeed, it is possible that there is more living matter within the microscopic pore spaces of the soil and rock beneath our feet than on the entire surface of the Earth.

During my visit with Woese, he took me into a large room lined with shelves from ceiling to floor that had been completely dedicated to the storage of these film sheets—thousands of them—now of historical significance. I was awed by this monument to the hours, weeks, and years of relentless pursuit of a scientific objective—the search for a pattern in the relationship among organisms. The sight brought home that leading a scientific revolution takes much more than genius. It also takes the stamina and tenacity of a bloodhound.

Before the Woesian revolution, our tree of life was essentially an "eye of the beholder" version of reality—based primarily on what creatures looked like, and what we could guess their ancestors looked like from the fossil record. Our evolutionary tree had advanced surprisingly little from the time of the ancient Greeks.

In the fourth century B.C., Aristotle described a *scala naturae*, or "ladder of life," which was a hierarchy that began with inanimate matter at its base and ascended through plants and animals to, of course, man at the top. About 2,000 years later, in 1735, Carolus Linnaeus published his masterpiece of taxonomy, the *Systema Naturae*, or *Natural System*, which has as its two great branches the same plant and animal kingdoms Aristotle described. Linnaeus's important contribution was his hierarchical classification scheme, still used today, that divided each of the kingdoms further into phylum, class, order, family, genus, and species.

The discovery of single-celled microbial life forms in the 17th century by Anton van Leeuwenhoek complicated things. Were they plants or animals? Most biologists and taxonomists took the easy way out and simply ignored Leeuwenhoek's microbes until, in the 19th century, Louis Pasteur demonstrated the important role they play in causing disease. After that, they could no longer be ignored. The problem was, and still is, that most living microbes and their fossils appear as nondescript rods or spheres, thereby preventing accurate classification. Even with the aid of powerful electron microscopes, the incredible diversity of the microbial world does not easily come into focus.

Rather arbitrarily, scientists decided to put the larger, motile single-celled organisms, named "protozoa," into the animal kingdom, and the relatively immobile fungi and tiny single-celled bacteria into the plant kingdom. That is the classification scheme I was taught in high school in the 1960s, even though by then many scientists had decided to lump the protozoa and bacteria into a third kingdom of their own. When I entered the University of California at Davis as a biology major a few years later, I learned the very latest dogma of the scientific community—a five-kingdom classification system proposed by Robert Whittaker of Cornell University in 1969. It raised the protozoa, bacteria, and fungi each to the status of individual kingdoms, alongside animals and plants.

By that time, detailed comparisons of organisms made possible by powerful scanning electron microscopes had revealed that all of Earth's life forms could be grouped into two "superkingdoms" based on cellular structure: the eukaryotes, which have cells with a well-formed nucleus, and the prokaryotes, whose cells lack a nucleus. Within the five-kingdom scheme, all multicellular plants, animals (including humans), and fungi, as well as the single-celled protozoa, are within the superkingdom of eukaryotes; only the bacteria are prokaryotes.

That is where things stood when Woese arrived on the scene. But Woese was not satisfied with the five-kingdom tree. He knew that the prokaryotes, the bacterial branch, represented most of the evolutionary history of life on the planet, and their living members had the metabolic diversity to survive in a wider range of ecological niches than the other four branches. Bacteria and their relatives have been evolving for at least 3.5 billion years, while the multicellular creatures emphasized in the five-kingdom tree have been around for less than one billion years. A tree based primarily on the visible characteristics of organisms would never do justice to the genetic diversity of the prokaryotes, or to the unicellular organisms that were at the base of the other branches.

So Woese pursued his molecular approach. One by one, he isolated the rRNA of individual bacterial strains and compared fragments for differences in nucleotide arrangement. During his first 10 years of effort at the University of Illinois, Woese gathered enough rRNA data on some 60 types of bacteria to begin publishing their genealogies—the shape of the prokaryote branch. Occasionally he would dabble with the eukaryotes, members of the other four branches of the five-kingdom tree. What became apparent from his comparisons was that within the bacterial branch there were sub-branches that differed as much from each other as plants differed from animals. In other words, if the difference in rRNA nucleotide sequence between plants and animals was to be used as the variable that would define separate kingdoms, he had evidence that required the bacterial branch itself to be divided into several separate kingdoms.

This was mind boggling enough, but Woese was in for an even bigger surprise. One day in 1976, his colleague Ralph Wolfe (no relation to the author) supplied him with a few colonies of methanogens. Not much was known about the methanogens at the time, except that they appeared to be bacteria; that they often inhabited subsurface soils, waters, and other places deficient in oxygen; and that they produced methane gas as a byproduct of their metabolism. Wolfe was one of the few well-established microbiologists who believed in Woese's approach, and he was curious as to where the methanogens might fit in the bacterial genealogy Woese was constructing.

Woese put the methanogen sample through his rRNA sequencing mill. When he examined the film that resulted, the sequences did not match up with anything he or anyone else had ever seen in a bacterium. They also differed from the nucleotide sequences of every kind of eukaryote—the protozoa, fungi, plants, and animals. For Woese, one of the few who could interpret and fully appreciate the rRNA sequence data, it was as startling as stepping into the backyard and seeing an alien.

Any scientist would be thrilled at discovering a new species, but Woese had unexpectedly dredged up an entire superkingdom. For the next several months, Woese put in even more hours at the lab to confirm his results. He examined other methanogens, and, on the basis of the rRNA data, they also turned out to belong in the unique group he eventually named Archaea.

Day by day the evidence accumulated, and soon it was abundantly clear to Woese that all life on Earth could be divided into three primary superkingdoms, or "domains," as they are now called: Bacteria, Archaea, and Eukarya (the last being the crowded home of the former kingdoms of plants, animals, fungi, and protozoa). These domains have "signature" nucleotide sequences in certain parts of their rRNA which establish that they represent the deepest, most fundamental branches of the universal tree of life.

Within a year of the initial discovery, Woese and Wolfe published their results in the *Proceedings of the National Academy of Sciences*. The findings did not go unnoticed by the popular press, and in November 1977 the discovery of the archaea made front-page news not only in Woese's hometown paper, the *Urbana News Gazette*, but in the *New York Times*.

What shocks people most about Woese's discovery is the implication that the vast diversity of life we see all around us, the multicellular plants, animals, and fungi, represents only three small twigs on one branch, the eukaryotic branch, of the universal tree of life. The discovery clarifies how our reliance on visual evidence has for thousands of years warped our perspective on the evolution of life on our planet. Most high school and introductory college textbooks on biology today continue to perpetuate this thinking by emphasizing the plant and animal kingdoms. The rRNA analyses tell us that within each of the three domains of life there are dozens of other kingdoms. And most of those kingdoms, representing most of Earth's genetic diversity, are microbial.

The prokaryotes, previously thought to be a single branch of primitive creatures within a five-kingdom tree dominated by large multicellular life forms, are now recognized as representing fully two-thirds of Earth's genetic diversity—the Archaea and Bacteria domains. By several orders of magnitude, there are greater diversity and evolutionary distance within the new domain of Archaea discovered by Carl Woese than exist among the plants, animals, and fungi combined.

Throughout the 1990s, the pace at which biologists sequenced the rRNA of new organisms and filled in the tree of life accelerated. By 1998, more than 5,000 organisms had been classified in this way. Researchers also sequenced the complete genome (not just rRNA fragments) of one methanogen, *Methanococcus jannaschii*, reporting their results in *Science* in 1996. Parts of the *M. jannaschii* genome were similar to bacteria, but other parts were more similar to eukaryotes. Overall, the results verified that archaea are a unique third domain, even though they *look* like bacteria. Since then, the complete genomes of several other archaea have been sequenced, and all of these findings tend to support the conclusion reached much earlier by Woese in his analysis of just fragments of rRNA.

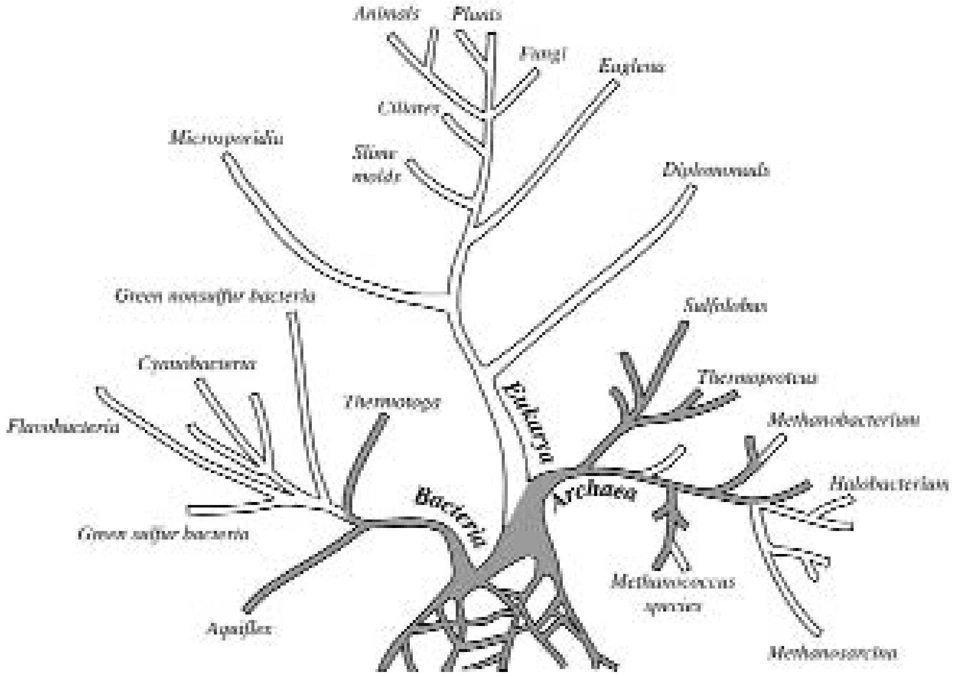
The universal tree provides a molecular-genetic approach to the study of the origin of life on Earth. The fact that single-cell thermophiles have the oldest evolutionary history (that is, are at the base of the universal tree) is weighty evidence in support of the hypothesis that life originated not in a shallow body of water on the surface, as conventional wisdom long held, but in a high-temperature habitat, such as the deep subsurface or within sediments near oceanic volcanic vents. The rRNA data suggest that all three domains—the Archaea, Bacteria, and Eukarya—arose from a common community of primitive life forms long ago, rather than one branch from another. This is a radical departure from the centuries-old belief that the multicellular eukaryotes represented “higher” life forms that had evolved from the more primitive prokaryotes.

It now appears that the three domains branched apart long ago and have for the most part evolved independently. However, near the very base of each domain within the universal tree the relationships get messy. These most ancient single-celled creatures are capable of “laterally” exchanging genetic material with distantly related organisms, even across domains. What occurs at this primitive level is like a 1960s “free love” festival of gene swapping, although it is all done in G-rated asexual fashion. Loose genetic material released by damaged cells of one species can be engulfed like food by active cells of another species and incorporated into their genome. It’s a “you are what you eat” method of gene transfer. As we gradually fill in the base of the tree over the next decade or two, it may come to resemble a network more than a simple branching pattern. And even with the powerful tools of molecular genetics, the precise location of the root of the tree may remain a mystery.

Many of the archaea are thermophilic. These amazing “extremophiles” eke out a living in environments in which no other organism can survive. Some species live thousands of feet underground, where they have been cut off from sunlight for hundreds of millions of years but have found other sources of energy, such as hydrogen gas, or perhaps other substances in the rocky layers. The apparent independence of these underground communities flies in the face of that lesson we learned in high school—that all life is ultimately dependent on solar energy. Some scientists now believe that the microbial organisms at the base of the “dark food chain” may be the direct descendants of Earth’s first life forms.

Archaea are also being discovered in other environments, some of them cold rather than hot, and others not very extreme at all. For example, scientists have found a very diverse and numerous group of archaea thriving in the cold ocean waters off Antarctica. Deep in the North Atlantic, archaea live among the bacterial communities devouring the *Titanic*. These microbial communities extract iron from the steel superstructure, producing huge, iron-rich “rusticles” that hang from the sunken ship. Scientists have also found that topsoils—previously considered to be an unlikely place to find archaea—are rife with these organisms. But the precise ecological role of the soil- and ocean-dwelling archaea is still largely unknown.

Carl Woese brought the study of evolution into the molecular age, and in so doing brought microbes of the underground into the Darwinian fold. In 1977, when Woese first went public with his findings about the methanogens, he knew that he had made a contribution most scientists can only fantasize about. He had, after all, discovered a third domain of life! But what



The Woesian tree of life, in which bacteria, eukarya, and archaea are shown to have evolved from a common set of ancestors. Dark branches represent thermophilic organisms, while the complex root system symbolizes the intricate, and still mysterious, genetic relationship among Earth's first life forms.

happened next, or rather, what did *not* happen, was discouraging.

After the initial few weeks of attention and newspaper reports, the requests for interviews dwindled. As the months passed, Woese's struggle to find funding to continue his work did not get any easier, nor was there a flood of eager graduate students clamoring for a post in his laboratory. Worst of all, Woese recalls, most microbiologists simply ignored the mountain of evidence he had so painstakingly accumulated. Some openly criticized his work; others privately scoffed at his conclusions and warned Woese's supporters that they were jeopardizing their own careers by remaining associated with him.

When I visited Woese, the battle to convince the scientific community of his revolutionary ideas was still being fought in some quarters. I asked him whether he felt there was something wrong with the scientific process, something in need of repair. To my surprise, he answered, "It's appropriate that science move cautiously on matters as profound as this. Corroboration from other laboratories just took time. Now that we have faster automated methods, and we're sequencing the entire genome of organisms, things should move more quickly; maybe some of the puzzles and inconsistencies can be resolved."

In retrospect, Woese recognizes that a significant part of the problem was his isolation. He loved his work, but he did not get much satisfaction from attending scientific conferences. With his background in physics and his molecular perspective, he spoke a different language than others involved in microbiology and evolutionary studies at the time. Only a small number of scientists were doing similar work and could comprehend the rationale of his approach or the implications of his results. Data from other labs to confirm or refute what he was finding were hard to come by. He preferred to be in the lab sequencing the rRNA for a new organism rather than socializing with fellow scientists and lobbying for them to support his interpretation of the data.

Fortunately, Woese's credentials and scientific methods were impeccable, and a slow but steady stream of his publications made it through the peer review process. He gained a

Dutch naturalist Anton Van Leeuwenhoek discovered the first microscopic organisms in 1674.

handful of well-respected and influential supporters, including Norman Pace, an evolutionary biologist at the University of California at Berkeley, Otto Kandler, a noted German microbiologist, and, of course, Ralph Wolfe, his University of Illinois collaborator. This small support group stood by him, its members often putting their own reputations on the line. The cold shoulder from the scientific community did little to dissuade Woese. Stubborn and self-confident by nature, he dug in his heels. He read Thomas Kuhn's *The Structure of Scientific Revolutions* (1976), and gained some comfort from learning that his struggle to introduce an unconventional new idea was not unique in the history of science.

Woese's story in many ways parallels that of Anton van Leeuwenhoek. In the 17th century, while Galileo was searching the sky for planets and stars, Leeuwenhoek, a cloth merchant by trade, was exploring droplets of pond water for microscopic "animalcules" and "wretched beasties," as he called them. Leeuwenhoek had a handful of supporters, most notably the famous British naturalist Robert Hooke, but for the most part he worked in anonymity, his findings receiving a lukewarm, at times even hostile, response. This may in part have been a consequence of his isolation from much of the scientific community. He was not a bona fide member of the academic club. Another problem was that Leeuwenhoek's lenses (which he ground himself) and technique were so superior that no one could duplicate his results. Leeuwenhoek took his rejection gracefully. In a letter to a friend, he wrote: "Among the ignorant, they're still saying about me that I am a conjuror, and that I show people what does not exist; but they're to be forgiven, they know no better. . . . Novelties oft-times aren't accepted, because men are apt to hold fast by what their Teachers have impressed upon them."

Luckily for us, Leeuwenhoek pursued his work and documented his findings. After he died, bacteria—those "wretched beasties"—would not be seen by human eyes again for at least another century. Finally, in the 19th century, others came along who were able to match his skills with a microscope and confirm his observations—and we began to recognize the potential significance of a microbial world.

Like scientists before him who have had the fortune, or misfortune, to be at the helm of a scientific revolution, Woese has had to take a lot of heat. But no scientific revolution can be credited to a single man or woman. This one, a revolution still in progress, is no exception. Carl Woese owes a great debt to Linus Pauling and other pioneer molecular biologists who preceded him. And by the late 1970s, Woese was no longer alone. There were others who independently recognized the advantages of the molecular approach to the study of microbial evolution. Kandler, for example, was making his own discoveries about the uniqueness of the methanogens by analyzing their cell walls, and was as convinced as Woese that the archaea represent a third unique domain of life thriving on our planet.

Gradually, during the 1980s, the tables turned, and the number of microbiologists who belittled the efforts of Woese began to diminish. The rRNA of several hundred organisms, representing all three of the major domains, was characterized. By the end of the decade, most scientists had at least come to accept that archaea represented the discovery of a unique life form, although many continued to dispute that the archaea deserved their own branch on the evolutionary tree. Woese, once shunned by many microbiologists, had become one of their leaders, and even a hero to some. His universal tree of life has entered into dogma among microbiologists, and the number of skeptics in other fields is dwindling. Virtually all of the scientific community now acknowledges the genetic uniqueness of the archaea, and most researchers would agree that rRNA analysis has become an important tool for clarifying evolutionary relationships.

During the plane ride home after my visit with Woese, I reflected on the modern scientific process. We are seeking truth, a deeper understanding of the world around us, but no one wants a wild-goose chase. The vast majority of the criticisms Woese has faced, and continues to deal with, are based on legitimate concerns of dedicated scientists. Peer review of grant proposals and publications, along with many other subtler barriers, has been established to prevent one renegade scientist from leading us all over the cliff and into the dreaded Abyss of False Theories. This is a good thing, of course, but for the scientist with a new perspective on an old problem, the process of convincing colleagues that he or she is right can be not only grueling and painfully slow, but a serious career risk.

Woese had recalled for me some of the things that kept him motivated all these years. Chiefly, it was the work itself, he said, and the confidence that he was making progress in tracing the genetic code back to its roots. But there were some pleasant surprises, too. In 1980, Kandler invited him to the first international conference on the archaea, in Munich, and Woese was treated like royalty upon his arrival. He found that, thanks largely to Kandler's considerable influence, his ideas were enthusiastically accepted in much of western Europe. And when the moment came for Woese to speak, a full choir and brass orchestra broke into celebratory music. Kandler had arranged the fanfare as an antidote to the emotional toll that criticism and lack of recognition were taking on Woese.

Just a decade after this event, Woese won worldwide recognition—at least within the field of microbiology. In 1990, he flew to Amsterdam to receive microbiology's highest honor, the Leeuwenhoek Medal, awarded by the Royal Netherlands Academy of Arts and Sciences. The medal is not given lightly or often. There have been only a dozen recipients in the past 125 years, among them Louis Pasteur in 1895. One is inclined to imagine that no name on the prestigious list of recipients would have pleased Leeuwenhoek more than that of Carl Woese.

I asked Woese whether receiving the Leeuwenhoek was his most gratifying moment. He thought briefly, then shook his head. "Here, let me show you something." He walked to a nearby office shelf and pulled down a 1991 edition of *The Biology of Microorganisms*, a widely respected textbook in microbiology that has gone through many editions. He opened the book, and there, on the inside front cover, was a complete diagram of his three-domain universal tree of life. "That," he said, pointing at the page, "that did it." ❑