

Phylogeny and Evolution of Microorganisms



Crafoord days

22 – 24 Sept 2003

Programme – Abstracts – The Crafoord lecture

CRAFOORD SYMPOSIUM

Phylogeny and Evolution of Microorganisms

Monday 22 September in Lund, Tuesday 23 September in Stockholm

- Chairperson:** *Torbjörn Fagerström, Vice President, Swedish University of Agricultural Sciences, Uppsala, Sweden*
- 09.00** **Opening of the Symposium**
Gunnar Öquist, Secretary General, the Royal Swedish Academy of Sciences
- 09.05** **Microbial Genomics –
Insights Into Physiology and Evolution**
Clarie M. Fraser, The Institute for Genomic Research, Rockville, USA
- 10.00** **Molecular Perspective on the Natural World**
Norman R. Pace, Department of MCD Biology, University of Colorado, USA
- 11.00** **Horizontal Gene Transfer and the Triumph of Darwin**
Gary Olsen, Department of Microbiology, University of Illinois, USA
- 12.00 – 13.00** **Lunch**
- 13.00** **Hyperthermophiles – Microbes in the Upper
Temperature Border of Life**
Karl O. Stetter, Lehrstuhl für Mikrobiologie, Universität Regensburg, Germany
- 14.00** **Archaea – a Goldmine for Molecular biologists**
Patrick Forterre, Institut de Génétique et Microbiologie, Université Paris-Sud, France
- 15.00** **Evolving Cellular Organization**
Carl. R. Woese, Crafoord Laureate 2003

CRAFOORD LAUREATE 2003



CARL R. WOESE was born in 1928 in Syracuse, New York, USA. He studied at Amherst College and at the University of Rochester before completing a PhD in Biophysics at Yale University in 1953, where he also did his post-doc. He became Professor in Microbiology at the University of Illinois at Urbana in 1969 and holds the Stanley O. Ikenberry chair at the same university since 1996.

Introduction to the Crafoord Prize 2003

Charles Kurland, Professor emeritus in Molecular Biology, Uppsala University, Sweden

The Royal Swedish Academy of Sciences decided on 12 February to award the Crafoord Prize in Biosciences 2003 to Professor Carl R. Woese, University of Illinois, Urbana, Illinois, USA: “for his discovery of a third domain of life”.

From Carl Linneaus to Carl R. Woese

Two major streams of biological thought are united in the work of Carl R. Woese. One of these is Carl Linneaus' (knighted von Linné) vision of a universal natural system of taxonomy for organisms (a taxonomy is the classification of organisms according to their relationship). The other is that of molecular genetics as initially envisioned by Watson, Crick and Gamov. They conceived a universal scheme based on the structure of DNA to describe how the genetic information for the structures of proteins is encoded in nucleic acid sequences. Woese provided the connection between these two seemingly separate fields of biology by employing the nucleic acids of the rRNA molecules themselves to make taxonomic comparisons and to derive phylogenetic order, i.e. summarize the evolutionary history in a phylogenetic tree.

The ribosome – a centrally placed informer

The choice of rRNA for this work was not gratuitous. In Woese's view the evolution of gene expression in general and the ribosomal mechanism for protein synthesis, in particular, is the defining process in the origin of cells. Thus, there is a universal ribosome-based translation mechanism and a universal genetic code that relates all organisms to each other, Archaea (the domain proposed by Woese himself, based on his findings), Bacteria and Eukaryotes alike. In Woese's view, the ribosome mechanism and the genetic code first evolved in a primitive population of organisms, collectively referred to as the progenote. Accordingly, the progenote population is identified as the common ancestor of modern organisms. Archaea, Bacteria and Eukaryotes diverge from this common progenote ancestor and they evolve by the selection of advantageous mutations in Darwinian lineages.

The sequence changes created by mutations in genes that define the evolution of species can be detected by sequence analysis of the nucleic acids of the DNA-molecule, or that of the RNA which is transcribed from DNA, or of the amino acids that constitute the end product, i.e. the proteins. Thus, these co-linear molecules are all related to each other by the Watson Crick base pairing rules and by the genetic code. In principle, the evolutionary sequence changes in any particular gene from any clade of organisms can be ordered in a natural phylogeny. If the analyzed sequence is present in all organisms, the resulting phylogenetic reconstruction should be universal.

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. Indeed, 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 rRNA complement. Two examples are known in which partial alien replacements are observed. In contrast there are reliable reports of dozens, perhaps hundreds of alien proteins transferred to organisms by Horizontal Gene Transfer.

The obscured diversity of microorganisms

Woese’s choice of rRNA as the molecular “window” through which to view the evolution of life on this planet was a wise one, indeed. He has introduced and developed a tool that has revolutionized medical microbiology, epidemiology and microbial ecology. However, it may be more important that Woese’s work has greatly changed our perception of biodiversity. Indeed, reflecting on the universal rRNA phylogenetic tree (figure 1) leads inevitably to the insight that our planet’s biota is totally dominated by microorganisms.

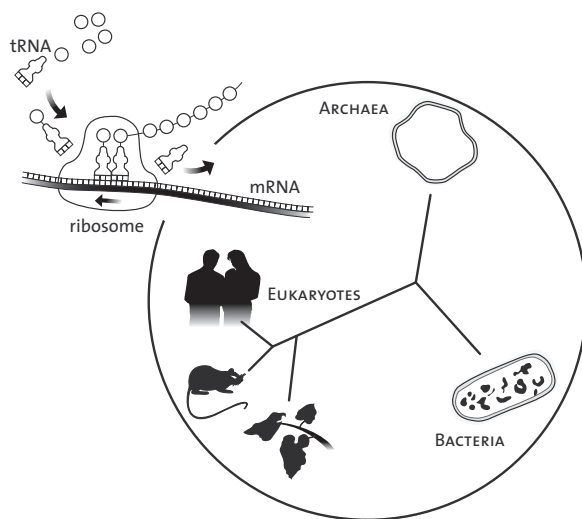


Figure 1. Woese realized that the ribosomes held the key for a proper construction of a phylogenetic tree of the main domains of life. The ribosomes interpret the messenger RNA molecules (mRNA) carrying the instructions from the DNA of the cell, and together with transfer RNA (tRNA) construct the proteins encoded in the genome. Woese showed that the nucleic acid sequence in the ribosomes, which themselves to a large extent consist of rRNA, can be used to construct the tree.

In conclusion it seems appropriate to cite Edward O. Wilson (Crafoord Laureate 1990). "In an ecological sense, the animals of rain forests and the abyssal benthos occupy opposite ends of the earth; one could say that they dwell on two planets. Their environments are as physically different as possible and their biotas share not a single species of plant or animal. Yet all the diversity they contain may be dwarfed by that of the bacteria, organisms that saturate the two extreme environments and every other place on earth. It is a common misconception among both biologists and non-biologists that bacteria are relatively well known because they are so important in medicine, ecology and molecular genetics. The truth is that the vast majority of bacterial types remain completely unknown, with no name and no hint of the means needed to detect them." Elsewhere, Wilson has written "If I could do it all over again, and relive my vision in the twenty-first century, I would be a microbial ecologist". A more fitting tribute to Carl R. Woese is difficult to find.

THE CRAFOORD LECTURE 2003

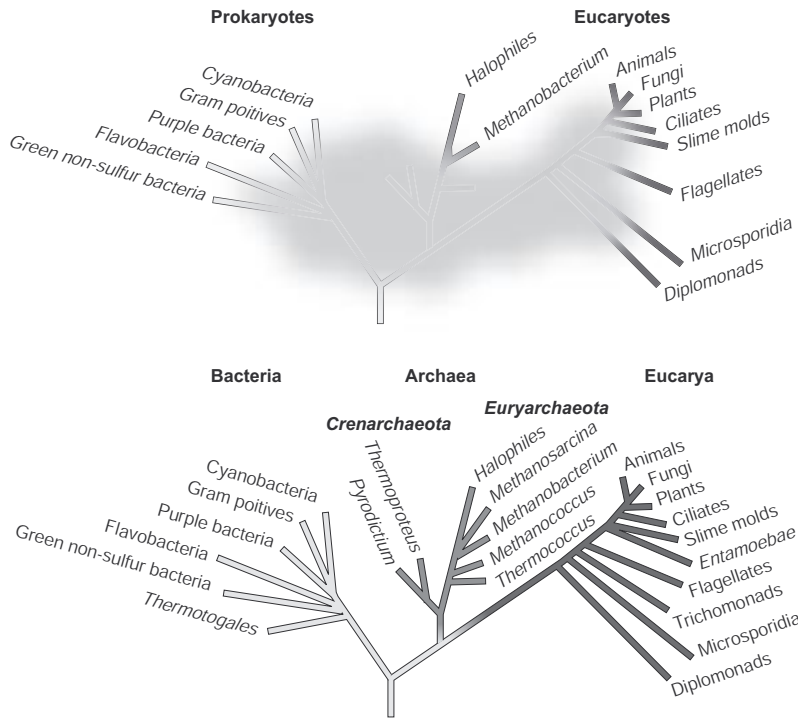
The Archaea and What They Represent

Carl R. Woese, University of Illinois, Urbana, Illinois, USA

Your Majesties, President of the Academy, members of the Crafoord family, members of the Academy, ladies and gentlemen, it is a great honor to have been given the Crafoord Prize this year by the Royal Swedish Academy of Sciences.

Many of the laureates who have stood before you could say: “Our work has solved or contributed to one of the important outstanding problems in ...”. Whether they would have chosen to put it that way is another matter. The DNA structure is a perfect case in point. Here was a problem central to all biology, the nature of the gene, that had in one sense been solved by that structure. Other laureates were entitled to say: “We made an unanticipated major discovery that did ...”. Here the discoveries of introns and penicillin come to mind. These were discoveries that, although not anticipated, served to refine, extend, or otherwise enrich their enveloping paradigms.

Standing here, I can say neither of these things. The discovery of the Archaea did not contribute to one of 20th century biology’s recognized major problems. Nor was it a serendipitous finding. I had set up a program to determine a universal phylogenetic framework, using molecular sequence comparisons. At the time, no one really knew what these relationships were, especially among the bacteria. The Archaea emerged as the program unfolded. It turns out that I was addressing a problem that Darwin and his contemporaries deemed important, but one that Darwin’s 20th century successors had paid little heed. Darwin had projected that eventually biologists would have (to put it in his words) “very fairly true genealogical trees of each great kingdom of nature”. Yet of all Darwin’s prophetic challenges, this is one whose urgency did not carry forth. Thus, the discovery of the Archaea did not enrich the prevailing biological paradigm. It was merely outside of that paradigm, incidental to 20th century biological thought. The Archaea were unexpected to begin with, and having arrived, they were unwelcome. This particular point needs understanding in that the situation is not unique to the Archaea.



This picture summarizes our work. It depicts Biology's knowledge of evolutionary relationships among organisms before our research program began and, then, a decade or so on into it. It is the background against which I now speak.

The Archaea are biologically significant on several levels. Let me begin with the most superficial, the significance of the Archaea as an organismal group. From time to time amazing and important organisms are discovered. The tube worms that inhabit the environs of deep sea hydrothermal vents are one such find; the coelacanths – which resemble our piscine ancestors – are another; as are bacteria that grow above the normal boiling point of water and fish that live below its freezing point. However, all such finds lie within the framework of established major taxonomic groups. They are like discovering major geological features on some continent. The discovery of the Archaea was different. It was more like discovering a whole new continent: the Archaea do not exist within any recognized higher biological taxon, they constitute a new highest level taxonomic unit in their own right. While they are microscopic, they have no specific relationship to the true bacteria, nor are they specifically related to eukaryotic cells. Thus, from a classical biological perspective, the Archaea are a truly major organismal find, the most significant one in modern scientific times. They have added a new trunk to the Tree of Life.

I have already said that the Archaea did not fit into the 20th century biology paradigm. Let me expand on that, for it introduces the second level of their discovery's significance, the opening of the Pandora's Box of Microbiology. When

first announced to the world the Archaea had been met with great public acclaim – for example front page coverage in the *New York Times*. That acclaim was matched only by the disdain accorded them by biologists in general, microbiologists in particular. The public had perceived their discovery as speaking to one of Mankind's eternal concerns – where we came from. Biologists received the discovery of the Archaea as anathema, which ran contrary to their conventional wisdom.

You need to feel the intensity of biology's reaction to appreciate it: Our chief collaborator in the characterization of the methanogens, which were the first of the archaeal groups to be recognized, was Ralph Wolfe, my colleague at Illinois. When the initial press coverage of our discovery appeared, Ralph received a telephone call from a prominent Nobel laureate whom he knew well and greatly respected. His friend advised him in no uncertain terms to dissociate himself publicly from this scientific fraud or his reputation would be ruined. Ralph, true scientist that he is, did nothing of the sort.

Our claim wasn't unscientific, the dismissive criticism of it was. How could that be? How could it be when the majority of biologists felt that way? Erwin Schroedinger in his little book "Nature and the Greeks" provides the answer: the hallmark of science, as opposed to other perspectives on the world, he says, is that scientists are willing to live with gaps in their knowledge, with questions unanswered. Unlike these other perspectives, science does not fill gaps in its knowledge with "guesswork" solutions, or "fakes" as Schroedinger calls them, but waits for valid science to do so. However, it turns out that microbiologists in the past had indeed filled such a gap with a scientific fake. Through no fault of their own microbiologists had for decades been unable to determine the evolutionary relationships among bacteria, and out of frustration, I believe, had ultimately resorted to a non-scientific, but comforting, guesswork solution; namely, the assumption that all bacteria were specifically related to one another at the highest level; they all were "prokaryotes". This meant that life on this planet comprised two basic organismal types, prokaryotes and eukaryotes – distinct both genealogically *and* in cellular organization.

Unfortunately, their belief rested completely upon authoritative assertion, not scientific data, and, worse, an assertion whose truth had been proclaimed self-evident and undeniable. Schroedinger had said that the power of guesswork solutions is such that (in his words) "the answer is missed even when, by luck, it comes close at hand". The Archaea provided a perfect example. We were not specifically looking for them, merely trying to find out how various organisms fitted into some large-scale phylogenetic picture – as I said before. True to Schroedinger's characterization, microbiologists had indeed missed the answer, not this once, it turns out, but a number of times, for their guesswork solution had removed the question. A question answered is a question dismissed. Thus, the truth was not only overlooked, but when confronted with it, biologists flat out denied it. Like all such fabrications, guesswork solutions are vulnerable and require dedicated defense if they are to persist.

Thus, on what I have chosen to call its second level of significance, the discovery of the Archaea brought to light a flaw in the conceptual structure of Microbiology. Bacteriology, like zoology and botany, is fundamentally an organismal discipline; its focus a group of organisms, which needs to be studied in four principal ways: First,

in structure and function, in order to learn how the organisms are built and work; second in the group's diversity, to bring to bear the power of comparative analysis; third, in their ecology, to understand the role the organisms play in the tangled, interconnected web of life, and finally, in terms of their evolutionary relationships, to make biological sense of it all. Meaningful development of the second and third of these turns upon the development of the fourth, evolutionary relationships. Otherwise the study of bacterial diversity amounts to no more than a catalog of disconnected vignettes about various microbiologists' favorite bacteria. And bacterial ecology exists in name only: how can you study ecology when you can't distinguish your "plants", as it were, from your "animals"? This is indeed the condition in which bacteriology found itself for the greater part of the 20th century: it possessed no phylogenetic framework, and as a result had no meaningful bacterial ecology or study of diversity. At base Bacteriology was not a true organismal discipline, because bacteriologists had no real concept of the organisms they were studying. And their guesswork invocation of the "prokaryote" had served only to obscure this all-important hiatus in their understanding.

Herein then, lies the real temporal worth of our overall research program: It finally provided bacteriology with a phylogenetic framework within which to structure itself as a full fledged organismal discipline. One can begin to see the salutary effects of this framework. Today talk of evolutionary relationships is no longer shunned, but is commonplace among microbiologists. Bacterial ecology has now come into its own and is fast becoming the dominant area of study in microbiology – just in time, I might add, because the problem of the global ecology, in which bacteria are absolutely central, is a pressing one.

In addressing bacterial ecology I would be remiss not to say that while a phylogenetic framework was necessary to the emergence of bacterial ecology, it alone wasn't sufficient. The vast majority of bacteria – and I mean well over 95% – cannot, for whatever reason, be readily *isolated* in laboratory culture. Norman Pace saw the way around this road block: given a molecular phylogenetic framework, he argued, meaningful identification of an organism requires only the characterization of some key gene, and that gene can be isolated from the organism regardless of whether it is in laboratory culture or cloaked in its natural setting. Pace's methodology for accomplishing this is what has made bacterial ecology feasible.

Finally, I come to the third, the deepest and most lasting, impact that our research program in general and the discovery of the Archaea in particular have had, namely helping to bring about the resurgence of interest in evolution. Throughout most of the past century evolution languished. By its nature the discipline of molecular biology had no interest in it. Evolution was simply a collection of idiosyncratic historical accidents, inexplicable and irrelevant to the understanding of Biology. As we have seen, evolutionary considerations were absent from Microbiology as well. And 20th century classical evolutionists failed to press the frontier of their discipline into the molecular area. The net result was stasis.

Once the universal phylogenetic tree appeared, however, it became difficult to ignore evolutionary relationships and evolution in general. What also became hard to ignore was that the molecular dissection of the cell was inadvertently providing the data needed to study how cellular organization evolved. I had been wanting to attack the evolution of translation since the early days of the genetic code. But it

was obvious that universal evolutionary problems could be approached only in the framework of a universal phylogenetic tree. And nothing even remotely approaching that tree existed in the 1960s. The microbial world was phylogenetic *terra incognita*. Consequently I spent over two decades of my career determining that tree. The reward for me has not been primarily in seeing the tree *per se* emerge, for the tree is only the framework. The reward has been in seeing unfold the new and fascinating biological realm that lies buried within its roots.

It is in probing the evolutionary depth of the cell where the Archaea are proving their full worth. Because the Archaea provide a third example of basic cellular organization, biologists thereby have the equivalent of binocular vision: they can now “triangulate” on problems of cellular evolution. And we all know how indispensable binocular discrimination is when the landscape is alien and complex.

If one steps back from the day to day bustle of biology – from the frenzy of genomics and the race to diagnose, cure, and bioengineer our way to a utopia – then one can glimpse the new vision of Biology that is emerging. It is a deeper and more integrated vision of Biology than its molecular predecessor. I would like to feel that what we have presented to Biology and to the World – a universal phylogenetic framework and a third primary type of cellular organization – is helping to bring this new and exciting Biology into being.

Microbial Genomics – Insights Into Physiology and Evolution

Claire M. Fraser, The Institute for Genomic Research, Rockville, USA

Since the publication of the complete *Haemophilus influenzae* genome sequence in 1995, the field of microbiology has undergone a revolution. With more than 100 bacterial and archaeal genome sequences available today, and at least twice that number of projects underway, we have begun to fully appreciate the extent of microbial diversity on Earth. These data suggest that the idea of a “model organism” in the prokaryotic world may not be valid, given the vast differences that are observed, even between related species. Complete genome sequences from representatives of the three domains of life have enabled a more comprehensive view of evolutionary relationships among organisms. It has become clear that many processes shape the evolution of microbial genomes including gene duplication, gene loss, and lateral gene transfer.

Microbial genomics has also had a profound impact on infectious disease research. Essentially all of the major human pathogens have been targeted for genome analysis and these data have already provided a large number of new targets for the development of anti-microbial compounds and the identification of novel vaccine candidates for some of the most devastating diseases known. In addition, genome analysis of closely related strains of pathogens (e.g., *Bacillus anthracis* and its relatives) has begun to reveal some of the key genetic differences responsible for differences in pathogenicity and virulence and has provided important comparative data for forensic and epidemiological studies.

Despite all of the initial excitement that has come from microbial genomics studies, it is important to remember that all of the work in that has been done to date has focused on organisms that can be readily grown in the laboratory. We know that this represents a very limited view of the prokaryotic world. One of the most exciting frontiers in microbial genomics will be in environmental microbial genomics – exploring the vast diversity of microbes that have never been cultured in the laboratory. Recent approaches have demonstrated that DNA can be isolated directly from the environment and used for whole genome analysis. However, in order to make sense out of this data, one still needs an anchor (e.g., ribosomal RNA) to link the DNA to the phylogenetic tree. These large-scale environmental approaches, together with new high-throughput methods for functional analysis of genes, will continue to provide exciting new insights into the wonders of the prokaryotic world.

Molecular Perspective on the Natural World

*Norman R. Pace, Department of Molecular,
Cellular and Developmental Biology, University of Colorado, USA*

The biosphere that we inhabit is absolutely dependent upon the activities of the diverse organisms that constitute the pervasive, yet little-known, microbial world. Humans have come to be aware of this microbial world only recently. The microscope was invented in the 17th Century, but remained a parlor curiosity until the 19th Century, when medical implications of microbes came to the fore. With the development of culture and biochemical techniques, in the 20th Century, our knowledge of particular model organisms expanded dramatically, even into the structure of their genomes. Still, our understanding of microorganisms in the environment has remained rudimentary. The underpinnings of the biosphere have remained obscure.

A main reason for the slow development of environmental microbiology has been a traditional requirement for the culture of microorganisms in order to detect and identify them. Yet, using standard techniques, microbiologists cannot culture more than 99.9% of the organisms seen microscopically in the environment. Moreover, the identification of even cultured microbes was problematic, based on physiological properties that often are anecdotal. Both of these situations changed radically with the advent of Carl Woese's ribosomal RNA approach to the description of biological diversity. This approach is embodied in sequence-based phylogenetic trees that can relate all life. From that molecular perspective we see that microbial life, whether archaeal, bacterial or eucaryotic, dominates the span of biological diversity. The results provide a quantitative view of biological diversification at the level of the genetic machinery, and a more solid understanding of the course of biological evolution.

Because this molecular-phylogenetic perspective is based on gene sequences, not on physiological properties, it was possible to identify and study environmental microbes without culture. Molecular sequences can be cloned directly from environmental DNA and analyzed to determine the kinds of organisms that are present in different ecosystems. The sequences also provide for tools, such as fluorescently labeled hybridization probes, with which to study organisms in the environment. For the first time, study of the natural history of the microbial world became possible. The application of these technologies in extreme, as well as familiar environments has expanded dramatically our view of the nature and diversity of the microbial life around us.

Horizontal Gene Transfer and the Triumph of Darwin

Gary Olsen, Department of Microbiology, University of Illinois, USA

One of the most exciting discoveries in recent years has been the tremendous flux of genes into and out of genomes. Since the time of the common ribosomal RNA ancestor, on the order of 100 genome equivalents of horizontally transferred DNA have flowed in and out of the lineage leading to any given present-day genome. With this flux of genes, does it make sense to even discuss lineages, or a tree of life? Is it more useful (or necessary) to think of the history of life as a complex mesh? In considering these questions, it is important to distinguish history from semantics; what we call something does not change what it is. Perhaps surprisingly, most of the history of life is a treelike evolution of lineages. The lineages comprising the tree are indeed interconnected by a metaphoric gauze of transferred genes, but this is in addition to, rather than instead of, the tree.

Darwin's *On the Origin of Species* includes only one figure, a tree illustrating evolution by modification and natural selection. This perspective is not altered by gene transfer. Although Darwin did not know its sources, he appreciated that variation within species was essential for his theory of evolution to work. Genetics and molecular biology led us to a perspective in which variation originated within the species. Horizontal gene transfer is an additional process that introduces variation into a lineage from other contemporaneous lineages. Clearly this latter pool is much larger. In addition, horizontal transfer can introduce whole new functions and systems, not just incrementally modify existing systems.

Is it necessary that a core of genes, or even a single gene, remain untransferred for a tree to be the appropriate framework for representing the history of life? I suggest that all that is necessary is a local continuity, that the ancestor of each organism be clear. The identity of an organism's immediate ancestor only becomes ambiguous when there is so much transfer within a single generation that the organism fails to receive a clear majority of its genes from a single parental genome. In this view, the most obvious exceptions to a treelike history are found at the extremes of the evolutionary scale. The first is the early stages in the origin and evolution of life, the history that spawned the three Domains of modern cellular life. The second exception is the intraspecies evolution of sexually reproducing eukaryotes.

Hyperthermophiles – Microbes in the Upper Temperature Border of Life

Karl O. Stetter, Lehrstuhl für Mikrobiologie, Universität Regensburg, Germany

Most microbial life forms known are mesophiles adapted to ambient temperatures within a range from 15 to 45 °C, well corresponding to the temperature of the human habitat. In contrast, communities of super-heatloving, “hyperthermophilic”, Archaea – and a few Bacteria – have been isolated which grow optimally at temperatures between 80 and 113 °C where mesophiles are killed within seconds e.g. in the Pasteurization process.

On Earth, hyperthermophiles are found in water-containing terrestrial and submarine environments of active volcanism where they represent life at the upper temperature border. In addition, hyperthermophiles have been discovered in geothermally heated subterranean oil reservoirs, some 3000 to 4000 meters below the surface. Members of the (non-spore-forming) archaeal genera *Pyrodicticum* and *Pyrolobus* were found to survive one hour autoclaving at 121 °C, a kind of cosmic impact scenario. As a rule, hyperthermophiles are unable to grow below 60 °C (*Pyrolobus* below 90 °C). They are adapted to distinct environmental factors including the composition of minerals and gasses, pH, redox potential, salinity and temperature. Most hyperthermophiles depend only on inorganic nutrients (“chemolithoautotrophic”): inorganic redox reactions serve as energy sources and CO₂ is the only carbon source required to build up organic cell material. The energy-yielding reactions represent anaerobic and aerobic types of respiration. H₂ serves as an important electron donor which may be a component of volcanic gasses. Other electron donors are sulphide, sulphur and ferrous iron. Electron acceptors are carbon dioxide, oxidized iron-, sulphur-, and nitrogen compounds as well as oxygen. Several hyperthermophiles are opportunistic heterotrophs. A great deal of hyperthermophiles exhibit very unusual cell shapes like disks, lobes, networks and “golf clubs”. Representatives of the Nanoarchaeota, a new kingdom of Archaea are *minicocci*, so tiny that they can hardly be recognized under the light microscope (0.4 micrometers in diameter) about the size of large viruses.

Seventy species of hyperthermophiles are known which are grouped into thirty genera in eleven orders. Surprisingly, within Woese’s small subunit rRNA-based phylogenetic tree of life, hyperthermophiles occupy all the short deep branches closest to the root. Therefore, by this feature they appear as the most primitive organisms. Similar hyperthermophiles could have already existed at the hot primeval Earth, about four billion years ago. Independent of oxygen and sunlight, hyperthermophiles could thrive even on other planets and moons that harbour thermal activity and liquid water.

Archaea – a Goldmine for Molecular Biologists

*Patrick Forterre, Institut de Génétique et Microbiologie,
CNRS UMR8621, Université Paris-Sud, Centre d'Orsay, France*

When Carl Woese first proposed the concept of Archaea (formerly archaeobacteria) in 1977, he rightly predicted that unique novel molecular features would be discovered in the third domain of life. Since the dream of all scientists is to put their hands on something really new, this prediction was a red flag for molecular biologists who had been used to work for decades with classical bacteria.

The reward turned out to be great for those who took the challenge seriously. The pioneer in the field, Wolfram Zillig, was able to show, as soon as 1979, that the RNA polymerase of Archaea (the major player in gene expression) was more similar to its eukaryotic than to its bacterial counterpart. This eucaryotic flavour was observed again and again in most aspects of the mechanisms that allow expression and replication of the archaeal genomes.

This has drastically changed our views of the procaryote/eukaryote transition. For instance, one cannot suggest anymore that the eukaryotic RNA polymerase contains more subunits than the bacterial one, just because eucaryotes are more complex than procaryotes (since Archaea are prokaryotes too). But Archaea are not simply “small eukaryotic models”. They exhibit several unique specific features (such as their lipids) and amazing mixtures of eukaryotic and bacterial traits in the same process. For instance, they replicate their chromosome in a bacterial-like fashion (a single origin and high speed) but with eukaryotic-like proteins and mechanisms (small Okazaki fragments). Archaeal studies also led to the discovery of entirely new viral families with morphologies never seen before in the living world. Surprisingly, some of these viruses are evolutionary linked to some nasty human killers, such as Poxviruses. The study of Archaea was especially rewarding for biologists fascinated by the topological problems raised by the double helical structure of DNA. Completely new unexpected enzymes were discovered, such as reverse gyrase, which produces positively supercoiled DNA. This enzyme turned out to be the only protein specific to hyperthermophiles and could testify for a hot origin of Archaea. The discovery of another of these “DNA-manipulating enzymes” in archaea has allowed to identify the protein that triggers genetic recombination in humans. Recently, this “archaeal enzyme” was found in plants, where it determines cell and body sizes!

Many more exciting findings should be expected for those working in the framework of the archaeal concept. More generally, the possibility to compare the major molecular mechanisms in three domains, instead of two, has allowed for the first time to put evolutionary thinking at the heart of molecular biology, once a purely descriptive science.

