Nanoarchaeum: How Low Can You Go?

By Mark Hartwig

Researchers from the University of Regensburg, Germany, are adding a branch to the "tree of life" after discovering a tiny new microbe in a submarine vent north of Iceland.

Measuring only 400 nanometers in diameter, the new microbe is among the smallest known living cells. It also boasts what appears to be the tiniest known cellular genome, containing some 500,000 DNA letters (i.e., nucleotide base pairs)--which is some 80,000 letters smaller than the previous champ, *Mycoplasma genitalium.* To get an idea of how small that is, the humble yeast contains about 12 million letters, while humans have about three billion.

Dubbed *Nanoarchaeum equitans*, the bug has been classed among the Archaea, one of life's three major divisions (the others being the Bacteria and Eukaryota--which includes organisms with nucleated cells, such as humans). The new bug is so unusual, however, that the Regensburg researchers had a chore figuring out what it is. And its classification is still not certain.

To help classify new microbes, scientists use what's called the *polymerase chain reaction* (PCR). The technique allows them to take an organism's DNA and quickly amplify, or mass-produce, a targeted segment. Once the segment has been mass-produced, it can then be sequenced.

The key to the whole thing is knowing part of the segment's sequence. Once you know that, you can create a "primer" (a short stretch of DNA) that attaches to the targeted segment and enables the PCR to proceed.

That sounds a bit like a catch-22. Fortunately, scientists have already sequenced the genomes of many organisms. Because these organisms share a number of genes, scientists can use selected bits of their sequences to fish for corresponding genes in new organisms. Even if the genes differ somewhat, those bits may still be the same.

When studying microbes, biologists like to use primers from genes that encode "small subunit ribosomal RNA" (ss rRNA). Such RNA is so important for life that every organism has a least one gene that encodes it. What's more, according to evolutionary biologists these genes are highly "conserved." That is, they've changed very little over billions of years.

According to microbiologists Yan Boucher and W. Ford Doolittle, this makes ss rRNA genes "the common currency of microbial taxonomy."[1] The idea is that the genes are similar enough for meaningful comparison, but different enough to distinguish one group of microbes from another.

Unfortunately, *Nanoarchaeum* is so "divergent" that none of the usual primers could find a stretch of DNA to attach to. That included "primers considered general for all Archaea as well as for all organisms ('universal')."[2] The researchers had to detect and amplify the organism's ss rRNA gene using other methods.

Sequencing the gene confirmed how unusual the new microbe is: "Its sequence turned out to be (so far) unique, harbouring many base exchanges even in the so-called 'highly conserved regions' that are usually employed as primer targets for ss rDNA PCR. This explains our initial failure to amplify this gene by PCR." [3]

Because its ss rRNA gene looks more like the genes of archaeal organisms than bacterial ones, the organism was classed in the Archaea. But it is so different from its fellow archaeons that researchers created a new phylum, *Nanoarchaeota,* to accommodate it.

More dubiously, they argue that *Nanoarchaeum* is a very early offshoot on the "tree of life," branching off from the Archaea before that group diversified. Indeed, "With its tiny cell and genome size, '*Nanoarchaeum*' resembles an intermediate between the smallest living organisms like *Mycoplasma genitalium* and big viruses like the pox virus and *Chlorella* virus CVK2, and is close to the theoretical minimum genome size calculated for a living being. …" [4]

They add, "No final conclusions can be drawn about a primitive or derived state of evolution of '*Nanoarchaeum*'. However, its high growth temperature and anaerobic mode of life correlates with probable early environmental conditions which suggest that the '*Nanoarchaeota*' are possibly still a primitive form of microbial life."

As tentative as these statements may sound, they are a huge stretch. Here's why.

Nanoarchaeum, *Mycoplasma genitalium* and other microbes of their genome size are either parasites or symbionts. They depend on preexisting life for their survival.

M. genitalium, for example, grows in human urinary and respiratory tracts, where it's bathed in nutrients. If you want to grow it in the lab, you have to supply it with a rich mixture of vitamins, cholesterol, amino acids and so on. It simply couldn't fend for itself in a world where those things didn't already exist--such as the early earth environment.

Nanoarchaeum may be even pickier. So far, researchers have only been able to cultivate it only when it can attach to another archaeon called *Ignicoccus.*

Boucher and Doolittle note, "So far, *Nanoarchaeum* has not been grown alone, even on *Ignicoccus* cell extracts or in the same vessel as live *Ignicoccus* (but separated from them by permeable membranes)." [5]

Neither of these organisms have the molecular machinery to survive in any realistic early earth environment, in which only the rawest materials exist. This "ecological simplicity,"

as biophysicist and origin-of-life researcher Harold Morowitz calls it, demands a more complex minimal genome. [6]

A more likely minimal genome, says Morowitz, would be in the range of the cyanobacteria, which have the smallest genome of "truly autonomous organisms." [7] The lightweight champion in that group so far (a strain of *Prochlorococcus marinus*) has a genome with some 1.66 million DNA letters-over three times the size of *Nanoarchaeum.*

Thus it is unreasonable to say-even tentatively-that *Nanoarchaeum* resembles an intermediate between viruses and "the smallest living organisms." For its simplicity testifies not to its own primitive status, but to the sophistication and complexity of the world on which it depends.

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[1] Yan Boucher and W. Ford Doolittle, "Something new under the sea," *Nature* 417 (May 2, 2002): 27.

[2] Harald Huber, Michael J. Hohn, Reinhard Rachel, Tanja Fuchs, Verena C. Wimmer & Karl O. Stetter, "A new phylum of Archaea represented by a nanosized hyperthermophilic symbiont," *Nature* 417 (May 2, 2002): 64.

[3] Ibid.

[4] Ibid., 66.

[5] Boucher and Doolittle, 27-28.

[6] Harold Morowitz, *Beginnings of Cellular Life* (New Haven, Conn.: Yale University Press, 1992), 68.

[7] Ibid., 66.

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